Controversies in Medical Physics: a Compendium of Point/Counterpoint Debates Volume 3

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American Association of Physicists in Medicine One Physics Ellipse College Park, Maryland, 20740

Published by: American Association of Physicists in Medicine, 1631 Prince Street, Alexandria, VA 22314, Phone 571-298-1300, Fax 571-298-1301

December, 2017

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PREFACE

The Point/Counterpoint series of debates in *Medical Physics* began in March 1998 and has continued unabated since. Point/Counterpoints continue to be among the most popular articles read in *Medical Physics* as demonstrated by consistently high online readership statistics. Indeed, they are usually the most downloaded of all articles in the monthly statistics. To commemorate the first 10 years of Point/Counterpoint debates (1998-2007) and, coincidentally, the first 50 years of existence of the American Association of Physicists in Medicine, the journal's Editorial Board decided to publish a compendium of the debates as a separate, free-access, online book with the title ―*Controversies in Medical Physics*. This was published in 2008, and was followed five years later by Volume 2 of *Controversies in Medical Physics*, which included all the Point/Counterpoint debates published from 2008-2012. This current Volume 3 contains Point/Counterpoints for the ensuing five years, 2013-2017. All three volumes are available on the *Medical Physics* website at http://medphys.org or the AAPM books webpage at http://www.aapm.org/pubs/books. Although the Point/Counterpoints here have been reformatted, they are essentially identical to those that appeared in the journal with one exception—the online version contains links to references within the text and to references cited by the authors. Readers will need to access the original articles in the online journal to take advantage of these citation links. Each Point/Counterpoint has a link to the original online Point/Counterpoint. All the Point/Counterpoints in this volume were moderated by Colin Orton and edited by either Bill Hendee (2013) or Jeff Williamson (2014-2017). The Moderator devised all of the Propositions, selected appropriate authors, edited their contributions, and wrote the Outlines. Persons participating in Point/Counterpoint debates were selected for their knowledge and communicative skills, and a disclaimer preceded all Point/Counterpoints to the effect that the positions of the authors for or against a proposition ―*may or may not reflect their personal opinions or the positions of their employers*. We hope you enjoy reading the Point/Counterpoint debates included in this volume.

Colin G. Orton, Jeffrey F. Williamson & William R. Hendee Editors

December, 2017

CHAPTER 1

General Radiation Therapy

1.1. Online adaptive planning for prostate cancer radiotherapy is necessary and ready now

X. Allen Li and Qiuwen Wu
Reproduced from *Medical Physics* **41**, Issue 8 Part1, 2014 (080601-1-3)
(http://dx.doi.org/10.1118/1.4883875)

OVERVIEW

In linear-accelerator based radiotherapy for prostate cancer, both target and normal tissues are known to change position and shape considerably during a course of therapy. The need to track and compensate for these motions is well established and adaptive planning is widely accepted. Some claim that this should be accomplished online while the patient is lying on the couch waiting for treatment and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is X. Allen Li, Ph.D. Dr. Li is Professor and Chief of Medical Physics in the Department of Radiation Oncology, Medical College of Wisconsin. He is certified in Radiation Oncology Physics by both the Canadian College of Physicists in Medicine and the American Board of Medical Physics. Dr. Li has served for the AAPM in the capacity of chair or member of various subcommittees and task groups including the Biological Effects Subcommittee, TG-74, TG-106, TG-166, and the Editorial Board of *Medical Physics*, and is a Fellow of the AAPM. He has been a peer reviewer for 14 scientific journals and seven public and private research funding agencies. He has edited a book entitled “Adaptive Radiation Therapy” and has authored over 125 peer-reviewed papers. Dr. Li's research interests range from adaptive radiation therapy, outcome modeling, and recently to MRI guided radiation treatment planning and delivery.

Arguing against the Proposition is Qiuwen Wu, Ph.D. Dr. Wu obtained his Ph.D. in Physics from Columbia University, New York, and subsequently worked in the Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, NY, the Department of Radiation Oncology, Virginia Commonwealth Univer-sity, Richmond, VA, William Beaumont Hospital, Royal Oak, MI, and Wayne State University, Detroit, MI, before moving to Duke University Medical Center where he is currently Professor in the Department of Radiation Oncology. He is certified in Therapeutic Radiological Physics by the American Board of Radiology, is a Fellow of the AAPM and is a member of the Board of Editors of the *Journal of Applied Clinical*

Medical Physics. Dr. Wu's major research interests include adaptive radiation therapy, online image guidance, and applications of flattening filter free linacs, for which he has published about 70 peer-reviewed papers.

FOR THE PROPOSITION: X. Allen Li, Ph.D.

Opening Statement

It has been widely reported that interfraction variations in both targets and organs at risk (OARs) can be substantial during radiation therapy (RT) for prostate cancer.[1] These variations, including translational and rotation shifts, deformation (e.g., volume and shape changes) and independent organ motions, can be systematic and random in nature. To account for these variations, large CTV-to-PTV margins are necessary to ensure adequate target coverage. These large margins inevitably result in increased doses to the OARs, leading to increased treatment-related toxicities that may prevent safe delivery of more effective and/or socially/economically favorable treatments such as dose escalated RT, hypofractionated RT, or stereotactic body RT (SBRT).

To address the negative impacts listed above, a large amount of effort has been expended in recent decades on the development of technologies and strategies to correct for interfraction variations.[2] Image-guided RT, where images acquired immediately prior to a treatment are used to guide patient repositioning, is currently the standard practice used to correct translational shifts and rotational errors, if the machine is properly equipped, but does not correct for anatomy deformations and independent organ motions. Adaptive RT (ART) that may be performed online or offline has been introduced to correct for this problem.[3] While offline ART may be used to account for systematic variations,[4] online ART that generates and delivers a new dosimetric plan optimized based on the anatomy of the day (fraction) can fully account for interfraction variations including both systematic and random (unpredictable) deformations and independent organ motions.[5,6]

Online replanning needs to be fast so that it can be completed within a few minutes while the patient is lying on the table waiting for treatment. Although such fast planning is generally challenging using conventional planning technologies, adaptive replanning does not need to start completely from scratch. For example, it can start with an initial plan fully optimized from the planning images for the same patient. Technologies on the quality of inroom imaging, image registration and segmentation, plan optimization algorithm, and computing hardware are advancing significantly and rapidly. For example, improved quality of onboard cone-beam CT, addition or integration of diagnostic-quality CT or MRI in the treatment room, graphic-processing unit accelerated autosegmentation and dose calculation,[7] rapid plan modification with aperture morphing algorithms,[6] and plan adaptation based on previous knowledge or a previously created plan library, are among the technological advances that can speed up adaptive planning significantly. Commercial treatment planning systems including some of these advances are becoming available.

Extensive literature indicates that the interfraction deformations of prostate, bladder, and rectum and independent motions between prostate, pelvic nodes, rectum, and bladder during RT for prostate cancer, are generally unpredictable and can be substantial. For example, based on the

MRIs acquired during the course of prostate RT, Nichol *et al.*[8] reported that prostate volume could decrease by 20% and its shape could deform by 13 mm. Patients with a transurethral resection of prostate were prone to prostate deformation.[8] It is necessary and possible to fully account for these variations by using online adaptive replanning for a treatment strategy requiring a small CTV-to-PTV margin. With online ART, a margin can reach as low as 3 mm, depending mainly on intrafraction variations. Such a small margin would be highly desirable to reduce treatment-related toxicities.

In conclusion, online adaptive planning for prostate cancer radiotherapy is necessary and ready now, particularly for cases with large deformations or for dose escalated RT, hypofractionated RT, or SBRT.

AGAINST THE PROPOSITION: Qiuwen Wu, Ph.D.

Opening Statement

With advanced onboard imaging systems, standard online image guidance (IG) techniques currently used in many clinics is efficient and can correct setup errors and rigid organ motions. The residues, including uncorrected rotations, execution errors, deformations, and intrafraction motions, are handled by the margins in treatment planning, which are significantly reduced from those used for conventional treatment planning without IG.[9]

In principle, online planning, either adapted geometrically to the target or dosimetrically to include dose from previous fractions, can compensate additionally for interfractional deformations of both targets and critical organs in real-time while the patient is still on the table, potentially allowing the use of minimal margins.[10] However, there are steep challenges ahead, both technically and practically. The crucial process in treatment planning is the delineation of regions of interest (ROIs). Unfortunately, current state-of-the-art online CBCT images are not adequate for this task for prostate cancer treatments.[11] Radiation oncologists need significantly longer time and yet with less confidence to manually contour on CBCT than conventional CT. Also, the accuracy of computerized segmentation and deformable image registration algorithms depends heavily on image quality and, therefore, margins for the uncertainty of ROI definition must be added. In addition, online adaptive planning will undoubtedly increase the time between imaging and treatment and therefore needs increased margin for intrafractional motion and deformation, which increase with time.[12] The potential savings in margins for online planning can *quickly* diminish. The prolonged treatment session is not economical either.

Many practical factors also limit the use of online planning. The physician is required to approve the ROIs on online CT as well as the treatment plan, which the planner needs to generate quickly. In addition, the physicist needs to validate the plan and perform quality assurance creatively with the patient on the table. In the meantime, the therapists need to check all *new* plan parameters. Ideally, all these tasks need to be done at the treatment console for efficient communication and minimization of errors. However, this is unrealistic for scheduling in many clinics since it requires additional personnel at the linac at the same time for each prostate patient.

There are competing alternatives to handle nonrigid organ motions such as the hybrid strategy combining online IG and offline adaptive planning.[13] The advantage is that time-consuming treatment planning is handled offline, the same way as traditional treatment planning. With no added burden to the online process, the online IG is the same efficient process that patients and therapists are used to. Many studies have shown that organ motion and deformation in prostate cancer are patient-specific in nature.[14,15] Offline or hybrid adaptive radiotherapy can take advantage of this by analyzing repeated images during early treatments and incorporating them into the treatment planning. Dose guided adaptive radiotherapy and equivalent margin reductions can be achieved.[16]

In summary, online adaptive planning faces many technical and practical challenges and is not yet ready for clinical implementation. Increased margins for target definition uncertainty and intrafraction motion offset the savings in margin for deformation. In the meantime, clinically proven alternative offline and hybrid adaptive strategies have been shown to be equally as effective.

Rebuttal: X. Allen Li, Ph.D.

The offline and hybrid adaptive strategies cannot adequately account for random (unpredictable) organ deformations and independent organ motions and hence they are certainly not as effective as the online adaptive approach. They would require larger margins for cases with moderate and large deformations. Also, I have to disagree with Dr. Wu on his point that the additional time for online adaptive planning required in order to increase margins to account for the increased intrafraction variations may diminish the benefits of online replanning. For cases with moderate and large deformations, the interfraction variation is dominant. It has been documented that the dosimetric loss due to the intrafraction changes during the application of online replanning is relatively small compared to the gain from the online replanning. Furthermore, the time required for online replanning can be reduced substantially (to a few minutes) with the recent advances in online imaging, image registration, replanning algorithms, and/or computing technology. Undoubtedly, large efforts and resources are needed for online replanning, similar to any other emerging techniques. However, the benefit of the reduced margins from online replanning is clear. These reduced margins would lead to reduced radiation injury to normal tissues and/or offer opportunities for more effective treatments (e.g., dose escalation, hypofractionation). For prostate radiotherapy, the increased effort can be socioeconomically justified in cases with large deformations or when using hypofractionated RT or SBRT.

Rebuttal: Qiuwen Wu, Ph.D.

Both Dr. Li and I agree that there are a variety of substantial interfractional organ motions in prostate cancer patients. We disagree on the effectiveness and efficiency of online adaptive planning to handle them as it stands now. Its advantage over alternatives is too little, and it is too soon for clinical implementation.

Many pelvic organ motions, including deformations and intrafraction motions, are not totally random but rather patient-specific; they can be characterized based on a few measurements from previous fractions, and compensated through either offline or hybrid adaptive planning. In

principle, in-room MRI could improve the accuracy and shorten the time of ROI delineation. However, either MRI-only based treatment planning must be clinically proven, or CT-MRI registration be shown to be equally as accurate as CT-CT registration.

Pretreatment verification of "a new dosimetric plan optimized based on the anatomy of the day" is a practical concern. With the standard of care of prostate radiotherapy moving toward IMRT and VMAT, the online adaptive plan must be verified before treatment as this is required by regulations. This poses considerable challenges while the patient is on the treatment table.

Current workflow in many radiation oncology clinics is sequential in nature, in which each task is performed by a specially trained staff member and completion of a task triggers the next one in line. It is not a trivial task to bring physicians, planners, physicists, and therapists together to the treatment console at the same time for each fraction.

All this being said, I believe that online planning represents the holy grail of prostate cancer IGRT, and I am all for the research toward its successful application. Pointing out its current deficiencies should provide us better directions to work on in the future.

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1.2. MRI/CT is the future of radiotherapy treatment planning

Carri K. Glide-Hurst and Daniel A. Low
Reproduced from *Medical Physics* **41**,110601-1-3 (2014)
(http://dx.doi.org/10.1118/1.4894495)

OVERVIEW

Use of magnetic resonance imaging (MRI) in radiotherapy planning has rapidly increased due to its exquisite high contrast, high resolution soft tissue visualization and functional imaging modalities that rival PET/CT in tumor visualization capability. These features, in combination with CT's freedom from spatial distortion, have led some to suggest that the future of radiotherapy lies more with MRI/CT than with either CT or MRI alone. This is the premise debated in this month's Point/Counterpoint

Arguing for the Proposition is Carri K. Glide-Hurst, Ph.D. Dr. Glide-Hurst obtained her Ph.D. in Medical Physics from Wayne State University in 2007, focusing her efforts on breast ultrasound tomography and utilizing acoustic parameters for breast density evaluation. She then spent two years in postdoctoral training in the Department of Radiation Oncology at William Beaumont Hospital, Royal Oak, MI, with an emphasis on motion management techniques in lung cancer, and is now Senior Staff Physicist at Henry Ford Health Systems in Detroit. Dr. Glide-Hurst is certified in Therapeutic Radiologic Physics by the American Board of Radiology. Her current interests include a hybrid of teaching, clinical duties, and translational research and, relevant to the topic of this debate, she is the Principal Investigator for a Henry Ford Health System Grant on optimizing MRI simulation (MR-SIM) for breast cancer radiotherapy.

Arguing against the Proposition is Daniel A. Low, Ph.D. Dr. Low obtained his Ph.D. in Physics from Indiana University, Bloomington and, after a postdoctoral fellowship at M. D. Anderson Cancer Center, Houston, TX, moved to Washington University Mallinckrodt Institute of Radiology, St. Louis, MO, where he eventually became Professor in Radiation Oncology. In 2010, he moved to his current position at UCLA, where he is Professor in Radiation Oncology and Vice Chair of Medical Physics. Dr. Low is certified by the American Board of Medical Physics in Radiation Oncology Physics. He has been very active in both the AAPM and ASTRO and currently serves as Chairman of the NIH Clinical Trials Committee of ASTRO, the AAPM Audit Committee, the AAPM Working Group for Radiation Oncology National Event Reporting System, the AAPM Working Group on Radiation Oncology Incident Learning System, and the AAPM Science Council. He is the current Treasurer of the AAPM Southern California Chapter. Dr. Low's major research interests include 4DCT, modeling respiratory motion, and applications of PET in radiotherapy. He is a Fellow of the AAPM and has published over 170 papers in refereed journals.

FOR THE PROPOSITION: Carri K. Glide-Hurst, Ph.D.

Opening Statement

Over the past few decades, CT simulation (CT-SIM) has been the primary modality used for radiotherapy treatment planning (RTP). CT offers excellent spatial resolution, high geometric integrity, short exam times, and accurate electron density information to enable dose calculation. Implementation of thinner slices, larger fields of view, and 4DCT has further improved spatial and temporal resolutions. Iterative reconstruction and dose modulation have yielded ~70% dose savings while maintaining comparable image quality.[1] One disadvantage of CT, however, is the lack of the soft tissue contrast which is essential for delineation of low contrast interfaces. To address this limitation, MRI is used as an adjunct to CT when soft tissue contrast is advantageous (e.g., abdomen, brain, and pelvis).

Compared with CT, MRI provides superior contrast resolution that can be further optimized by varying parameters. MRI can resolve tumor boundaries and differentiate between normal tissue and surgical beds. In addition, functional MRI offers potential for identifying dominant lesions or serving as a biomarker of tumor/organ at risk (OAR) response. However, the geometric accuracy of MRI can be hindered by magnetic field distortion and gradient nonlinearity, resulting in spatial distortions as large as 3–4 mm for gradient and spin echo acquisitions and ~20 mm for echo planar imaging.[2] Furthermore, patient-induced field distortions (e.g., chemical shifts and susceptibility) may introduce distortions of 3–4 mm due to different magnetic field susceptibilities between interfaces.[3] Given the high degree of accuracy and high dose per fraction required for stereotactic radiosurgery and body radiotherapy, even small errors in target localization may cause >20% undertreatment of the tumor while overdosing adjacent OARs.[4] Thus, the synergistic effects of CT and MRI combined yield the most complete tumor delineation,[5,6] with the highest geometrical accuracy afforded by CT-SIM.

Recently, MR-SIM platforms have been introduced with added components (e.g., flat tabletops and laser systems) that will undoubtedly improve image registration accuracy between MR-SIM and CT-SIM. Nevertheless, MR-SIM for single modality simulation is being explored via generation of synthetic/pseudo CT-SIM datasets, but low signal intensity of cortical bone on MRI remains a limitation. Caution must be exercised when using only MRI for delineation. Evaluating MRI prostatic tumor volumes revealed only 2 of 20 estimates were within 10% of actual volumes determined via prostatectomy, while 11 were underestimated.[7] Most importantly, excellent outcomes have already been observed for CT-based delineation. To justify implementing MRI-alone simulation, large prospective trials spanning decades would be necessary for evaluating outcomes and survival.

Currently, MRI is not indicated for all anatomies. MRI has shown limited clinical advantages in the thoracic region, where low proton density, respiratory/cardiac artifacts, and magnetic susceptibility artifacts pose challenges. Not all patients are candidates for MRI due to contraindications such as implanted devices. Finally, ~25% of cases are designated as palliative intent, thereby making it difficult to justify MRI's high cost and long examination times.[8] Overall, CT-SIM will maintain its prominent role in RTP. MRI will continue to complement CT-

SIM and provide soft tissue contrast for delineation, but only when indicated for a subset of qualified patients.

AGAINST THE PROPOSITION: Daniel A. Low, Ph.D.

Opening Statement

There is no controversy that MRI provides superior image quality when compared against CT for almost all treatment sites. There are two options for integrating MR into the clinical workflow: to acquire images using both modalities or replace the CT simulator with a MR simulator and develop a strategy for replacing the data we currently receive from CT.

One of the important considerations when determining whether to replace an existing paradigm with a new one is cost. For most treatment sites and regimens, the current billing structure reimburses only for a single simulation modality. Broad implementation of MR + CT planning would require a significant increase in cost to payers or would require clinics to subsidize uncompensated imaging costs. This would be especially challenging given the high cost of MR scanners and the need to have specially trained staff to operate them. Not only do such simulations require two acquisitions but also they require the planner to fuse the image datasets to allow structures from one image dataset to be used on the other. This fusion adds additional workload to the clinic.

The capital and operational costs could be reduced by using MR-only simulation. Challenges to this include questionable spatial integrity, the need to develop robust methods for obtaining electron densities from the images, the need to develop robust methods for obtaining digitally reconstructed radiographs for comparison against radiographic and fluoroscopic patient positioning imaging methods, and the need to develop adequate 4DMR image sequences for lung and upper abdominal tumors.[9–13]

A second consideration is benefit. MR imaging for cervical cancer brachytherapy is common in some countries,[14] and MR has long been used for planning treatments of brain lesions.[15] However, there is little evidence that the improved soft tissue imaging of MRI actually leads to improved outcomes. Easier segmentation does not necessarily relate to dose distributions that more accurately conform to tumor volumes. In the current and future medical economic climate, the prospect of increased cost with uncertain, if any, benefit is unlikely to lead to substantial acceptance.

Given the unknown benefits of MRI-based simulation outside of its current limited uses, the unmet challenges of implementing MR-only simulation, the lack of credible evidence as to the benefit of the improved image contrast and flexibility, and the degrading medical economic climate that is unlikely to improve in the near future, it is unlikely that MR/CT simulation will be a dominant imaging modality for radiation therapy in the future. It has its place, even in the current paradigm, but broad adoption in the long-term future is at best uncertain, at worst nonexistent.

Rebuttal: Carri K. Glide-Hurst, Ph.D.

Dr. Low and I agree on many issues regarding the role of MRI/CT in radiation oncology, including that the benefits of MRI will apply to a subset of patients and that MRI poses many technical challenges, particularly with image distortion. While Dr. Low is correct that we currently bill for a single simulation modality, it is important to note that the standard of care is constantly changing as technology evolves. For example, in 2014, a Current Procedural Terminology (CPT) code (77293) was introduced for respiratory motion management simulation. This CPT code came *eight years* after TG-76—The Management of Respiratory Motion in Radiation Oncology—was first published and long after 4DCT and other motion management approaches were integrated into most clinics. Despite the technical costs (specialized equipment and management of hundreds of "uncompensated" images) and significant personnel burdens (extended imaging times and physician review/delineation) associated with 4DCT acquisition, we did not forgo 4DCT for patients who may have benefited from motion management just because a procedure code was not available.

When MRI is critical for target delineation and the patient is being treated with curative intent, the workload and expense of MRI in addition to CT are justified. This practice has, and will continue to be, well supported by clinical trials and cooperative groups.[14] While a direct association between MRI utilization for delineation and improved outcomes is currently unproven, preliminary studies suggest that functional MRI (i.e., diffusion-weighted and dynamic contrast-enhanced) can identify dominant lesions and elucidate early tumor response.[16] Having this noninvasive, nonionizing imaging feedback may facilitate adaptive dose escalation strategies and personalized treatment selection, thereby offering potential to improve therapeutic ratios. Given MRI's unparalleled soft tissue contrast and functional information that cannot be obtained via CT alone, MRI/CT will play an even greater role in radiotherapy treatment planning in the future.

Rebuttal: Daniel A. Low, Ph.D.

My esteemed colleague had an excellent point that I had failed to mention, that CT iterative reconstruction and dose modulation have yielded a large dose savings while maintaining comparable image quality. This work has been prompted by public health concerns about the increasing medical radiation burden on the population, which has climbed a factor of 6 from 1980 to 2006.[17] However, the doses delivered by CT scans to most radiation therapy patients pale in comparison to even the scattered and leakage doses from their treatments. Therefore, we can and should be pursuing the uses of these techniques not to lower the dose but to improve CT image quality by reducing the effects of noise and consequently increasing the CT soft tissue contrast. In fact, Sheng *et al.*[18] presented at the 2014 AAPM Annual Meeting their work on improving CT soft tissue contrast with postprocessing. Finally, phase-contrast CT has the potential for greatly improving image quality and has only recently been investigated for clinical imaging.[19]

CT scanners are ubiquitous, relatively inexpensive, provide outstanding spatial integrity, deliver essentially inconsequential doses, and have the potential for further improvements in soft tissue contrast. What's not to love?

ACKNOWLEDGMENTS

C.K.G.-H. would like to acknowledge Joshua Kim and Indrin Chetty for their valuable feedback and that Henry Ford Health Systems holds research agreements with Philips Healthcare.

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1.3. Within the next ten years treatment planning will become fully automated without the need for human intervention

Michael B. Sharpe and Kevin L. Moore
Reproduced from *Medical Physics* **41**, 120601-1-4 (2014)
(http:// dx.doi.org /10.1118/1.4894496)

OVERVIEW

Radiotherapy treatment planning is rapidly becoming more-and-more automated or, at least, semiautomated, in order to relieve the human planner of tasks that can be readily handled by computers, such as autosegmentation and optimization. How far this can go in removing the need for human intervention is controversial, but some believe that treatment planning can be fully automated within the next ten years. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Michael B. Sharpe, Ph.D. Dr. Sharpe obtained his Ph.D. in Medical Biophysics in 1997 from the University of Western Ontario, London, Canada, having worked for several years at the London Regional Cancer Centre before moving to William Beaumont Hospital, Royal Oak, MI, in 1995. He worked there until 2002 at which time he moved to the Princess Margaret Cancer Centre, Toronto, where he is currently Associate Head of Radiation Physics and Associate Professor in both Radiation Oncology and Mechanical and Industrial Engineering, University of Toronto. Since 2010, he has also served as Radiation Physics Quality Lead, Radiation Treatment Program, Cancer Care Ontario. He is certified in Radiation Oncology Physics by the American Board of Medical Physics. Dr. Sharpe's major research interests are focused on advancing practice through the development, validation, and application of radiotherapy and imaging technologies on which he has published over 70 papers in peer-reviewed journals and 11 book chapters, and has authored several patents.

Arguing against the Proposition is Kevin L. Moore, Ph.D. Dr. Moore obtained his Ph.D. in Physics from the University of California, Berkeley, subsequently training and working at Washington University in St. Louis before moving back west to the University of California, San Diego. He is certified in Therapeutic Radiological Physics by the American Board of Radiology and is currently Associate Physics Director and Medical Physics Residency Director in the UC San Diego Department of Radiation Medicine and Applied Sciences. Dr. Moore's major research interests lie in knowledge-based treatment planning, treatment plan quality control, and informatics applications in clinical radiotherapy. He has published nearly 30 peer-reviewed papers and one book chapter, and is lead inventor on a patent regarding knowledge-based dosimetric prediction.

FOR THE PROPOSITION: Michael B. Sharpe, Ph.D.

Opening Statement

Within a decade, radiation treatment planning will become fully automated without the need for human intervention because (i) we will exploit pertinent trends in the manufacturing and informatics industries, (ii) the precedent is already established, and (iii) it is imperative to improving quality and continuing advancements in care.

Impressive technological advances have occurred in radiation oncology over the past two decades. Image-based planning, optimization, and guidance progressed rapidly from compelling concepts to routine tools because outside influences like high-performance computing, networking, and robotics became widespread and affordable. IMRT and IGRT have become ubiquitous tools and have altered the paradigm of treatment. But we wish to do more for our patients. The "adaptive" concept was also described more than 15 years ago. The concept has been developed extensively and now includes biologically motivated adaptation.[1] However, more effort is needed to overcome the complexities and impact on workflow to realize adaptation as it was conceived. Future efforts will benefit surely from the "third wave of computing" from which image processing and information technologies will produce insights from large quantities of unstructured treatment planning data.

The need to estimate dose distributions made automation central to the earliest developments of computerized treatment planning. Today, even more advanced functions are automated, such as image registration, organ delineation, and dose optimization. Using commercial tools, it is now possible to control workflow so as to fully create, evaluate and document a plan with minimal intervention.[2–4] Interestingly, applications involving tangential breast irradiation remain controversial: In spite of the obvious improvements in personalization and efficiency afforded by IMRT and related automation techniques, modern innovation is discouraged because entrenched reimbursement guidelines confuse the technologies and the "modality" they enable.[5]

Providing healthcare is one of the most complex and demanding of human endeavors. Radiation oncology treatment relies on distributed decisions and tasks that are shared across highly skilled medical and technical staff. We strive to assess and respond to each patient's personal needs; but our tools, skills, and processes are stretched to the limit. Procedures can become error prone, sometimes with tragic and very public consequences.[6] Consequently, practice guidance is limited to the structures and inspections required to achieve safety today.[7] The dynamic nature of patients and their response to treatment were recognized long ago as a control problem. Adaptive control provides a means to account for anatomical and physiological variations and supports highly personalized treatment.[1] Adaptive radiation therapy must become "more than safe." It must embrace a broader definition of quality to ensure that clinical decisions and technical procedures are evidence based, effective, equitable, timely, and highly tailored to each patient.[8] A higher level of robust quality is required and we must do more than embrace automation. Robust quality is achieved by design rather than through organic innovation followed by inspection for quality control.[9] Adaptation requires a framework to achieve robust quality that is safe, consistent, and highly customized. Within such a framework, care will become more complex unless automation is used to make it "merely complicated."

AGAINST THE PROPOSITION: Kevin L. Moore, Ph.D.

Opening Statement

As someone who intends to spend the next decade working to advance the proposition, I nonetheless contend that the odds of fully automated treatment planning being the norm in ten years' time must be rated as extremely unlikely.

A close read of the proposition could make my task relatively easy, i.e., interpreting "fully automated" treatment planning to imply end-to-end automation, whereby all steps between radiotherapy simulation and first treatment are performed without human intervention. Impressive though the last decade has been for the field of autosegmentation, it strains credulity that a decade's time would be enough to herald a universal autosegmentation platform that not only identifies all normal anatomical structures across all imaging modalities but also flawlessly incorporates every patient's unique clinical circumstances into fully automated tumor volume contouring.

Making my task somewhat more difficult, we could interpret the proposition to "merely" imply full automation from segmentation to treatment. Both my opponent[3] and I[10,11] have clinically implemented automated treatment planning using present-day technologies, and, undoubtedly, research and commercial offerings in this space will advance in the next ten years. However, we should appreciate the enormity of the challenge in effecting universal automation for all clinical scenarios. Using the impressive work of my opponent as an example, tangents in early-stage breast cancer can clearly be automated to a great effect, but I am skeptical that this algorithm can be easily extended to all breast cancer treatments, e.g., bilateral postimplant chest wall irradiation with internal mammary chain and axillary lymph node involvement, including electron scar boosts, for a patient with cardiac comorbidities. Such a case is both complicated and outside of normative experience, making the work of algorithmic development simultaneously more difficult, more time consuming, and less beneficial (in a utilitarian sense). As automated treatment planning advances, by necessity it will expand from common and standardized treatment sites to infrequent and nonstandardized cases. To automate everything we treat in radiotherapy will take time, and ten years is simply not enough of it.

In fairness to the spirit of the proposition, I feel I should stake my own claim for 2024. Semiautomated (i.e., computer-assisted) treatment planning will be used in the large majority cases, with some form of knowledge-based and/or computer-aided multicriterial optimization removing most of the present-day human variability from the optimization process.[12,13] The clinical expertise of humans will still be regularly employed to evaluate and adjust plans for patients whose circumstances fall outside of normative treatments. Automated software systems will be commonly available for online plan adaptation. Some reductions in treatment planning staff will occur, although job descriptions might expand to encompass increased needs in clinical informatics and adaptive plan management. Ironically, human-driven planning will probably retain the largest foothold in 3D-conformal/palliative treatments, where patient anatomical variations can be very large and nonstandard clinical considerations are a frequent occurrence.

These changes will be breathtaking and practice altering, but will fall short of delivering fully automated treatment planning by the year 2024. As for 2034…

Rebuttal: Michael B. Sharpe, Ph.D.

I appreciate Dr. Moore's flexible viewpoint and the challenges he presents. Indeed, image segmentation is a major hurdle; contours are vital for communicating decisions and intent. We are poised to exploit vast stores of images and manually delineated organs,[14] but current clinical practices may not provide what is required for algorithm training. We do build on "shifting sands" to some degree as technologies and practice standards evolve. But, the proposition does not "strain credulity" if manual contouring is approached with consensus and consistency.

Dr. Moore believes clinical variation limits our capacity to automate planning. I agree to the extent that the "Pareto Rule" governs progress; i.e., 20% of our efforts will succeed for 80% of the cases. Clearly outliers require significant human effort, but reducing arbitrary variation and building anatomically related evidence to support continuing development could help.

Dr. Moore also speculates that automation will reduce staffing, but concedes it could free skilled staff to add value to challenging cases and to advance appropriately personalized adaptation. As automation is introduced, it influences the tasks remaining, i.e., what staff are asked to do. Will we continue in familiar territory, or will new tasks differ qualitatively or become disconnected? We must also assure that it is possible to monitor and compensate for system deficiencies. If these deficiencies are ignored, there is a risk of new types of errors and system failures. In short, automation does not solve all problems.[15]

In his opening statement, Dr. Moore contends that the "odds" of fully automated treatment planning being the norm in ten years' time must be rated as extremely unlikely. In my opinion, the future should not be left to chance. We must move to achieve robust quality by design. I conclude by quoting Dr. Dennis Gabor, the Nobel Laureate who invented holography: "*The future cannot be predicted, but futures can be invented*."[16]

Rebuttal: Kevin L. Moore, Ph.D.

I absolutely align myself with the large portion of Dr. Sharpe's statement dedicated to how automation could improve radiotherapy, and thus will focus on the narrow portion of my opponent's argument that attempts to explain how automated treatment planning might come to pass.

Relying on a third wave of computing to make this happen perhaps confuses more data with more knowledge. I would respond that analyzing prior information is a necessary but not sufficient condition, and while we must exploit prior information, we cannot expect that the mere possession of large quantities of data will herald miraculous gains. The recent advance of knowledge-based planning yielded useful predictions only when new techniques were brought to widely available data.[2,11,13,17,18] Extending automation will rely on further research and development and, as argued in my opening statement, this will take time to expand to all clinical scenarios.

As for the precedents that Dr. Sharpe introduced—image registration, organ delineation, and dose optimization—I would argue that none of these are yet fully automated. Image registration comes close, but in my experience automatic registrations are ultimately adjusted more often than not. I have contended (with great respect) that autosegmentation is not fully automated even

after more than a decade's development. As for optimization, this is unfortunately the least automated of all, demanding further technological development to eliminate human-caused variability.[12]

Examples of full automation in radiotherapy are actually very few. One example is beam aperture definition, now automated by programmed multileaf collimators. Arguably the elimination of human block cutters did occur on a decade's timescale, but mere citation of this does not inform predictions for other technologies.

In closing, I am not at all pessimistic about the future of automation in treatment planning; deployed in tandem with the clinical expertise of highly trained human beings, automation will improve patient care and make radiotherapy more efficient. We should, however, work toward this future with eyes open about the significant effort that remains to achieve fully automated treatment planning.

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1.4. Radiotherapy is an appropriate treatment to consider for patients infected with the Ebola virus

Wilfred F. Ngwa, Roland Teboh
Reproduced from *Medical Physics* **42**, 1149-1152 (2015)
(http://dx.doi.org /10.1118/1.4903900)

OVERVIEW

The Ebola virus has been spreading rapidly in West African countries and the medical profession has been urgently seeking ways to treat patients infected with the disease in order to stop it spreading further. The predicament in Africa is desperate and totally unproven treatments are being tried on patients. It has been proposed that even some forms of radiotherapy (RT) should be considered, and this is the suggestion debated in this month's Point/Counterpoint.

Arguing for the Proposition is Wilfred F. Ngwa, Ph.D. Dr. Ngwa earned his B.S. in Physics/Computer Science from the University of Buea, Cameroon and his M.S. and Ph.D. degrees in Physics/Biophysics from the University of Leipzig, Germany. He then had postdoctoral training in Medical Physics at M.D. Anderson Cancer Center Orlando, FL and the joint Department of Radiation Oncology at Brigham and Women's Hospital and Dana Farber Cancer Institute, Boston, MA. He is currently Faculty Medical Physicist in Harvard Medical School and the University of Massachusetts, Lowell. He also codirects a Radiation Oncology Global Health Initiative Towards Elimination of Cancer Disparities. Dr. Ngwa's major research interest is nanoparticle-aided radiotherapy for the treatment of prostate cancer, lung cancer, and retinal diseases, for which he has several grants.

Arguing against the Proposition is Roland Teboh, Ph.D. Dr. Teboh is an ABR board-certified Radiation Oncology Physicist and Head of Service, CyberKnife and Stereotactic Radiosurgery/Radiotherapy (SRS/SRT), Division of Medical Physics at the Johns Hopkins University School of Medicine, where he also completed his Fellowship. He earned a B.Sc. (Hons) in Physics from the University of Buea, Cameroon, an M.S. in Physics from Michigan Technological University, Houghton, MI, and a Ph.D. specializing in Medical Physics from the University of Texas Health Science Center at San Antonio. He is a two-time recipient of the ACMP Young Investigator Award and has authored/coauthored over 50 articles and abstracts in peer-reviewed journals.

FOR THE PROPOSITION: Wilfred F. Ngwa, Ph.D.

Opening Statement

The 2014 Ebola outbreak has captured the world's attention, as healthcare professionals and scientists work ardently to find vaccines and treatments for this swiftly spreading, high mortality disease. Ebola infection is characterized by low normal white blood cell count, fever, persistent

fatigue or weakness, easy bleeding/bruising, joint/bone pain, etc., and ultimately potential death from severe bleeding, shock, or organ failure.[1] These characteristics are reminiscent of blood cancers like leukemia and lymphomas whose treatment often involves radiotherapy. Also, the Ebola virus belongs to the virus family Filoviridae, which has been shown to be one of the most radiosensitive of viruses.[2] Following infection, the virus also replicates at a usually high rate, which would render infected cells unusually radiosensitive. This high radiosensitivity, and precedent for using radiotherapy in the treatment of blood cancers with similar disease characteristics, provides a strong rationale for investigating radiotherapy as a treatment approach for patients infected with the Ebola virus.

One potential radiotherapy treatment approach that could be considered is total body irradiation (TBI). TBI is currently used with increasing sophistication to treat leukemia and other blood cancers (destroying abnormal/infected blood cells) and/or for suppressing a patient's immune system in preparation for stem cell transplantation.[3,4]

From what is currently known about the Ebola virus, its primary targets in the early phase of infections are the blood leukocytes that provide innate immunity.[1,5] The virus swiftly renders the innate immune system ineffective, particularly inhibiting dendritic cells from initiating an adaptive immune response and hence disrupting a crucial connection between the patient's innate and adaptive immune system needed to develop antibodies to fight the disease. To make matters worse, the virus then "hijacks" the helpless leukocytes to help propagate the infection by (1) helping transport the virus throughout the body to vital parts such as the lymph nodes, spleen, brain, and liver. It is the ultimate failure of such parts, such as the liver due to chronic hepatocyte infection, that can cause death; (2) releasing a cocktail of proinflammatory cytokines that destroy the vascular endothelium, causing bleeding, and excessive activation of the blood clotting cascade that causes death in some patients.[6]

Cognizant of this, TBI, or a low dose adaptation of it, presents as a viable disruptive approach for consideration for the treatment of Ebola patients. The example of using TBI in the treatment of leukemia and other blood cancers[3,4,7] serves as a precedent for such a disruptive approach. And, as with leukemia treatment, such an approach could be combined with adjuvant administration/transfusion of a fresh supply of blood stem cells and/or chemotherapy. Actually, bleeding problems for Ebola patients are currently addressed by blood transfusions, so this also has precedent.

Another radiotherapy approach that could be considered is radioimmunotherapy (RIT). A recent study shows promise for using this approach to eradicate HIV virus infected cells.[8] Radioimmunotherapy could be considered as an option for targeting the Ebola envelope glycoprotein, which is also a main target of drugs currently under investigation.[9]

AGAINST THE PROPOSITION: Roland Teboh, Ph.D.

Opening Statement

Renewed interest in the quest for a cure for the Ebola virus disease (EVD) is due in part to the recent outbreak originating in the West African countries of Guinea, Sierra Leone, and Liberia.

This is a global public health concern that desperately needs a viable treatment modality but, regretfully, I have to argue against consideration of RT as a solution to EVD mainly because the side effects will limit the dose that can be used such that it cannot be curative.

Furthermore, there is a dire need for RT in so-called low and middle income countries (LMICs) such as this region of the world. The need for RT is for the treatment of cancer, not Ebola. The projected estimate is that cancer incidence will rise to 9.3×10^6 new cases per year by 2020 in LMICs, constituting two-thirds of all new cases in the world. Disproportionately, the distribution of teletherapy machines based on a 2010 report shows that the average number of such machines per million people was 1.99 for the whole world: 8.6 for high-income countries, 1.6 for upper middle-income countries, 0.71 for lower-middle-income countries, and 0.21 for low-income countries.[10] Because more than 50% of all cancer patients receive some form of RT as part of their care,[11] lack of RT resources means that a diagnosis of cancer in this part of the world usually leads to distress and a painful death. The need for RT is thus critical and, if no action is taken now, a severe crisis looms that will be of far greater consequence than that currently due to EVD. A consideration of RT as a solution to EVD is an unnecessary digression and could trivialize a true need, especially in the eyes of the authorities that matter, including local governments, business leaders, philanthropists, etc.

Finally, several promising solutions are under development. For example, the World Health Organization has approved the use of an untested drug ZMapp (Mapp Biopharmaceutical, Inc., San Diego, CA) for EVD patients.[12] This is the so-called "secret serum" that was administered to two US aid workers who fell sick with EVD while working in Liberia.[13] There are several other efforts reported in the literature with experimental drugs that have been proven effective in animal models.[14] It does appear that lack of funds and global interest is what has prevented the next step, namely, testing the efficacy and safety in humans.[14] Therefore the immediate focus should be to mobilize world resources to support current scientific efforts so that a safe drug for EVD can be developed.

To conclude, RT has a true and urgent need in LMICs. It is for cancer care and not EVD.

Rebuttal: Wilfred F. Ngwa, Ph.D.

Dr. Teboh makes an excellent point about safety. Beyond taking the right precautions, the development of vaccines and treatments for Ebola will reduce this concern. Human trials of vaccines for Ebola are being conducted.[15] However, while investigations for these vaccines are being expedited toward preventing infection, including among healthcare workers, different treatment options also need to be investigated in parallel.

This brings us back to the question of whether radiotherapy merits consideration as a treatment option. Dr. Teboh prematurely dismisses such consideration. His main argument is that considering radiotherapy for this is a digression from cancer care. However, for the Ebola patient who may potentially have this as the only treatment option, it will not be a digression as it could be a life saved. Also, it is always better to have as many tools/treatment options as possible to combat a disease. Now is a good time to investigate other potential treatment options in parallel with ZMapp, especially given the growing urgency to find a cure.[16] Moreover, we know that

sometimes a combination of treatments could work more effectively for some diseases, depending on the stage of presentation. Finally, the point on digression discusses Ebola as if it is only a problem/concern for low and middle income countries, where resources needed to treat cancer are in short supply. However, other countries are, rightfully, also concerned because of the potential for bioterrorism.[2,17]

In conclusion, low-dose TBI (Ref. 18) (with relatively fewer side effects and risks than high-dose TBI), using Co-60 units, for example, whose sources have decayed too much to be useful for conventional radiotherapy (to address Dr. Teboh's argument about digression from cancer care), radioimmunotherapy,[8] or adaptations of these approaches, should be considered in developing a radiotherapy approach for treating Ebola. My opening statement on precedent, expected high radiosensitivity of Ebola-infected cells and *in-vivo* evidence in using such radiotherapy approaches to treat other virus-infected cells,[8,19] provide a compelling rationale for such consideration.

Rebuttal: Roland Teboh, Ph.D.

Dr. Ngwa suggested TBI and radioimmunotherapy (RIT) as possible RT modalities that can be considered for EVD. I believe that the problems associated with these treatments make this unlikely.

As TBI involves irradiation of all cells, in theory, differential radiosensitivity is crucial if the goal is to eradicate residual EVD cells with curative intent. My colleague stated that the EVD virus is highly radiosensitive albeit relative to other viruses. Studies show that viral inactivation requires high doses, up to kGy,[20] therefore it is likely that high doses are required for EVD response. Toxicity then becomes a major concern, keeping in mind that the LD50, the total-body dose for 50% lethality, is about 4.5 Gy.[21] Furthermore, radiosensitivity is not the only factor. For example, TBI, once considered for Ewing's sarcoma, a highly radiosensitive cancer, has been shown to cause toxicity without disease control.[22]

Given that TBI is largely used as part of the preparatory regimen for hematopoietic stem cell transplant (HSCT), one could envisage a low-dose version of TBI playing the same role toward EVD. One must emphasize, however, that for HSCT, TBI is mainly used as a means to immunosuppress the host so as to prevent rejection of the donor marrow cells, not as a cure. Also, experience with HSCT for viral infections like HIV is inconclusive in that the first patient reported to have been functionally cured of HIV, received a bone marrow transplant from an HIV-resistant donor.[23] Also, two HIV patients who were treated with HSCT and initially seemed to have been cured of HIV, had the infection return.[24]

There is no question that monoclonal antibodies (mAbs) in the 1970s revolutionized antibody therapeutics[25,26] and gives hope today that RIT could be used to treat infections like HIV (Refs. 27 and 28) and, potentially, EVD. A major disadvantage, however, is the cost, since the high specificity means that more than one antibody might be needed to target microorganisms with high antigenic variation, which is possible with EVD given its five distinct species: BDBV, EBOV, RESTV, SUDV, TAFV.[29]

In all, the cost/benefit ratio has to be considered especially given competing alternatives such as ZMapp. Indeed, the first two patients administered ZMapp are now EVD free.[30] Although it is unclear if ZMapp helped, this is welcoming news and encourages further assessment.

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1.5. GPU technology is the hope for near real-time Monte Carlo dose calculations

Xun Jia and X. George Xu
Reproduced from *Medical Physics* **42**, 1474–1476 (2015)
(http://dx.doi.org /10.1118/1.4903901)

OVERVIEW

Monte Carlo (MC) dose calculations are recognized as being the most accurate modality for radiotherapy treatment planning but, because of the excessive computational time required, they cannot presently be used for near real-time dose calculations. Currently, the most common way to accelerate MC dose calculations is to use clusters of central processing units (CPUs), but some believe that the future of near real-time MC dose calculations lies not with clusters of CPUs but with the use of graphics processing unit (GPU) technology. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Xun Jia, Ph.D. Dr. Jia received his Masters degree in Applied Mathematics and Ph.D. degree in Physics, both from UCLA. He is currently an Assistant Professor in the Department of Radiation Oncology, University of Texas Southwestern Medical Center. Dr. Jia's research focuses on GPU-based high-performance computing for medical physics and medical imaging. He has developed several Monte Carlo packages to improve efficiency for photon, electron, and proton transport. Dr. Jia's research has been supported by government and industrial grants and he has published 60 peer-reviewed papers. He is currently a section editor of the *Journal of Applied Clinical Medical Physics*.

Arguing against the Proposition is X. George Xu, Ph.D. Dr. Xu obtained his Ph.D. in Nuclear Engineering from Texas A&M University, College Station, TX and, for the past 20 years, he has been on the faculty of Rensselaer Polytechnic Institute, Troy, NY, where he currently holds the Edward E. Hood Endowed Chair of Engineering. Dr. Xu's research has centered around applications of Monte Carlo methods to problems in radiation protection, imaging, and radiation therapy. He has been continuously funded by the NIH over the past ten years, including an R01 grant to develop a new Monte Carlo code, archer, for heterogeneous computing involving GPUs and coprocessors. He is the author of more than 150 journal papers and book chapters, and 270 conference abstracts. Dr. Xu is a Fellow of the American Association of Physicists in Medicine, the Health Physics Society, and the American Nuclear Society. In 2014, he was re-elected to a 6-yr term as a council member of the National Council on Radiation Protection and Measurements.

FOR THE PROPOSITION: Xun Jia, Ph.D.

Opening Statement

Clinical applications of MC dose calculations have been limited by the long computation time to achieve a sufficient precision level. Over the years, great efforts have been devoted to

accelerating MC simulations. Recently, with the success of GPU-based high-performance computing,[1,2] particularly for MC simulations, near real-time (e.g., seconds or subseconds) dose calculation is becoming feasible. Achieving this will not only facilitate its routine utilization, but also realize novel applications to advance radiotherapy practice, such as MC-based inverse treatment planning. To date, the computation time for a typical photon plan has been reduced to less than a minute with ~1% uncertainty using only one GPU, and the speed can be further boosted with multiple GPUs by a factor proportional to the number of GPUs. Also reported are computation times as low as seconds to tens of seconds for different applications.[3,4] Notably, the group at UT Southwestern[5] has developed a GPU application to visualize an MC-reconstructed dose delivery process in almost real-time during beam delivery, with a refresh frequency of >10 Hz. These achievements have clearly demonstrated the potential of near real-time MC dose calculations.

Besides advantages in speed, GPUs also hold other favorable features for clinical applications. First, GPUs are orders of magnitude lower in cost than a conventional high-performance-computing structure with a similar processing power. Second, GPUs are locally hosted and managed. This is particularly important for problems aiming at near real-time applications, since data-transfer and job-scheduling times cannot be neglected if the computation facility is remotely placed and shared by many users. Patient privacy may also be a concern when transferring medical data to a remote facility.

Of course we cannot neglect disadvantages of using GPUs for MC. As a new platform, redevelopment of codes is necessary. However, burdens of initial code development have been overcome to a large extent, and several packages have been successfully built. Efforts have also been initiated to write MC packages in OpenCL to increase portability.[6] While there are also technical issues hindering computational efficiency, e.g., thread divergence and memory writing conflicts, many solutions exist to remove or alleviate them.[4,7]

I would also like to mention a strong competitor of the GPU, the Intel many integrated core (MIC) processor. What makes this particularly attractive is its x86 compatibility, which can run existing CPU codes with minor modification. However, just like for GPUs, substantial effort is needed to achieve optimal performance.[8] Simply running an existing code may not achieve high acceleration, because parallel-computing specific issues such as memory access and vectorization were not considered sufficiently in the conventional CPU code. As of today, there has been only limited study regarding MC dose calculations on MIC processors. While it holds the potential to improve efficiency, a lot of research is needed.

In conclusion, GPU technology has the capability of substantially accelerating MC simulations. Its advantages and extensive research efforts demonstrate the hope for near real-time dose calculations.

AGAINST THE PROPOSITION: X. George Xu, Ph.D.

Opening Statement

Since the invention of computers in the 1940s, MC codes have been developed for nuclear engineering, high-energy physics, and, recently, medical physics applications. However, most radiation treatment planning is done currently using dosimetry algorithms that are extremely fast, but only "approximately" correct.[9] Given the lasting interest in accelerating MC methods, the recent hype related to the GPU is not surprising. Originally marketed by NVidia as household devices, GPU-based game consoles offered amazingly fast graphics at an affordable price. It did not take long, however, for the scientific community to realize that these desktop toys were actually parallel computers. As summarized in two review papers,[1,2] GPU adopters from the medical physics community wasted no time in reporting overwhelmingly positive experiences, including a dozen studies that focused specifically on MC dosimetry. Impressive, but inconsistent, "speedup factors" ranging from single digits to several hundreds were reported within months, sometimes by the same group. It has become a cliché to highlight how fast an MC-based dose calculation can be done with a GPU. Such results indeed attracted a lot of attention from medical physicists who are notoriously busy and seeking expediency.

There are two strong indications that GPU technology is only hype and not the hope for near real-time, fully MC dose calculations.

First, we have not seen any convincing evidence that the GPU is indeed better than traditional solutions for running MC dose calculations. Both of the above review papers[1,2] enjoyed referencing the rapidly increasing number of GPU-related journal articles—which only reinforces the concept of a "hype cycle." Furthermore, the authors of the GPU-accelerated MC studies obscure the issue by omitting details on how they compared GPU performance with traditional CPUs. CPU-based clusters are currently so cheap that one can assemble a desk-side 32-core cluster for about $3000US—the cost of a high-end CPU/GPU system. Using software optimization schemes and hyperthreading, such a CPU cluster may achieve a speedup similar to the best reported for GPUs, without the painful process of rewriting the MC code for the GPU/compute unified device architecture (GPU/CUDA) environment. But few of the GPU enthusiasts optimized the CPU code in order to make fair performance comparisons. It has been observed that a lack of "fair comparison" measures is responsible for exaggerated GPU performance.[10]

Second, competing technologies are mostly ignored by GPU adopters. Intel's Xeon Phi coprocessor, for example, which comes with 60 embedded Pentium cores, is capable of achieving a similar level of parallelism as GPUs.[11–13] Adopting the coprocessor is relatively easy and a large number of them are, in fact, used in Tianhe-2—the world's number-1 supercomputer. The "heterogeneous computing" era has just begun and it is uncertain which hardware (and software) technology will dominate the market.[14]

The excitement brought by the GPU has reignited our interest in achieving real-time MC dose calculations and one should take full advantage of the research opportunities.[15] However, an inflated expectation can be counterproductive, especially when investing in a single technology that may be obsolete in ten years.

Rebuttal: Xun Jia, Ph.D.

I agree that variations in reported GPU-acceleration factors exist due to different degrees of software/hardware utilization and optimization. However, it is quite difficult, if not impossible, to conduct an absolutely fair comparison. For example, I would like to mention the software aspect that unfairly treats GPUs: Software optimization schemes, such as variance reduction techniques widely employed in CPU-based MC packages, have been barely explored for GPUs. The deterministic nature of such algorithms is expected to be particularly favorable for GPU's single-instruction-multiple-thread structure. Yet it is absolute computational efficiency, rather than performance relative to CPUs, that determines the feasibility of near real-time MC calculations. The fact that a single GPU can already compute dose in seconds strongly supports this feasibility. Practicality should also be considered. While a low-end cluster with 4–8 computers may offer high speed, it is more advantageous in a clinical environment to use GPU-enabled computers in terms of energy efficiency, ease of management, etc.

The utilization of GPUs in scientific computing is *absolutely* more than hype. Among the world's top 500 supercomputers, 46 of them use GPU-based coprocessors compared to only 17 systems with MIC coprocessors. A few major vendors in radiotherapy, e.g., RaySearch and Elekta, already employ GPUs in their products.

I agree that multiple options are available to substantially accelerate MC in this era of booming technology. Intel MIC is a great example. Nonetheless, it too may be hype which only emphasizes the ease of programmability based on existing CPU codes but hides the required efforts of performance tuning. There is probably no single technology that is undoubtedly better than others. However, based on the overall consideration of GPU's advantages and developments so far, I believe that GPU technology is the hope for near real-time MC dose calculations.

Rebuttal: X. George Xu, Ph.D.

I agree with Dr. Jia that the capability of real-time MC dose calculations is within reach owing largely to the innovative technology and marketing strategies by Nvidia. The greatest roadblock to GPU is the fact that the effort to translate legacy MC codes to the new CUDA programming environment is prohibitively expensive. GPU also faces tough technological challenges, including limited memory and data bandwidth.[14] Given the steep investment and market risk, for *everyone* to jump onto the GPU wagon is costly and unwise.

To CPU enthusiasts, multithreading techniques such as OpenMP and Pthreads are readily available for parallel computing. Intel CPUs come with hyperthreading for concurrent execution, and various compiler options can be used for optimization. As a competing architecture, Intel's MIC is much easier to adopt.

To avoid “unfair comparison” between GPU and CPU,[11] one should consider the above-mentioned software optimization techniques and pick a “multicore” CPU (instead of a “single-core”) at a similar price to the GPU implementation. Comparative studies should also consider software related labor expenses. When we recently compared the performances of ARCHER—an MC dosimetry code developed from scratch by my Ph.D. students[11–13]—in the CPU, GPU, and MIC platforms, we found that GPU's advantages as a dose engine are less dramatic than some of those reported in the literature. All things considered, traditional CPU clusters and MIC

remain serious competitors to GPUs when energy efficiency is not the priority. In the next five years, all these technologies are expected to evolve rapidly.

The potential waste of capital and human resources due to hype and misleading information should be avoided. To this end, peer-reviewed journal publication and grant application processes should emphasize balanced GPU studies that offer the best methodologies and practices to the medical physics community.

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1.6. Evaluation of treatment plans using target and normal tissue DVHs is no longer appropriate

Christopher F. Njeh and Brent C. Parker
Reproduced from *Medical Physics* **42**, 2099–2102 (2015)
(http:// dx.doi.org /10.1118/1.4903902)

OVERVIEW

It is standard practice to evaluate dose distributions in different tissues, organs, and tumors through visualization of dose-volume histograms (DVHs) and/or analysis of quantities derived from DVHs. The DVH does not contain spatial information and has several other shortcomings, however, and some have suggested that evaluation of treatment plans using DVHs is no longer appropriate. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Christopher Njeh, Ph.D. Dr. Njeh graduated with a Ph.D. in Medical Physics from Sheffield Hallam University, United Kingdom and, after graduation, he worked at the Addenbrooke's Hospital in Cambridge and Queen Elizabeth's Hospital, Birmingham, United Kingdom. He later joined the Department of Radiology at the University of California, San Francisco as a Visiting Postdoctoral Fellow where he was subsequently appointed as Assistant Professor. Dr. Njeh transitioned to therapeutic medical physics by completing a Medical Physics residency at Johns Hopkins University, Baltimore. He has since served as Chief Medical Physicist at Texas Oncology in Tyler, TX and held an adjunct faculty position at the University of Texas at Tyler. He is currently Radiation Physicist at California Cancer Center, Fresno, CA. Dr. Njeh is certified in Therapeutic Radiologic Physics by the ABR. His major research interests include image-guided radiation therapy and accelerated partial breast irradiation. He is an author or a co-author of over 60 journal papers and 10 book chapters, and is a co-editor of two books. He is an Associate Editor of the British Journal of Radiology, a member of the ASTRO Education Committee, and a Fellow of the AAPM.

Arguing against the Proposition is Brent C. Parker, Ph.D. Dr. Parker earned his M.S. and Ph.D. degrees in Medical Physics at the University of Texas-Houston Health Science Center Graduate School of Biomedical Sciences, Houston, TX while he was working as a Graduate Research Assistant in the M.D. Anderson Cancer Center, Houston. He subsequently worked as Medical Physicist at The University of Texas Medical Branch, Galveston, TX from 2004 to 2007 and the Mary Bird Perkins Cancer Center, Baton Rouge, LA from 2007 to 2011, after which he returned to the University of Texas Medical Branch, Galveston, where he is currently Director, Division of Physics and Engineering, and Associate Professor in the Department of Radiation Oncology. Dr. Parker is certified in Therapeutic Radiologic Physics by the ABR and has served as the President of the AAPM Southwest Chapter. His major research interests include stereotactic radiosurgery, and radiotherapy treatment planning, delivery, and quality assurance, on which he has published 17 papers in refereed journals.

FOR THE PROPOSITION: Christopher F. Njeh, Ph.D.

Opening Statement

The fundamental tenet of radiation therapy is to deliver a tumoricidal dose to the target while limiting the dose to the normal tissues and organs at risk (OARs), and the goal of treatment planning is to optimize these objectives. The DVH was introduced in the 1980s as a simple way to evaluate plan quality by condensing a 3D dose distribution into a 2D graphical representation of the dose distribution throughout the target volume and each of the OARs.[1] In today's era of modern radiation therapy with competing techniques such as IMRT, VMAT, and proton therapy, it is my opinion that DVHs are no longer the best tool for plan quality evaluation. Let us start by identifying some of the shortcomings of the DVH.

By the very nature of the DVH, there is a loss of spatial information of the dose in the volume under consideration.[1,2] When comparing competing plans, such information about the location of hot and cold spots can be critical to determination of the effectiveness of that treatment.[3] The DVH can only be calculated for the defined volume of interest and its shape may be misleading.

The accuracy with which the DVH is estimated depends highly on the accuracy with which the target or OARs is delineated.[1] Accurate target and OAR delineation is a serious problem in radiation therapy.[4] DVH accuracy is also dependent on the accuracy of the dose distributions computed by the treatment-planning system. This is affected by several sources of uncertainty, such as algorithm limitations, measurement uncertainty in the data used to model the beam, and residual differences between measured and computed dose.[5] Furthermore, when delivery uncertainties are present, the DVH may not always accurately describe the dose distribution actually delivered to the patient.[6,7]

It has long been recognized that for some normal tissues such as rectum and bladder, the dose distribution of importance is that to the surface rather than the whole volume.[8–10] Radiation doses delivered to the contents of the rectum or bladder are of no consequence to the normal tissue complication probability (NTCP).

Another limitation of DVHs is that the interpretation of the plot is rather subjective. There is a need to better understand the implication of small differences between DVHs. This is more urgent in today's practice of RT with competing techniques to treat the same target.

It is clear that dose distributions in targets and OARs are just surrogates for tumor control probability (TCP) and NTCP. DVHs do not provide any information about the biological response of the tumor and OARs. A truly objective score of a treatment plan should be linked to the potential clinical outcome. Thus, one needs tools that can objectively quantify the probability of an end point of interest such as TCP or NTCP as a function of delivered dose distribution.[11]

On the basis of the above stated shortcomings of DVHs, it is my contention that the DVH in today's highly conformal radiation therapy environment is no longer an adequate tool for plan quality evaluation.

AGAINST THE PROPOSITION: Brent C. Parker, Ph.D.

Opening Statement

Since its introduction more than 30 years ago, the DVH has become a staple of plan evaluation in radiation oncology.[12] So why put it out to pasture now?

There is no question that the traditional planning DVH has its limitations: representation of a single time point; no biological or functional information; cannot account for tissue motion or deformation; and contains no spatial dose distribution information. But these limitations will apply to any metric that is based on a plan at a single point in time. I argue that we can address many of the shortcomings of the DVH as opposed to eliminating it. Recent and current topics of clinical research have served to address some of these issues. Image guided radiation therapy (IGRT) has been shown to reduce setup error prior to initiation of treatment.[13] Gated delivery has the potential to minimize anatomic deviations during treatment compared to the initial plan geometry.[14] Tumor tracking can potentially account for intrafraction motion of the target.[15] Deformable image registration has the potential to account for changes in the shape of the target and surrounding normal tissues and relate the delivered dose distribution back to the original structure DVHs.[16] Functional information can be used to modify the DVH to evaluate only tissue that may be adversely impacted by the delivered radiation.[17] In theory, combining all of these developments can make the treatment planning DVHs more meaningful than ever.

As physicists, we seek to develop objective and quantitative metrics to make plan optimization and evaluation more efficient and meaningful. For example, we have moved from visually evaluating dose distributions, to DVH curves, and now to biological models (TCP, NTCP, EUD) to evaluate and rank plan quality. In each step of the process some information is lost, but additional information is gained. However, we should be mindful that every metric has associated uncertainties that must be acknowledged in their use. For example, studies have shown that the specific biological and treatment delivery parameters used can significantly influence plan optimization, evaluation, and ranking.[18,19]

Even as we have moved through the various methods of plan evaluation, we have not completely eliminated older methods. Our physician colleagues still evaluate dose distributions relative to the patient anatomy in order to evaluate plan quality. We cannot ignore the fact that there is still a subjective component to plan evaluation using metrics that are well-established and familiar.

In conclusion, while the DVH is not *the* appropriate choice for plan evaluation, it is still *an* appropriate choice. While it should not be the sole method for evaluating treatment plans, I predict that it will continue to be used with past, present, and future evaluation methods to help us generate the best possible treatment plans for our patients.

Rebuttal: Christopher F. Njeh, Ph.D.

Dr. Parker has articulated strongly his support for DVH but I disagree with his opening argument that we should accept the status quo. The field of medical physics has advanced to where it is today because those who came before us questioned, revised, and improved upon the status quo. Hence, we should strive towards a better way of evaluating plans so that competing techniques can be properly assessed.

Dr. Parker and I both agree that the DVH in its present form has significant limitations. He goes further to present some of the recent developments that could potentially improve the accuracy of DVHs. However, if any new tool is a derivative of DVH, then the inaccuracies inherent in DVH will be propagated along with it. Hence, the plethora of indices or metrics[20] that have been used as quantitative indices of DVHs are bound by the same uncertainties. This makes it imperative to find a tool that is less sensitive to the uncertainties in dose computations and volume delineation.

Some of the shortcomings of the DVH can never be totally eliminated. It is not surprising that over the years, different researchers have proposed alternative approaches. For example, to address the loss in spatial information in the DVH, the zDVH,[1] the 2D dose–volume scoring-function histogram (DVSH),[21] and slice base plan evaluation,[22] have been proposed. The biologically effective dose DVH has also been proposed[23] to account for the effect of dose on the given tissue taking into consideration the fraction size, overall treatment time, etc. However, as stated in my opening statement, with increased knowledge of tumor and normal tissue radiation responses and advances in molecular imaging, biologically based evaluation must be the best way forward.[24]

In conclusion, if we agree that DVH is flawed, then we must also agree that a better tool is required because these flaws might be impacting our decision on what we consider the optimal plan for our patients. We need an appropriate tool to guide us to make the right decisions and thus achieve our goal of improved tumor control.

Rebuttal: Brent C. Parker, Ph.D.

If my colleague is going to argue that the DVH is no longer appropriate for plan evaluation, then he should identify how his suggested replacement metrics address their shortcomings.

I agree that there is a loss of spatial information in the DVH, and I addressed that issue in my opening statement. I also agree that some organs should be evaluated by dose-surface or dose-wall histograms. But that is not an inherent limitation of the DVH itself, only an indicator that we need to use a different evaluation tool that more accurately reflects the structure of the tissue of interest.[8]

As for the other limitations identified by my colleague (structure delineation, dose distribution accuracy, algorithm limitations, delivery uncertainties, measurement uncertainty in commissioning data, etc.), their impacts are not limited solely to the DVH. Errors or uncertainties in any of these quantities will manifest in any metric that is used to evaluate competing treatment plans. He suggests that we should use end-point-of-interest metrics such as TCP and NTCP. Studies have shown that systematic errors in calculated dose (e.g., inaccurate dose algorithms, and inaccurate commissioning data) can significantly impact the calculated values of these parameters.[25,26] Additionally, the choice of biological model, as well as uncertainties in the model itself (e.g., tissue sensitivity), will also impact the calculated values.[27] The dose evaluation metric is only as good as the data used for its calculation. As I stated in my opening argument, all metrics have some associated uncertainty that must be acknowledged in their use.

During a patient's course of treatment, our goal is to make the delivered dose (magnitude and location) match that of the treatment plan. The more we can reduce the uncertainties in the treatment planning and delivery process, the more accurate and relevant the DVH (or any evaluation metric) becomes.

Given that DVHs remain a primary method of plan quality evaluation, we should seek to correlate our DVH experiences with new metrics as they develop and mature so as to ensure clinical experience continuity throughout the transition. In any case, the sun has still not set on the DVH in radiation oncology.

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1.7. Treatment planning evaluation and optimization should be biologically and not dose/volume based

Joseph O. Deasy and Charles S. Mayo
Reproduced from *Medical Physics* **42**, 2753–2756 (2015)
(http:// dx.doi.org /10.1118/1.4916670)

OVERVIEW

The ultimate goal of radiotherapy treatment planning is to find a treatment that will yield a high tumor control probability (TCP) with an acceptable normal tissue complication probability (NTCP). Yet most treatment planning today is not based upon optimization of TCPs and NTCPs, but rather upon meeting physical dose and volume constraints defined by the planner. It has been suggested that treatment planning evaluation and optimization would be more effective if they were biologically and not dose/volume based, and this is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Joseph O. Deasy Ph.D. Dr. Deasy obtained his Ph.D. in Physics from the University of Kentucky in 1992 and subsequently was a postdoctoral fellow at the University of Wisconsin, Madison in Rock Mackie's group, where he met Jack Fowler, who stimulated his interest in predicting outcomes. He subsequently held several faculty positions, including professor from 2008 to 2010 at Washington University in St. Louis, where he established a division of Bioinformatics and Outcomes Research within the Department of Radiation Oncology, before moving to Memorial Sloan Kettering Cancer Center in 2010 as Chair of the Department of Medical Physics. His research interests include applying statistical modeling to the analysis of large complex datasets in order to understand the relationship between treatment, patient, and disease characteristics and the probability of local control and normal tissue toxicity and applying statistical methods to information derived from medical images, a growing field called “radiomics.” Dr. Deasy is a very active in the AAPM, ASTRO, and chairs several committees and task groups. He has held numerous grants to support his research and has published over 100 papers in peer-reviewed journals.

Arguing against the Proposition is Charles S. Mayo, Ph.D. Dr. Mayo obtained his Ph.D. in Physics from the University of Massachusetts, Amherst in 1991 and was a post-doctoral fellow from 1990 to 1993 specializing in proton therapy at the Harvard University Cyclotron Laboratory, Cambridge, MA. After holding several positions in New England hospitals, he moved to the Department of Radiation Oncology, Mayo Clinic, Rochester, MN in 2010, where he is currently Assistant Professor of Medical Physics. He has been very active on AAPM Committees and Task Groups and currently serves as chair of TG 263 on Standardizing Nomenclature for Radiation Therapy. He has served as President of the New England Chapter and is a fellow of the AAPM. Dr. Mayo's major research interests include effects of reduced treatment time on tumor radiobiology, normal tissue tolerance to radiation, modeling effects of motion on TCP/NTCP, design and analysis of patient outcomes databases, and design of web

interfaced/database solutions for managing clinical practice, on which he has published extensively.

FOR THE PROPOSITION: Joseph O. Deasy, Ph.D.

Opening Statement

The goal of radiotherapy should be to give a highly effective tumor treatment with an acceptably low risk of toxicity. I believe that we have reached the tipping point, where predictive NTCP and TCP models, when validated against relevant datasets, should be placed in the hands of clinical practitioners, alongside accepted dose–volume metrics, such as those in QUANTEC reviews.[1,2]

Today, prescriptions for standard external beam radiotherapy are often written in categories of "one-prescription-dose-fits-all," with little personalization to the patient's disease, despite the fact that we know very clearly that normal tissue tolerance is strongly related to organ/tissue volumes irradiated. To give just one example, most locally advanced lung cancer patients treated in the U.S. receive 60 Gy in 30 fractions, despite wide variations in tumor volume, shape, and location within the lungs. Just as importantly, our current obsession with dose flatness, and with overly generous margins, has little radiobiological support and is likely to be counterproductive.

In many cases, commonly used dose–volume planning limits (for normal tissues) and dose–volume goals (e.g., the PTV D95, the maximum dose in the coldest 5% of the planning target volume) are likely to be poor substitutes for NTCP and TCP prediction models derived from adequately powered datasets. Dose–volume constraints typically have higher uncertainty with respect to their impact on outcome, because they are inherently less general and only represent part of the (dose and fractionation) picture that biological/NTCP models attempt to integrate into a useful estimate. It follows that driving IMRT optimization using outcome-based functions could result in significantly more effective dose distributions for many patients.

The radiobiological modeling in TCP and NTCP functions throws the foundations of the conventional planning paradigm into question. In particular, the practice of worshipping flat dose distributions, accompanied by large margins overlapping with normal tissues ("paranoid target volumes"), should lose its unearned credibility and be superseded by a more rational approach to choosing dose limits.

Currently, there is a good reason to consult relevant NTCP models (and in a few cases, TCP models) on a routine basis, but this is not as easy to do in commercial treatment planning systems as it should. Furthermore, to properly use NTCP and TCP models, new protocols need to be written and established which allow for greater treatment customization based on the anatomical details of each patient's case.

Other technologies will be crucial for optimizing radiotherapy treatment plans. Probabilistic treatment planning, which accounts for residual geometrical uncertainties relevant to a given treatment situation, is another piece of the puzzle for rationally optimizing radiotherapy, and can help avoid overly generous margins. Together with increasingly accurate online tissue localization (for example, using in-room MRI), a much more aggressive approach could be

taken: steep dose gradients could be routinely placed close to the edge of the tumor (or regions of suspected occult disease), thus increasing the likelihood of complete disease sterilization due to the hotter dose over most of the target, while lessening the impact on normal tissues spared by the rapid dose falloff.

Although TCP and NTCP models are improving significantly with continued publications, there are many areas where better models are needed, and the imperative to pool the data necessary to improve the models is greater than ever.

Even today, routine treatment planning would benefit from referencing TCP and NTCP functions, alongside accepted dose–volume constraints. It is logical to expect that the increasing integration of TCP and NTCP models into clinical practice, over time, will result in more therapeutically effective (nonuniform) dose distributions, and a rationalized personalization (within limits) of prescription dose and fractionation.

AGAINST THE PROPOSITION: Charles S. Mayo, Ph.D.

Opening Statement

Can we accept the proposition that we know enough about the reliability and errors associated with biological models and the resultant impact on dose distributions (among the many treatment planning systems) produced by using these models in optimization and evaluation of patient plans, to take the extreme position of discarding several decades of clinical experience based on DVH metrics as the fundamental benchmarks? Dr. Deasy *et al.* have elegantly summarized one argument against the Proposition: "*Despite a large number of dose-volume-outcome publications, made possible by the revolution in three-dimensional treatment planning, progress in normal tissue complication probability (NTCP) modeling to date has been modest. The QUANTEC reviews, though helpful, have demonstrated the limited accuracy of existing risk protection models*."[1]

Models are still evolving to improve and demonstrate predictive ability.[2,3] There can be wide variability among existing models and challenges in accurately predicting clinical outcomes. Classic models often do not have means to adequately reflect the clinically observed impact of nondosimetric factors such as age, chemotherapy, surgery, setup reproducibility, or even fractionation. Efforts to improve models have highlighted a richer set of interactions to explore such as heart–lung codependence[4] or nerve–vasculature interactions. Development of radio-genomics databases have helped pave the way for models factoring in single-nucleotide polymorphisms to improve predictive power of NTCP models.[5] Imaging based biomarkers[6] may be used to improve models. Monte Carlo approaches to TCP/NTCP estimations and *in-silico* modeling of outcomes and mechanisms are very promising.[7] Concluding that we are ready to specify which models the community should use may be premature.

Is it more efficient or reliable to set constraints using radiobiological metrics during optimization rather than DVH metrics? After all, is not an experienced treatment planner intuitively factoring in an EUD calculation when considering dose–response in setting constraints on dose regions of the DVH curve? However, when evaluating the plan, consumers of the results are mindful of

extensive literature, trial results, and personal experience correlating DVH metrics with outcomes. A few clinics have long experience examining correlations of NTCP and DVH metrics with outcomes to shape their perspective on clinical decisions.[8] In the larger community, when a benchmark DVH metric has not been met but the radiobiological metric has, replanning to also meet the DVH metric is the likely outcome. Relying only on biologically based metrics rather than considering both for plan optimization and evaluation is less effective.

To reach the goal of more reliance on radiobiologically based metrics, we need to greatly improve the community's personal experience with use of these metrics. A useful strategy would be to routinely calculate these metrics along with DVH metrics in plan evaluations, saving the results in databases to correlate with outcomes monitored in those clinics, pooling results among institutions to explore the impact of variations from one clinic to another in order to find consensus. The Proposition sets forth a great vision, but one that the community as a whole is not ready for right now.

Rebuttal: Joseph O. Deasy, Ph.D.

It is admittedly awkward to argue against quotes from my work with my QUANTEC coauthors, but my own position has evolved, given the steady stream of TCP and NTCP models and analyses that have been published since QUANTEC.[9–14] We are in an exciting age of predictive model development. This is an opportunity that we should not ignore: given the mathematical nature of these models, only medical physicists are equipped to lead the effort of clinical adoption (e.g., see the Biosuite software system developed by Nahum and colleagues).[15] Meanwhile, standard practice creeps along, based on rather arbitrary, DVH-based measures of treatment plan quality which have long been understood to have limited predictive value.[16] As one example: there is currently little clinical evidence that either the D95 or D98 of the PTV is a good predictor of tumor control. I am happy to concede to my debate opponent that our knowledge of NTCP and TCP models is incomplete, with many holes requiring further improvements, and that the clinical use of predictive models should proceed cautiously.[3] A wholesale replacement of standard DVH guidelines with NTCP and TCP models is not to be recommended. Nonetheless, the use of published, validated models to inform physicians and planners concerning tradeoffs in toxicity risk against disease control is highly desirable and would, I believe, amount to a real (though admittedly incremental) improvement in treatment planning.

Consider the historical parallel of the argument previously advanced against using heterogeneity-corrected dose calculations in lung because our clinical experience was (at that time) based on water-equivalent calculations. It is now well-accepted that those simplified algorithms were dangerously misleading (resulting in incorrect doses and undersized apertures). Analogously, we can continue to rely on relatively arbitrary traditional DVH metrics, or we can make a serious, sustained, concerted effort to put validated outcome prediction models into the hands of physicians, physicists, and treatment planners, who could use the resulting predictions (alongside other considerations, such as age, performance status, and the patient's input) to improve clinical decision making.

Rebuttal: Charles S. Mayo, Ph.D.

There is too little multi-institutional data available on tumor control or normal tissue complications documenting correlations of traditional DVH metrics with TCP/NTCP models and contrasting confidence intervals for predicting outcomes. Without this clinical data, the arguments in favor of prioritizing biological models over DVH metrics for clinical decision making are weaker than they should be. Using models to add to what we know from the DVH metrics falls short of the goal of the Proposition, but it is a very good and plausible first step.

Treatment planning systems should make it easy to routinely calculate, report, and record sets of DVH and radiobiological model metrics. If this had been true for the last decade, it is unlikely that we would be having the current debate and speculation. QUANTEC might then have been able to report on a literature summary table of recommend radiobiological constraints in addition to one of DVH metrics.

We should be cautious about the potential for overstating the impact of use of these models in optimization and evaluation. Sculpting steep dose gradients and margin reduction have steadily improved with improvements in MLC design, IMRT/VMAT optimization algorithms, and IGRT technologies. Radiobiological models are less the limiting factor than the physics of the beams and the planning systems' practical abilities to push limits. For proton beams, models that reflect effects of variation of LET in range of the Bragg peak may result in change for how we evaluate some plans. TCP models produce less uniform dose distributions, but the range of values that will pass is still going to be limited. Until there are data demonstrating outcomes as good or better, it is unlikely that a clinician would accept extremely cold regions in a CTV or hot regions in a PTV, despite having acceptable TCP values.

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1.8. Calibration of radiotherapy ionization chambers using Co-60 is outdated and should be replaced by direct calibration in linear accelerator beams

Ramanathan Ganesan and Malcolm R. McEwen
Reproduced from *Medical Physics* **42**, 5003–5006 (2015)
(http:// dx.doi.org /10.1118/1.4922710)

OVERVIEW

Most medical linear accelerators worldwide are calibrated using ionization chambers that are themselves calibrated by a standards laboratory, or secondary standards laboratory, in a Co-60 beam. Because these chambers are actually used to calibrate high-energy x-ray beams, it has been suggested that calibration against Co-60 is outdated and should be replaced by calibration in linear accelerator beams. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Ramanathan Ganesan, Ph.D. Dr. Ganesan earned his Ph.D. in Physics from the University of Mumbai in 2001, having previously worked for many years as Scientific Officer in the Radiation Standards Section, Radiation Safety Systems Division, BARC, Trombay, Mumbai, India. Subsequently, he spent some time working at the National Physical Laboratory, Teddington, Middlesex, UK, and NIST, Gaithersburg, MD, USA, before he moved to his current position as Senior Radiation Scientist, Radiotherapy Section Medical Radiation Services Branch, Australian Radiation Protection and Nuclear Safety Agency, Yallambie, Victoria, Australia. His major research interests are calorimetry measurements of photon and electron beams, calibration of dosimeters, small field dosimetry, development of diamond and diode detectors, and calibration of environmental radiation dosimeters.

Arguing against the Proposition is Malcolm R. McEwen, Ph.D. Dr. McEwen earned his Ph.D. in Radiation Physics from the University of Surrey, UK, in 2002, having previously worked for many years at the Centre for Ionising Radiation Metrology, National Physical Laboratory, UK. He then moved to his current position as Research Officer at the Ionizing Radiation Standards Group, National Research Council of Canada, Ottawa, Canada, where he is Director of the Ottawa Medical Physics Institute and Adjunct Professor within the Department of Physics, Carleton University. Dr. McEwen is Chairman of the Consultative Committee for Ionising Radiation Section I of the Bureau International des Poids et Mesures and has been very active in the AAPM including having served as Chair of the Working Group to review and extend data in the AAPM TG-51 dosimetry protocol for radiotherapy, and he is the current Chair of the AAPM Calibration Laboratory Accreditation Subcommittee. His major research interests are improvements in reference dosimetry for radiation therapy, experimental and theoretical works on the performance and application of secondary dosimeters in high energy photon and electron beams, investigation of novel dosimeters/applications in dosimetry at radiotherapy dose levels,

and development of high-accuracy experimental benchmarks for testing Monte Carlo radiation transport codes used, for example, in the commissioning of medical linear accelerators.

FOR THE PROPOSITION: Ramanathan Ganesan, Ph.D.

Opening Statement

The success of radiation therapy depends on the accuracy of the prescribed dose delivered. The starting point in the dosimetry chain deciding this accuracy is the dissemination of absorbed dose standards in the calibration of radiotherapy reference ionization chambers. Two methods of dissemination are available: one based on direct calibration of ionization chambers in megavoltage photon beams and the other based on the use of a correction factor, k_Q, applied to the calibration coefficient determined in a Co-60 beam.

Linear accelerators have totally replaced Co-60 for radiotherapy treatment in many countries and are becoming more common in others. The cost and difficulty in obtaining replacement Co-60 sources caused by increasing security concerns that treat Co-60 therapy sources as high risk, and the need to safely dispose of decayed sources, inhibit their use in hospitals and calibration laboratories.[1]

Several standards laboratories are equipped with Linacs.[2] The experimental measurement of the absorbed dose to water calibration coefficient $N_{D,w,Q}$ and beam quality factor K_{Q,Q_0} for the user chamber at primary standards dosimetry laboratories is the preferred option in IAEA TRS-398.[3] Observed chamber-to-chamber differences, which include the effect of waterproof sleeves (also seen for Co-60), justify the recommendation in IAEA TRS-398 for k_Q values specifically measured for the user chamber.[4] Also, the new formalism by the IAEA/AAPM working group for reference dosimetry of small and nonstandard fields recommends the direct calibration of the dosimeter in a conventional broad beam and machine-specific-reference fields against a primary standard without the Co-60 calibration.[5]

The accuracy of a calculated k_Q factor depends on the precision of the chamber geometry (including any deviations from the specified geometry). To use a measured k_Q only requires that the chamber response be reasonably insensitive to photon energy, so that users can interpolate between beam quality indicies.[6] Relative standard uncertainties for the experimental measurements of k_Q factors for the most commonly used chambers have been reported as 0.3%.[7] Although similar relative standard uncertainties of <0.5% have been achieved recently for Monte Carlo calculated k_Q values,[8] theoretical calculations are limited by the energy-dependent uncertainties of W/e and stopping power values. This is to be contrasted with the combined uncertainty for the direct calibration method such as the uncertainties achieved at the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) that are around 0.6%–0.7%, which are less than the estimated 1.1% with a reference beam quality of Co-60 and the TRS-398 energy correction.[10] Furthermore, for the calibration of flattening filter free beams, the published k_Q factors reported in IAEA TRS-398 have to be corrected,[9] adding to the uncertainties in using Co-60 calibration.

After the release of the IAEA TRS-398 and AAPM TG-51 protocols in 2000, several new ion chambers have been introduced in the market. Direct calibration may be used for these new or rare chamber types for which calculated k_Q factors are not available in IAEA TRS-398 or the addendum to AAPM TG-51.[11]

Calibration of radiotherapy ionization chambers using Co-60 is outdated for the above mentioned reasons and should be replaced by direct calibration in linear accelerator beams.

AGAINST THE PROPOSITION: Malcolm R. McEwen, Ph.D.

Opening Statement

At the heart of this proposition would appear to be the fact that for reference dosimetry of linear accelerator beams, the majority of clinical medical physicists worldwide must use a chamber calibrated in a Co-60 beam together with calculated k_Q factors. These factors, and the method to apply them, are provided by protocols such as AAPM TG-51 or IAEA TRS-398.[11–13] The reason to change from this approach is, presumably, that these calculated factors are used "on faith" and could lead to significant dosimetric errors when combined with any particular ionization chamber.

Fifteen years after the IAEA TRS-398 recommendation that users obtain calibrations in linear accelerator beams, the literature is surprisingly silent on the need to do so. Only one country in the world currently requires calibrations in linear accelerator beams. The National Physical Laboratory in the UK has carried out Linac calibration of ion chambers since 1989, and their own data[14] show no significant variation in chamber k_Q factors, to the extent that one can apply a generic calibration curve with an uncertainty better than 0.2%. Muir *et al.*[15] compared Monte Carlo k_Q factors to measurements and found very good agreement (0.25% or better) for a wide range of chamber types over the full range of Linac photon energies. Andreo *et al.*[4] compared the older TRS-398 calculations to the same experimental data set and concluded that no revision of those semianalytical k_Q factors was required. The National Research Council in Canada has been offering MV calibrations since 2007 and analysis of these data showed that, although one sees up to 1% variations in Co-60 $N_{D,w}$ coefficients, the *standard deviation* of k_Q factors for reference-class ionization chambers was only around 0.15%.[16] One can therefore reasonably ask, "What problem needs to be solved?"

On a more pragmatic note, although it is perhaps easy for the clinical medical physicist to view Co-60 as "outdated," I would argue that Co-60 is the ideal calibration beam. A Co-60 irradiation unit is simple and very reliable to use, has a very predictable output over multiple years, and is much cheaper to operate than a linear accelerator. Leaving the economics of the calibration laboratory aside (although in some areas of the world this is a very important consideration), moving from a Co-60 irradiator to a linear accelerator for calibration would immediately result in a loss of precision and a loss in the ability to monitor the long-term stability of reference-class ionization chambers. Linear accelerator beams are simply not stable enough to provide that long-term reference field. Since the accuracy gain one might achieve by moving to Linac calibrations is, based on the literature, only a few tenths of one percent, this loss in baseline QA of the detectors results in a negative cost-benefit analysis. Linear accelerators may be the obvious

choice for absorbed dose delivery but Co-60 remains the best choice for absorbed dose calibration.

Rebuttal: Ramanathan Ganesan, Ph.D.

Dr. McEwen has raised several important points regarding the calibration of radiotherapy ionization chambers. However, his comment that "*Fifteen years after the IAEA TRS-398 recommendation that users obtain calibrations in linear accelerator beams, the literature is surprisingly silent on the need to do so*" is not entirely correct. As I mentioned in my opening statement, a number of standards laboratories are installing Linacs, establishing primary standards, and measuring absorbed dose to water, the prime quantity needed for calibration, validated through international intercomparisons (e.g., BIPM.RI(I)-K6).[17] Also, there are a number of publications on experimental measurements of k_Q factors at megavoltage energies for several ionization chambers.[18]

Regarding his point that calibration data from the National Physical Laboratory in the UK show no significant variations in chamber k_Q factors, the chambers (NE 2561/NE 2611) were designed in-house and built specifically as secondary standards. Andreo *et al.*[4] observed significant chamber-to-chamber variations in Co-60 beams in a study of 91 NE 2571 chambers, which are the industry standard. The observation by Muir *et al.*,[15] who compared Monte Carlo k_Q factors to measurements and found very good agreement (0.25% or better), is valid only if possible variations of W/e with energy are ignored and assuming correlated uncertainties in photon cross sections. Larger deviations (~0.5%) between measured and theoretical k_Q factors occur at higher energies.

Dr. McEwen argues that replacement of Co-60 with linear accelerators for calibration would immediately result in a loss of precision and a loss in the ability to monitor the long-term stability of reference-class ionization chambers. This argument is contradictory to his claim that the MV calibration data from the National Research Council in Canada since 2007 have shown the standard deviation of k_Q factors for reference-class ionization chambers to be around 0.15%.

Rebuttal: Malcolm R. McEwen, Ph.D.

The rising cost of Co-60 re-sourcing is indeed a concern for many calibration laboratories but must be considered in the context of the price tag for a linear accelerator, which is the proposed alternative. If you take the optimistic assumption of a 20-yr Linac lifetime, you can do the math and conclude that you do not come close to the same capital costs for a Co-60 irradiator over that time period, even if you re-source every half-life. And that is before accounting for maintenance costs, which are significantly more for a Linac compared to a Co-60 unit. Economics are, therefore, not a driver for a change in the calibration basis.

The chamber-to-chamber variations cited are also illusory. The much larger data set from the US ADCLs analyzed by Muir[19] shows very tight tolerances on $N_{D,w}$ coefficients, and I would reiterate that there are no data in the literature that suggest a significant chamber-to-chamber variation in k_Q for any particular chamber type.

Direct calibrations in MV beams do indeed result in a potentially lower uncertainty in clinical reference dosimetry, although one could argue whether the improvement is significant. However, there is one issue where MV calibrations offer a clear advantage, and I am surprised it was not brought up by my opponent. A calibration in a MV photon beam is also a precise test of the user's chamber in a beam very similar to that in which it will be used. It answers that "*What if my chamber is atypical*?" question and is a QA test clearly missing from the present Co-60-based approach. Whether that, alone, is enough to warrant a wholesale change in calibration practices is for the user community to decide.

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1.9. Radiotherapy using hard wedges is no longer appropriate and should be discontinued

Christopher F. Njeh and Tae Suk Suh
Reproduced from *Medical Physics* **43**, 1031–1034 (2016)
(http:// dx.doi.org /10.1118/1.4939262)

OVERVIEW

Because of the widespread use of dynamic and virtual wedges with modern radiotherapy machines, and the concomitant decrease in use of hard (physical) wedges, some would argue that the use of hard wedges is no longer appropriate and should be discontinued. This is the claim debated in this month's Point/Counterpoint

Arguing for the Proposition is Christopher F. Njeh, Ph.D. Dr. Njeh is a graduate of Birmingham University, Aberdeen University, and Sheffield Hallam University, UK. He started his professional career at the Addenbrooke's Hospital in Cambridge and Queen Elizabeth's Hospital, Birmingham, UK. He later joined the Department of Radiology at the University of California, San Francisco as a Visiting Postdoctoral Fellow where he was subsequently appointed as Assistant Professor. Dr. Njeh transitioned to therapeutic medical physics by completing a medical physics residency at Johns Hopkins University, Baltimore. He has since served as Chief Medical Physicist at Texas Oncology in Tyler, TX and held adjunct faculty positions at the University of Texas at Tyler and California State University, Fresno. He is currently Chief Medical Physicist and Radiation Safety Officer at Franciscan Health, Indianapolis, IN. Dr. Njeh is certified in Therapeutic Radiologic Physics by the ABR. His major research interests include osteoporosis, image-guided radiation therapy, and accelerated partial breast irradiation. He is author or coauthor of over 65 peer reviewed journal papers and 10 book chapters and is coeditor of two books. He is an Associate Editor of the British Journal of Radiology, a member of the ASTRO Education Committee, and a Fellow of the AAPM.

Arguing against the Proposition is Tae Suk Suh, Ph.D. Dr. Suh received his Ph.D. in Medical Physics from the University of Florida in 1990. He subsequently returned to his home country of Korea as Professor and Chair in the Department of Biomedical Engineering of the Catholic University Medical College in Seoul, Director of the Research Institute of Biomedical Engineering, and Director of the Research Institute of Magnetic Resonance Imaging. Dr. Suh is known for his work with his colleagues on the development of radiotherapy planning, multimodality imaging, and, in particular, radiosurgery. He has served on the editorial boards of many international journals, including *Medical Physics*. In 2006 and again in 2012, Dr. Suh was honored with the Korean Government's Award for the Best Academic Achievement.

FOR THE PROPOSITION: Christopher F. Njeh, Ph.D.

Opening Statement

The use of physical wedges to modify dose distributions with multiple fields to make them more homogeneous is a well established technique. However, there are several well-known problems with physical wedges. First, they are designed for limited field sizes and wedge angles. Typically, only four physical wedge angles of 15°, 30°, 45°, and 60° have been implemented by all manufacturers. Second, the wedge factor is dependent on many variables including beam energy, field size, depth of measurement, and type of accelerator.[1] This is because of beam degradation and hardening by the physical wedge. These problems can cause dosimetric issues in treatment planning and also any occasional misalignment of the wedge can produce significant dosimetric error in treatment delivery.[2] Last, physical wedges are heavy and cumbersome to use clinically for the therapists (usually must be lifted overhead) and present a safety concern for the patient.

One alternative to physical wedges is the use of computer controlled movement of one of the collimator jaws and variation in output rate during treatment.[3,4] Compared with physical wedges, these nonphysical wedges have several advantages such as reduction of treatment time, less scatter dose to areas outside the treatment field, potential for any arbitrary wedge angle and, in many cases, extended field size capabilities. For breast treatment in particular, there is improved dose distribution and reduction of dose to the contralateral breast,[5] thereby reducing potential carcinogenic effects.

The synergistic advances in therapy planning techniques, radiation technology [such as the introduction of the multileaf collimator (MLC)], computing, and 3D imaging have caused a monumental paradigm shift in the way radiation therapy is delivered.[6] It has made it possible to improve dose homogeneity by moving the MLC either by forward planning [such as field-in-field (FIF)] or inverse planning (IMRT) techniques. Several studies have reported that the use of the FIF technique gives better dose homogeneity than the traditional wedge technique, especially the reduction in cold and hot spots. Also, for breast radiotherapy, FIF has improved axillary node coverage and decreased doses to the heart and lungs compared to the traditional technique.[7]

In general, IMRT provides the ability to create highly conformal dose distributions, with normal tissue sparing. The increased tissue sparing can reduce both acute and late toxicity without compromising tumor control.[8] With IMRT, this gives the potential for dose escalation with increased probability of tumor control. With overwhelming clinical use of IMRT, it is not surprising that Princess Margaret Hospital, Toronto, Canada has either physically removed or disabled the use of physical wedges since 2007.[9] This came after their study demonstrated that, as IMRT was gradually implemented, the use of physical wedges steadily declined. More importantly, the decline in the use of physical wedges led to a statistically significant decrease in the rate of radiation incidents caused by accessory errors.[9]

It is evident that physical wedges have significant drawbacks that can be overcome by using nonphysical wedges, IMRT, or FIF, where appropriate. Hence, we should discontinue the use of physical wedges.

AGAINST THE PROPOSITION: Tae Suk Suh, Ph.D.

Opening Statement

Wedge filters are commonly used to modify dose distributions in radiation therapy to optimize target volume coverage.[10] With IMRT, nonphysical wedges (virtual or dynamic) are at the center of attention.[11] Nevertheless, due to technical issues, hard wedges should still be used in certain circumstances.

There are a few clinical cases that require the use of hard wedges rather than nonphysical ones. One of the major limitations of nonphysical wedges is direction. Enhanced dynamic wedges in Varian linear accelerators operate with only one pair of independent jaws (Y-upper jaws). Virtual wedges with Siemens accelerators require choosing one pair of jaws to generate dynamic movements and the other pair to operate during beam-on time as a jaw to define field size.[12] While hard wedges require no rotation since they offer 4-way wedge rotation (Right-Left-In-Out), nonphysical wedges, which have two-wedge orientations, 2-way (In-Out), require the collimator to be rotated either 90° or 270°.[13] These limitations of nonphysical wedges might make treatment planning for certain concave-shaped clinical cases impossible because multileaf collimator leaves are perpendicular to their wedge direction.

Since the introduction of IMRT, respiratory intrafractional organ motion during IMRT treatment has been examined but the effectiveness is not yet clear. Additionally, plenty of respiratory gating techniques with IMRT include interplay effects caused by similar velocities of tumor motion and collimators leading to a regular perturbation in the dose distribution. These have been reported and raise significant issues.[14] However, implementation of gating therapy in conjunction with IMRT using hard wedges does pose the same issue, but several studies have demonstrated better dosimetric outcomes utilizing hard rather than nonphysical wedges, with and without gating.[15]

Furthermore, the implementation of nonphysical wedges on our Varian linear accelerator requires an extensive quality assurance process. For example, the segmented treatment table from Varian requires more than 100 measurements to be made.[16] The measurement method for nonphysical wedges is much more complicated than that used for hard wedges for several reasons. Standard ion-chamber measurement in a water phantom cannot be applied for measurements for nonphysical wedges. This is because, with simultaneous 2-way (In-Out) movement during ion-chamber measurement, it is impossible to carry out the continuous measurement. Also, the standard 2D array measurement equipment is not appropriate for measuring nonphysical wedges owing to the lack of resolution in treatment planning systems. Most TPS manufacturers strongly suggest the importation of measurement data with 2 mm resolution, which requires more than one time measurement to achieve this resolution, which is extremely time-consuming. Therefore, a specialized linear ion-chamber array in a water phantom is recommended to fulfill all required measurement conditions for nonphysical wedges. Quantitative Gafchromic EBT film or electronic portal imaging dosimetry are potential solutions, but they are still inconvenient.[17]

In summary, there are a few applications of hard wedges that cannot be completely eliminated. Additionally, technical issues such as those mentioned above need to be resolved before nonphysical wedges can totally replace hard wedges for radiation treatment.

Rebuttal: Christopher F. Njeh, Ph.D.

Dr. Suh has provided justification for continued use of physical wedges. I put forward the following counter arguments to each of the points he has made.

It is understandable to advocate for varied tools in order to provide optimal care of our patients. However, we live in an era of evidence-based medicine.[18] My Opening Statement clearly demonstrates that physical wedges add very little to the optimal care of our patients.

The directional limitations of the EDW indicated by Dr. Suh can be overcome simply by rotating the collimator.

It is accepted that respiratory motion has an impact on dose delivery using IMRT or dynamic wedges.[19] However, studies have shown that the interplay between organ and MLC motion may average out with a large number of treatment fractions.[20] In addition, the interplay may also be reduced by careful application of motion management techniques such as breath hold.

Implementation of EDWs into treatment planning systems such as Pinnacle[4,21] and Masterplan[22] has been simplified by use of the golden segmented treatment table (GSTT) provided by Varian. The use of the GSTT has significantly improved the consistency of EDW generation on the accelerator as well as the efficiency of computer modeling of EDWs for treatment planning. The computer modeling is a convolution of the GSTT based field intensity matrix with the pencil beam kernel derived from the basic field beam data. As with physical wedges, the accuracy of the models generated by the TPS has to be verified by the physicist using films or diode/ion detector arrays such as MapCheck.

Dr. Suh has failed to provide strong evidence to support continued use of physical wedges. I believe that, in today's age of modern linacs with thin leaf MLCs, high dose rates, and computer controlled collimation, highly conformal and homogenous dose to a target can be achieved at any anatomical site without the need of physical wedges.

Rebuttal: Tae Suk Suh, Ph.D.

With rapidly developing radiotherapy technology at present, it may seem to be an outdated view to cling to the physical wedge. Occasionally, however, there are situations where simple methods such as using physical wedges can work as well as complicated ones.

I recognize Dr. Njeh's claim of weaknesses/issues with hard wedges such as limited field sizes, limited wedge angles, a large amount of measurements needed for various wedge factors, heavy weight, and inconvenience in use. However, the statement about the wedge factors has to be reconsidered since nonphysical wedges (virtual or dynamic) also require considerable measurement data as described in my Opening Statement. Furthermore, unlike hard wedges, nonphysical wedges are more prone to cause systematic errors that might be more difficult to discover because of their fully automated processes, and the consequences of such systematic errors are likely to be more severe.

My opponent states that field-in-field and intensity modulated radiation therapy provide excellent alternatives to the use of wedges, and in some respects, I agree with his statement.

Nevertheless, some clinics might have difficulty in utilizing such advanced treatment techniques due to lack of resources. It is well understood that significant resources are needed for the accurate and safe implementation of such advanced radiotherapy techniques. Note that the consequence of an error is much more severe with advanced techniques compared to conventional ones, as clearly reported in the New York Times paper.[23] While most major hospitals, by virtue of abundant financial and human resources, are able to keep up with the latest treatment technologies such as therapy machines, software programs, and auxiliary devices, some local clinics or even major hospitals in developing countries might not be able to do so because of the lack of either financial or human resources, or both.

In summary, it is premature to replace physical wedges by other techniques completely, even though there are no *technical* issues in realizing advanced radiotherapy technologies. Although the recent trend of radiation treatments in developed countries shows a rapid decrease in hard wedge utilization, the speed of catching up with necessary infrastructure in underdeveloped countries is not as fast as desired, leaving them no choice but to continue to use hard wedges in many cases. Thus, I believe that it is not yet the time to completely eliminate the use of hard wedges.

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1.10. EPID-based daily quality assurance of linear accelerators will likely replace other methods within the next ten years

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Reproduced from *Medical Physics* **43**, 2691–2693 (2016)
(http:// dx.doi.org /10.1118/1.4944423)

OVERVIEW

Daily quality assurance (QA) on linear accelerators (linacs) is both a time and resource consuming exercise. It has been suggested that it would be more efficient and cost-effective to perform daily QA using the electronic portal imaging devices (EPIDs) already present on most linacs. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Sasa Mutic, Ph.D. Dr. Mutic obtained his M.S. in Medical Physics from the University of Colorado, Denver, CO and his Ph.D. in Nuclear Engineering from the University of Missouri, Columbia, MO, and completed a medical physics residency at Washington University School of Medicine, St. Louis in 1996, where he has been ever since and currently is Professor of Radiation Oncology and Director of Medical Physics. He has served the AAPM in numerous capacities, including as a member of the *Medical Physics* Editorial Board. His current interests include decision support in RT, adaptive RT, MR, and CT guided RT, and use of systems engineering principles for design of QA programs. His group has published several articles on automation of QA activities in RT and design of algorithms and software applications for more consistent and effective performance of RT. He is a cofounder and Chief Technical Officer of Radialogica LLC, a company focused on software applications in oncology informatics. He is also a cofounder of the TreatSafely Foundation (http://treatsafelyfoundation.org), a nonprofit organization helping make radiation therapy safer around the world.

Arguing against the Proposition is Todd Pawlicki, Ph.D. Dr. Pawlicki is Professor and Vice-Chair in the Department of Radiation Medicine and Applied Sciences, University of California, San Diego. He obtained his M.S. in Physics from De Paul University, Chicago and his Ph.D. in Medical Sciences from the Medical College of Ohio, Toledo. He currently serves the AAPM as a member of the *Medical Physics* Editorial Board, Vice-Chair of the *ad hoc* Committee on Medical Physics 3.0, the Board of Directors as Secretary, and a number of other committees. His major research interest is the application of quality and safety engineering tools to radiation therapy. He is also a cofounder of the TreatSafely Foundation.

FOR THE PROPOSITION: Sasa Mutic, Ph.D.

Opening Statement

For almost two decades, there have been numerous reports on use of EPIDs for QA of virtually every aspect of linac performance, including daily QA.[1,2] These publications have thus far mostly addressed commercial EPID-based QA solutions focused on patient-specific-QA and less

on machine performance evaluation. Recent work by Clivio *et al.*[3] describes a linac vendor-provided EPID-based routine for automatic selfintegrity check of linac performance which would be performed daily. From the EPID-based linac daily QA processes described by Sun *et al.*[2] and the Clivio *et al.*,[3] one can foresee a fully automated, highly reliable, and commercially available solution for EPID only based daily QA. If a commercial solution for automated EPID-based linac daily QA is available, the question then becomes why would we not adopt such a tool to replace other daily QA methods. EPIDs provide a larger coverage area with higher resolution and offer significantly larger degree of automation which can be very important for efficiency and scope of daily QA. As both Sun[2] and Clivio[3] show, EPID-based daily QA can test many more linac performance aspects than conventional QA devices in the same or shorter amount of time. When properly calibrated and maintained, EPIDs also provide stable and reliable performance, one that many institutions trust for routine patient-specific-QA.[4] The only two practical obstacles to the adoption of EPID-based daily QA would be (1) perception that the EPID does not offer sufficient independence as a dosimeter for linac QA and (2) concerns with cost of EPID-based QA.

(1) *The EPID as an independent dosimeter:* the EPID, beam delivery mechanism, and mechanical linac components are all independent parts of the same machine. Having an EPID evaluate the performance of beam production and mechanical components is an independent QA but with a dosimeter which is mounted on the linac and which far exceeds the capabilities of conventional daily QA devices. A simple fault-tree analysis[5] would demonstrate that it is impossible for other linac components to malfunction and for the EPID to compensate for that malfunction and create false negative results. While there may be a perception that an EPID is not an independent dosimeter, there is no evidence that it is not nor that the existing daily QA devices offer a greater degree of independence. In the end, we must manage QA based on data rather than on perceptions.

(2) *Cost of EPID-based QA:* EPIDs would obviate the need for third-party electronics and would only need software and a simple phantom to be purchased for performance of daily QA. Elimination of additional electronics and use of automation would result in at least as cost effective if not cheaper daily QA with greater efficiency and scope of testing. The majority of our field has been moving in the direction of higher efficiency and effectiveness and daily QA should progress in that direction as well.

AGAINST THE PROPOSITION: Todd Pawlicki, Ph.D.

Opening Statement

EPIDs have been in clinical use for over 30 years in one technological form or another.[6] EPIDs were initially developed to replace radiographic film as an online method to verify patient position and then was readily applied to linac QA.[7] In the ensuing 30 years, the use of EPIDs has become an integral part of the patient setup and treatment process. Why, then, has not the use of EPIDs been extended to QA of linear accelerators over that same time frame? The proposition as stated (i.e., that it is *likely*) only refers to the *probability* that EPID-based daily linac QA will replace other methods within the next ten years. As they have not become part of our routine QA procedures over the last 30 years, it seems unlikely that EPIDs will replace other methods for

daily linac QA within the next ten. Here are a number of reasons that the prediction of the proposition seems improbable.

Even though the technological issues with EPID-based radiation beam measurements are now fairly well understood, EPIDs are still only being investigated for routine linac QA.[2,8] This is in part because EPID measurements are highly derived quantities that are not easily related to the gold standard for radiation therapy, namely, absorbed dose measurements in water. Additionally, EPIDs are complicated pieces of hardware and software that require significant QA checks and calibrations themselves. A robust daily linac QA device should be simple to operate, the results easily interpreted, and exhibit greater stability and reliability than the device it is intended to assess, which is not necessarily the case for EPIDs.

A robust daily linac QA device (hardware and software) should also be completely independent of the equipment it is designed to check. EPIDs are tightly integrated into the linac hardware and software systems. Therefore, using an EPID for daily linac QA requires the fox to guard the henhouse. This should give considerable pause to anyone responsible for the safe operation of their department's linacs.

Furthermore, linac vendors already have built-in redundant checks of linac operation. EPID-based daily linac QA would ultimately be just another redundant check provided by the linac vendor meaning that there is no *independent* daily linac QA being performed.

Finally, to provide EPID-based daily linac QA, the linac vendors would need to get into the "QA market" and compete against the established radiation therapy QA vendors. New company divisions would need to be created, software developed and maintained, as well as marketing efforts to promote their products. This would require a substantial resource investment that distracts the linac vendors away from their core businesses. In addition, daily linac QA is a "solved" problem; the existing QA vendors have robust and effective solutions. The expense of existing daily linac QA methods (device, software, and maintenance) is a minuscule part of the cost and maintenance of a linac. Therefore, while a handful of academic centers may employ EPID-based daily linac QA, it is decidedly *unlikely* that EPIDs will replace other methods within the next ten years.

Rebuttal: Sasa Mutic, Ph.D.

Addressing Professor Pawlicki's individual arguments/hypotheses:

"*…EPID measurements are highly derived quantities…EPIDs are complicated pieces of hardware…*"—Published data[2,3] and vast experience with EPID-based patient-specific-QA show that daily QA with EPIDs is practical and possible. The data show that these procedures can be automated and can also be used to test many more parameters than conventional methods. There is plenty of evidence that automation leads to greater efficiency and robustness.

"*…using an EPID for daily linac QA requires the fox to guard the henhouse…*"—Again, no evidence is offered to support this statement and that EPIDs are not independent QA devices or how their use could result in false QA.

"*…to provide EPID-based daily linac QA, the linac vendors would need to get into the QA market…*"—EPID-based daily QA will likely be offered by third-party companies. The automation of testing can be done through the treatment management system (Mosaiq, Aria, etc.) and images can be fully analyzed by third-party software. This paradigm already exists with EPID-based patient-specific-QA.

"*….daily linac QA is a solved problem…*"—History is full of examples where problems were solved with robust and effective solutions only to be upstaged with more effective and more robust solutions.

Finally, regarding what will happen in the next ten years, Bill Gates said "*We always overestimate the change that will occur in the next two years and underestimate the change that will occur in the next ten. Do not let yourself be lulled into inaction.*"[9] The question is not only what will happen with daily QA but rather which QAs (monthly, annual, commissioning, etc.) will be performed mainly with EPIDs within the next ten years, and I would further propose that most of linac QA tasks, including commissioning, will be performed with EPIDs.

Rebuttal: Todd Pawlicki, Ph.D.

While I agree with some of Dr. Mutic's points in his opening statement, they have not convinced me that EPID-based daily QA of linacs will likely replace other methods within the next ten years.

It is true that EPIDs provide a larger coverage area and higher resolution. However, modern day linacs are highly developed machines with sophisticated preventive maintenance schedules. Subtle performance degradation that would only be identified by a more comprehensive daily check of the linac (beyond current daily checks) is unlikely. Therefore, it is unclear how an EPID-based daily linac QA system would provide a higher degree of quality than what currently exists.

I agree that a commercial EPID-based daily linac QA solution *could* be available within the next ten years, but this does not mean that it *should* be adopted or that medical physicists would feel comfortable using such a solution. The perception that the EPID is not an independent dosimeter is supported by the fact that the EPID, associated control software, and maintenance are provided by the linac vendor. Conversely, the QA vendors provide a daily linac check that is independent of the linac vendor. With excellent existing daily linac QA solutions that are independent, is the increased level of integration afforded by an EPID-based solution worth the risk?

EPIDs do provide a larger degree of automation and daily linac QA may be completed faster than using existing solutions. But this would come at the expense of more work for medical physicists (or medical physics assistants). One should not underestimate the increased workload in having to develop, implement, and maintain a robust QA program for the EPID and associated components of an EPID-based daily linac QA solution.

While an intriguing proposition, it is unlikely that EPID-based daily linac QA will replace other methods within the next ten years.

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1.11. Within the next five years most radiotherapy treatment schedules will be designed using spatiotemporal optimization

Minsun Kim and David L. Craft
Reproduced from *Medical Physics* **43**, 2009–2012 (2016)
(http:// dx.doi.org /10.1118/1.4943383)

OVERVIEW

Currently, treatment plans are optimized for each patient's anatomy as far as the spatial configuration of beams is concerned, while the same fractionation employed for the course of therapy is that used for all patients who fall into the same category and is not optimized for each patient. Hence there is personalized spatial optimization for each patient, but not temporal optimization. It has been suggested that within the next five years, treatment schedules will be designed using both spatial and temporal optimizations. This is the claim debated in this month's Point/Counterpoint.

Arguing for the proposition is Minsun Kim, Ph.D. Dr. Kim earned her M.S. in Applied Physics and Applied Mathematics from Columbia University, and her Ph.D. in Applied Mathematics from the University of Washington (UW). She started her career as a medical physicist at Memorial Sloan Kettering Cancer Center and became board-certified through the ABR in 2006. She is currently an assistant professor and the associate director of the medical physics residency program in the Department of Radiation Oncology at UW. Her research interests include spatiotemporally optimal radiotherapy, multimodality (photons, protons, and neutrons) treatments, and optimal, time-dependent decision-making in cancer therapy (surgery, chemotherapy, and radiotherapy). She actively participates on the ABR Examination Committee.

Arguing against the proposition is David L. Craft, Ph.D. Dr. Craft earned his B.S. in Mechanical Engineering from Brown University and his Ph.D. in Operations Research from the Massachusetts Institute of Technology. He then became a postdoctoral fellow in the Department of Radiation Oncology, Massachusetts General Hospital, where he is currently an assistant professor. His research interests include developing multiobjective planning ideas for radiotherapy, treatment planning optimization, and implementation of biological modeling.

FOR THE PROPOSITION: Minsun Kim, Ph.D.

Opening Statement

The key to the success of radiotherapy is to deliver the right amount of radiation in the right place at the right time to maximize tumor damage while minimizing normal tissue toxicity. Spatial optimization of radiation dose by ever more sophisticated hardware and software has been of high interest in the last decades and has achieved success. Multileaf collimators, intensity-modulated radiotherapy (IMRT), and image-guided radiotherapy (IGRT) focus on delivering a radiation dose to the right location, i.e., a highly concentrated dose within the tumor,

reducing dose to nearby healthy tissues. However, the temporal distribution of radiation dose has been only crudely optimized, i.e., the total dose is delivered in a predetermined number of fractions while keeping the dose/fraction constant.

The widely implemented standard fractionation (1.8–2.0 Gy/fraction) exploits the difference in the repair capability between tumor and normal tissues based on empirical observation that normal tissues recover from radiation damage between fractions better than tumors.[1] However, hypofractionation, such as with stereotactic body radiotherapy (SBRT), has recently become more prevalent because normal tissues receive much less dose than tumors owing to the developments of IMRT and IGRT. Although studies indicate that the success of SBRT in clinical outcome is correlated to the larger biologically effective dose (BED) delivered to the tumor,[2,3] the nonstandard fractionation schedules used are still mostly empirical and limited to certain classes of tumor type and/or tumor size. It would take thousands of clinical trials to find optimal treatment schedules for all cancer types by a heuristic search.

The basic idea of fractionation schedule optimization (FSO) is to systematically derive the most effective fractionation schedule that maximizes tumor BED while keeping the organs-at-risk (OARs) BED constant.[4] The key factors determining an optimal fractionation schedule in this framework are the relative dose between tumors and OARs, as well as radiobiological parameters used for the BED calculations, which could vary significantly between patients. Fortunately, recent advances in mathematical modeling and functional imaging have enhanced our understanding of tumor dynamics.[5,6] Research, such as that of Swanson *et al*. that modeled individual glioma patient's tumor growth from two sequential MRIs,[5] shows that patient-specific, radiobiological parameters are no longer just theoretical. By incorporating tumor characteristics and calculated relative dose between tumor and OAR for each patient into FSO, it is possible to optimize fractionation schedules that lead to the maximum tumor BED for each patient.[7]

Radiation oncology, in line with the rest of medicine, is moving toward evidence-based, personalized therapy.[8] The ultimate goal of radiotherapy is to allow patients to have longer and healthier lives. It is time to utilize optimal treatment schedules using FSO to achieve the maximum tumor BED feasible for a given patient geometry and tumor characteristics. Delivering spatiotemporally optimal dose distributions, tailored to the individual patient's physical and biological condition, will improve clinical outcome for many tumor types and benefit a broad spectrum of patients.

AGAINST THE PROPOSITION: David L. Craft, Ph.D.

Opening Statement

In order for spatiotemporal optimization to become the norm for radiotherapy planning in five years, reliable models that map the treatment plan (dose distributions and the timing of delivery) to various measures of patient outcome (probabilities of various grades of organ damage, probability of tumor eradication) must exist. Ideally these models should be individualized to the patient rather than defined on a population level. We are unfortunately still far from having suitable models ready for clinical deployment. The most likely candidate for such a model is the linear-quadratic (LQ) model, which is the most widely used model to make fractionation

decisions in radiotherapy.[2,9] Although it is often defended as a mechanistic model, it originates from a study of the irradiation of plant pollen and so its biological basis is only partially relevant to humans.[10] Effects such as vascular damage and immunomodulation complicate the story, as well as the coadministration of targeted drugs.[11] Furthermore, the LQ model is based on a uniform dose hitting a target, but all radiotherapy plans see a nonuniform dose to various targets and organs, for which there is not a validated workaround. At best, the LQ model should be viewed as a second order approximation to a complex patient-specific input–output relationship. Even macroscopic fractionation decisions, such as whether to hypofractionate or not in a certain clinical setting, are not decided based on modeling: they are implemented after performing clinical trials (albeit which are often justified by LQ-based reasoning).[12] If spatiotemporal optimization is to become commonplace in radiotherapy schedule design, then quality predictive models must exist first.

There are two imaginable paths to reliable predictive models in radiotherapy: (1) deep systems-level biology models able to predict human cellular-, tissue-, and organism-level behavior and are informed by measurable patient characteristics or, (2) statistical/machine learning type models that model input–output relationships without detailed biology, but still involve patient biomarkers that are reasonable to obtain. In the near term, it appears that (2) is the more likely route. For that, large shared databases are needed due to the vast heterogeneities of humans and their cancers. Although some efforts have been initiated,[13] the majority of clinical data are not saved in any format amenable to analyses. Even in the best case scenario, where patient and treatment details and outcome data, including adverse effects, are stored and widely accessible for pooled analysis, the model-building will be very difficult. Predicting how a patient will respond to a given course of therapy is predicting how an extraordinarily complex system will respond to multiple input controls. While it is tempting to hope that the patient's genetic signature will be the key to unlocking the relationship between treatment and outcome, there is surely much more to the story (hypoxic tumor environment influencing response and number of tumor clonogens are but two examples).[14,15]

It is likely that spatiotemporal optimization can improve patient care, and the roadmap is clear: shared databases with biological analysis. I just think it will take us longer than five years to get there.

Rebuttal: Minsun Kim, Ph.D.

I agree with Dr. Craft's opening statement that "*In order for spatiotemporal optimization to become the norm for radiotherapy planning in five years, reliable models that map the treatment plan to…patient outcome…must exist*," and the exact models are not readily available at this time. Nonetheless, numerous studies have already reported that the tumor BED calculated from treatment plans is positively correlated with clinical outcomes such as median survival and local control for many different sites, modalities, and fractionation schedules.[1,16–19]

BED models currently available may well be "*at best a second order approximation to a complex patient-specific input–output relationship*." However, Dr. Craft also pointed out that "*macroscopic fractionation decisions…are implemented after performing clinical trials* (*albeit which are often justified by LQ-based reasoning*)." Waiting to find ideal radiobiological models

that are valid both microscopically and macroscopically before utilizing spatiotemporal optimization would be suboptimal for current cancer patients. A better option is to safely improve treatment efficacy using knowledge currently available to us. In fact, various fractionation schedules have already been tried empirically without systematic optimization procedures. SBRT for early stage, inoperable nonsmall cell lung cancer is a successful example. It should not be necessary to obtain the most accurate model to connect treatment plans to clinical outcomes before making efforts to improve the therapeutic ratio. Spatiotemporal optimization, which systematically optimizes a treatment schedule leading to the maximum tumor BED feasible for a given patient's physical and biological conditions, can also be used in designing clinical trials cost-effectively.

With newly available tools such as functional imaging and mathematical models to better estimate the patient-specific, radiobiological parameters used in the BED model, I believe spatiotemporal optimization will enhance current efforts to find more effective treatment schedules to improve patient outcome.

Rebuttal: David L. Craft, Ph.D.

There are currently 183 cancer drugs approved by the FDA, 18 of which were approved in 2015. In the 20th century when radiation therapy was emerging, the “key to the success of radiation therapy” was to optimize this single modality for the best therapeutic ratio. Before the days when we could assay patients and begin to capitalize on their specific biology, it made sense to use macroscopic models such as LQ/BED to guide fractionation decisions.

Today, the goal of the radiation therapy research community should be to figure out how to best combine radiation with drugs. Focusing on the question of fractionation schedule optimization alone is unlikely to result in large treatment gains. Swanson's model of GBM,[5] while capturing some dynamics, does not offer any biological insights into actually curing these patients. On the other hand, a detailed understanding of the active biochemical pathways (including DNA repair, proliferation, and apoptosis) should pave the way to increased curability.

Stated in another way: we can focus our efforts on maximizing BED, but if the maximum effect we can obtain through radiation alone is limited, we should look elsewhere. A wellspring of genomic cancer data is now available for free public usage[20] along with a host of tools to infer gene regulatory networks,[21] metabolic networks,[22] and general signaling networks,[23–25] from such data. Packaging these together to optimize clinical care is a formidable task, but it is the one we should embark on rather than attempting to squeeze as much as we can out of radiotherapy as a standalone treatment technique.

Spatiotemporal radiotherapy and drug optimization will be part of the future care of cancer patients. We should admit that this problem will require a dedicated effort to learn and incorporate the biological subtleties that make some treatments work and others fail.

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1.12. Within the next five years, adaptive hypofractionation will become the most common form of radiotherapy

Marco van Vulpen, Lu Wang
Reproduced from *Medical Physics* **43**, 3941–3944 (2016)
(http:// dx.doi.org /10.1118/1.4951735)

OVERVIEW

In the past few years, innovations such as on-board imaging have made it possible to adjust each radiation beam on a daily basis to account for any changes in anatomical positions of target and normal tissues. This “adaptive radiotherapy” has made it possible to reduce margins so as to decrease the risk of normal tissue damage, enabling safe and effective delivery of higher doses/fraction (hypofractionation). It has been proposed that such technological advances will allow adaptive hypofractionation to become the most common form of radiotherapy within the next five years. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Marco van Vulpen, M.D., Ph.D. Dr. van Vulpen obtained his M.D. from the University of Amsterdam and his Ph.D. from the University of Utrecht, both in the Netherlands. After graduation as a radiation oncologist, he completed a fellowship at the Cross Cancer Institute, Department of Radiation Oncology in Edmonton, Alberta, Canada, where he participated in the Image-Guided Adaptive Radiotherapy (IGART) program within the Center for Biological Imaging and Adaptive Radiotherapy and where he was appointed Full Professor in 2011. In 2013, he returned to The Netherlands to chair the Department of Radiotherapy at the University Medical Center, Utrecht, where he is currently Clinical Chair of the Center of Image Guided Oncological Interventions, where a 1.5 T MRI linear accelerator is being developed. He is the Clinical Chair of the International Consortium, ATLANTIC, on the worldwide clinical introduction of the MRI linear accelerator. He currently serves as Adjunct Professor in the Department of Radiotherapy at the University of Texas MD Anderson Cancer Center, Houston, TX. His major research interests include the development and clinical introduction of different adaptive MRI-guided oncological interventions. He has published over 130 papers in peer-reviewed journals.

Arguing against the Proposition is Lu Wang, Ph.D. Dr. Wang obtained her Ph.D. in Medical Physics from Rush University, Chicago, IL, and then completed a Postdoctoral Fellowship and Medical Physics Residency in the Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, NY. She subsequently moved to the Department of Radiation Oncology, School of Medicine, University of Pennsylvania, Philadelphia, PA as an Instructor and then moved to the Department of Radiation Oncology at Fox Chase Cancer Center, Philadelphia, where she is currently an Associate Professor and SRS/SBRT Program Leader. Dr. Wang has served on many AAPM committees and task groups including the Medical Physics Editorial Board, and, currently, is the Vice-Chair of the Work Group on Treatment Planning. She is a Fellow of the AAPM and is certified in Therapeutic Radiological Physics by the American Board of Radiology. Dr. Wang's major research interests include dose prescription and image guidance for hypofractionated radiotherapy treatments, and applications of cone-beam CT for SBRT.

FOR THE PROPOSITION: Marco van Vulpen, M.D., Ph.D.

Opening Statement

We are facing a paradigm shift in radiotherapy. In the last century, radiotherapy was predominantly used in conjunction with surgery to assure the killing of unremoved microscopic spread. For this purpose, moderate homogeneously distributed doses were administered with large and often rectangular fields. Since the beginning of this century, major technical developments have been introduced.[1] Treatment planning has evolved from x-ray based to MRI-based.[2] Delivery techniques have advanced from opposing beams to rotating beams, allowing dose sculpting with steep dose gradients.[1,2] The introduction of on-board imaging techniques, like cone-beam CT, brought major changes in radiotherapy practice, such as for the treatment of lung and prostate cancer and brain metastases. Extreme hypofractionation with an inhomogeneous dose seemed safe and feasible and was able to compete with surgery while providing organ preservation.[3] These technical changes have resulted in safer treatments and sometimes higher cure rates.[1,3]

Surgery itself seems to be shifting toward the "elimination of invasion."[4] In radiotherapy, this tendency is supported by several examples, the oldest being the preservation of the larynx in laryngeal cancer by (chemo-)radiation. Patients benefit hugely from preserving their ability to speak and reducing the risk of infections. This tendency extends to other solid tumors such as the preservation of rectal function, safely, by chemoradiation in rectal cancer.[5] Chemoradiation alone is likely to prevent low anterior resection syndrome, which occurs in the majority of surgery patients, and has a significant burden on quality of life.[6] This trend toward organ sparing and less surgery changes the use of radiotherapy and increases the demand for high precision and dose painting.

These different perspectives on fractionation rules and dose homogeneity led to other discussions, like whether ICRU reports 50, 62 and 83 are still appropriate, the validity of linear quadratic theory assumptions, clinical validity of radioresistance, along with the re-evaluation of radiotherapy indications,[7] retreatment rules, the use of the CTV-PTV concept, and even setting minimum or maximum dose limits.

These discussions lead to a paradigm shift in radiotherapy, moving from "elective" to an "ablative," more surgical-like, approach. Here, geometric precision goes beyond biological considerations. High dose needs to be confined to the tumor alone, demanding meticulous precision and a pure geometrical distinction between target and normal tissue.[1] In extreme hypofractionation, online intrafraction monitoring and correction of organ motion becomes a necessity.[1,3] New technologies have become commercially available, from real-time adaptive tumor tracking/trailing to intrafraction monitoring with triggering of the treatment sequence/beam.[1,2,8]

The advent of online soft tissue image guidance will greatly enhance these developments and will expand the ability to deliver high-precision hypofractionation to all body parts.[1,2] Image guidance feedback loops will allow for treatment optimization, treatment adaptation, response assessment, and retreatment, if necessary.[2] Currently, major studies are being conducted by

international multiplatform groups to prove benefit.[2,8] A variety of technical solutions with real-time adaptation[8] already seem to be significantly outperforming nonadaptive methods and therefore offer our patients the best possible treatments.

AGAINST THE PROPOSITION: Lu Wang, Ph.D.

Opening Statement

The choice of an appropriate fractionation schedule requires a clear understanding of the radiobiological principles that govern the tumor or normal tissue responses to radiation therapy, as well as the goals and expected outcomes for the individual patient. According to the well-accepted linear quadratic model of cell killing,[9,10] the dose response of a tumor or a normal tissue depends on its α/β ratio. For tumors, a low α/β ratio indicates low sensitivity to low doses of radiation, so a larger fraction size may offer a radiobiological advantage. Certain tumors such as breast and prostate adenocarcinomas, melanomas, and sarcomas often have low α/β ratios.[11–13] However, reducing the number of fractions may compromise vital process such as reoxygenation for hypoxic tumor cells, and this would diminish local control.[14] A high α/β ratio implies relatively high sensitivity to low doses of radiation. For tumors with a high α/β ratio surrounded by low α/β ratio tissues, delivering small ($\leq$2 Gy) daily dose fractions with a large number of treatments may be preferred in order to yield the highest therapeutic ratio while maintaining the same level of late effects.[10] Tumors of the head and neck (H&N), cervix, skin, and nonsmall cell lung cancers (NSCLCs) are often in this category. Although treatment of early stage NSCLC tumors with stereotactic body radiation therapy (SBRT) using extreme hypofractionation is currently routine,[15,16] the late effects are not a concern due to the quasiparallel structure of the surrounding lung tissue which results in a similar effective α/β as the tumor.[17]

Ultimately, optimal hypofractionated regimens should be designed by carefully analyzing clinical outcomes from hypofractionated trials; however, such clinical trials for certain types of cancers are either unavailable or on-going, and consistent outcome data are sparse. For example, there are no existing RTOG randomized hypofractionation trials for H&N cancers. Although a few institutional studies have demonstrated a slightly superior local control when comparing accelerated hypofractionation with conventional fractionation for early glottis carcinoma,[18–20] a higher incidence of late complications has also been associated with the higher fraction size.[21] Even for prostate radiotherapy treatment, to date there are no conclusive results that show hypofractionation to be more effective or safer than conventional fractionation in the treatment of localized prostate cancers (PCs).[22–24] Hypofractionation is considered to be an emerging approach that has not thus far been established for PCs. Moreover, hypofractionation has more of an impact on late-responding-tissues compared to early responding-tissues, and it takes longer to demonstrate those responses.

Since adaptive-hypofractionated radiotherapy reduces the number of treatments while increasing the demand for technical support compared with conventional radiotherapy, it requires increased man-power or shifting of the workload from therapists to dosimetrists or physicists, and increased physician involvement for approving contours. In addition, plan authorization and physician presence for initializing treatments are also required. All of these may require reimbursement changes in order to address the new demands. Also, the time requirement for

online or offline adaptive radiotherapy (ART) is so extensive that, with current technology, it is difficult to do ART for each patient on a routine basis.

Rebuttal: Marco van Vulpen, M.D., Ph.D.

The pace of innovation in interventional oncology is high, and the window of opportunity for evaluation narrow. Financial incentives, marketing hypes, industry pressure, and patients' demand for "high-tech" treatments have led to widespread implementation of innovations without robust clinical evidence of improved patient outcomes or time/cost savings.[25] Proton treatment and intensity modulated radiotherapy have been implemented widely without robust evidence of superiority over standard treatment.[26–28]

Ideally, before implementation, all innovations in radiation oncology would be evaluated in a systematic manner where, ultimately, one would test the new technology against the standard treatment and evaluate whether it can accomplish the task faster, cheaper, with less toxicity, better local control and survival. Implementation of the new technique would be justified if it would be time or cost saving, while clinical outcomes stay similar. Alternatively, implementation of more expensive or time-consuming techniques may be justified if these would lead to improved patient outcomes.

Until now, the traditional phase 1, 2, and 3 trial framework has been applied to evaluate safety and efficacy of new radiotherapy interventions. However, this may not be the most efficient and desirable framework in the radiotherapy setting[29–31] and will lack a timely value proposition.[32,33]

Radiotherapy innovations are complex interventions, the evaluation of which is complicated by team and operator dependence, learning curves, and differences in levels of experience and quality control. Recommendations for the assessment of innovations, based on a description of the surgical development process (IDEAL), may be used for this purpose.[34,35] Also, registry or cohort based evaluations are currently being introduced, as model based comparisons and new ways of randomized trials.[36–39]

We are facing a paradigm shift in radiotherapy. The move from elective to a more ablative radiotherapy strategy demands astute ways to perform proper evaluations. Within the next five years, adaptive hypofractionation will have become the most common form of radiotherapy. It is unstoppable.

Rebuttal: Lu Wang, Ph.D.

The significant advancements in radiotherapy technology, such as 3D imaging and treatment planning and computer-controlled intensity-modulated radiation dose delivery combined with sophisticated image-guidance technology, undoubtedly provide us with unprecedented geometric precision, and thus the ability to deliver higher doses to tumors without compromising normal-tissue toxicity. In addition, adaptive radiotherapy further improves dose conformality to the target while minimizing dose to the surrounding tissue by correcting for tumor/normal tissue variations during the course of treatment through online or offline modification of target and normal tissue volumes and treatment plans.

However, the moderate dose escalation afforded by these technological advancements is not the major factor contributing the paradigm shift mentioned by Dr. van Vulpen. As explained in my opening statement, it is the radiobiological factors that govern the choice of dose fractionation. Historically, we found that the 4Rs of radiobiology (repair, repopulation, redistribution, and reoxygenation) played an important role in radiation treatment outcomes. More recently, other biological factors concerning overall time and delayed proliferation after irradiation, the effect of dose per fraction, and the volume effect for late-reacting normal tissues have been understood. This increase in understanding of biological factors, as well as tumor radiobiology and histologies, has led to fractionation alterations in radiotherapy, including hypofractionation. Although clinical gains have been reported from the use of hypofractionated schedules, consistent and convincing outcome data are still sparse and take time to acquire. Specifically, hypofractionation has a greater impact on late-responding-tissues compared to early responding-tissues and it takes longer for these to become evident.

Certainly, since an increased fraction dose generally results in more effective cell-killing, hypofractionation should be a better approach for improving tumor control, but only for certain types and stages of cancers. However, to expect this paradigm to become the most common form of radiotherapy within the next five years is overly optimistic.

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1.13. The future of MRI in RT belongs to the integrated MR-EBRT system, not the standalone MR-Sim

Vladimir Feygelman and Frank Lohr
Reproduced from *Medical Physics* **44**, 791–794 (2017)
(http://dx.doi.org /10.1002/mp.12090)

OVERVIEW

The use of MRI in radiotherapy planning and simulation is increasing rapidly and is beginning to be integrated into the external beam radiation therapy (EBRT) treatment process. Some have suggested that integrated MRI-linac systems, not the standalone MRI-Sim, represents the future of MRI in radiotherapy, and this is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Vladimir Feygelman, Ph.D. Dr. Feygelman received his 5-year (M.S.-equivalent) degree in Laser Physics in 1982 and his Ph.D. in Physical Chemistry in 1985, both from the Rostov State University in the former USSR. Upon landing in the US, he discovered the profession of Medical Physics and, after on the job training, became ABR-certified in Therapeutic Radiological Physics in 1995. Since then, he has held both purely clinical and research-oriented positions and, currently, is an Associate Member faculty physicist at Moffitt Cancer Center in Tampa, FL, USA. He is a member of the team charged with evaluating and implementing new technologies for the Radiation Oncology Department. Dr. Feygelman's current research interests center primarily around quality assurance equipment and procedures for advanced treatments, and he has over 60 peer-reviewed publications. He serves on several AAPM committees and task groups, and is an Associate Editor of both *Medical Physics* and the *JACMP*.

Arguing against the Proposition is Frank Lohr, M.D. Dr. Lohr received his medical degree from Heidelberg University, Germany, followed by a residency in the Department of Radiation Oncology of Heidelberg University and the German Cancer Research Center, Heidelberg. During residency, he spent 2 years in radiobiological research on hyperthermia-induced gene therapy at Duke University, NC. Following his residency, he joined the team at the Department of Radiation Oncology at University Medical Center Mannheim, University of Heidelberg, as an attending physician, where he became the vice chairman in 2004 and the associate adjunct professor in 2005. Recently, he moved to his current position as the Director of Radiotherapy at the University Hospital, Modena, Italy. He is specially interested in precision radiotherapy techniques such as IMRT, VMAT (performed the second VMAT treatment in Germany), IGRT, and SBRT. His main clinical and research interests are lung, gastric, H&N, CNS and prostate cancers, interdisciplinary optimization of surgery, systemic therapy (particularly immunotherapy), and radiotherapy, as well as the optimization of local radiotherapy based on optimal integration of imaging modalities such as MRI (e.g., iron oxide nanoparticles) and PET. Dr. Lohr has contributed to more than 130 peer-reviewed scientific articles, textbook chapters and textbooks, and is co-editor of a German standard radiotherapy textbook.

For the proposition: Vladimir Feygelman, Ph.D.

Opening Statement

There is no argument about the increasingly important role of MRI in radiation oncology.[1-3] We disagree only on what is the best approach to even tighter integration of MRI into the radiotherapy process.

In order to argue that the integrated MR-guided radiation therapy (IMGRT) system is, on balance, the optimal solution, all one has to do is to compare suitability and necessity of IMGRT *vs.* MR-Simulator (MRS) for the following list of tasks pertinent to radiation oncology.

1. *The interrelated processes of initial target delineation, tissue segmentation, simulation, and planning*. Neither IMGRT nor MRS is truly needed. The concept of MR-only simulation was introduced over a decade ago.[4] However, the publication list since then is much more persuasive in terms of *technical feasibility* of the approach, rather than the measurable *benefits*. Over the last 10 years, deformable image registration algorithms have gained greatly in quality, availability, and acceptance. Diagnostic MRI scans are easily and routinely incorporated in the treatment planning process through registration with the planning CT. Interestingly, the Utrecht group, which has a great deal of experience in, and knowledge of, MRI, still chose to use CT to define the geometry for treatment planning and fuse MR images to it.[1]
2. *Patient positioning*. IMGRT is suitable for the task while the MRS is not. An intermediate solution, in-room MR on rails registered to the treatment isocenter,[5] is theoretically usable but cumbersome, particularly for repeated intrafraction imaging.
3. *Adaptive re-planning*. An integrated system is clearly advantageous, allowing for both offline and online geometrically adaptive re-planning, including the "dose of the day" re-optimization and treatment to the isotoxicity of organs-at-risk (OARs). Only offline re-planning is possible with the typical stationary MRS.
4. *Motion management*. IMGRT, and IMGRT only, is capable of directly tracking/gating the target and surrounding tissues in real time, anywhere in the body, with MRI-quality contrast and no external surrogates, invasive fiducials, or ionizing radiation.
5. *Functional imaging biomarkers*. While the long-standing, but yet to be fulfilled, promise of using functional MR imaging to individualize radiation therapy is great, so are the challenges,[6] one of the most insidious being reproducibility.[7] Whether reliable and practical functional MRI biomarkers are ever found (and that is, statistically speaking, not an easy feat[8]), both systems have advantages and disadvantages for discovering and exploiting them. Potentially better image quality and more sophisticated scanning protocols in MRS may or may not balance out the value of high frequency (daily) IMGRT scans.

To summarize, in every conceivable clinical or research category, IMGRT capabilities are either superior to, or on par with the MRS. Right now and in the foreseeable future, it is an ultimate SBRT tool, "*making radiotherapy more of an interventional radiology process*", as was elegantly stated by Lagendijk et al.[1] IMGRT combines immediately available, neatly integrated motion management and daily dose adaptation capabilities with future research

experience in functional imaging, which is way more than can be plausibly speculated about the MRS standalone system.

Against the proposition: Frank Lohr, M.D.

Opening statement

There is no doubt that the ideal situation for radiotherapy would be a treatment under more or less static conditions in an ideal dosimetric situation with permanent online image-based control of the position of tumor, OARs, and patient surface. Online MR-guidance is therefore an appealing concept and it has already been applied to brachytherapy.[9] However, to provide clinical results beyond what current image guidance strategies in external beam radiotherapy can achieve, several requirements must be fulfilled on the way, and the allocation of a large amount of resources has to be justified.

We have already come very close to the objective of treating a quasi-static geometric situation if advanced image guidance strategies already available at moderate cost are fully used. Several such strategies are now available but are underutilized, typically for lack of funding or perceived complexity. Recent developments, such as flattening-filter-free (FFF)-delivery and fast collimators have, however, dramatically shortened treatment time and thus rendered advanced imaging strategies more feasible. Considerable expertise is needed, as it is also for MR-guidance. Continuous 2D-tracking based on fiducials placed by minimally invasive procedures has entered the clinical routine for the ablation of small lesions without complex interference of OARs and achieved precision is near-perfect.[10]

3D-imaging with CBCT, particularly in conjunction with breath-hold strategies,[11] still has considerable potential. Accuracies in the range of 3 mm can be consistently achieved across treatment targets using deep inspiration breath-hold, resulting in favorable dose distributions and straightforward dose accumulation. 4D-approaches are available, and ultrafast “snapshot” volume imaging is ready to be deployed clinically.[12] Ultrasound, where applicable, allows not only for positioning but also for tracking in 2D and 3D.[13] Surface scanning as a complementary positioning and gating tool not using ionizing radiation may simultaneously provide patient surveillance and gating signals during a therapy session, further improving overall precision of a treatment.[14]

The integration of functional MR-data into the treatment process is desirable, but the possibilities at the currently available field strengths in integrated machines are limited. Another aspect is that non-coplanar treatment strategies have recently gained renewed interest outside the cranial area[15] and high-LET radiation, too, may have further potential to improve clinical results independent of imaging strategy. Both strategies are currently not feasible in conjunction with in-room MR-guidance. Finally, local control of small, mobile lesions is already excellent. For larger lesions, overcoming integral dose limits using particle strategies may be more important than minimally further improving geometric precision.

In conclusion, if online MR-guidance is necessary, then there is a general necessity for broad use of advanced image guidance strategies, particularly as successful screening programs such as

those for lung cancer and, potentially, even pancreatic cancer, are established, as this potentially leads to more localized disease being treated. These opportunities should be exploited immediately with available technology while, in parallel, online MR-guidance is scientifically developed to provide added value in applications such as intratumoral dose painting, conformal treatment of individual lymph nodes identified as positive by novel markers, or other situations not yet identified that go beyond just providing geographic precision.

Rebuttal: Vladimir Feygelman, Ph.D.

My distinguished opponent has chosen to shift the debate away from the relative merits of IMGRT vs. MRS. It is understandable, given the paucity of reported clinical accomplishments of MRS in the last 15 years. Instead, the strategy of the opposing Opening Statement is to enumerate different existing IGRT approaches, with the aim of convincing the reader that IMGRT is an unnecessary luxury. In reality, each one of those techniques comes with a sizable disclaimer. Some only work for certain disease sites. Others require implanted fiducials or rely on external surrogates, and/or provide no information beyond (hopefully) tumor location. My opponent and his co-authors seem to advocate that breath-hold is the ultimate answer to the problem of motion in radiotherapy and are willing to resort to extraordinary measures to induce prolonged breath-holds beyond normal physiology.[16] However, in the same breath the authors "*emphasize the urgent need for more research on the position changes of both tumors and healthy tissue throughout breath-holding*." This in itself contradicts my opponent's main postulate that the current image guidance strategies have already achieved the saturation point of clinical impact. To further dispel that assertion, early reports from the clinical IMGRT sites, admittedly anecdotal so far, indicate that there may be a subgroup of patients, previously considered untreatable, that can now be offered beneficial radiotherapy.

Unlike the other IGRT techniques, IMGRT is universally applicable to any disease site and provides direct visualization, with best image quality currently available, of the tumor and surrounding OARs, for both adaptive re-planning and real-time motion management. While the cost of an MR-guided system currently is roughly double that of the nicely equipped accelerator, once one adds up the costs of separate IGRT systems best suited for every clinical situation, the cost gap narrows appreciably, yet without matching the image quality and seamless workflow of IMGRT.

Rebuttal: Frank Lohr, M.D.

There is no doubt that online MR-guidance will further simplify current IGRT workflows, and this may already be a value in itself, as was the transition from 2D to 3D X-ray based imaging that has made precision treatments easier than before. If the clinical advent of MR-guidance raises the awareness that 3D imaging should be used in most instances, this would be another positive, as the need for CBCT and advanced motion management is still not commonly agreed upon within the community. The systems being placed now should be systematically used to clarify issues that are open, some of which were also highlighted by my opponent:

1. To what extent is there an added value (useful functional imaging) of MR over pure geometric accuracy at relatively low field strengths?

2. Can functional data from higher field strengths be easier/better integrated into the daily image datasets when MR-base datasets are matched?
3. What are the relative merits of tracking in different clinical situations (with potentially suboptimal cumulative dose distributions in OARs for larger targets) vs. inspiration breath-hold gating (with potentially better dosimetric characteristics and easier dose cumulation)?
4. Do adaptive strategies really have merit in H&N and lung cancer, where conclusive data is still elusive?
5. And, finally, can the concept of online MR-guidance be transferred to particle therapy, where dose distributions depend more on anatomical geometry than for photon therapy and the case for online MR-guidance is therefore stronger?

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1.14. Within the next five years, deep learning will play a significant role in radiotherapy and imaging Implanted fiducial markers are no longer needed for prostate cancer radiotherapy

Ge Wang and Mannudeep Kalra
Reproduced from *Medical Physics* **44**, 2041–2044 (2017)
(http:// dx.doi.org /10.1002/mp.12204)

OVERVIEW

With impressive progress in machine learning, there has been increasingly more interest in its relevance to medical physics, which involves both medical imaging and radiation treatment planning. However, because it is still generally unclear how to identify unique niches, utilize big data, and optimize neural networks, machine learning is yet to have a major impact on medical physics practice. Nevertheless, there are optimistic opinions that machine learning will have a major impact on medical physics and radiology within the next 5 years. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Ge Wang, Ph.D. Dr. Wang received his Ph.D. in Electrical & Computer Engineering from the University at Buffalo in 1992. Upon graduation, he assumed a junior faculty position at the Mallinckrodt Institute of Radiology, Washington University School of Medicine. In 1997, he joined the University of Iowa as Associate Professor, then in 2006 Virginia Tech as Pritchard Professor, and in 2013 he moved to his current position as Clark & Crossan Endowed Chair Professor at the Rensselaer Polytechnic Institute, where he leads the Biomedical Imaging Center. He has made original contributions to spiral/helical cone-beam/multislice CT, bioluminescence tomography, interior tomography, energy-sensitive CT, and multimodality fusion, and has authored or co-authored over 400 peer-reviewed journal papers. Dr. Wang is a member of the *Medical Physics* Board of Associate Editors and is a Fellow of the AAPM, AIMBE, OSA, SPIE, IEEE, and AAAS.

Arguing against the Proposition is Mannudeep Kalra, M.D. Dr. Kalra completed his diagnostic radiology residency in India in 1999. He subsequently became a research fellow at the Massachusetts General Hospital (MGH) and then at Emory University Hospital. In 2005, he started a clinical fellowship in the thoracic and cardiac imaging sections and then joined as an attending radiologist at MGH. He has authored or co-authored over 300 peer-reviewed journal articles and book chapters. He has co-edited five textbooks and special journal issues in radiology. Currently, he is Associate Professor of Radiology with the Harvard Medical School and Director of the Webster Center for Quality and Safety. His interests include imaging technology assessment, radiation dose optimization, and deep learning applications in radiology.

For the proposition: Ge Wang, Ph.D.

Opening statement

I view machine learning as a truly disruptive technology, or more accurately a *paradigm shift*,[1] and believe that it has *transformative* potential in the medical physics field, valid for both medical imaging and treatment planning. Clearly, the interest in machine learning seems much greater than that in compressed sensing, as evidenced by my quick PubMed search for the title to contain "*machine learning*" and "*compressed sensing*", respectively. The number of hits for "*machine learning*" has increased from 151 to 450 over the past 5 years, while the number for "*compressed sensing*" has only gone from 84 to 102. Given the successes of machine learning in other areas, I have little doubt that machine intelligence will reshape medical physics, and more generally radiology, and we should immediately make major efforts toward this direction.

Intelligence is essentially the capability to extract knowledge that allows comprehension and prediction, which can be in most cases performed *computationally*. When data are becoming diversified and explosive in either medical imaging or radiotherapy, the classic methods cannot model and utilize huge data effectively and efficiently. It seems that big data and deep learning promise numerous opportunities for medical physicists. Instead of trying to enumerating all the possibilities, without loss of generality, let me discuss this *transformative* approach as related to two *transforms*: the Radon transform (from an underlying image to its projections) and radiation treatment planning (from a source distribution to therapeutic beam profiles).

This year is for the first centenary celebration of the Radon transform, which is fundamental to not only CT but also other tomographic modalities. In practice, Radon data are never ideal; for example, in x-ray imaging, projections are compromised by source spot size, beam hardening, detector imperfection, geometric mismatch, patient motion, metal artifacts, photon fluctuations, and other factors. Over the past decades, excellent analytic and iterative reconstruction methods have been developed. However, the assumed data model is only approximate and compromises image quality; for example, it is challenging to convert photon-counting data into linear integrals, especially when radiation dose is low. In this aspect, image quality can be potentially improved via a deep neural network. This is to perform the Radon transform via machine learning, a freshly new way to recharge the existing reconstruction algorithms for more quantitative results.

The optimization of a therapeutic plan needs to ensure tumor killing while sparing healthy/sensitive tissues for the best prognosis.[2-7] In this context, there is a critical need for a high-quality predictive model which integrates a huge amount of heterogeneous data via machine learning,[8, 9] including electronic health records, tomographic and therapeutic images, and genomic profiles. Tomographic images can be improved via machine learning to reduce metal artifacts,[10] estimate an attenuation background,[11] target tumors,[12] and so on. Hence, the potential of machine learning ought to be significant for radiotherapy. We expect that the ultimate therapeutic system will be able to reconstruct images and design plans with high confidence, and keep learning from huge, distributed, and living data sources.

Against the proposition: Mannudeep Kalra, M.D.

Opening statement

If a big company's AI makes a mistake, it might get sued for a billion-dollars! A skeptical radiologist might opine that malpractice is the most important issue with artificial intelligence (AI) replacing him over the next few years. This concern is accentuated by unexpected and undetectable behavior of "*black box*" deep learning techniques in a multidimensional feature space. Errors with AI can result when confounding factors are correlated with pathologic entities in the training datasets rather than true signs of diseases. In fact, applications so far have been limited to low level, narrow task-specific pursuits such as detection of pulmonary nodules, rather than the spectra of abnormalities found in the real clinical environment with unbound, unstructured inputs from multiple scanners, entities, and institutions. This might take more than a few years to validate and then gain acceptance. Yet, patients tend to trust the decisions of physicians but question the diagnoses made by a machine.[13]

Doubts have been raised on aspirations of AI to unseat human radiologists.[14, 15] If neural networks have high generalization performance, why should adversarial negatives of regular examples confound them?[15] While human vision could not delineate subtle changes engineered in test images, blind spots in neural networks led to several misclassifications including a dog labeled as an ostrich!

Deep neural networks expressed 99% overconfidence for classifying unrecognizable images such as labeling of a red crayon as a syringe.[14] "*Fooling*" of these networks raises questions about their true generalization capabilities in face of tremendous biological and physical variations in patients and imaging modalities. Dr. Bryan observed that variations between intersite and multivendor measurements limited AI applications for cerebral blood flow imaging techniques in Alzheimer Disease.[16] Such variations can be robustly normalized in human vision but need considerable advances in deep learning to avoid dangers from underappreciated and underrepresented statistical errors.

Alternative use of large, nonhomogeneous data with flexible learning algorithms is challenged by the general lack of annotated imaging data for training. Manual segmentation is severely limited by human resources and inability to demarcate diffuse or heterogeneous abnormalities. Multiple instance learning can overcome certain aspects of weakly labeled image database[17, 18] but still requires standardized labels of specific diagnoses, which are often not available. Natural language processing to parse radiology reports requires a full syntactic parser trained on radiology reports. This is immature, partially due to lack of integration between radiology findings and clinical, pathology and laboratory results from claims and electronic medical records databases.[19, 20]

Other challenges include the cost of producing labeled datasets not confined to single diagnostic entities and that of time-consuming, intensive computation requiring in depth know-how of graphics processing units, and systematic rigorous cross-validation for clinical acceptance of machine learning. Radiology extends beyond medical physics to interpretation of radiology findings and correlation with clinical context. AI can help medical physics but its ability to replace radiologists in the context of interpretation of radiology findings and correlation with clinical and laboratory findings is unlikely within the next 5 years.

Rebuttal: Ge Wang, Ph.D.

I agree with most of what my opponent has said. In principle, all the challenges can be met over time, but how soon will machine learning plays a significant role in hospitals and clinics? I would imagine that it could be as soon as within the next 5 years. This view is based on my resonance to the prophecy that the singularity of artificial intelligence is near.[21] Many of us share a feeling that the scientific advancement is at an accelerated rate due to the combinatory effect of knowledge and tools, as demonstrated by the data fitting into the Moore's law as well as the surge of machine learning and high-performance computing (including quantum computing) research. Now, machine intelligence has competed with, or already outperformed, humans in a number of tasks, such as chess playing, image classification, and speech recognition. Hence, the efforts along this direction are well justified in medical imaging, therapeutic planning, and beyond.

Two examples are supportive of my optimism. The first is the software *Master* (an upgrade of *AlphaGo*) that recently defeated the world's best Go players in several dozen games in a row. Not long ago, when *AlphaGo* won over Lee Sedol 4-1, Ke Jie watched and claimed that "*it can't beat me*." Recently, however, Ke lost three games to *Master*. The team *DeepMind* behind *Master* is actively working on machine learning methods for other applications, including healthcare, and so are many other teams including ours. In January, 2017, Nature reported that a machine learning algorithm developed at Stanford performed on par with 21 board-certified dermatologists in the diagnosis of skin cancer.[22] Their single neural network, which was trained on a dataset of 129,450 clinical images consisting of 2032 different diseases, clearly showed potential for highly variable tasks across many fine-grained object categories. They pointed out that "*Outfitted with deep neural networks, mobile devices can potentially extend the reach of dermatologists outside of the clinic*." I feel confident that machine learning would impact radiology similarly and quite soon.

Rebuttal: Mannudeep Kalra, M.D.

Dr. Wang makes several claims in favor of machine learning. Without being a procrastinator, I cite the following contrary arguments. First, the opinion in Forbes on accidents involving self-driving cars raised the probability of carmakers getting sued for hefty fines.[23] Such libels will stifle progress, and our legal system is underprepared for a fully autonomous AI driver or a machine radiologist in the current context. While car accident lawsuits are the most common type of personal injury claims, medical malpractice suits are among the most complex ones!

Second, the FDA approved computer-aided diagnosis (CAD) for mammography in 1998 based on its comparable performance with, or outperformance of, human observers. Over the past two decades, CAD programs remain relegated to being a second reader without any exception in clinical radiology practices around the world! Are these not the very same programs that AI hopes to improvise based on training data labeled by human observers?

Third, applications of AI in the physics domain (such as image reconstruction and equipment calibration) might be ripe opportunities but, in clinical practice, AI will face challenges to experts at work on creating the most intelligent deep learning algorithms. Such nontrivial challenges stem from the lack of decent theories and labeled datasets, and validation of AI algorithms against dissenting human radiologists and its acceptance among radiologists, ordering

physicians, and the patients. Like existing CAD programs, AI algorithms should also undergo a prolonged phase of enquiry and verification in clinical practice, a task without trims or short cuts. As a second reader, AI will learn from humans while helping them in return to take better care of their patients.

Finally, AI fares pretty well on "low hanging" targets of sharply defined skin cancers in colorful 2D photographs[22] but will face challenges from 3D gray scale, fuzzy radiology images where lesions are often subtle or diffuse, differentials are wider, and artifacts masquerade.

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1.15. Implanted fiducial markers are no longer needed for prostate cancer radiotherapy

Christopher F. Njeh and Brent C. Parker
Reproduced from *Medical Physics* **44**, 6113–6116 (2017)
(http:// dx.doi.org /10.1002/mp.12633)

OVERVIEW

For many decades, it has been common practice to implant fiducial markers within the prostate of patients undergoing radiotherapy in order to enhance the visualization of the target before, during, and after treatment. Some argue that, with the widespread use of cone-beam CT, prostate visualization without the use of fiducial markers is now possible, and such markers are no longer needed. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Christopher F. Njeh, Ph.D. Dr. Njeh is a graduate of Birmingham University, Aberdeen University, and Sheffield Hallam University, UK. He started his professional career at the Addenbrooke's Hospital in Cambridge and Queen Elizabeth's Hospital, Birmingham, UK. He later joined the Department of Radiology at the University of California, San Francisco as a Visiting Postdoctoral Fellow, where he was subsequently appointed as Assistant Professor. Dr. Njeh transitioned to therapeutic medical physics by completing a medical physics residency at Johns Hopkins University, Baltimore. He has since served as Chief Medical Physicist at Texas Oncology in Tyler, TX and held adjunct faculty positions at the University of Texas at Tyler, and California State University Fresno. He is currently Chief Medical Physicist and Radiation Safety Officer at Franciscan Health, Indianapolis, Indiana. Dr. Njeh is certified in Therapeutic Radiologic Physics by the ABR. His major research interests include osteoporosis, image-guided radiation therapy, and accelerated partial breast irradiation. He is author or co-author of over 65 peer reviewed journal articles and 10 book chapters, and is co-editor of two books. He is an Associate Editor of the British Journal of Radiology, a member of the ASTRO Education Committee, and a Fellow of the AAPM.

Arguing against the Proposition is Brent C. Parker, Ph.D. Dr. Parker earned his M.S. and Ph.D. degrees in Medical Physics at the University of Texas-Houston Health Science Center Graduate School of Biomedical Sciences, Houston, Texas while he was working as a Graduate Research Assistant in the M.D. Anderson Cancer Center, Houston. He subsequently worked as Medical Physicist at The University of Texas Medical Branch, Galveston, TX from 2004–2007 and the Mary Bird Perkins Cancer Center, Baton Rouge, LA from 2007–2011, after which he returned to The University of Texas Medical Branch, Galveston, where he is currently Director, Division of Physics and Engineering, and Associate Professor in the Department of Radiation Oncology. Dr. Parker is certified in Therapeutic Radiologic Physics by the ABR and has served as the President of the AAPM Southwest Chapter. His major research interests include stereotactic radiosurgery,

and radiotherapy treatment planning, delivery and quality assurance, on which he has published over 20 papers in refereed journals.

For the proposition: Christopher F. Njeh, Ph.D.

Opening Statement

Prostate cancer is a significant health problem being the most common cancer among men in the US, with an estimated 1,80,890 newly diagnosed cases in 2016.[1] Radiotherapy is a treatment option for localized prostate cancer.[2] The effectiveness of radiotherapy depends on the delivery of a high dose of radiation to the tumor while limiting collateral damage to surrounding structures. In today's era of conformal radiation therapy dose escalation is possible; however, there is a need for higher geometric accuracy than when using the earlier approach. Geometric accuracy can be improved by imaging the target during treatment. Broadly speaking, this approach is called image-guided radiation therapy (IGRT). There are various IGRT techniques available for prostate radiotherapy.[3] Fiducial markers (FMs) were initially introduced for use with electronic portal imaging (EPI) as the prostate is not easily visualized on portal images. The clinical utility of FM in prostate cancer radiotherapy is well established.[4] However, FMs have some shortcomings which include:

1. Implantation of FMs into the prostate is an invasive surgical procedure which carries associated risks including pain, rectal bleeding, hematuria, prostate inflammation, and urinary infection. Loh et al.[5] reported that 2.8% of patients required hospital admissions due to infective complications following the FM procedure. Because of the associated risks some patients are unwilling to undergo this invasive procedure.
2. Not all patients are candidates for FMs. FMs are contraindicated for patients with coagulopathies, prothrombin time/partial thromboplastin time greater than 1.5 times normal, and patients with platelet counts of less than 50,000.[3]
3. The efficacy of FMs is based on the assumption that each marker will remain fixed in position between simulation and the duration of the treatment. There is potential for seed migration, albeit small.[6, 7]
4. Edema and inflammatory responses resulting from implantation may be present during treatment planning. These may then resolve before or during treatment resulting in volume changes or deformation. This could potentially alter the position of the FMs and introduce systematic positioning errors.[7]
5. FMs, depending on their composition, have the potential to cause significant dose perturbation in the planned dose distribution.[8, 9] Using Monte Carlo simulation, Vassiliev et al.[8] found up to 58% dose increase and 47% dose decrease at the entrance and exit surface of FMs, respectively.
6. There are extra costs associated with FM implantation. FM implantation requires gold seeds, needle placement, and transrectal ultrasound, for a total estimated cost according to Das et al.[3] of approximately $335.
7. Lastly, FMs act only as a surrogate of prostate position and do not provide information on deformation of the prostate, localization of the seminal vesicles, or changes in the surrounding normal tissues.

Considering these drawbacks of FMs, kilovoltage cone-beam CT (CBCT) without FMs may provide a better alternative. One advantage of CBCT includes good quality soft tissue image resolution compared to EPI. Studies have shown that CBCT provides localization accuracy comparable to that with FMs.[10] CBCT also provides better visualization than EPI of the prostate, seminal vesicles, and the adjacent structures at the time of treatment. Given the low risk of alternative techniques, there are no reasons why FMs are still needed for prostate IGRT.

Against the proposition: Brent C. Parker, Ph.D.

Opening Statement

One definition of fiducial is "taken as a standard of reference".[11] In radiation oncology, implanted prostatic fiducials are frequently used as the standard for target position during patient setup. With 2D orthogonal imaging used for patient positioning, fiducials allowed for 3D position corrections. With the advent of cone-beam computed tomography (CBCT), however, 3D volumetric imaging information could be directly used in patient positioning. This may lead one to conclude that fiducials are no longer needed in prostate radiotherapy. Indeed, studies have shown that the use of implanted fiducials imaged with orthogonal planar imaging is not superior to CBCT for patient positioning.[12] Thus, there is intrinsically no "need" for fiducials in the traditional use of initial patient positioning. The flip side to that position, though, is that neither is CBCT superior to fiducials. In that situation, the decision becomes a matter of other issues.

Instead, I argue that the "need" for fiducials depends on how the prostate is to be treated and how the fiducials are to be used after the initial patient setup. While CBCT may negate the need for the use of fiducials in initial target positioning, it does not address intrafraction prostate displacement. This intrafraction motion can be determined by imaging of radiopaque fiducials or acquisition of data from transponder fiducials. For target tracking, implanted transponder fiducials (e.g., Calypso, Varian Medical Systems) allow for continuous, real-time tracking of intrafraction prostate displacement without the need to interrupt treatment for volumetric imaging.[13] X-ray IGRT systems can allow for imaging of radiopaque fiducials during treatment delivery to evaluate prostate displacement as a function of time.[14] Studies have shown that beacon and radiographic fiducials provide comparably accurate intrafraction prostate motion measurements.[15]

While intrafraction motion is typically small, it can be clinically significant at times, leading to treatment deliveries that do not meet clinical goals depending on the specifics of the treatment plan (e.g., margin size).[16, 17] Additionally, we may expect these displacements to increase in magnitude with an increase of the overall fraction delivery time.[17] In these cases, prostate position will need to be corrected back to its nominal position or larger margins will be required to ensure adequate target coverage. However, larger margins will lead to increased normal tissue doses and possible increases in complications. With the increasing popularity of hypofractionated prostate radiotherapy, the ability to reduce margins while ensuring adequate target coverage becomes even more important.[18] This will require accurate real-time measurement of intrafraction prostate displacement using fiducials to determine if treatment intervention is required.

In conclusion, while prostate fiducials are not needed for initial patient setup, they will play an important role in the evolution of adaptive and hypofractionated radiation therapy of the prostate.

Rebuttal: Christopher F. Njeh, Ph.D.

I agree with Dr. Parker that FMs are not superior to noninvasive techniques such as CBCT in the initial setup alignment of prostate patients.[12] Dr. Parker went further to present an argument for an alternative role for FMs whereby they are used to monitor prostate intrafraction motion. However, the data do not justify this. For example, studies have found that intrafraction motion only becomes clinically significant for long duration treatments.[19-21] Langen et al.[21] reported that, from the initial setup, only 13% of patients have displacements above 3 mm by 5 min, rising to 25% by 10 min. Furthermore, such movements are accounted for in the treatment planning margins.

Dr. Parker implied that intrafraction monitoring is critical for hypofractionated regimens because of increased fraction time and the need for reduce treatment margins. The increased fraction time is true with CyberKnife, where prostate treatments typically take up to 45 min per fraction.[22] With the implementation of volumetric modulated arc therapy (VMAT) on traditional linacs; however, the treatment time for prostate cancer has significantly decreased to a mean of 4.6 min.[20] In addition, with flattening filter-free (FFF) treatment delivery with dose rates up to 2400 MU/min, it possible to deliver hypofractionated doses within a few minutes.[23, 24] Hence, there is not enough time for clinically significant prostate motion.[24]

Dr. Parker also indicated that intrafraction motion, if not corrected, will necessitate higher treatment margins. However, the greatest contributors to prostate treatment margins are systematic errors such as target delineation, not random errors such as intrafraction motion.[25] Studies have also cautioned against excessive margin reduction around CTVs when using IGRT.[26]

It is therefore logical to conclude that for prostate cancer radiotherapy, FMs are no longer required.

Rebuttal: Brent C. Parker, Ph.D.

My colleague has made a number of arguments against the use of fiducial markers, and I will address them sequentially.

1. *Surgical risks*: The results of Loh et al.[5] were based on retrospective self-reported data from patients. It is possible that the results are biased based on the demographics of the responding patients. Moman et al.[27] reported a urosepsis rate of only 0.2% in 914 patients with either transrectal or transperineal implantation of fiducials.
2. *Not all patients are candidates*: While there may be a subset of patients who are not candidates for FMs, this does not address the efficacy of FMs in patient setup. FMs still provide intrafraction target motion information not readily available with CBCT.
3. *Seed migration*: Kumar et al.[28] demonstrated an average FM migration < 1 mm. Their results indicated that a margin of 1–3 mm would account for the vast majority of

variations in seed position. Additionally, a large migration of a single seed would be readily apparent in imaging review and that seed could be eliminated from consideration in the image guidance process.

4. *Errors due to edema*: Kumar et al.[28] demonstrated that prostate volume showed an average change of 1.4% between FM implant day and 1 week after FM placement. Waiting 1 week after FM placement to simulate the patient would minimize any effects due to edema or inflammation.
5. *Dose perturbation*: Vassiliev et al.[8] showed that the dose perturbation effects are an issue in fiducials made of high Z materials such as gold with essentially no dose perturbation from carbon fiducials. Therefore, dosimetric issues are a consequence of the selection of fiducial material, and not an inherent limitation of the use of fiducials in general.
6. *Extra costs*: Data show that Medicare reimbursement for a course of prostate IMRT is approximately $30,000.[29] Given that the submitted charges are even higher than the reimbursement amount, FM placement is not a significant component (1.1%) of the overall cost of treatment.
7. *Missing information*: Beyond the initial setup imaging, CBCT does not provide this information either without interrupting treatment. As I presented in my opening statement, however, FMs allow for intrafraction monitoring of prostate motion and deformation to determine if intervention is required.

While I agree that FMs are not necessary for initial prostate positioning, they can provide essentially real-time intrafraction displacement data. This may allow for smaller margins and potentially reduced normal issue complications.

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CHAPTER 2

Highly Conformal Radiotherapy: IMRT, Tomotherapy, Stereotactic Radiosurgery, Proton Therapy

2.1. TG-142 is unwarranted for IGRT QA

Scott Dube and Jennifer O'Daniel
Reproduced from *Medical Physics* **41**, 101601-1-3 (2013)
(http:// dx.doi.org /10.1118/1.4766437)

OVERVIEW

The AAPM Task Group Report 142 is a comprehensive document dealing with quality assurance for medical accelerators.[1] Recommendations in this report are being used to prescribe the types of tests and their frequency for image-guided radiation therapy (IGRT) but some believe that these are overly onerous and, hence, unwarranted for IGRT. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Scott Dube, M.S. Mr. Dube received his M.S. degree in Radiological Sciences from the University of Colorado in 1979. Subsequently, he worked for Rocky Mountain Medical Physics, Mid-Pacific Medical Physics, Northwest Medical Physics Center, The Queen's Medical Center in Honolulu, and Queen of the Valley Medical Center in Napa, CA. Mr. Dube is certified by the American Board of Radiology in Diagnostic Radiologic Physics, Medical Nuclear Physics, and Therapeutic Radiologic Physics. In the AAPM, he has served as a member of the Clinical Practice and Professional and Public Relations Committees, and the Joint Medical Physics Licensure Subcommittee. He served as President of the San Francisco Bay Chapter for 2011/2012.

Arguing against the Proposition is Jennifer O'Daniel, Ph.D. Dr. O'Daniel obtained her M.S. and Ph.D. degrees from the University of Texas at Houston Graduate School of Biomedical Sciences Medical Physics Program, MD Anderson Cancer Center, where she completed a Medical Physics residency in 2008. She is currently an Assistant Professor in the Department of Radiation Oncology at the Duke University Medical Center, Durham, NC. She is certified in Therapeutic Radiological Physics by the American Board of Radiology. Her major research interests include IMRT, VMAT, CBCT, and associated quality assurance. Dr. O'Daniel is a member of several AAPM committees and subcommittees and is a member of the Board of Editors of the JACMP.

FOR THE PROPOSITION: Scott Dube, M.S.

Opening Statement

The AAPM Task Group Report 142 recommends many tests which provide quality assurance for medical accelerators.[1] When applied to IGRT, however, some physicists believe that, while the procedures are sound, they do not yield a favorable cost/benefit analysis outcome (personal communications). In other words, they consider the procedures to be unwarranted for IGRT. Specifically, they find the following tests found in Table VI for monthly checks of the imaging modes to be unnecessarily onerous:

- Planar imaging (MV and kV)—scaling, spatial resolution, contrast, uniformity, and noise.
- CBCT imaging (kV and MV)—geometric distortion, spatial resolution, contrast, HU constancy, uniformity, and noise.

Let us consider a qualitative cost/benefit analysis and first look at the cost components:

- Time—The image acquisitions, image analysis, and reporting can require many hours per machine each month. This can be reduced considerably using commercially available software, which leads to the next component.
- Money—Many physicists feel compelled to purchase specialized software for the image analysis and data tracking. Furthermore, although there are specialized phantoms provided with the imaging system, many physicists feel compelled to purchase additional phantoms to perform the QA tests. In fact, TG-142 has been a boon for those vendors who sell products related to linac QA for IGRT.
- Risk—The American College of Radiology as well as certain States have, or will, consider compliance with TG-142 to be a requirement. Therefore, any deviation from the recommendations puts the facility at risk for being judged as noncompliant with unfavorable consequences to follow.

Now let us consider the benefits derived from performing monthly imaging QA as described in the TG-142 Report, specifically for the detection of component image degradation. Certainly degradation of image quality can undermine the IGRT process. But it is important to keep the issue of image quality in perspective. First, these images are not, and do not, need to be of diagnostic quality. In the case of planar imaging, the staff look at structures such as fiducial markers and bones, which are readily seen. In the case of cone-beam CT (CBCT), there are the additional structures such as soft tissue interfaces, which are useful even at degraded contrast. Second, the IGRT images are always compared to a reference image such as from a planning digitally reconstructed radiograph or CBCT. So each IGRT session provides a comparison of the IGRT image with a reference image. Finally, what is the consequence of image degradation? Again, these images are not used for diagnosis. So the only potential risk is uncertainty in the mind of the therapist and/or physician performing the IGRT procedure. Should that occur, they should notify the physicist to investigate further on an *ad hoc* basis.

In the final analysis, implementation of TG-142 for monthly imaging QA does not yield a favorable cost/benefit analysis for many physicists who find the recommendations unwarranted.

AGAINST THE PROPOSITION: Jennifer O'Daniel, Ph.D.

Opening Statement

IGRT recommendations in the AAPM TG-142 Report provide a comprehensive list of QA requirements to ensure safe, high quality application of imaging systems in the radiation treatment room.[1] The principle goal of IGRT is to improve the accuracy of patient positioning and target localization, thereby reducing delivery errors and improving dosimetric outcomes.[2–4] Currently, x-ray imaging is the primary means to perform IGRT.[5] The AAPM TG-58 and TG-104 reports provide detailed descriptions of existing MV and kV x-ray imaging devices available for in-room image guidance.[6] During acceptance testing/commissioning, the imaging system baselines are established, including geometric accuracy, positioning/repositioning accuracy, image quality, and imaging dose. The geometric and positioning/repositioning accuracy are used to determine appropriate planning margins. Image quality affects how accurately the images may be used for alignment. The imaging dose should be as low as possible while maintaining sufficient image quality.

The purpose of QA is to ensure that these baselines are maintained. Any unexpected hardware or software deviations/malfunctions could affect the specific characteristics of the imaging device. For example, geometric accuracy could easily be reduced by mechanical defects and loss of calibration factors. Image quality could be degraded by detector stability and responses. Positioning/repositioning accuracy could be put out of specification by many factors such as mechanical motion inaccuracies and software errors. These could be clinically significant. For example, a 3 mm positioning inaccuracy could cause about a 20% increase in cord dose for a typical spinal radiosurgery case. At present, such potential deviations are not automatically monitored. Therefore, it is important to maintain a vigilant QA program.

The appropriate frequency of measurements and the associated acceptance criteria/action levels depend upon the accuracy requirements for different treatments. A comprehensive model for determining site-specific recommendations is being developed (AAPM TG-100). Given the importance of IGRT, until a comprehensive statistical model is available, the recommendations from TG-142 are the most appropriate guidance for IGRT QA. In fact, the actual QA program should go beyond TG-142 to include process and staff QA, as the majority of errors that reach the radiotherapy patient have a human error component.

Although I expect that error incidence for IGRT is rare, a single incident could diminish patient confidence and impact facility credentialing, not to mention the detrimental effect it might have on that patient. It is our primary responsibility as therapeutic medical physicists to ensure safe, high quality treatments for every radiotherapy patient.

Rebuttal: Scott Dube, M.S.

My opponent stated "*I expect that error incidence for IGRT is rare*." I agree with that statement. In fact, this was demonstrated in a recent publication for a Novalis Tx accelerator.[7] Coincidentally, the authors of this paper were from the same academic institution as my opponent. They concluded that the linac demonstrated excellent compliance with TG 142

guidelines over this one-year period. They also stated that additional hardware may be required for the testing and that this may take 3–5 h of a physicist's time per linear accelerator per month.

It is not surprising compliance was excellent. If IGRT systems were unreliable, manufacturers would include ongoing inspections as part of their service contracts. Yet Varian provides an IGRT system inspection of the mechanical and imaging performance only every six months, while the Elekta frequency is every 12 months (personal communication). Surely these frequencies are based on a demonstrated history of *stable* performance.

Also, the IGRT systems are designed with failure detection feedback mechanisms in place. Any loss of mechanical calibration generates an interlock, which must be investigated and cleared before proceeding. And failure of the imaging system is immediately identified by the therapist who examines the 2D and CBCT images on a daily basis.

At the 2012 AAPM meeting, a slide was presented by a speaker discussing QA testing which read, "If you can dream it, you must do it."[8] The speaker was being facetious by altering a famous quotation from Walt Disney. His point was the design of quality assurance programs is often developed with great imagination but not equal consideration of the necessity or cost of the procedures.

As said in my Opening Statement, the IGRT QA program should fit the scope of clinical practice in a particular center. The TG-142 Report provides an excellent source of procedures to consider. However, there is little evidence to justify the frequency of the testing.

Rebuttal: Jennifer O'Daniel, Ph.D.

While QA for IGRT may be time consuming, it is nonetheless necessary to ensure its proper functioning. Image quality and spatial accuracy, singled out by my opponent, are just some of the aspects that should be tested according to the TG-142 Report but there are many others.[1] Collision interlocks prevent significant injury/damage from patient-imager collisions. The coincidence of imaging and treatment isocenters as well as the accuracy of patient positioning/repositioning help avoid patient misalignments. Monitoring imaging dose and quality ensure that the patient does not receive any unnecessary dose, increasing their risk of secondary cancers without providing any benefit.

Of course, spatial accuracy and image quality should be monitored. Clearly, errors in scaling and/or geometric distortions can lead to misalignment. Spatial resolution, contrast, noise, and uniformity indirectly affect the alignment accuracy by degrading image quality. While my opponent suggests relying on the physician or therapist to report these problems, it would be difficult to detect scaling or geometric distortion errors during routine clinical use. Similarly, image quality is best evaluated on a phantom, where a baseline may be known, instead of qualitatively on a constantly changing patient population. Ultimately it is the responsibility of the medical physicist to ensure that geometric accuracy and adequate image quality are maintained. Future technology developments (e.g., an integrated QA phantom) could improve our efficiency.

While providing recommendations on specific tests, TG-142 allows for deviations in their frequency, stating "institutional deviations from some of these recommendations are expected based upon the institution's policy and procedures; the clinical significance… may be mitigated by other control methods…."[1] For example, if all patient shifts are based on kV imaging, then the frequency of the MV positioning/repositioning test may be reduced. Or if only a single mode of CBCT is used clinically (e.g., pelvic scans), then the frequency of testing other modes (e.g., head scans) could be likewise reduced. On the other hand, if the linac is treating a large number of radiosurgery patients using IGRT, the frequency of certain tests may be needed to be increased. When the TG-100 Report is published, physicists should feel comfortable performing the analysis to determine the appropriate frequency of testing for their particular clinic.

The IGRT QA recommended by TG-142 covers all aspects necessary to ensure safe clinical usage, and allows for deviations in their frequency based on the policies of individual clinics. Therefore, TG-142 is not unnecessarily onerous for IGRT QA.

ACKNOWLEDGMENT

J.O'D wishes to thank Fang-Fang Yin for helpful discussions on this topic

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2.2. DASSIM-RT is likely to become the method of choice over IMRT and VMAT for delivery of highly conformal radiotherapy

Lei Xing and Mark H. Phillips
Reproduced from *Medical Physics* **41**, 020601-1-3 (2014)
(http:// dx.doi.org /10.1118/1.4773025)

OVERVIEW

Recently, a novel form of treatment planning and delivery for IMRT called dense angularly sampled and sparse intensity modulated radiation therapy (DASSIM-RT) has been introduced as a means of improving dose distributions.[1] The authors claim that DASSIM-RT is superior to conventional IMRT and volumetric modulated arc therapy (VMAT) and will likely become the method of choice for highly conformal radiotherapy. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Lei Xing, Ph.D. Dr. Xing obtained his Ph.D. in Physics from the Johns Hopkins University in 1992 and received his Medical Physics training at the University of Chicago. He has been a member of the Radiation Oncology faculty at Stanford since 1997, where currently he is the Jacob Haimson Professor of Radiation Physics and Director of the Radiation Physics Division of the Radiation Oncology Department. He also holds affiliate faculty positions in Medical Informatics, Bio-X, and the Molecular Imaging Program at Stanford. His research has been focused on inverse treatment planning, tomographic image reconstruction, optical and PET imaging instrumentation, image guided interventions, nanomedicine, and applications of molecular imaging in radiation oncology. Dr. Xing is an author on more than 200 peer reviewed publications, a coinventor on many issued and pending patents, and principal investigator or coinvestigator on numerous NIH, DOD, ACS, and corporate grants. He is an AAPM fellow and has served on the editorial boards of a number of journals in radiation physics and medical imaging including *Medical Physics*.

Arguing against the Proposition is Mark H. Phillips, Ph.D. Dr. Phillips obtained his Ph.D. in Atomic Physics from the University of Wisconsin, Madison and his Medical Physics education at Harvard University, Boston, MA. Since 1991 he has been at the University of Washington, Seattle, where currently he is Professor in the Department of Radiation Oncology. He is certified in Radiation Oncology Physics by the American Board of Radiology. His major research interests include IMRT optimization, decision theory application in treatment planning, and applications of PET in radiotherapy.

FOR THE PROPOSITION: Lei Xing, Ph.D.

Opening Statement

The holy grail of modern radiation therapy (RT) is to produce and efficiently deliver highly conformal dose distributions. IMRT was developed to meet this challenge and has had a significant impact on radiation oncology practice. In general, the quality of IMRT depends on beam configuration and intensity modulation. Limited by the available dose optimization and delivery techniques, little effort has been devoted to investigate systematically the role of beam angular sampling and the interplay between this and intensity modulation. Two technical advances in RT have been made recently, which are changing the current RT landscape and making a new type of treatment scheme, coined DASSIM-RT, possible.[1] First, in treatment planning, a compressed-sensing based inverse planning strategy has been proposed,[2] which allows the user to optimally control the level of intensity modulation of the incident beams. Second, in treatment delivery, a new generation of digital linacs with autofield sequencing has become commercially available, which dramatically improves the delivery efficiency.

The clinical need for DASSIM-RT stems from the fact that conventional IMRT (with 5–10 beams) often does not possess sufficient angular sampling required to spatially spread the dose.[1] In contrast, current VMAT (with 1–3 arcs) oversamples the angular space and does not provide the desired intrabeam modulation in some or all directions. Switching beam energy between the gantry angles is impossible in rotational arc delivery. DASSIM-RT explores a large area of uncharted territory in terms of the number of beams (including noncoplanar and/or nonisocentric beams) and level of intensity modulation, and bridges the gap between IMRT and VMAT. Technically, DASSIM-RT is achieved by increasing angular beam sampling while eliminating dispensable segments of the incident fields through the use of emerging compressed-sensing based dose optimization.[2,3] The removal of dispensable intrabeam modulation and autofield sequencing make DASSIM-RT extremely efficient in delivery. A number of variants of DASSIM-RT are possible, such as segment boosted arc therapy in which segmented delivery at some fixed gantry angles and rotational arc delivery are intertwined to achieve a much improved dose distribution without relying on the use of multiple arcs. Of course, the boosting segments at a gantry position can also be distributed over a small angular interval and delivered rotationally by slowing the gantry rotation.

In summary, DASSIM-RT is likely to replace conventional IMRT and VMAT for delivery of highly conformal radiotherapy. It represents a truly optimal RT scheme with (1) uncompromised beam sampling, (2) beam collimation,[4] couch rotation[5] and/or energy modulation, (3) elimination of dispensable intensity modulation, and (4) highly efficient delivery. DASSIM-RT overcomes the limitations of existing treatment schemes and empowers the radiation oncology community with the best possible tools for the next-generation of conformal RT.

AGAINST THE PROPOSITION: Mark H. Phillips, Ph.D.

Opening Statement

First, I would like to congratulate Drs. Li and Xing for their work on DASSIM-RT.[1] Similar to the search for the Higgs boson, they have confirmed what many suspected, which is that there exists a multidimensional space of plans that fills the gap between VMAT and conventional IMRT plans.

Although I hesitate to predict the collective actions of the radiation therapy community, I do see a number of reasons why the introduction of DASSIM-RT does not herald a paradigm shift in optimization and delivery. In reverse order of importance:

- I believe that there will be pushback from administrators who have already invested hundreds of thousands of dollars in getting VMAT up and running. They will not be amenable to requests for purchasing new licenses for planning and delivery.
- Do the differences in speed between VMAT, IMRT, and DASSIM-RT really matter? Clinically, not in many cases. While intrafraction motion occurs for some tumor sites, the slow type of drift that is of interest in this comparison may not provide any operational differences between these methods with respect to the need for reimaging.[6] Faster motions, i.e., respiration-induced, create the same problems for all methods and, in fact, fixed beam methods are more amenable to gating. The speed is more of an administrative/clinic issue. As the examples show, the time differences between DASSIM-RT and IMRT plans are only about a minute, and 2–3 minutes longer than a comparable VMAT plan. This seems a small effect on which to base treatment decisions.
- Is there a clinical benefit to the dosimetric differences? The published examples are not definitive and the differences are not dramatic.[1] Strictly speaking, none of the methods dominates the others,[7] although overall the advantage goes to DASSIM-RT. The move to VMAT was not instigated by better plan quality, nor is this likely to be the case with DASSIM-RT. What makes a greater difference are the optimization objectives, including the functional form and parameters.[8,9] Current methods of evaluating plans are still crude, and comparisons between plans even more so. Until more comprehensive models are developed, it is very difficult to convert the array of dosimetric differences of the magnitudes reported into anything approaching significant clinical outcomes.

Clinics are used to accepting plans that are "good enough" and, once a program is established, they do little exploration of plan space. Current planning systems do not provide good tools for doing so and this would require a lot of time and effort on the part of the user. The advantages of DASSIM-RT, therefore, which I am convinced are real, are not dramatic enough given the current state of treatment planning for any sizeable shift away from whatever system in which a clinic has invested. Without some other source of pressure, the advantages that physicists perceive will not yield any winds of change.

Rebuttal: Lei Xing, Ph.D.

I like the Higgs boson analogy but, for radiation oncology, I want to emphasize that proving what we suspected is not, should not, and will not be the end of story. Instead, it is only the beginning of a new digital RT age. Let us not forget that it took more than a decade for IMRT to go from conception to clinics worldwide. VMAT has taken even longer, apparently for the reasons rightfully listed by Dr. Phillips.

Not that I am overly optimistic about technology transfer, which may have multiple causes of failure even for a totally sensible technology, but I am passionate about DASSIM-RT because of its enormous potential. Although not widely realized, radiation therapy is stepping into a digital era in which treatments will be done "station by station" instead of "beam by beam," In a

nutshell, a station (alternatively, a control point or a node) describes the state of a delivery system (including linac configurations such as beam energy, aperture shape and weight, gantry/collimator angle, and auxiliaries such as the couch). When the auxiliary equipment is stationary, a station is no different from an MLC or jaw-shaped beam. A conventional intensity-modulated beam consists of a collection of stations with the same gantry angle but different MLC segments. Next-generation RT will be all about the optimization of station-mediated intensity and spatial distribution, which I call station parameter optimized RT (SPORT). VMAT and IMRT are simply two special, and often nonoptimal, cases of SPORT, as explained in my Opening Statement. DASSIM-RT represents an important region in the SPORT map.[1]

The functional form and parameters of the optimization objectives do make a difference in inverse planning, as they define the solution space.[8–11] SPORT also enlarges the solution space through improved angular and intensity sampling of the stations.[1]

About current plan evaluation methods, I rebut that they capture the main features of treatment plans and are thus useful clinically. At the bare minimum, the evaluation is like choreography—people can tell the difference when SPORT and conventional plans are placed side-by-side. That is one of the reasons that VMAT has prevailed over IMRT in the past few years.

To recapitulate, SPORT/DASSIM-RT advances RT to a new paradigm through optimal modulations of station-mediated parameters. The new planning and delivery techniques will replace the existing IMRT/VMAT.

Rebuttal: Mark H. Phillips, Ph.D.

Dr. Xing believes that DASSIM-RT will replace conventional IMRT and VMAT because new developments (compressed sensing and autosequencing linacs) will provide users with what they desire (efficient delivery of highly conformal dose distributions). His subsequent description of the essentials of DASSIM-RT is very convincing to mathematical physicists. But is it convincing to the physicians and administrators? As nearly all who have delved into such comparisons between methods will attest,[3] the differences in the resulting plans (a) are often small and not consistent, and (b) are dependent on the skills of the particular planner. Similarly, the results presented in the original paper[1] are within the variations in plan metrics that physicians see in plans produced for different patients by different planners. The delivery efficiency is only as good as or worse than that of VMAT, which does little to open the wallets of the administrators.

I would be more convinced of DASSIM-RT's future if there were reliable methods to improve inverse planning. In that way, the stochastic nature of current plan quality could be overcome and the benefits of DASSIM-RT would more clearly emerge from the noise. However, our current planning environments provide few tools for systematically searching for better objectives. In addition, the limited correspondence between optimization algorithms and clinical outcomes has placed us in the curious position where clinical trials are now written to accommodate the limitations of our planning, rather than our planning being improved to accommodate clinical trials.

My conclusion is that, since many institutions have already spent significant dollars for the latest planning and delivery techniques, there will not be sufficient arguments from physicians to effect any change in current habits. Perhaps, it is like new generations of smart phones, where each generation is a bit more capable than its predecessor, but where it takes a significant step forward before any but the most devoted technophile discards the old for the new.

LX wishes to thank Dr. Ruijiang Li for his contributions during the development of SPORT/DASSIM-RT. He also acknowledges useful discussions with Drs. Benjamin Fahimian, Gary Luxton, Karl Bush and Daniel Chang.

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2.3. IGRT has limited clinical value due to lack of accurate tumor delineation

Christopher F. Njeh and Lei Dong
Reproduced from *Medical Physics* **41**, 040601-1-4 (2013)
(http:// dx.doi.org /10.1118/1.4789492)

OVERVIEW

Image-guided radiation therapy (IGRT) is only as good as the imaging it requires. It has been suggested that, because current imaging techniques are insufficiently accurate for adequate delineation of tumors, IGRT is only of limited clinical value. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Christopher Njeh, Ph.D. Dr. Njeh obtained his Ph.D. degree in Medical Physics from Sheffield Hallam University, UK and, after graduation, he worked at the Addenbrooke's Hospital in Cambridge and Queen Elizabeth's Hospital, Birmingham, UK. He then came to the USA as a Visiting Postdoctoral Fellow at the University of California, San Francisco where he was subsequently appointed an Assistant Professor of Radiology. He later completed a Medical Physics residency at Johns Hopkins University, Baltimore was Chief Medical Physicist at Texas Oncology Tyler. He is now the Medical Physics director at National Medical Physics Services, Tyler, Texas and holds an adjunct faculty position at the University of Texas at Tyler. Dr. Njeh is certified in Therapeutic Radiologic Physics by the ABR. His major research interests include image-guided radiation therapy and accelerated partial breast irradiation. He is author or coauthor of over 50 papers and 10 book chapters, and is coeditor of two books.

Arguing against the Proposition is Lei Dong, Ph.D. Dr. Dong obtained his Ph.D. in Biomedical Sciences/Medical Physics from the University of Texas Graduate School of Biomedical Sciences, Houston, Texas. After a brief period at Baylor College of Medicine, he moved to the Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, where he attained the rank of Professor before moving to the Scripps Proton Therapy Center, San Diego in 2012, where he is currently Director and Chief Medical Physicist. Dr. Dong is certified by the American Board of Radiology in Therapeutic Radiation Physics, is a Fellow of the AAPM, and a Senior Associate Editor for the *International Journal of Radiation Oncology, Biology, and Physics*. He is active on several committees in the AAPM and is Chairman of the Imaging for Treatment Verification Work Group. His major research interests include IMRT, IGRT, deformable image registration, proton therapy, and dose/volume modeling, for which he has obtained numerous grants and patents and has published well over 100 papers in refereed journals.

FOR THE PROPOSITION: Christopher F. Njeh, Ph.D.

Opening Statement

The fundamental tenet of radiotherapy is the delivery of a high dose of radiation to the tumor while limiting the dose to the surrounding normal tissues. To achieve this goal, all uncertainties in the multifaceted radiation therapy process have to be minimized. These include radiation output, geometric, and tumor delineation uncertainties.[1] Developments broadly termed "image guided radiation therapy" have recently been introduced to reduce geometric uncertainties.[2] There is growing evidence that these techniques have improved tumor localization in the treatment room.[3] However, my key contention is that any improvement gained by the application of IGRT may be negated by inaccuracy in tumor delineation.

Tumor delineation has been identified as the weakest link in the search for accuracy in radiation therapy.[4,5] A high degree of uncertainty in target volume has been demonstrated for most cancer sites. For example, the target contours drawn for the same case by different physicians, or by the same physician on different days, show enormous differences. Weiss and Hess, for example, went as far as saying that "*inter-observer variability in tumor delineation is a major - for some tumor locations probably the largest - factor contributing to geometric inaccuracy*."[6] Major sources of variations in tumor volume delineation are: visibility of the target, including its extensions (impact of imaging protocol), disagreement on target extension, and interpretation (or lack of) delineation protocols.[5,6] It is reasonable to assume that variation in tumor delineation increases the probability of geometric miss of parts of the tumor, thus increasing the risk of recurrence.

Errors in tumor delineation (contouring) generate systematic errors that remain constant during the course of radiation therapy and, therefore, can have a large impact on outcome.[5] No level of image guidance can eliminate this error. This also brings home the difference in precision and accuracy. Proper contouring of the target volume improves accuracy whereas image guidance improves precision. In other words, you can consistently hit a wrong target (high precision, poor accuracy). But what is required is to consistently hit the right target (high precision, high accuracy) during the course of treatment. Hence, accurate radiation therapy involves knowing exactly where the tumor is at the time of treatment.

Finally, treatment margins may be overly reduced because IGRT gives a false sense of security in target localization. However, cancer has a complicated and mostly poorly understood disease spread and biology. It is likely that the incidental dose around the margins, the feathering effect from setup errors and generous planning target volume (PTV) margins, is needed to take care of the microscopic disease spread that may be present but not visible by current imaging techniques.

Hence, IGRT is only as good as the accuracy with which the target is known. So, I suggest that the improvement in accuracy rendered by IGRT is limited by the accuracy of target delineation.

AGAINST THE PROPOSITION: Lei Dong, Ph.D.

Opening Statement

I am arguing against the proposition because image guidance is so critical for radiation therapy that it is almost unethical not to use image guidance technology if it is available. Biological effects will be produced whenever tissues (tumors or normal organs) receive sufficiently high radiation doses.[7] Geometric accuracy, therefore, is essential if high doses are to be delivered where they are needed and avoided where they are not.

It is true that that IGRT requires accurate tumor delineation. Without defining a target, IGRT is impossible. I believe that the argument is whether or not the accuracy of target delineation is good enough to make IGRT clinically valuable. Interobserver contouring studies have, indeed, demonstrated large differences between radiation oncologists in target delineation for some treatment sites.[8,9] Nevertheless, the value of precise target delineation is difficult to demonstrate clinically because treatment outcome depends on many other factors, including patient setup errors.

Regardless of these uncertainties in target delineation, we should not ignore the other important aspect of image guidance in radiation therapy, which is to protect normal tissues and improve the patient's quality of life after radiation therapy. Compared to target delineation, it is fair to say that the accuracy of normal organ delineation is adequate. The use of IGRT in protecting normal tissue deserves its own clinical value. For example, a recent study of patients treated for localized prostate cancer demonstrated that the use of IGRT reduced grade 2 or higher urinary toxicity from 20.0% to 10.4% when compared with a group of similarly treated patients without using daily IGRT.[10] The authors believed that the enhanced accuracy associated with IGRT caused a reduction in the volume of bladder or bladder neck exposed to the high prescription dose of 86.4 Gy used in the treatments. A Cox regression analysis also identified IGRT as one of the predictors for PSA relapse-free survival in the high-risk cohort. This was a retrospective analysis, however, and not a randomized clinical trial (RCT). Direct comparison of IGRT vs non-IGRT is rare. It will be morally difficult to conduct prospective randomized trials for such head-to-head comparisons because of the potential risk of underdosing the target and/or increasing normal tissue doses in the non-IGRT group.

Finally, IGRT plays a role in providing quality assurance of daily patient setup.[3] Large setup errors can be visualized and corrected before each treatment. IGRT makes treatment more consistent and eliminates one of the key uncertainties that will affect treatment outcome. Tight quality control of daily treatment will eventually improve our target delineation because we can better differentiate the outcome of “a correct target treated consistently” and “an incorrect target treated consistently.” The experience learned will help us to define the target better in the future. Therefore, I conclude that IGRT has great clinical value both now and for the future.

Rebuttal: Christopher F. Njeh, Ph.D.

Clinical value can be measured by reduction in early and late toxicity and improved disease control. As Dr. Dong has rightly pointed out, it will be impossible, or rather unethical, to conduct a RCT to measure these values for IGRT, as well as it is unethical to carry out a RTC to demonstrate the effects of tumor delineation inaccuracy. However, the lack of evidence of IGRT's deleterious effects is not proof of its clinical value. Radiation therapy should be evidence based, and history has shown that not all scientifically sound developments have clinical value or

improve previous approaches.[11] It is for this reason that many commentaries in scientific journals have cautioned against the blind application of technology without clinical evidence of its efficacy.[12]

It can also be pointed out that margins that are applied to account for delineation uncertainties can be reduced if tumor delineation accuracy is improved. Since tumor abuts normal tissue, it is fair to assume that if the tumor is delineated accurately, so also will be the normal tissues.

While Dr. Dong points to retrospective studies documenting the clinical utility of IGRT, there are reports casting doubts on IGRT's clinical effectiveness. For example, Engels *et al.*[13] demonstrated increased biochemical failure in patients with distended rectum on the planning CT, in spite of image guidance by implanted markers.

Dr. Dong has failed to also address the fact that there is a plethora of techniques lumped under the umbrella of IGRT, with different precisions in target localization.[14] For instance, the residual error for prostate localization using CBCT and fiducial markers was less than 2 mm, while it was approximately 4 mm for daily ultrasound. Consequently, as we try to tease out the value of accurate tumor delineation on IGRT, we should be cognizant of the fact that the diversity in IGRT techniques may mask the true benefit of IGRT.

I do not doubt that IGRT has *potential* clinical value for radiation therapy, but such benefit will be harvested only if there is improved accuracy in tumor delineation. More research is required to improve target delineation using advancements in imaging techniques such as molecular imaging, and also to identify which IGRT technique is best for which cancer type.

Rebuttal: Lei Dong, Ph.D.

Dr. Njeh has brought several important points to the debate. The incidental dose around the geometric margin is an important one that people tend to ignore. The incidental dose creates a “dosimetric margin” which depends on the particular treatment technique. The dosimetric margin, instead of the geometric margin, ultimately determines the success of radiation therapy; of course, assuming that the target is appropriately defined. We should be mindful when changing practice. IMRT is a good example where the sharp dose falloff near the PTV and critical structure boundary represents a dosimetric risk for underdosing the target. Fortunately, geometric setup margins have not been reduced in most clinical practices when IGRT has been introduced. A combination of sharp dosimetric penumbra and aggressive reduction of setup margin with IGRT can result in treatment failures.[13] I agree that physicists should not get the false impression that the geometric margin is the only concern when designing the PTV. On the other hand, we should not expect the unreliable incidental dose to take care of the microscopic disease. Microscopic disease extension should be explicitly included in the clinical target volume (CTV) definition, rather than in the PTV. Unfortunately, defining CTV is not an easy job.

Despite some reports of interobserver variability in defining the CTV,[8,9] target delineation uncertainties are clearly site and application-specific. It is unfair to state that target delineation is the weakest link for *all* treatment disease sites or treatment techniques. For example, for early-stage disease, some well-defined small tumors are commonly treated with stereotactic body

radiation therapy (SBRT). Target delineation is relatively accurate in this case while organ motion and setup error are the biggest challenges, especially for mobile lung or liver cancers.[15–17] IGRT plays a critical role and perhaps is the enabling technology in delivering accurate doses to these small targets with good results.[16,17]

In general, I agree with Dr. Njeh that target delineation is challenging. As Sir William Osler once said, "*Medicine is a science of uncertainty and an art of probability*." Obviously, IGRT has made improvements in target delineation accuracy a high priority for the future.

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2.4. Submillimeter accuracy in radiosurgery is not possible

Tewfik Bichay and Sonja Dieterich
Reproduced from *Medical Physics* **41**, 050601-1-4 (2013)
(http:// dx.doi.org /10.1118/1.4790690)

OVERVIEW

With most external beam radiotherapy treatments an accuracy of ±3 mm is usually considered desirable and achievable. With stereotactic radiotherapy, however, a somewhat greater accuracy is desired and, with modern techniques, can be achieved, and some claim that even submillimeter accuracy is achievable. This is the topic debated in this month's Point/Counterpoint.

Arguing FOR the Proposition is Tewfik Bichay, Ph.D. Dr. Bichay obtained his B.Sc. degree in Human Physiology from McGill University, Montreal, his M.Sc. in Radiation Biology from Concordia University, Montreal, and his Ph.D. in Medical Biophysics from the University of Western Ontario, London, Canada. He is currently Director of Medical Physics, Radiation Oncology, The Lacks Cancer Center at St. Mary's Health Care, Grand Rapids, MI. He started his career as a radiation biologist before transitioning into medical physics with a residency at the Ottawa Regional Cancer Center. He is certified in Radiation Oncology Physics by the ABMP and his present research interests center around applications of the TomoTherapy system and improvement in treatment accuracy with IGRT.

Arguing against the Proposition is Sonja Dieterich, Ph.D. After completing her Ph.D. in Nuclear Physics at Rutgers University in 2002, Dr. Dieterich received training in Medical Physics at Georgetown University Hospital, Washington, DC, from 2002 to 2003. In 2003, she accepted a faculty position at Georgetown. From 2007 to 2012, she worked at Stanford University Hospital as Clinical Associate Professor and Chief of Radiosurgery Physics. Since April 2012 she is an Associate Professor and Physics Residency Co-Director at the University of California Davis. Dr. Dieterich is Chair of the AAPM Task Group 135 “QA for Robotic Radiosurgery” and a member of the ASTRO Physics and Multi-Disciplinary QA Committees. Her current research interests are the development of QA/QM programs for new technologies, image-guided brachytherapy, and Veterinary Radiation Oncology.

FOR THE PROPOSITION: Tewfik Bichay, Ph.D.

Opening Statement

The advent of cranial radiosurgical therapy has allowed a nonsurgical approach to the treatment of cranial lesions.[1] The obvious benefits apply to both malignant as well as benign lesions. Historically a rigid invasive frame, attached to the patient's skull via small screws, acted as both immobilizer and localizer. With such devices, the frame defines a 3D coordinate system within which the skull and targeted lesion are intended to remain fixed from the time of the planning CT scan to the completion of treatment. More modern radiosurgical systems may use 3D “image-

guided" positioning for exact alignment. Accuracy of radiosurgery has often been considered as ultimately relying on the rigidity of the immobilizer, as opposed to the treatment system as a whole. This ignores multiple other factors that must also be included. Typical quoted values for frame-based immobilization accuracy are 0.3–0.6 mm.[2–4] This measure relates only to flex between the frame and the skull, and the stability of the treatment apparatus. The system accuracy as a whole must also include end-to-end uncertainties that result from the spatial resolution of the original CT, resolution and linearity of the MRI scan, contouring uncertainty, treatment planning grid resolution, algorithm errors, CT to MRI registration uncertainty, etc. The now-dated AAPM report 54 (Ref. 5) suggested that the total uncertainty can reach 2–3 mm.

The planning system is designed to calculate an optimized dose distribution around a physician-determined region of interest (ROI). Since the physician-drawn ROI is a function of the window and level differences on CT and MRI, there is variability between physicians, which even for well-identified normal structures (let alone often less distinct targets) can exceed 1–2 mm.[6] A recent study by a Canadian group demonstrated a shift in tumor isocenter of 1.4 mm by simply altering the time of CT imaging after injected contrast.[7] An analysis of the registration accuracy of CT with MRI for several algorithms determined typical errors along the *x*, *y*, and *z* axes of approximately 0.68, 1.04, and 0.60 mm, respectively. When added in quadrature this amounts to a vector of 1.4 mm.[8] Others have published even greater variability.[9] A recent Gamma Knife end-to-end study, evaluating the distance to agreement, determined that the uncertainty was better than expected based on quadrature-sum but still over 1 mm.[10]

The planning system dose grid is unlikely to have a resolution of less than 1 mm and the dose calculation algorithm will itself contain some uncertainty in placement of dose within the grid due to imperfect modeling of radiation transport. Since a significant percent of target definition is done on MRI datasets it is important to note that even for MRI systems compliant with ACR guidelines, the distortion can reach up to 2 mm.[11]

Taking all of the above uncertainties into account is essential in deriving a realistic overall accuracy for SRS treatment. It is apparent that radiosurgery treatment using current technology and considering human factors, when observed from end-to-end, cannot reach submillimeter accuracy.

AGAINST THE PROPOSITION: Sonja Dieterich, Ph.D.

Opening Statement

The crux of this debate is the definition of "Accuracy in Radiosurgery." In the literature, there is significant confusion caused by imprecise language.

If we are debating the mechanical accuracy of the delivery system to align to isocenter, the answer is straightforward and supported by literature. Current mechanical engineering techniques meet this standard easily.[3,12,13]

Frameless, image-guided radiosurgery adds the requirement to match the imaging isocenter to the mechanical isocenter. A look at the QA tables contained in TG-142 confirms that the expert authors consider this an achievable goal for standard QA.[14]

The next level of achieving submillimeter accuracy is to match the radiation isocenter to the mechanical isocenter using image-guidance. This task can be achieved by, for example, using an end-to-end (E2E) test. A literature search confirms submillimeter accuracy in E2E tests is achievable on CyberKnife,[3] Truebeam,[15] and Gamma Knife[13] machines. We should assume similar E2E accuracy for other delivery systems (to be published soon).

Radiosurgery targets are not always spherical or elliptical. Patient-specific delivery QA (DQA) is done to assess how mechanical, imaging, treatment planning, and radiation isocenter uncertainties combine *in a rigid phantom*. In IMRT, gamma criteria of 3%/3 mm are customarily used. To argue my case, I must argue that a reduction to 3%/1 mm is possible.[15] This is the point where the argument becomes too complex to support a binary answer to our hypothesis. First, the 1 mm criterion. Everyone who has performed a DQA is aware that working on an accuracy scale of 1 mm is a very time-intensive undertaking. The two QA devices we have available to reach this resolution are film and gels. Other QA devices have been shown to be unable to detect mechanical shifts of 1 mm in delivery.[16] Therefore, we cannot use them to verify that a radiosurgery device is accurate to <1 mm.

What about the 3% dose uncertainty: does it belong in this argument? I could choose the easy way out and argue that we are mixing units, hence it should be excluded. But as I like to point out, any uncertainty in dose, may it originate from dose calculation algorithms, delivery uncertainties, or any other possible cause, is equivalent to moving an isodose line.

Up to this point, we have been working in the physics realm of phantom testing for which we have confirmation of our ability to achieve submillimeter accuracy, so this proves the Proposition to be invalid. Once we step out of the phantom world and apply radiosurgery to patients, I have to concede. Even in as seemingly simple a task as contouring, we are still limited by imaging, causing contouring uncertainties of several millimeters among expert physicians. Not to mention residual patient motion or changes in internal anatomy. Since this is a physics publication, I am going to claim these factors are beyond this discussion, and still claim to have disproved the Proposition.

Rebuttal: Tewfik Bichay, Ph.D.

What an interesting approach to this debate. My esteemed colleague initially claims that 1 mm accuracy is achievable, then executes an elegant *demi-tour* and concedes that it cannot be met, only to follow with another *demi-tour*, discounting any parameters that are inconvenient, and claims victory! I applaud Dr. Dieterich's breakdown of the components of radiosurgery. My colleague states that, when these parameters are applied to a phantom, using certain specialized tools, assuming that a 3% dose error is nonexistent, ignoring contouring uncertainties, ignoring organ motion, ignoring imaging uncertainties, etc. we can achieve 1 mm accuracy! The reasoning is that this is a medical physics publication; hence clinical realities that affect accuracy can be excluded from the equation. Not so I say! After all, as medical physicists we can hardly

modify the accuracy of our linear accelerator's isocenter. This is determined by a vendor over which we have little control. The accuracy of our imaging system, our treatment planning system, registration software, etc. are also predetermined for us. We can measure their accuracy, but cannot modify them. Similarly, we can measure the clinical uncertainties that exist, from one clinician to another in contouring, for example, or how windowing levels affect contouring, or organ motion during respiration. We can measure those parameters but not affect them. They are still part of the equation. This reality of accuracy should hold whether the debate takes place in *Medical Physics* or in the *International Journal of Radiation Oncology, Biology, Physics.*

Because physicists concentrate largely on parameters that are within their control and can be readily applied to a phantom, such as physical or dosimetric measurements, we sometimes forget, or choose to ignore, the big picture. Our physician colleagues hear us tell them that our treatments are accurate within a certain tolerance, and they believe us. We need to step back and look at the reality from a larger perspective that includes all relevant parameters. The weakest links, be they imaging, mechanical, dosimetric, or clinical, must be identified and addressed. When we do take these parameters into consideration, submillimeter accuracy in a patient is currently not achievable.

Rebuttal: Sonja Dieterich, Ph.D.

Dr. Bichay states: "It is apparent that radiosurgery treatment using current technology and considering human factors, when observed from end-to-end, cannot reach sub-millimeter accuracy." This is in direct contradiction to peer-reviewed papers[3,15,17–19] demonstrating submillimeter accuracy with end-to-end tests for several radiosurgery methods. Furthermore, he is offering no supporting literature for his statement that the planning system dose grids are unlikely to have dose grid resolutions of less than 1 mm. Modern treatment planning systems have dose grid resolutions matching (Accuray MultiPlan) or exceeding[20] the voxel resolution of the CT image. At 512 × 512 with a field of view of 250 mm for a cranial scan, this is equivalent to 0.5 mm. The interpolation between dose points pushes the resolution even higher, because for photon treatments dose gradients are relatively smooth.

It is also no longer true that *a significant percentage of target definition is done on MR data sets* alone. The fraction of radiosurgery patients with plans generated on MR-based planning systems has been declining; more widely used modalities such as linac based SRS use CT based treatment planning, with MR being used as an additional, complementary component of the contouring process. Even where MR is used for target definition (but not for localization), the 2 mm MR distortion Dr. Bichay references is measured over the extent of the MR phantom (>100 mm). Over the typical diameter of a large brain metastasis, 20– 30 mm, the expected distortion is less than 0.5 mm.

I do agree with Dr. Bichay that there is significant variability in defining the target volume. Quantitative imaging of disease has not reached the quality or resolution needed to achieve submillimeter accuracy. While I disagree with Dr. Bichay when I maintain that we can achieve submillimeter accuracy spatially and most likely dosimetrically (at least for rigid targets in homogeneous areas of the body), I do agree with him that submillimeter accuracy in contouring is as yet beyond our reach.

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2.5. The future of IMRT/SBRT lies in the use of unflattened x-ray beams

Chihray Liu and Michael G. Snyder
Reproduced from *Medical Physics* **41**, 060601-1-3 (2013)
(http:// dx.doi.org /10.1118/1.4793410)

OVERVIEW

Until the introduction of Tomotherapy and Cyberknife units, all linear accelerators used for radiotherapy utilized flattening filters (FF) to produce photon fields with uniform crossbeam dose distributions, primarily because it made dosimetry measurements and treatment planning feasible with the relatively crude linacs and computers used at the time. With the highly sophisticated treatment planning and delivery systems available today, however, it has become possible to use unflattened x-ray beams. In fact it has been suggested that, for the IMRT and SBRT treatments commonly used today, flattening-filter-free (FFF) accelerators will soon become the norm. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Chihray Liu, Ph.D. Dr. Liu obtained his Ph.D. degree in Physics from the University of Nebraska-Lincoln, Lincoln, Nebraska in 1988 and completed postdoctoral clinical training at Thomas Jefferson University, Philadelphia, PA in 1992. Since 1993 he has worked in the Department of Radiation Oncology, University of Florida, where he is currently Professor and Chief of Physics. Dr. Liu is a member of several committees and task groups in the AAPM including serving as Chair of Task Group No. 210—Conventional LINAC Acceptance Testing, and member of the Working Group on Recommendations for Radiotherapy External Beam Quality Assurance. He is certified by the American Board of Radiology in Therapeutic Radiological Physics and his main research interests revolve around technical improvements in delivery of radiation such as image registration and image-guided radiation therapy, computer modeling of dynamic therapy, and treatment planning optimization.

Arguing against the Proposition is Michael G. Snyder, Ph.D. Dr. Snyder obtained his Physics Ph.D. in 2006 from the University of Texas at Austin. He subsequently moved to Wayne State University School of Medicine where he completed his M.S. degree in Radiological Physics in 2010. Since then he has been a medical physicist in the Department of Radiation Oncology at Wayne State where he is currently an Assistant Professor. He serves as a member of the AAPM Task Group No. 244 (Treatment Planning System Commissioning and QC/QA), Task Group No. 231 (Cognitive Science and Education Resources), and the Work Group on IMRT. Dr. Snyder's current research interests include infrared depth-map imaging to increase accuracy in radiotherapy delivery; HPV, tumor metabolism and radiosensitivity in head and neck cancer; and radiotherapy enhancement using gold nanoparticles: dose characterization and clinical strategies.

FOR THE PROPOSITION: Chihray Liu, Ph.D.

Opening Statement

IMRT and SBRT have gained popularity over the last decade. These modalities minimize normal tissue toxicity; SBRT provides ablation of small volume tumors. A concern with these modalities is that the longer treatment times can jeopardize patient comfort, leading to excess patient movement and inconsistent breathing. This compromises treatment delivery, i.e., normal tissue sparing and CTV coverage suffer.

Delivery time is a function of three main variables: (1) Gantry rotation speed and subsequent field setup and loading, (2) multileaf (ML) movement, and (3) maximum dose rate for delivery. Gantry rotation and field setup/loading speed may be optimized by using dynamic arc delivery, which gives continuous gantry movement. ML movement between gantry angles is also optimized in dynamic arc delivery through minimization of the leaf movement. However, when a hypofractionated treatment is required (e.g. SBRT), the primary time-limiting factor is dose rate. For these cases, FFF beams will reduce the delivery time since the dose rate for FFF beams is higher by a factor of 2–3 over that achievable with conventional FF beams.

For IMRT: Comparable dose delivery time between FF and FFF beams

Since the standard dose delivery monitor units (MUs) for IMRT are much less than for SBRT (high dose per fraction), the FFF higher dose rate does not significantly improve on IMRT delivery time compared to SBRT. The limiting factor for IMRT is the position-to-position leaf movement. Nevertheless, the delivery time with the FFF beam remains comparable to that of a conventional flattening-filter beam. Sometimes, fewer total MUs are necessary with FFF beams than with FF beams, although the reverse may be true.

For SBRT: FFF beams provide delivery time advantage over FF beams

Typical SBRT treatments use field sizes of 5×5 cm^2 or less, with 10–20 Gy per fraction. Since FFF and FF beams have similar profiles for these field sizes, the dose delivery time will be much less if the ML moves at its maximum speed (assuming gantry rotation speed is also maximized). Since the field size is small, the ML movement range is also limited.[1,2]

FFF beams provide simpler physics with reduced head leakage, hence simpler treatment planning system (TPS) model and less whole body dose than FF beam

The FFF beam provides simpler physics characteristics over the FF beam.[3,4] These are: (1) minimum variation in head scatter factor for field sizes larger than 10×10 cm^2, (2) minimum variation in the shape of the depth dependent off-axis profiles since the beam softening effect is less, and (3) half the head leakage radiation of a conventional FF beam. These characteristics: (1) result in a more accurate beam model than that of the FF beam since variation in the energy-dependent beam softening factor is significantly reduced and there is less change in the output factor for larger field sizes, and (2) reduce the total scatter dose to the patient.

AGAINST THE PROPOSITION: Michael G. Snyder, Ph.D.

Opening Statement

Within the context of intensity modulated treatments, the superiority of FFF delivery seems self-evident. In a modern world with accurate dose calculation engines and inverse planning algorithms, the flattening filter is an anachronism, without purpose, and is quite literally in the way. However, the oft stated advantages of removing the flattening filter—increased dose rates, reduced head scatter, etc.—may not prove to be as clinically relevant as expected and, when the potential disadvantages of flattening filter removal are considered, the decision to cast-off this seemingly unnecessary component becomes less straightforward. The question must be asked: will removing the flattening filter substantially improve patient care?

Take first an increased dose rate. Without the use of a flattening filter it is currently possible to increase the dose rate to two to four times that of conventional treatment.[5] Radiobiological considerations aside, the primary advantage of an increased dose rate presumably is shorter treatment times. If it is accepted for the moment that shorter treatment times are better for the patient, how much shorter is clinically impactful? In their study of the time dependence of intrafraction motion, Hoogeman *et al.*[6] found that targets tend to drift linearly with time. Based on their estimations, the extra margin required for a 15-min, hypofractionated treatment of the spine would need to be a mere 2.0 mm. For a 5-min treatment of the same type, the margins could be reduced further to 1.0 mm. These numbers will vary based on treatment type, but the results seem to indicate that shorter treatment times should lead to smaller margins and, therefore, less dose to normal tissue.

However, subtle drifts do not tell the whole story. Preliminary data from Verbakel *et al.*[7] simulating the dosimetric impact of large, low-probability target movements (e.g., coughing) during SBRT spine treatments indicate an average increase in dose to the spinal cord of 8% for conventional treatments, rising to 22% for FFF treatments. Given an average treatment time of 6.7 min with flattening filter and 2.8 min without, the benefits of introducing this risk into treatment are, at most, submillimeter margin reductions.

The other major advantage of removing the flattening filter is a reduction in head scatter and leakage and, hopefully therefore a reduction in peripheral dose. However, the removal of the flattening filter also tends to increase inpatient scatter.[8] Despite reductions in head scatter and leakage, when all three components of peripheral dose are taken as a whole, the effective dose can actually be greater in FFF treatments.[9,10]

It is granted that a flattening filter is not essential for either IMRT or SBRT. However, there is as of yet no compelling argument that a flattening filter already in place should be removed. If removing the flattening filter potentially increases the effect of patient motion on treatment accuracy, and if the only real, tangible benefit to the patient is ~4 fewer minutes of their time, it seems unreasonable to completely reinvent an already functional modality.

Rebuttal: Chihray Liu, Ph.D.

Continuous improvement in technology is essential to future progress in the field of radiation therapy. Predating today's computer technology, flattening filters were introduced many years ago for the purpose of creating a simple flat photon beam to easily provide dose coverage to the tumor. However, use of a flattening filter unnecessarily complicates the physics of the photon beam and creates larger dose calculation uncertainties. Outcome improvement is a motivating force for the introduction and utilization of newer technologies. Elimination of the flattening filter simplifies the TPS physics model, reduces head leakage by approximately half and, for SBRT treatments, significantly reduces beam delivery time.

Simplification of the physics model

For a Monte Carlo based TPS, the most complex and uncertain aspects of the beam model are due to the flattening filter; its elimination would appreciably simplify the modeling process. Calculation accuracy for the current convolution based TPS would also improve due to: (1) slower variation in the field size dependent output factors for field sizes > 10×10 cm^2 and (2) the resultant insignificance of off-axis energy spectrum dependence.

Head leakage reduced by half

Induction of secondary cancer is an important concern. Reduction of head leakage by approximately half would, statistically, almost certainly benefit the patient.

Significant reduction in beam delivery time

Optimized delivery time is a critical aspect of patient treatment. A shortened treatment time can greatly reduce patient discomfort brought about by the immobilization device, mental stress, or the illness itself. Reduced delivery time also greatly increases the reliability of the breath-hold technique for SBRT.

In summary, the FFF approach for treatment delivery, while optimizing the clinical benefits of the photon beam, also enhances the benefits of radiation therapy, thus, it is a worthwhile technological investment for the improvement of patient care.

Rebuttal: Michael G. Snyder, Ph.D.

It appears that, for unflattened beams, every advantage brings with it an equal or greater disadvantage. In lung SBRT treatments, the removal of the flattening filter could potentially allow an entire port to be delivered within a single breath-hold, yet in free-breathing treatments flattening filter removal leads to significant interplay effects.[5,7] The lack of a flattening filter reduces head scatter, yet the softer spectrum increases patient scatter and delivers more skin dose.[11] For each positive, there seems to be a negative, and upon this basis it can be said that, at present, the clinical arguments for moving to unflattened beams fail to convince.

The physics arguments are another story entirely. The flattening filter is a kludge, a brute-force solution to the unfortunate realities of $4\pi r^2$ and bremsstrahlung angular distribution. It is ugly. It is inelegant. However, it also happens to be part of a system that has been used effectively for

decades—a system about which an entire generation of collective knowledge exists. Of course, the mere fact that this knowledge exists cannot impede the advancement of the field, but do unflattened beams represent a significant clinical advancement?

In the future, the removal of the flattening filter may prove to open modes of treatment that are far-and-away superior to any that could be performed with a conventional linac. However, it appears that those treatments do not yet exist, and it is certainly possible to imagine a future where FFF delivery has been relegated to a niche therapy. An intolerable cynic might even envision a future where FFF delivery—like so many alternate modalities before it—has fallen into disuse entirely, still stubbornly clinging to its theoretical superiority.

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2.6. Patient-specific QA for IMRT should be performed using software rather than hardware methods

Ramon Alfredo C. Siochi and Andrea Molineu
Reproduced from *Medical Physics* **41**, 070601-1-3 (20130
(http:// dx.doi.org /10.1118/1.4794929)

OVERVIEW

Measurement-based patient-specific quality assurance (QA) for IMRT is both time-consuming and potentially inaccurate, since the measurements are made in phantoms rather than actual patients. It has been suggested that it would be more accurate and considerably less time consuming to perform such QA with software rather than hardware, and this is the topic debated in this month's Point/Counterpoint.

Arguing for the Proposition is Alfredo Siochi, Ph.D. Dr. Siochi received his Ph.D. in Physics from Virginia Tech in 1990 and his M.S. in Radiological Physics from the University of Cincinnati in 1995. He holds over 20 patents and has more than 40 publications in radiotherapy. He developed over 17 in-house software applications, including an IMRT QA plan check suite and an IMRT sequencing algorithm in use in several treatment planning systems. He is Director of Medical Physics Education and IT Operations in the Radiation Oncology Department at the University of Iowa, and a member of many AAPM Committees and Task Groups including Chair of the AAPM Work Group on Information Technology and TG201 (Quality Assurance of External Beam Treatment Data Transfer), and Co-chair of the Radiation Safety Stakeholders Initiative. Dr. Siochi is certified by the American Board of Radiology in Therapeutic Radiological Physics.

Arguing against the Proposition is Andrea Molineu, M.S. Ms. Molineu obtained her M.S. in Medical Physics from the University of Kentucky, Lexington in 1999 and then moved to the Department of Radiation Oncology, St. Elizabeth's Medical Center, Boston, where she held a Medical Physicist appointment until 2001. She then moved to the Radiological Physics Center, Department of Radiation Physics, Division of Radiation Oncology, UT M. D. Anderson Cancer Center, Houston, TX, where she is currently a Senior Medical Physicist and Associate Director of the MD Anderson Phantom Laboratory. She is certified by the American Board of Radiology in Therapeutic Radiological Physics and her major research interests include anthropomorphic phantoms and radiotherapy QA, especially IMRT. She is a member of many AAPM committees and Task Groups and is the current Chair of the Working Group on Clinical Trials.

FOR THE PROPOSITION: Ramon Alfredo C. Siochi, Ph.D.

Opening statement

"Patient-specific QA" is a misnomer. What we really need is "Quality Control (QC)".[1] Every service for each patient is tested to ensure that it meets our safety and quality specifications. There is general agreement that, in IMRT, the specification is that the actual delivered dose (or location) should be within 3% (or 3 mm) of that planned. But what is the actual dose? Film measurements are reliable only to within 5%. Diode arrays are typically only used on a beam-by-beam basis and provide no composite information, leading to a lack of predictive power for "clinically relevant patient dose errors."[2] When arrays are used in a composite setting, there are inaccuracies due to anisotropy of response with gantry angle. Also, arrays are low-resolution devices that could potentially miss errors in un-sampled areas.

Apart from measurement inaccuracies, there is also the issue of troubleshooting combined system measurements. If something is wrong, how do you know which subsystem has the problem? Is it the linear accelerator? Or has the treatment planning system been pushed to the limits of beam modeling accuracy? Measured IMRT QA cannot parse the errors from the treatment database, planning system, and linear accelerator.

An approach that solves these issues is to treat each subsystem separately. QA is performed on the delivery system at a high enough frequency to ensure that the system is operating as needed to achieve the accuracy required for IMRT.[3] These tests should be done regardless of the number of patients receiving IMRT. QC is performed on the patient's planned dose distributions by using an independent, secondary, composite dose calculation system. Absolute dose is calculated using treatment planning system (TPS)-determined radiological depths to a single point. Treatment beam parameters used in the calculation are taken from the treatment delivery database. QC is also performed on the patient's treatment delivery parameters in the delivery system's database, to ensure that they match the values in the treatment plan.

The patient-specific portion of "IMRT QA" can be done in software.[4] This has the advantage of a quick turnaround on IMRT plan checks, reducing this from 2 h down to just 15 min. Every patient is checked, avoiding QA models that sample a few IMRT cases. We have used this method at the University of Iowa, where ROC tests, using 100 retrospective IMRT cases and 8 physicists, confirmed that our calculated "virtual film" allowed us to make better decisions than those made with film measurements.[5] This is consistent with studies showing the potential for calculations to replace measurements via control charts.[6] Furthermore, every time our calculation showed possible errors, subsequent film measurements confirmed our results. We have been successfully using this method and providing more consistent treatment planning quality control for all our IMRT patients for over five years.

AGAINST THE PROPOSITION: Andrea Molineu, M.S.

Opening statement

Why do we do patient-specific QA for IMRT? None of us wants to have the kind of errors reported by the New York Times or any smaller, yet dosimetrically significant, inaccuracies.[7] We want to ensure that the treatment we deliver is close enough to the plan we created that the patient receives the desired clinical outcome. For static 3D conformal radiotherapy fields, this can easily be achieved using software methods, because the shaped fields are defined by the user

to be something that the planning system was commissioned to accurately model. The complexity and inverse planning aspects of IMRT QA, however, require a more robust mechanism to verify that all of the small fields that are delivered have been modeled well enough so that they add together to achieve the expected dose. The dynamic aspect of the delivery along with the possibility of large dosimetric impacts due to small size differences in small fields means that we also want to verify that the planned delivery is physically achievable by the delivery system, i.e., that all of the moving parts are able to position themselves in ways that are fast enough and accurate enough to produce the planned delivery.

For this type of verification we turn to hardware, specifically measurement. Reports that often-used verification techniques may not adequately predict clinically meaningful differences may make us eager to get rid of the measurements, because we all want to spend our limited time and resources in efficient, effective ways.[2,8] However, in a report on over 13 000 plans, an analysis showed that 2.3% of the patient-specific IMRT measurements did not meet the passing criteria, and the Radiologic Physics Center has reported a pass rate of only 82% for their independent head and neck phantom measurements, so we know that not all plans meet our standards and that not all treatments are delivered as planned.[9,10] Measurement is still our best way to discover this before treating a patient with a plan that does not meet our delivery criteria, so we should work to improve our measurements, as well as our analysis, rather than rush to dismiss measurement. Measurement and analysis depend heavily on software, and we should take advantage of appropriate software advances. One such recent advance is the ability to use measurements to recalculate DVHs. This can detect clinically relevant dose errors better than the widely used gamma criteria.[11,12]

While we should be careful not to become overly dependent on computer technologies to the point that we are unable to detect mistakes or unintended outcomes of software that are certain to occur, we should continue to look for ways for software to improve how we spend our time.[13] Though software developments are important, we are not ready to abandon all measurements for patient-specific IMRT QA. Measurement gives us the best method to confirm that the plan we created can be delivered accurately. Yes, incorporate meaningful software, analyze wisely, and improve types of measurements. But it is not yet the time to get rid of measurements.

Rebuttal: Ramon Alfredo C. Siochi, Ph.D.

IMRT QA must be considered in two parts: the periodic QA for the system, and the QC for each patient. When commissioning the planning system, small field and MU limits for the desired accuracy are determined; dosimetrists must respect those limits. Verifying those limits requires measurement as part of the system QA. Checking that dosimetrists follow the constraints does not require measurement.

The types of errors reported in the New York Times[7] can be detected by software methods for verifying data transfers.[14] As for small field models, most discrepancies occur in the penumbral toe and tails. If the independent calculation uses a different model in this region from the planning system, a large number of small fields will yield differences large enough to catch the problem. Also, these regions can be modeled accurately in a solid water phantom.[5]

With respect to the IMRT delivery capabilities of the Linac, these can be verified on a periodic basis as part of the system QA. Once the limitations of the Linac have been identified at commissioning, they can be incorporated as constraints in the planning system or in the physics plan check (QC). Separating TPS QA and QC from linac QA provides a more accurate view of the IMRT system's ability to deliver the desired quality, since the source of errors can be more readily identified and efficiently monitored.

I am quite sure that most of the centers that failed the RPC credentialing tests used measurement-based methods (calculation methods are not widely implemented). While improving measurement based methods may solve these issues, developing robust 2D calculation QA could also provide a solution, while simultaneously making the process more efficient and cost-effective. (Our institution passed, by the way.) However, I do not advocate eagerly abandoning measurements. One must carefully verify through measurement that a calculation based QC process works as well as or better than hardware methods, as we did with our ROC testing. While it may not yet be time to eliminate measurements, it is always timely to improve our IMRT QA and QC processes.

Rebuttal: Andrea Molineu, M.S.

We agree that efficiencies in patient-specific QA should be found and employed when appropriate. However, I am not willing to automatically write off differences between secondary calculations and measurements as inaccuracies in measurements rather than inaccuracies in the dose calculations. We should have an understanding of why we sometimes get positive results with film and not with software calculations. Are those results truly false positives? Assuming measurement inaccuracies only for false positives, without addressing why we do not uniformly see inaccuracies, is an insufficient reason to choose software checks over measurements. We should investigate whether there is something unique or different about those cases that explains having measurement inaccuracy that would not also logically predict the same inaccuracy in the true negative cases.

As the RPC's head and neck phantom data from 2012 indicates,[10] we are still having problems accurately modeling and commissioning our primary treatment planning systems to accurately predict all of the complexities that are present in some patient treatments. There is no reason to think that a secondary system, which is not currently an option for many clinics, would not have many of the same differences.

Certainly statistical process control can and should be implemented in software checks as well as measurements, which should improve both our accuracy and efficiency. Measurements have limitations that we should understand, but I am not convinced that we are ready to summarily throw out patient-specific measurements.

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2.7. The more important heavy charged particle radiotherapy of the future is more likely to be with heavy ions rather than protons

Oliver Jäkel and Alfred R. Smith
Reproduced from *Medical Physics* **41**, 090601-1-4 (2013)
(http:// dx.doi.org /10.1118/1.4798945)

OVERVIEW

Over the past decade there has been considerable interest and progress in the use of heavy ions such as protons and carbon in an attempt to improve the effectiveness of radiotherapy. Both have a physical advantage over photons because of their Bragg peaks, but only heavier ions such as carbon have a potential biological advantage. This has led to the claim that the most important heavy charged particle radiotherapy of the future is more likely to be with heavy ions rather than protons, and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Oliver Jäkel, Ph.D. Dr. Jäkel completed his Ph.D. in Theoretical Physics at the University Erlangen, Germany in 1994. He then moved to the Department for Medical Physics, German Cancer Research Center (DKFZ), Heidelberg, where he is currently Full Professor and Director of the Heidelberg Ion Beam Therapy Facility of the University Hospital. Dr. Jäkel is a member of the Editorial Board of *Physics in Medicine and Biology* and has served on the Board of Editors of *Medical Physics*. His major research interests are treatment planning, new dosimetry techniques, optimizing quality assurance procedures, and imaging with particle beams.

Arguing against the Proposition is Alfred R. Smith, Ph.D. Dr. Smith obtained his Ph.D. in Physics from Texas Tech University, Lubbock, TX, in 1970. After completing a Postdoctoral Fellowship in Medical Physics at The University of Texas, M. D. Anderson Hospital and Tumor Institute, he held faculty positions at several institutions until he moved back to M. D. Anderson in 2002 as a Full Professor and Director of Proton Therapy Development, a position he held until 2010. Dr. Smith is a Fellow of the AAPM and the ACMP. His most recent major research interest has been in proton therapy, although over the years he has published extensively on other exotic forms of therapy such as neutrons, pions, and Cf-252 brachytherapy, for which he has published over 80 papers.

FOR THE PROPOSITION: Oliver Jäkel, Ph.D.

Opening Statement

I would like to make two opening statements to underline my viewpoint and explain these in more detail below:

> (i)With respect to their physical properties, heavier ions can do everything that can be done with protons, but better.

(ii)With respect to biology, heavier ions have the potential to significantly improve clinical results at least for selected indications, including especially hypoxic tumors.

Ions heavier than protons provide superior physical dose distributions due to reduced lateral scattering, reduced range straggling, and an increased ratio of dose in the target relative to the entrance region.[1] In this regard, helium ions could replace protons leading to improved dose conformation at a comparable technical complexity (i.e., price) while maintaining biological properties comparable to those of protons.[2,3]

Another physical aspect is connected with accurate targeting. In many cases, the clinical advantage of ions may be seriously limited if the range cannot be controlled accurately, e.g., in the presence of heterogeneous tissues, setup errors, or organ motion. The related uncertainties largely prevent beam directions with organs at risk directly behind the Bragg-peak. In some clinical cases, the use of ions may, in fact, be inferior to modern photon techniques, as the latter are much more robust against these uncertainties. This is, of course, a common problem of heavy charged particles and challenges the often stated superiority of ions over photons. Heavier ions, however, offer some possibilities to measure the range *in vivo* and thus to verify accurate positioning of the Bragg-peak. These *in vivo* measurements make use of tissue activation,[4] radioactive beams, or prompt secondary particles produced in nuclear reactions, and are not feasible with protons.[5,6]

The most important rationale for heavier ions, however, originates from the biology of high-LET radiation.[7,8] This is the increased RBE in the tumor relative to the normal tissue and the increased effectiveness in hypoxic tumors.[9] Probably not all patients will benefit from this, but for some dedicated indications, especially when highly resistant tumors and hypoxia are involved, this may make a great difference. Currently, evidence for the clinical benefit of high-LET radiation is still lacking and the necessary clinical trials are just being initiated. But even if this biological advantage would finally not be significant, the physical advantages remain and, leaving aside financial considerations, heavier ions would be the modality of choice in the future.

Finally, the clinical benefit resulting from the dose sparing potential of protons relative to photons may in some cases be too small to justify the additional costs for proton facilities in the long term. This is especially the case in view of the enormous and still ongoing improvements achieved in photon RT.

In conclusion, I think that both the substantial physical and biological potential of heavier ions will make them more important in the future than protons: more important in terms of clinical research opportunities and more important for some patients with tumors which cannot be cured with low-LET radiation.

AGAINST THE PROPOSITION: Alfred R. Smith, Ph.D.

Opening Statement

I will use the term “carbon ions” here as a surrogate for high-LET charged particles; they are the only high-LET charged particles to be used extensively in clinical investigations. Clinically,

protons are considered to be low-LET particles. Carbon ions and protons have similar *physical* dose distributions; however, carbon ions have a presumed biological advantage arising from high-LET, which leads to higher RBE and lower OER. The rationale for carbon therapy is based on the hypothesis that high-LET carbon ions are more effective in killing oxygen-deficient tumor cells that are radioresistant to low-LET photons and protons. High-LET biological effects are complex, depending on a number of treatment and tissue factors and will not be discussed here.[1,10]

Approximately 95 000 patients have been treated with protons and 13 000 with carbon ions. The argument against the stated proposition is based on the following factors:

- Carbon ion facilities cost ~2–3 times more than proton facilities.
- Due to the large size and cost of isocentric gantries for carbon therapy, most treatments have been given with fixed beams having less clinical flexibility than isocentric gantries.
- Large uncertainties in the RBE in the carbon spread-out Bragg peak (SOBP) (~1.5–3.4) can result in large variations in the delivered biological dose in the target volume. RBE values for normal and tumor tissues are not well known for protons or carbon ions.[10]
- Carbon ions, due to their high/variable RBE, have the potential for increased risk of normal tissue damage.[10]
- Due to fractionation effects, tumor cells that are initially oxygen-depleted may reoxygenate during a course of proton treatment—this may diminish/eliminate the hypothesized advantage of carbon ions.
- Carbon ion depth-dose distributions exhibit a "tail" of particle fragments created by fragmentation of carbon ions in the primary beam due to nuclear interactions. This tail contains high-LET components and continues for a distance (depending on initial ion energy) into normal tissues distal to the target volume.[1] Proton beams do not have a tail in their dose distribution.[10]
- The theoretical advantages of carbon ions over protons have not been proven in a clinical setting. Studies performed this far have shown an approximate equivalence of both modalities.[1,10–12]
- In the USA, there is no FDA certification; there are no approved treatment procedure codes; and there is no approved reimbursement for carbon ion therapy.

Modern proton therapy systems have substantially reduced the cost of proton facilities. Small hospitals/cancer centers and large clinical practices are now able to provide proton therapy; the growth curve for new facilities is steep. This situation is opposite for carbon ions: Carbon ions are biologically complex; facilities are too expensive; and there are too few facilities to conduct proton vs carbon prospective and randomized clinical trials required to compare the two modalities. Extremely high costs and the lack of data showing clinical superiority are major deterrents for carbon therapy. It is highly unlikely that carbon ions will replace protons in cancer treatment.

Rebuttal: Oliver Jäkel, Ph.D.

My opponent points out several problems for carbon ion therapy: higher costs, lack of evidence, lack of gantries, and large RBE uncertainties. All these arguments are valid, but I think they all hold likewise against protons and they conceal the potential of heavier ions.

The lack of FDA approval and reimbursement and unrealistic costs for carbon therapy may be specific to the USA (the average reimbursement in the USA for protons is $36k vs €19k for carbon in Europe) so cost may not hinder the development of ion therapy elsewhere. While technology is likely to reduce the cost for carbon ions in the future, both modalities will remain costly. These costs may be worthwhile if a clinical benefit can be gained.

The lack of clinical evidence is, of course, as critical for protons as it is for carbon: a recent critical review of proton therapy for brain tumors showed that, despite reduced integral doses, no reduction of adverse events could be demonstrated.[13] Also, the ASTRO Emerging Technology Committee concluded that further clinical research is needed.[14] One reason may be biology: while the variable RBE is modeled in detail for ions, the simplification of proton RBE as commonly used in clinics may be associated with substantial uncertainties.

The FDA approval of protons in the US facilitated clinical application but may have reduced the urge for clinical trials. Also, commercial interest resulted in the development of some low-cost solutions for protons which may not allow for the highest treatment quality. Some proton vendors even sacrificed gantries, which have just been introduced successfully for carbon. There will soon be 10 carbon facilities in operation in Asia and Europe,[15] which will give ample possibilities for clinical trials.

Currently, ion therapy relates to carbon only but it may turn out that other ions can do better for specific indications, be it due to physics or biology. Anything that protons can do, heavier ions can do better! It is our task to continue exploring the full clinical potential of heavy ions and not just the cheapest, easiest, but potentially least beneficial ion species.

Rebuttal: Alfred R. Smith, Ph.D.

My colleague correctly states that heavy ions have sharper lateral penumbras than protons. They have higher charge, greater mass, and require higher energies per nucleon for the same range in tissue. Therefore, multiple Coulomb scattering of the primary beam is smaller for heavy ions than for protons.[16] However, heavy ions have a “fragmentation tail” that penetrates beyond the range of the primary beam and this dose tail contains some relatively high RBE components. This unwanted/unnecessary dose must be explicitly included in treatment planning to avoid unanticipated “hot-spots” in adjacent normal tissues.[16] For equivalent range in tissue, Bragg-peak dose distributions of proton and carbon beams show that protons have a lower relative entrance dose and stop at the end of their range without having a fragmentation tail.

He also states that heavier ion ranges can be measured *in vivo* but fails to mention that such techniques, e.g., positron tomography, have been shown by many authors to be effective also for proton beams.[17–19]

The *theoretical* biological advantage offered by carbon ion beams is based on the existence of hypoxia in tumor cells and/or an increased RBE in the tumor relative to normal tissues. To date, this *potential* advantage has not been demonstrated in clinical studies; in fact, studies have shown a relative equivalence in clinical results from proton and carbon ion treatments.[16–19]

My colleague correctly states that, "Currently, evidence for the clinical benefit of high-LET radiation is still lacking …" and yet he concludes, "… and leaving aside financial considerations, heavier ions would be the modality of choice in the future." This is not logical; if there is no demonstrated clinical benefit and the cost differential is quite large, the conclusion that heavier ions would be the modality of choice in the future is unfounded.

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2.8. The disadvantages of a multileaf collimator for proton radiotherapy outweigh its advantages

Juliane Daartz and Richard L. Maughan
Reproduced from *Medical Physics* **41**, 020601-1-3 (2014)
(http:// dx.doi.org /10.1118/1.4824437)

OVERVIEW

Multileaf collimators (MLCs) are commonly used to shape fields for photon beam radiotherapy but only rarely for protons. Early proton therapy machines used customized shielding blocks to shape individual fields, much like the cerrobend blocks used for photon therapy, whereas the latest proton machines use pencil beam scanning, whereby beams can be shaped electronically. Despite this new technology, however, some have chosen to employ MLCs for shaping proton beams, primarily because of their superior efficiency. Others, on the other hand, claim that the disadvantages of MLCs used in proton therapy outweigh the advantages. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Juliane Daartz, Ph.D. Dr. Daartz obtained her Ph.D. in Physics in 2011 from the University of Heidelberg, Germany. Prior to that she was a physicist in proton therapy at the Massachusetts General Hospital, Boston from 2006 to 2010, and at the Paul Scherrer Institut, Villigen, Switzerland in 2010, after which she returned to MGH, where she is currently a physicist in the Radiation Oncology Department and Instructor at Harvard Medical School. Dr. Daartz's major research interests include evaluation of the use of MLCs for intensity modulated proton therapy (her Ph.D. thesis topic), proton and photon radiosurgery, and dosimetry of small proton fields. She is certified in Therapeutic Radiological Physics by the American Board of Radiology.

Arguing against the Proposition is Richard L. Maughan, Ph.D. Dr. Maughan obtained his Ph.D. in Nuclear Physics in 1974 from the University of Birmingham, England. From 1974 to 1983, he worked as a member of the scientific staff of the Cancer Research Campaign Gray Laboratory at Mount Vernon Hospital in England, where he was involved in basic radiation physics, chemistry, and radiation biology research. He moved to the USA in 1983 when he took a position as a medical physicist and a member of the faculty in the Radiation Oncology Department of Wayne State University, Detroit, where he played a major role in development and application of a superconducting cyclotron for neutron radiation therapy. In 2000, Dr. Maughan moved to the University of Pennsylvania as Professor and Director of the Medical Physics Division, where he is currently Department Vice-Chair. His research interests are particle therapy with neutrons, heavy ions, and especially protons.

FOR THE PROPOSITION: Juliane Daartz, Ph.D.

Opening Statement

In conventional therapy, multileaf collimators are used for 3D conformal and intensity modulated dose delivery. This debate on proton therapy mostly revolves around the use of MLCs for simple final collimation.

Gottschalk[1] describes the potential detriment of employing a universal MLC (a single device for all patients) for this purpose in passively scattered proton fields. The bulky device necessitates a large air gap which, in combination with a large double-scattering source size, degrades the lateral penumbra. The effect is aggravated by the range compensator, an additional source of scatter placed far away from the patient surface. Decreased distal conformality is an additional consequence of a large air gap. Depending on leaf size, the scalloping effect, even though mitigated at treatment depth by multiple Coulomb scattering, worsens lateral conformality and falloff. Additional issues arise from thick collimators, ranging from even further degradation of lateral penumbra to added complexity in dose modeling.

For a significant fraction of proton indications, the dosimetric effects listed above will result in lower target doses due to the target's proximity to critical structures. The optimum dose distribution is achieved by a thin collimator as close to the patient surface as possible. This holds true for uniform (US) and pencil beam scanning (PBS) deliveries, albeit to a lesser extent given the smaller source sizes. Efficiency in today's proton therapy is still not on a par with conventional photon radiotherapy. The use of MLCs could help but, unlike many other improvements the proton community is presently tackling, it comes at the cost of compromised dose distributions. Pencil beam scanning is generally regarded as the future of proton therapy delivery, replacing passive scattering as the primary mode for large proton field production. PBS systems promise great flexibility in dose application, comparatively simple system QA, and much more efficient treatment planning and delivery. PBS permits intensity modulated proton therapy. This can also be achieved with a multileaf collimator, analogous to conventional therapy. The general feasibility has been shown,[2] but its performance depends on implementation and the properties of the delivery system. Treatment time may prove problematic, and maximum field size continues to pose a challenge.

In summary, the use of MLCs for final collimation in passive scattering and scanned beam delivery comes with degradation of the dose distribution. Use for intensity modulation in passive scattering may improve the quality of dose distributions, but is linked to increased effort in quality assurance and will most likely be outperformed by pencil beam scanning systems.

AGAINST THE PROPOSITION: Richard L. Maughan, Ph.D.

Opening Statement

The use of a multileaf collimator for proton therapy has not been widely investigated. The HIMAC facility in Hyogo, Japan, uses an MLC with a ^{12}C beam in the treatment of extracranial lesions.[3] Daartz *et al.*[4] investigated the use of a mini-multileaf collimator (MMLC) for use in passively scattered proton beam therapy for intracranial lesions. At the University of Pennsylvania Roberts Proton Therapy Center, four MLCs are used on gantry mounted nozzles for shaping passively scattered and uniformly scanned beams for all treatment sites. These MLCs were built in a joint collaboration between the University of Pennsylvania, Ion Beam

Applications, SA (Louvain-La-Neuve, Belgium) and Varian Medical Systems (Palo Alto, CA). The primary reason for installing these devices was to improve beam delivery efficiency.

The MLC has a leaf width giving a 5 mm projection at the isocenter and beams of up to 25 × 18 cm^2 are delivered in double scattering and uniform scanning mode. Data show that the 20%–80% penumbra achieved with a beam of range 22 cm, modulation 10 cm, measured using film at the isocenter, at depth of 17 cm in solid water, with a collimator-to-surface distance (CSD) of 16 cm, and a 10 × 10 cm^2 field size is 9.6 ± 0.6 mm. This penumbra can be compared with data from Fig. 3 of Safai *et al.*[5] where the penumbra for an unmodulated beam of 22 cm range, with a CSD of 10 cm and a brass aperture, of unspecified size, is 7.9 ± 0.2 mm. Oozeer *et al.*[6] showed that penumbral width as a function of depth is practically independent of modulation and that variations with field size are also small. The differences in these penumbras can most likely be attributed to the differences in the CSD, which introduces more air scattering in the case of the MLC measurements.

CSD may be an issue with an MLC, since their large dimensions compared to brass apertures when used for treating small and intermediate sized fields, dictate that the MLC be positioned at a greater CSD than for an aperture. The collimator housing, therefore, is designed to have a D-shape allowing access over the patient's shoulder, minimizing the air gap for brain and base of skull treatments. For head-and-neck patients many fields are large, extending below the shoulder, which require larger air gaps even with brass apertures. The collimator has tungsten leafs; concerns about leaf activation and excessive neutron dose[7,8] have proved to be unsupported.[4,9,10]

The University of Pennsylvania experience in using an MLC with double scattered and uniform scanning beams has shown it to be convenient in use and well suited to a department where a large number of complex treatments are delivered with two or more fields. It increases efficiency and eliminates the need for the storage of brass apertures. Our clinical experience confirms the conclusions of Daartz *et al.*[4] that there are "only small differences in the dose distributions obtained with brass apertures and the MMLC."

Rebuttal: Juliane Daartz, Ph.D.

We are focusing the debate on the dosimetry of multileaf collimators as used for final collimation. Once more we end up in a stalemate between "penumbra is always worse" and "but not significantly." It seems that we agree: it is worse. How much worse? That depends on the device. It should be obvious that the results of our 2009 study performed using a mini-MLC with 2.5 mm leaf size and a maximum field of 8 × 6 cm^2 cannot be transcribed to a large universal MLC, necessitating larger CSD, with 5 mm leaf thickness.[2]

The penumbra in a collimated beam is a function of depth, energy, CSD, SAD, source size, and range compensator thickness. Unless obtained under the same conditions, since the varying parameter is the mode of collimation, penumbral widths should not be compared. Dr. Maughan mentions penumbral widths for a single beam energy, without information on source size or SAD, CSD varying by 6 cm and a depth of measurement of 17 cm for the MLC and 21 cm for the aperture. But assuming this comparison is valid—even with a D-shaped MLC housing, minimizing CSD, there is little doubt that air gap is still larger than for custom-milled apertures.

Considering the cranial component of a head-and-neck treatment plan, where the most critical organs are to be spared, the air gap with apertures is 2–3 cm. Widening of the penumbra by 2 mm will result in notably decreased target coverage. In addition, these numbers neglect the effect of a range compensator—amplifying the impact of increased CSD.

This reasoning disqualifies the use of a large, thick-leaf universal MLC from application to cranial sites. Does the argument of gained efficiency still hold if one has to employ a different mode of collimation for a rather large subset of our typical proton patients? Other than qualitative statements, there are no data quantifying the effect of universal MLCs on efficiency. Commissioning and routine quality assurance for an MLC are a substantial effort. In addition, it is one more device that potentially fails during operation and causes downtime. The limitation in field size necessitates splitting fields into abutting areas more frequently.

Despite the promise, MLCs have not been widely adapted in the field. Perhaps, the practical advantages are not that convincing after all.

Rebuttal: Richard L. Maughan, Ph.D.

As pointed out by Dr. Daartz, the future of proton therapy lies in the development of more efficient pencil beam scanning systems; this requires faster scanning times and, more importantly, faster layer switching times. PBS has multiple advantages over passive scattering; better dose conformality (especially on the proximal field edge), the ability to treat large fields (up to 30×40 cm^2) without field matching or patching, and the possibility of intensity modulated proton therapy. However, presently the treatment of moving targets with PBS remains problematic, since gating, breath-hold, and over scanning all reduce efficiency significantly.

The University of Pennsylvania's five treatment room system was originally configured with two gantries with passive scattering, US, and PBS, two gantries with passive scattering and US, and a fixed horizontal beamline with PBS only. Experience treating with PBS in the fixed beam and in one gantry room has convinced us that our final room configuration will comprise three PBS rooms (two gantries, one fixed beam) and two gantries with passive scattering.

With this combination, it will be possible to select the patients best suited for treatment with MLC based passive scattering and those requiring the improved dose conformality of PBS beams, which have beam-spot diameter σ-values of 3 and 4 mm in air at 230 MeV, for the fixed beam and gantry rooms, respectively. Targets with appreciable motion will be treated with passive scattering until robust solutions for motion management of PBS delivery are established. The use of an MLC with PBS will be challenging as the MLC required to treat large fields would be impractically large. Developing beams with a smaller sigma may be a better solution for improving penumbra. In conclusion, we find that using an MLC for proton beam shaping does not compromise our treatment plans, but leads to greater efficiency in handling the patient throughput.

ACKNOWLEDGMENT

RLM acknowledges that this work was supported in part by the US Army Medical Research and Materiel Command under Contract Agreement No. DAMD17-W81XWH-04-2-022. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the US Army.

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2.9. A 3D-conformal technique is better than IMRT or VMAT for lung SBRT

Jing Cai and Harish K. Malhotra
Reproduced from *Medical Physics* **41**, 040601-1-4 (2014)
(http:// dx.doi.org /10.1118/1.4856175)

OVERVIEW

Most clinical studies of stereotactic body radiation therapy (SBRT) for the treatment of lung cancers have employed 3D conformal radiotherapy (3DCRT) techniques. Recently, however, there has been a trend toward using the more technologically advanced intensity modulated radiation therapy (IMRT) or volumetrically modulated arc therapy (VMAT) for these treatments. Some claim, however, that 3DCRT is better than IMRT or VMAT for lung SBRT, and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Jing Cai, Ph.D. Dr. Cai obtained his Ph.D. degree in Engineering Physics in 2006 from the University of Virginia where he subsequently completed a one-year Postdoctoral Fellowship and a two-year Medical Physics Residency. He moved to Duke University Medical Center in 2009, where he is currently an Associate Professor in the Department Radiation Oncology. He is certified in Therapeutic Radiologic Physics by the American Board of Radiology. Dr. Cai's major research interests include image-guided radiation therapy, 4D imaging and planning, stereotactic-body radiotherapy, brachytherapy, and MRI. He has published over 40 papers on these topics and regularly provides scientific reviews for peer-reviewed journals, scientific conferences, and grant applications. His research has received federal, charitable, and industrial funding.

Arguing against the Proposition is Harish K. Malhotra, Ph.D. Dr. Malhotra joined the faculty of Roswell Park Cancer Institute (RPCI) in 2002 and is a Senior Physicist in the Department of Radiation Medicine. He serves as Assistant Professor in the Department of Molecular and Cellular Biophysics in RPCI's Graduate Division of the State University of New York. Dr. Malhotra earned his doctorate in physics from the University of Mumbai, India, and completed a post-doctoral fellowship in Medical Physics at Montefiore Medical Center, Albert Einstein College of Medicine, New York. He is certified in Therapeutic Radiologic Physics by the American Board of Radiology and is licensed by the State of New York to practice Therapeutic Medical Physics. Dr. Malhotra is a Section Editor of the *Journal of Applied Clinical Medical Physics*, has served on the Board of Chancellors of the ACMP and as President of the Upstate New York Chapter of the AAPM. He has published about 30 papers in refereed journals and has been the major advisor to five M.S. students.

FOR THE PROPOSITION: Jing Cai, Ph.D.

Opening Statement

Recently there has been an increase in use of IMRT and VMAT to treat SBRT of the lung. Comparison treatment planning studies have shown that IMRT and VMAT usually result in more critical structure sparing than 3DCRT.[1,2] However, lung SBRT is a complex treatment, involving multiple steps (imaging, planning, delivery, and quality assurance of each step) with multiple layers of uncertainties. Debating the relative merits and drawbacks of different techniques for lung SBRT should take into account every aspect of the process. A good technique not only generates good plans but also delivers them without deviations. 3DCRT has unique advantages over IMRT and VMAT in this regard. First, 3DCRT is not susceptible to the interplay effect between MLC leaf motion and tumor respiratory motion. Similarly, compared to IMRT and VMAT 3DCRT is less affected by patient movement during treatment, MLC positioning errors, and the limited accuracy of MLC modeling in treatment planning systems. 3DCRT therefore is expected to have a better agreement in target coverage between the plan and delivered treatment than IMRT and VMAT, especially when there is large respiratory tumor motion or significant modulation in IMRT or VMAT. Second, 3DCRT allows for cine MV imaging during treatment delivery. These images not only verify tumor position in real-time during beam-on, but also provide information that can be used for determining the true 4D dose delivered to the tumor[3] and for developing more effective lung SBRT treatments, such as tumor trailing,[4] probability-based treatment planning,[5] and adaptive radiation therapy.[6] Cine MV imaging is not applicable to IMRT or VMAT since the moving MLC leaves block the majority of the beam view.

Furthermore, in our current health care environment where cost is increasingly important, cost-effectiveness needs to be taken into consideration when selecting the technique. 3DCRT is less expensive than IMRT and VMAT.

Obviously not *all* lung SBRT cases are best treated with 3DCRT. Lung tumors vary in location, size, motion, and grade. Some may be more effectively treated using a specific modality than others. Nevertheless, institutional experiences at Duke University Medical Center suggest that the majority of lung SBRT cases (~70%) can be treated effectively with 3DCRT.[7] IMRT and VMAT are used only for carefully selected patients with large tumor size, small tumor motion, or whose dose sparing cannot be achieved with 3DCRT due to the proximity of critical structures.

ASTRO recently initiated its national *Choosing Wisely* campaign to question the use of treatments that are commonly ordered but may not always be appropriate. In echo with this initiative, I conclude my opening statement by recommending that one should not routinely use IMRT or VMAT for lung SBRT without considering 3DCRT.

AGAINST THE PROPOSITION: Harish K. Malhotra, Ph.D.

Opening Statement

The arrival of 3DCRT into mainstream clinics in the 1980s was an important milestone in the evolution of radiation therapy. Parameters like number of fields and their spatial orientation with respect to tumor and organs at risk, and limited beam modulation options (beam energy, weight, wedges, blocks, etc.), were iteratively adjusted to get a clinically acceptable treatment plan but

one which may not have been the optimal plan. The skill and experience of the planner played an important role in such 3DCRT planning.

The turning point in the evolution of modern radiation therapy came in the 1990s with the advent of IMRT. The synergy of an inverse optimization engine, better dose computation algorithms, linear accelerators supporting precise dynamic motions, and the ability to target the tumor better with image guided radiation therapy (IGRT), etc., significantly boosted technical abilities. The optimization engine has been much more forgiving (number of beams and their spatial orientation) and searched for global minima, thereby producing consistently better plans. VMAT further improved work flow efficiency by ensuring that the entire treatment could be delivered in 1–2 arcs.

Recently, lung SBRT has shown excellent local control.[8] In the past, SBRT has most often been delivered using 3DCRT. Though SBRT in general has been well tolerated, Fakiris *et al.*[9] reported 17% grade 3–5 toxicities, while Timmerman *et al.*[8] reported 12.7% grade 3 toxicities. There are also reported cases of rib fractures.[10] Many 3DCRT plans have dosimetric minor deviations which could be improved with IMRT/VMAT. In a recent study, IMRT/VMAT plans were shown to consistently outperform their respective 3DCRT plans in almost every dosimetric aspect.[11] SBRT for advanced central lung cancers requiring nodal irradiation along with primary disease is also being attempted.[12] In our preliminary experience, this requires treating complex geographically separated volumes requiring different simultaneous prescription doses for the primary and nodal beds that can be handled better with IMRT/VMAT.

There is concern that in the absence of any synchronization between a moving tumor and dynamic motions inherent in IMRT/VMAT techniques, there may be significant underdosage of portions of the tumor volume. In ten patients, Rao *et al.*[13] found that both VMAT and IMRT plans experienced a negligible MLC interplay effect with a 400 MU/min repetition rate. Similarly, two arcs and ≥2 fractions have been shown to reduce the MLC interplay effect to an apparently clinically insignificant level for FFF beams.[1] If respiratory gating is employed or a simple abdominal compression is used to dampen the tumor motion, the results are expected to be even better.

Whilst it is possible to generate an acceptable SBRT plan for peripheral lung tumors using 3DCRT, it becomes much more challenging for central lung tumors, including advanced tumors, because of the close proximity of critical structures, which can be better handled consistently with IMRT/VMAT. If low dose to large volumes of normal tissues is not of clinical concern, VMAT can even deliver it quickly making the procedure better tolerable to the patient, with reduced intrafraction motion, and less loss of biological effect due to prolonged fraction delivery.[14] Improvement in work flow efficiency and optimal use of departmental resources is the icing on the cake.

Rebuttal: Jing Cai, Ph.D.

My opponent argues in favor of IMRT/VMAT mainly from three perspectives: plan quality, planning ability, and work flow efficiency. First, I agree that IMRT/VMAT usually exhibits a dosimetric advantage over 3DCRT, especially when the target volume is geographically complex

or is in close proximity to critical structures. In the majority of lung SBRT cases, however, the target volume has a simple geometry and 3DCRT can generate plans that are clinically equivalent to those with IMRT/VMAT. Any slight dosimetric advantages of IMRT/VMAT will be diminished in practice due to various uncertainties.

Regarding planning ability, my opponent argues that skill and experience of the planner play an important role in 3DCRT planning, while IMRT/VMAT produces consistently better plans using inverse optimization. Although this is generally true, it should not matter for lung SBRT since the planning is relatively simple due to the small target volume and the simple geometrical relationship between target volume and critical structures. Furthermore, IMRT/VMAT planning has its own challenges, such as limited beam arrangements and couch angles for VMAT in noncoplanar planning, and interplay effects for large tumor motion and the high dose rate for FFF beams.

Finally, I want to address the issue of work flow efficiency. IMRT/VMAT requires patient-specific QA, demanding substantial time for preparation, delivery, and documentation. In addition, image verification contributes significantly to the overall treatment time. 3DCRT allows for real-time verification using cine MV imaging during beam on, thus eliminating the need for pre- and post-treatment image verification that are usually required in IMRT/VMAT. Furthermore, the high dose rate with FFF beams (1400 or 2400 MU/min) can improve delivery efficiency for 3DCRT but not much for VMAT, for which treatment delivery time is largely limited by the gantry rotation speed.[2]

Rebuttal: Harish K. Malhotra, Ph.D.

My opponent agrees with me that IMRT/VMAT SBRT plans are dosimetrically superior. He has concerns, however, about their suboptimal delivery and robustness but has not supported this with any literature. Modern linacs are pretty reliable[15] and are well modeled in treatment planning systems. Their parameters are monitored every 10–50 ms for compliance with interlocks for out-of-tolerance behavior. Thousands of patients are getting IMRT/VMAT treatments every day, with satisfactory pretreatment QA. SBRT lung plans usually do not have high modulation[6] and high dose/fraction allows MLC leaves and gantry to move slowly,[13] thereby reducing dose delivery uncertainties. As with other radiotherapy techniques, end-to-end testing provides necessary confidence in the entire SBRT dose delivery chain. Better immobilization, coupled with gating/abdominal-compression, minimizes motion-related concerns.

Cine MV-imaging for intrafraction motion is not supported on new flattening-filter-free beams which now have better alternatives which do not degrade throughput (simultaneous kV-imaging, radiofrequency tracking, etc.). Manufacturers usually cap MV-imaging to 100 MU/min, which increases treatment times substantially. Is it ethical to deny patients access to better IMRT/VMAT plans with the justification that cine MV-imaging data may pave the way for a better delivery?

That 3DCRT for SBRT is inexpensive is a myth. IGRT requirements for SBRT (Ref. 16) require higher-end linacs which have IMRT and/or VMAT capabilities anyway. Slow 3DCRT delivery

represents underutilization of resources, affects throughput and hence possible revenue. If the total cost of treatment delivery is calculated including the time commitment of staff-members (physician, physicist, therapists), 3DCRT might be the costliest.

Eventually, everything boils down to clinical results. In a recent study comparing early results for 132 nonsmall-cell lung patients (86-3DCRT, 46-VMAT), the one-year local control rates for VMAT (100%) and 3DCRT (92.5%), favored VMAT ($p = 0.03$).[17] These statistically significant results demonstrate robustness of the IMRT/VMAT dose delivery chain and should allay my opponent's concerns. I wholeheartedly support research initiatives but without sacrificing better IMRT/VMAT plans. Our patients deserve the best modality currently available.

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2.10. Because of the advantages of rotational techniques, conventional IMRT will soon become obsolete

Richard A. Popple and Peter A. Balter
Reproduced from *Medical Physics* **41**, 100601-1-4 (2014)
(http:// dx.doi.org /10.1118/1.4885996)

OVERVIEW

In recent years, a variety of intensity modulated radiation therapy (IMRT) delivery techniques have been developed that have provided clinicians with the ability to deliver highly conformal dose distributions. The delivery techniques include step-and-shoot IMRT, sliding window IMRT, volumetric modulated arc therapy (VMAT), and tomotherapy. A key development in the field of IMRT was the introduction of new planning algorithms and delivery control systems in 2007 that made it possible to coordinate the gantry rotation speed, dose rate, and multileaf collimator leaf positions during the delivery of arc therapy. With these developments, VMAT became a routine clinical tool. The use of rotational techniques has continued to increase in recent years and some would argue that this will soon make conventional IMRT obsolete, and this is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Richard A. Popple, Ph.D. Dr. Popple obtained his Ph.D. from Rice University, Houston, TX, and, after 2-yr postdoctoral fellowships at Rice and the University of Texas MD Anderson Cancer Center, Houston, moved to the Department of Radiation Oncology, The University of Alabama at Birmingham, where he is currently Professor and Medical Physics Residency Director. Dr. Popple is certified in Therapeutic Radiologic Physics by the American Board of Radiology. He has been active on several AAPM committees and serves as a Section Editor for the *Journal of Applied Clinical Medical Physics*. His major research interests include volumetric modulated arc therapy, dosimetry of small fields, treatment planning optimization, and quality assurance, and he has published over 50 papers in peer-reviewed journals.

Arguing against the Proposition is Peter A. Balter, Ph.D. Dr. Balter obtained his Ph.D. in Medical Physics from the University of Texas Houston Graduate School of Biomedical Sciences, Houston, TX, having already worked as a Medical Physicist for several years in the Department of Radiation Physics, Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, where he is currently Associate Professor and Associate Director of the Accredited Dosimetry Calibration Laboratory. Dr. Balter is certified in Therapeutic Radiologic Physics by the American Board of Radiology and examines on the Board. He has been active on several committees in the AAPM and has served as President of the Southwest Chapter. His major research interests include Cyberknife stereotactic radiosurgery, 4D-CT simulation and CT perfusion, advanced volumetric imaging and adaptive radiotherapy for detecting and correcting for interfractional change, flat-panel based cone beam CT for 3D chest imaging, and proton therapy. He has published over 50 papers on these and related topics in peer-reviewed journals.

FOR THE PROPOSITION: Richard A. Popple, Ph.D.

Opening Statement

From the beginning of civilization, increasingly sophisticated technologies have replaced older, less efficient ones. Conventional IMRT using stationary gantry locations will not escape this paradigm and will be displaced by rotational techniques. The first rotational technique for delivery of intensity modulation was proposed by Mackie and coworkers in 1993.[1] Although tomotherapy, first serial and then helical, was adopted by a modest number of centers, widespread adoption was limited by the need for specialized equipment. Shortly after the introduction of tomotherapy, Yu proposed intensity modulated arc therapy (IMAT), a rotational technique based on dynamic multileaf collimation (MLC).[2] IMAT did not require specialized equipment and had the potential for broad implementation on ubiquitous C-arm linear accelerators but was complex to plan and no more efficient than fixed gantry IMRT. Consequently, IMAT remained confined to a handful of academic centers. Rotational techniques languished while static gantry intensity modulated radiation therapy techniques (conventional IMRT) entered widespread clinical use. The situation changed dramatically in 2008 with the introduction of new planning techniques that, in combination with variable dose-rate delivery, were capable of creating treatment plans having dose distributions comparable to static gantry IMRT using a single arc.[3] Consequently, IMAT became substantially more efficient in terms of treatment time than stationary field techniques.

IMAT is a stage in the ongoing evolution of radiation therapy, during which the roles of computer optimization and computer control have been steadily increasing. Static techniques in which the human operator sets machine parameters have given way to dynamic techniques and increasing automation. The dynamic wedge introduced preprogrammed motion of a single collimator jaw during irradiation.[4] Dynamic multileaf collimation increased treatment complexity by moving tens of MLC leaves in a prescribed, patient-specific trajectory.[5] IMAT added gantry rotation to dynamic MLC motion,[2] and VMAT added variable dose rate.[3] Treatment planning has undergone a similar evolution, progressing from the human planner selecting a handful of machine settings and calculating the resulting dose, to the human planner specifying the desired dose distribution characteristics and the computer optimizing the positions and trajectories of hundreds of machine parameters.

Treatment-machine control systems are becoming more sophisticated, providing programmed control of all machine parameters while the machine is delivering radiation. This allows, for example, an entire conventional IMRT plan to be delivered without intervention of the human operator, blurring the distinction between fixed gantry and rotational techniques. Should such a treatment be considered fixed gantry or a “step-and-shoot” type of rotational treatment? Work is underway to optimally mix fixed gantry modulation with IMAT.[6] These hybrid plans can be presented to the machine control system as a single set of control points, further blurring the line between conventional IMRT and rotational techniques. Advanced control systems allow motion of the table and collimator as well, and there is active work on planning techniques that exploit machine trajectories.[7]

Because of the efficiency of rotational techniques, IMAT is displacing conventional IMRT in many clinics. Furthermore, improvements in linear accelerator control systems and nascent developments in machine trajectory optimization are blurring the distinction between rotational

techniques and conventional IMRT. Rotational techniques will make conventional IMRT obsolete, just as rotational techniques as we know them today will themselves be displaced by methods which exploit patient-specific optimized machine trajectories.

AGAINST THE PROPOSITION: Peter A. Balter, Ph.D.

Opening Statement

The case for VMAT replacing traditional IMRT is based on the increased speed in delivery. This, however, comes at high costs in complexity, machine reliability, and, potentially, in plan quality and delivery accuracy.

Many publications have demonstrated the improvement in delivery time in VMAT vs fixed field IMRT.[8–13] These tend to be reductions of treatment time by 50%–80%, which corresponds to a decrease in on-table time of only 2–5 min.[14] Automated field sequencing for fixed field IMRT would somewhat reduce these differences. In addition, the total room cycle time is limited by other aspects of the treatment including time to transport the patient, to setup the patient on the table, and to image and shift. These times can often be on the order of 10 min or twice the treatment delivery time.

Plan quality in VMAT has been evaluated by a number of groups who found VMAT to be noninferior rather than superior. Fundamentally, the greatest degrees of freedom for plan optimization come from fixed field step-and-shoot IMRT with noncoplanar beams. In these cases, beams angles are only limited by the patience and creativity of the planner and can be enhanced by automated beam angle selection and IMRT optimization systems.[15] VMAT, by contrast, is limited by the minimum and maximum allowable dose rates, leaf speeds, and gantry speeds effectively reducing the possible solution space for the optimized plan.[13] More optimal IMRT plans may be realized by delivering fields with different couch positions and angles,[16] which is not possible with VMAT. The increased calculation times required by VMAT optimization would make the planners more willing to accept plans that are “good enough” rather than optimal.[17] In addition to these concerns, lesions that are away from the center of the patient may also require that VMAT use a physical isocenter away from the center-of-mass of the tumor, violating many of the assumptions made in our QA processes and daily imaging procedures.

VMAT has many higher costs than fixed field IMRT that should force each institution to examine the cost/benefit ratio of switching to this technology. To upgrade an existing Linac to VMAT requires a small amount of hardware changes but a large software license fee for the Linac, the R&V system, and the treatment planning system (TPS). VMAT calculations are also much more computationally demanding, often requiring an upgrade of the TPS hardware to enable planning of these cases. VMAT also results in lower reliability of Linac. Step-and-shoot IMRT is very forgiving of dose-rate variations and MLC performance. VMAT not only increases the wear on the MLC but also has more demanding tolerances for its motion. VMAT also adds an extra QA burden on the physics staff,[18,19] adding a planned extra 30 min to monthly QA in addition to the large amount of unplanned QA due to the increased number of MLC failures when using the machine for VMAT treatments.

In conclusion, VMAT has high costs, and the only theoretical benefit is decreased delivery time which may be offset by the decreased reliability of the Linac. Fixed field IMRT has proven to be robust and reliable, and our ability to fully optimize IMRT, including couch angle and position for each beam, is just beginning to be explored. Fixed field IMRT will always be needed for some cases due to tumor locations, will be equal or superior to VMAT for all cases and, for lesions that are away from the center of the patient, will avoid violating many of our assumptions.

Rebuttal: Richard A. Popple, Ph.D.

The argument against the proposition rests on two premises. The first is that VMAT is less accurate and less reliable than conventional IMRT. The second is that the improved efficiency of VMAT is not significant.

The assumption that VMAT is less accurate is contradicted by the literature. MLC leaf positioning is equally accurate for VMAT as for fixed fields.[20] Furthermore, VMAT plans are not more sensitive to MLC errors than conventional IMRT plans and may be more robust against leaf positioning errors than complex step-and-shoot plans.[21] Finally, the proof is in the pudding: VMAT plans are no less likely to fail QA testing than conventional IMRT plans.[22,23] With regard to reliability, there is no reported evidence to support the supposition that VMAT increases MLC failures.

The advantage of VMAT is expressed by the Latin proverb *ex granis acervus*: from grains, a heap. For a linear accelerator treating 15 IMRT patients per day, conversion to VMAT results in saving approximately an hour each day, thus reducing operating cost. Although the savings are partially offset by additional planning and QA, technology development will decrease planning and QA time. Furthermore, treatment time is an important component of plan quality. Radiation therapy is uncomfortable and, while a few minutes may not seem long to the team outside of the vault, it is significant to the patient inside. Furthermore, reduced treatment time has the potential to reduce targeting errors resulting from target motion during treatment.[24]

The advantage of VMAT is improved delivery efficiency. All other things being equal, reduced treatment time is better. For VMAT, all other things *are* equal and consequently rotational techniques will displace conventional IMRT.

Rebuttal: Peter A. Balter, Ph.D.

Dr. Popple has done an excellent job demonstrating that VMAT is on the high end of the technology spectrum and that many treatments will naturally move toward this end. He did not demonstrate a clinical benefit for this move, only a perceived efficiency benefit, which he did acknowledge is made smaller by the advent of autofield sequencing on many of the modern treatment units. He also emphasized that in the future, radiotherapy will be delivered by highly complicated plans including multiple couch positions highly optimized by IMRT autoplanning systems with little human intervention in either planning or delivery. Both machine design and safety concerns will limit the use of rotational therapy with automated combinations of multiple

couch positions and angles thus, to best use the optimized benefits of multiple couch positions, it will be necessary to continue using fixed field IMRT in these cases.

I agree with Dr. Popple that technology will inevitably move forward. In order to fully utilize the benefits in treatments made possible by the advent of automated treatment planning with the most possible degrees of freedom, including couch positions and angles, fixed field IMRT will continue to be an important tool and thus will not be replaced by rotational techniques. I also recognize that not all centers will have the resources to support the top-of-the-line planning and delivery equipment to deliver treatments that may be slightly faster but are no better than existing technology, providing another venue where rotation techniques will not replace fixed field IMRT.

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2.11. Non-coplanar beams improve dosimetry quality for extracranial intensity modulated radiotherapy and should be used more extensively

Ke Sheng and David M. Shepard
Reproduced from *Medical Physics* **42**, 531–533 (2015)
(http:// dx.doi.org /10.1118/1.4895981)

OVERVIEW

The past few years have seen widespread adoption of rotational beam-delivery techniques such as tomotherapy and volumetric modulated arc therapy (VMAT) for the delivery of extracranial intensity modulated radiotherapy (IMRT) treatments, resulting in better quality plans and more efficient delivery than previously possible with stationary beams. Because these techniques require the use of coplanar beam arrangements, there has been a reduction of interest in application of noncoplanar beam arrangements. Some argue, however, that noncoplanar beams improve dosimetry quality for IMRT treatments and thus should be used more extensively, and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Ke Sheng, Ph.D. Dr. Sheng received his M.S. and Ph.D. degrees in Medical Physics from the University of Wisconsin, Madison. He then worked as a faculty medical physicist at the University of Virginia, Charlottesville until 2011 at which time he moved to his current position as Associate Professor at UCLA. He is certified by the American Board of Radiology in Therapeutic Radiologic Physics. His major research interests include innovations in cone beam MVCT imaging, stereotactic body radiosurgery and motion management, modeling lung motion during radiotherapy, 4π radiotherapy planning and delivery, and small animal irradiation, for which he has numerous grants and has published over 60 papers in peer-reviewed journals.

Arguing against the Proposition is David M. Shepard, Ph.D. Dr. Shepard obtained his M.S. and Ph.D. from the University of Wisconsin where he worked in the tomotherapy research group. He joined the faculty at the University of Maryland School of Medicine in 1999. In 2006 he moved to his current position as Director of Medical Physics, Swedish Health Services, Seattle, WA. He is certified by the American Board of Radiology in Therapeutic Radiologic Physics, is a fellow of the AAPM, and has served as President of the Northwest Chapter. Dr. Shepard's major research interests include developments in volumetric modulated arc therapy, image guided radiation therapy, motion management, and optimization, for which he has several patents and grants and has published over 30 papers in peer-reviewed journals.

FOR THE PROPOSITION: Ke Sheng, Ph.D.

Opening Statement

In principle, coplanar beam geometry is a subset of noncoplanar solution space and the latter should yield superior dosimetry. The dosimetric advantages of noncoplanar beam geometries have been clearly demonstrated for intracranial treatments via Gamma Knife and Linac machines.[1] As a result, noncoplanar beams are systematically used for intracranial stereotactic radiosurgery treatment.

The usefulness of noncoplanar beams in extracranial treatments, however, is less clear. I believe that differing utilization rates of noncoplanar beams in intracranial and extracranial treatments are due, not to the noncoplanar approach itself, but to the limited *quality* and *quantity* of noncoplanar beams applied to practical extracranial plans. Since hemispherical beam templates typically utilized in intracranial radiosurgery are not feasible for extracranial treatment, the beam orientation has to be selected. Unfortunately, manual selection of noncoplanar beam orientations is neither intuitive nor optimal. Automated beam orientation optimization has been previously researched, but more practical and robust beam orientation optimization algorithms to solve the complex integrated noncoplanar beam orientation and fluence optimization problem were not reported until recently. Breedveld *et al.*[2] developed an automated beam orientation and optimization program, termed iCycle, to manage a large number of noncoplanar beams. They showed that noncoplanar plans consistently outperformed coplanar plans.[3] More interestingly, using the same algorithm, Rossi *et al.*[4] showed substantial dosimetric gains by increasing the number of noncoplanar beams from 12 to 25. Similarly, our group has optimized both the beam orientations and fluence maps for 12 lung SBRT cases using a 4π algorithm for both coplanar and noncoplanar plans.[5] We have demonstrated that with fewer than ten beams, the difference in R_{50} (coplanar vs noncoplanar), defined as the ratio of the 50% isodose volume to that of the PTV, is insignificant and can be compensated for by using more coplanar beams, findings that have been previously observed. However, with more than 20 beams, R_{50} of the noncoplanar plan is 30% less than that of the coplanar plan and can no longer be matched using more coplanar beams. Using the same method, we showed that clinical plans using primarily coplanar beams could be meaningfully improved for lung and liver SBRT patients.[5,6] For example, using 4π planning, the mean normal liver volume receiving <15 Gy was increased by 51 cm^3 (range 21–107 cm^3) with a 31% reduction of the mean normal liver dose, when compared against two partial arc VMAT plans. For lung SBRT patients, the critical organ doses were reduced by 32%–72%. The substantial improvement in critical organ sparing would allow a 40% target dose escalation. Even for the prostate that is centrally located, a significant reduction in the V50%, V80%, and V90% values for the rectum was achieved using 4π.[7] Concerns about integral dose were alleviated by a recent study showing comparable noncoplanar and coplanar integral doses.[8] The effect of longer x-ray paths in noncoplanar plans was offset by a shorter average beam entrance-to-target distance.

In view of the newly emerged evidence, we believe that noncoplanar plans should be more extensively used for extracranial treatment since they consistently outperform coplanar plans.

AGAINST THE PROPOSITION: David M. Shepard, Ph.D.

Opening Statement

The negative consequences of using of noncoplanar beams in radiation therapy include (1) added treatment planning complexity, (2) greater potential for setup errors, (3) increased risk of collisions, and (4) longer treatment times. Consequently, noncoplanar beam arrangements are used infrequently in clinical practice and are rarely employed in the treatment of extracranial targets with IMRT. In fact, IMRT has largely obviated the need for noncoplanar beam arrangements. This is because IMRT uses optimized intensity patterns to overcome the geometric deficiencies of any individual beam angle.

The introduction of rotational IMRT techniques such as tomotherapy and VMAT has further simplified the process of selecting beam angles. These rotational IMRT techniques provide enormous flexibility in shaping the dose distribution. As a result, the addition of noncoplanar beams generally provides only an incremental dosimetric benefit.[9] This is evidenced by treatment planning studies comparing coplanar and noncoplanar delivery. These studies have not demonstrated a significant clinical advantage to the use of noncoplanar beams.[9–15] Additionally, the use of noncoplanar beams in treating extracranial targets will generally result in longer radiation pathlengths through the patient and a corresponding increase in the integral dose.

Noncoplanar beam arrangements complicate both the planning and the delivery process. In the treatment planning phase, the manual selection of noncoplanar beams can prove tedious because of the enormous number of possible beam configurations.[16] Several researchers have examined automated techniques for determining the optimal configuration of noncoplanar beams. This is a highly complex mathematical problem. Consequently, there is no robust commercial solution that optimizes the beam angle selection for noncoplanar IMRT.[9,10]

A significant concern with the use of noncoplanar beams is their negative impact on treatment times. The delivery process is encumbered by the need to move the treatment couch and gantry through an arrangement of noncoplanar beam angles. Additionally, great caution must be exercised when delivering noncoplanar beams due to the risk of collisions between the patient and the head of the linear accelerator.[11] This is why the use of automated couch rotations from the treatment console is often ill advised. Treatment planning systems generally lack sophisticated collision prediction algorithms. As a result, it is not uncommon to discover that a planned noncoplanar beam arrangement is in fact undeliverable.

This stands in contrast to coplanar VMAT where complex treatments can be delivered in a highly efficient manner using one or two arcs. VMAT offers a simplicity and efficiency that has led to its rapid clinical adoption and has further reduced the utilization of noncoplanar beam arrangements.

Overall, the more widespread adoption of noncoplanar beams for extracranial IMRT is unjustified at this time. The incremental dosimetric gains are generally not sufficient to outweigh the negative impact on both the clinical workflow and patient comfort, along with increased risks of intrafraction organ motion, setup errors, and collisions.

Rebuttal: Ke Sheng, Ph.D.

When IMRT was first introduced, it had many flaws. It was slow, the multileaf collimators were unreliable, the optimization algorithm was complex and commercially unavailable, and the quality assurance program was notoriously tedious. Moreover, the integral dose increased due to both increased leakage and beam angles. Now, some 20 years later, the technical difficulties associated with early IMRT development have largely dissolved. The worries over integral dose have subsided with a few exceptions such as breast treatments, where IMRT is used sparingly. Similarly, technical challenges related to noncoplanar IMRT are surmountable. The computational complexity of integrated beam orientation and fluence optimization is manageable using the current generation of calculation platforms, which will only become faster. Automation, which many newer C-arm Linacs equipped with robotic couch and gantry are technically capable of, allows efficient plan delivery. Collisions can be prevented with pretreatment 3D modeling and the use of proximity sensors.

I agree with my colleague that rotational IMRT has significantly advanced radiotherapy by providing good quality yet efficient plans. The question we have to ask is whether or not the good plans meet all our needs. A recent study shows that, for centrally located and larger lung tumors treated with coplanar beams, normal tissue toxicity is still a major roadblock to the delivery of an effective tumor control dose.[17] Similarly, for patients with recurrent head and neck cancer, delivering a high dose to the tumor while sparing previously treated normal tissues is challenging.[18] In many cases, normal organs mediolaterally encompass the tumor exposing a fundamental limitation of the coplanar platform that cannot be compensated for by intensity modulation alone. Therefore, instead of affixing to the current technical hurdles that will be overcome, I claim that the dosimetric gains made possible by using advanced noncoplanar IMRT will surely benefit many patients and should be used more extensively.

Rebuttal: David M. Shepard, Ph.D.

The treatment planning studies cited by Dr. Sheng have demonstrated a dosimetric benefit to the use of beam arrangements incorporating 20 or more noncoplanar beams. These plans do not serve as practical clinical solutions. The routine delivery of beam arrangements incorporating large numbers of noncoplanar beams would require the development and commercial availability of each of the following: (1) software capable of comprehensive optimization of noncoplanar plans including selection of the beam configuration; (2) software and hardware with sophisticated collision prediction and detection systems to ensure safe delivery; (3) tools to optimally sequence the delivery to maximize efficiency while accounting for all of the delivery limitations; (4) tools to deliver these plans in an automated fashion without the need to enter the room between beams. Additionally, treatment planning vendors would need to address the time consuming and resource intensive nature of these complex noncoplanar dose calculations and optimizations.

The use of exotic beam arrangements and complex noncoplanar arc paths is an area that merits further investigation. Significant work remains, however, to demonstrate a consistent dosimetric benefit and to mitigate the negative impact on the clinical workflow. In the meantime, clinicians will continue to use coplanar rotational IMRT as a safe, efficient, and effective delivery technique for extracranial IMRT.

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2.12. Systemic alpha-particles are likely to yield more important advances in radiotherapy than are protons

Barry J. Allen and Alexei V. Chvetsov
Reproduced from *Medical Physics* **42**, 3785–3787 (2015)
(http:// dx.doi.org /10.1118/1.4919281)

OVERVIEW

New treatment modalities aimed at increasing tumor control and decreasing complications include proton and heavy ion external beam radiotherapies and systemic targeted alpha-particle therapy (TAT). Although proton therapy (PT) has received the most press recently, some would argue that systemic α-particles are likely to yield more important advances than are protons. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Barry J. Allen, Ph.D. Dr. Allen earned his Ph.D. from the University of Wollongong, Australia in 1979 and his D.Sc. from the University of Melbourne in 1983. Subsequently, he worked as Chief Research Scientist at the Australian Nuclear Science and Technology Organisation, and Principal Hospital Scientist, Cancer Care Centre and Clinical School at St George Hospital in Sydney. Dr. Allen's recent research interests include the development of preclinical studies of internal targeted alpha therapy for melanoma, breast, ovarian, prostate, and pancreatic cancers. He is the initiator and Study Director of the world's first two trials of intralesional and systemic targeted alpha therapy for metastatic melanoma, with some 51 patients treated in these phase 1 trials. He has published over 300 papers on neutron capture gamma rays, resonance cross sections, stellar nucleosynthesis, *in vivo* body composition, neutron capture therapy, macro- and microdosimetry, microbeams, and targeted alpha therapy. He is past-president of the Asia Oceania Federation of Medical Physics, the International Organization for Medical Physics, and the International Union of Physical and Engineering Sciences in Medicine.

Arguing against the Proposition is Alexei V. Chvetsov, Ph.D. Dr. Chvetsov received an M.S. in radiation protection and dosimetry and a Ph.D. in radiation physics from the Moscow Engineering Physics Institute, Moscow, Russia. He was certified in radiotherapy physics by the CCPM in 2003 and the ABR in 2004. Dr. Chvetsov held faculty positions at several institutions, including the University of Florida Proton Therapy Institute in Jacksonville (2008–2011). He is currently Associate Professor in the Department of Radiation Oncology at the University of Washington Medical Center, Seattle, WA. Dr. Chvetsov's major research interests are tumor response assessment, image-guided radiation therapy, and proton therapy. He is coauthor of the AAPM Task Group 202 Report “Physical uncertainties in the planning and delivery of light ion beam treatments.”

FOR THE PROPOSITION: Barry J. Allen, Ph.D.

Opening Statement

The therapeutic objectives that must be addressed for each stage of cancer development are to kill isolated cancer cells in transit in the lymphatic and vascular circulation, eliminate avascular cell clusters, and to induce tumor regression. A targeted *systemic* therapy could be successful in controlling cancer at each stage, whereas external beam *local* therapy is applicable only for tumor regression and local prophylactic therapy.

The exploitation of the Bragg peak for cancer therapy is perhaps the ultimate fusion of high energy nuclear physics and precision radiotherapy, whereas internal, targeted, high linear energy transfer (LET) therapy may be the ultimate fusion of nuclear physics and biology. As such, both approaches should find application in the management of cancer.

External PT is a mature and effective technology with many clinical results comparable to photon therapy.[1] Results for PT of central nervous system tumors were found to be similar to those reported for photons, except for base of skull chordomas. PT results for ocular tumors show good results for eye preservation, but the key issue is the impact on long term survival. As such, PT is a high cost *local* therapy with minimal or unproven impact on metastatic cancer and ultimate survival.

Immunotherapy is having considerable success for metastatic cancer and there are a number of antibody therapies now with FDA approval. However, their efficacy is often of short term duration. Efficacy can be enhanced by radiolabeling with α emitting radioisotopes. Phase 1 trials of internal TAT show remission of tumors that are refractory to β radiation, with favorable acute and midterm toxicity at therapeutic effective doses for, *inter alia*, acute myelogenous leukaemia[2] (now in phase 2) and neuroendocrine tumors.[3]

Phase 1 trials of intralesional[4] and systemic[5] TAT for metastatic melanoma showed high efficacy for the former and, for the latter, 10% partial response and 40% stable disease without any adverse events at all, being well below the maximum tolerance dose.[6] Uveal melanoma was one of the first successes for PT, but intralesional TAT followed by systemic TAT is expected to not only control local disease but could impact survival by eliminating melanoma cells in transit and subclinical cell clusters. This hypothesis remains to be tested.

Radioimmunotherapy with the β emitter ^{177}Lu for castration-resistant prostate cancer was efficacious but limited by the tolerance dose.[7] TAT is expected to achieve efficacy below the tolerance dose and change survival outcomes. This hypothesis also remains to be tested.

The first alpha therapy approved by the FDA is radium chloride ($^{223}RaCl_2$, Alpharadin, or Xofigo) for metastatic prostate cancer to the bone. This is a palliative therapy with significant life extension that targets osteoblasts as a calcium analogue.

TAT is a systemic therapy[8] designed for metastatic disease that is intractable to chemotherapy and new age immunotherapies. Whether it achieves its potential for important advances in systemic radiotherapy depends on funding support to test the above hypotheses.

AGAINST THE PROPOSITION: Alexei V. Chvetsov, Ph.D.

Opening Statement

Both targeted therapy with α-particles[9,10] and radiotherapy with proton beams[11,12] are expected to produce fewer complications and improved or at least achieve the same tumor control compared to therapy with standard radiation sources (β-particles and x-rays, respectively) because they utilize dosimetric advantages of heavy charged particles. However, the impact on advances in radiation therapy will be different for α-particle therapy and proton therapy because they have different practical potentials in treatment of primary solid tumors, hematological tumors, and metastatic malignancies.

The results of several studies suggest that α-particle immunotherapy may be more effective in the treatment of microscopic or small-volume disease than in the treatment of large-volume solid tumors.[9] First, solid tumors provide a natural diffusion barrier that delays penetration of antibodies/targeting molecules into the tumors. Therefore, the therapeutic effect of α-particles depends on the tumor's vascular supply, which can deteriorate in hypoxic areas. Second, due to the very short pathlength (<100 μm) of radionuclide emitted α-particles with energy 4–8 MeV, targeted cells can receive high radiation dose, whereas adjacent tumor cells (for example, cells to which the targeting molecule is not directly bound) might not receive any dose at all. Taking into account these two reasons and the short half-life of α-emitting radionuclides, it is difficult to guarantee a uniform dose distribution without unpredictable cold spots. A uniform dose distribution is required to maximize tumor control probability.[13] Therefore, proton therapy will apparently outperform internal targeted α-particle therapy in treatment of most solid tumors where proton therapy can deliver, with known uncertainties,[14] practically any prescribed dose distributions to tumors of any shape and size.

Targeted α-particle therapy also has some limitations and risks in normal tissue sparing compared to proton therapy. First, for α-emitting radionuclides with a half-life of several hours, distribution of antibodies after administration may yield residence times comparable to the residence times achieved in targets. Second, there is a risk of toxicity due to unforeseen accumulation of radionuclides elsewhere in the body.

The conclusion is that the current state of external proton beam radiotherapy offers more advantages for treatment of most solid tumors. Due to significant progress in the development of compact superconducting cyclotron technology and single treatment-room centers, proton therapy has become available to small radiotherapy clinics.[15] Taking into account the improved quality of proton dose distributions and the availability of protons thereby to small clinics, the number of patients treated with proton beams will apparently grow, changing overall approaches to radiation therapy. At the same time, internal alpha-particle therapy can be used for hematological tumors,[9,10] metastatic malignancies,[16] and some primary solid tumors such as glioblastoma multiforme.[9] Also, internal α-particles can be considered as part of a multimodality approach for elimination of minimal residual and micrometastatic disease.[9] This multimodality approach may include external beam radiotherapy which is followed by systemic adjuvant curative targeted alpha-particle therapy. However, the number of metastatic cases may decrease in the future because of improved diagnostic procedures and treatment of primary solid tumors.

Rebuttal: Barry J. Allen, Ph.D.

Dr. Chvetsov makes some good points in his opening statement with regard to the dosimetric advantages of heavy ions. His comments on solid tumors ring true. Hypoxia could be a real problem for TAT as is uniform dose distribution in tumors, even with long lived radioisotopes such as Ac-225 and Ra-223. However, preclinical and phase 1 trials may virtually eliminate concerns about the unforeseen uptake risk in normal tissues.

The real issue is whether TAT can make *more important advances* to cancer treatments than external beam protons. The alleged superiority and cost effectiveness of protons over modern photon-beam radiotherapy technology were not addressed. As such, the modest gains that protons might achieve need to be compared with the potential, major gains of systemic TAT for cure or palliation.

TAT offers highly targeted toxicity for cancer cells in transit, which have escaped into the vasculature before tumor regression by PT is achieved. Also, TAT can target metastatic cancer spheroids and small tumors via the vascular system, none of which are clinically evident and cannot, therefore, be treated by external radiation beams.

Protons can be used to eliminate clinical tumor, whether primary or metastatic, but cannot address widespread metastases, for which there is a spectrum of tumor sizes as well as subclinical disease. On the other hand, targeted alpha immunotherapy has achieved some success with hematological disease and solid tumors.

Therapeutic efficacy for tumors may well be enhanced by targeting vascular receptors or perivascular cancer cells, shutting down leaky tumor capillaries and blood supply, regressing tumors. This approach would eliminate concerns about tumor hypoxia and uniform dose distributions in tumors.

We both agree that external protons and internal alphas have different potential applications and, in the end, we need both approaches to achieve cancer control.

Rebuttal: Alexei V. Chvetsov, Ph.D.

I agree with Dr. Allen that targeted alpha therapy has potential in controlling metastatic cancer. However, radiolabeled antibodies have been less successful in treatment of large solid tumors, which may be related to the diffusion barrier and perfusion limitations. Therefore, external beam therapy and one of its most advanced forms—proton therapy—will apparently remain the primary modality in treatment of large solid tumors.

Comparing proton therapy to x-ray therapy, Dr. Allen criticizes the high treatment cost and low improvement in clinical results with protons. However, the cost of proton therapy can be reduced, for example, by using treatment machines with compact superconducting cyclotrons mounted on gantries, such as those implemented recently.[15] Improvements in local control outcomes have been reported for head and neck cancer treated with proton beams.[11] Tumor control can be improved by using higher doses with protons; however, another advantage of proton therapy would be reducing normal tissue complications because of unique dose distributions. These improvements are associated, for example, with decreased posttreatment

testosterone suppression in prostate patients and improved quality of life in pediatric patients.[12] The advantages of proton therapy are especially important for pediatric patients, for whom lifetime follow-up treatment costs associated with x-ray therapy (for example, mental retardation and secondary cancers) may far exceed the cost of proton therapy.

However, I agree that proton therapy cannot be used to control occult metastatic cancer. When earlier diagnosis and treatment of primary tumors fail, TAT may be used to eliminate the metastatic disease. However, several problems should be solved for practical implementation of this therapy. For example, cost-efficient α-particle radionuclide production and *in vivo* verification of radionuclide distribution are needed.[9]

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2.13. Proton therapy is the most cost-effective modality for partial breast irradiation

Valentina Ovalle and J. Keith DeWyngaert
Reproduced from *Medical Physics* **42**, 4419–4422 (2015)
(http:// dx.doi.org /10.1118/1.4922709)

OVERVIEW

Construction of new proton therapy facilities is expanding rapidly, despite the order-of-magnitude higher expense of building them compared to conventional radiotherapy. Despite this, many have argued that proton therapy is cost effective, at least for some types of cancer and some populations of patients. In this month's Point/Counterpoint, we debate the claim that proton therapy is the most cost-effective modality for partial breast irradiation (PBI).

Arguing for the Proposition is Valentina Ovalle, M.D. Dr. Ovalle earned her M.D. degree from the Universidad de Los Andes Medical School, Santiago, Chile. She then completed a Clinical Residency in Radiation Oncology at the Universidad Diego Portales-Instituto de Radiomedicina, Santiago, and is now a Postdoctoral Research Fellow, Breast Radiation Oncology, at the University of Texas MD Anderson Cancer Center, Houston, TX. Her major research interests include the treatment of early and late stage breast cancer, partial breast irradiation, and proton therapy, on which she has published several papers and one book chapter.

Arguing against the Proposition is J. Keith DeWyngaert, Ph.D. Dr. DeWyngaert earned his Ph.D. in Physics from Brown University, Providence, RI and subsequently completed a Postdoctoral Fellowship in Medical Physics at the Joint Center for Radiation Therapy, Harvard Medical School, Boston, MA. He then worked for 13 yr in the Department of Radiation Oncology Mount Sinai School of Medicine, NY and, since 1997 has worked in the Department of Radiation Oncology, New York University Medical Center, NY, where he is currently Associate Professor and Director of Physics. His major research interests include radiotherapy for breast cancer, especially partial breast irradiation and cone beam CT to investigate interfraction motion. He has published over 50 papers and two book chapters. Dr. DeWyngaert is certified in Therapeutic Radiologic Physics by the ABR and has served as the President of the AAPM New York Chapter, RAMPS.

FOR THE PROPOSITION: Valentina Ovalle, M.D.

Opening Statement

Proton beam irradiation has become the modality of choice for tumors difficult to treat with other modalities. Among those clearly supported by the literature are the treatment of intraocular melanoma, tumors near or at the base of skull, and those requiring treatment with craniospinal irradiation.[1] Proton therapy value—meaning benefit as a function of cost—in the treatment of other diseases is more difficult to show. The case of prostate cancer has become the center of a

growing discussion on the cost-effectiveness of protons in terms of clinically meaningful gains of expensive new technologies.

In this context, it is not intuitive that using protons for accelerated partial breast irradiation (APBI) would be a good value. Yet the data show that proton APBI compares favorably to all the external beam and brachytherapy alternatives.[2–5] The dose is very homogeneous within the target region and delivers negligible dose to nontarget breast, heart, and lung. The initial clinical outcomes of proton APBI have been reported from three institutions, and additional Phase II studies are ongoing. Two of these experiences have been updated recently with up to five years of follow-up showing excellent local control rates and high patient satisfaction.[6,7] The group at Loma Linda University has the largest published experience with proton beam APBI showing good to excellent cosmetic outcomes in 90% of patients. Problems seen with other types of APBI—high infection rates, declining cosmesis with time, and fat necrosis—have not been seen with proton therapy. In particular, the poor cosmesis seen in the TARGIT-A and RAPID trials suggests that Linac-based APBI may not be a favorable option.[8,9]

Because of this promising clinical role for protons in the treatment of early stage breast cancer, cost becomes relevant. Only one cost analysis comparing proton APBI to other breast irradiation techniques has been published to date.[5] In 2006, Taghian *et al.* found protons to be more costly than 3D-conformal partial breast irradiation with photons and classic whole breast irradiation (WBI) with a boost. At PTCOG-NA, Ovalle *et al.* presented their analysis of current costs of proton APBI compared to seven other partial- and whole breast irradiation techniques.[10] Using 2014 Medicare reimbursement rates, proton APBI costs were similar to six weeks of whole breast irradiation including a boost, and less costly than APBI with interstitial brachytherapy using a multilumen device or IMRT whole breast treatments. The key factors in these unexpected results are that (1) the small number of treatments required by proton APBI offsets the higher costs per fraction and that (2) reimbursement rates for the various options have significantly changed in the last decade.

With lower costs than multilumen brachytherapy APBI or whole breast IMRT, proton APBI appears to be an appealing alternative for the treatment of early stage breast cancer and deserves further investigation.

AGAINST THE PROPOSITION: J. Keith DeWyngaert, Ph.D.

Opening Statement

In general, one would not dispute the proposition that with protons one should be able to design a dosimetrically superior treatment plan compared to external beam Linac-based treatments. What may be surprising is the notion that a marvelous physics-rich modality as proton therapy can be considered a less expensive alternative to conventional photon-based treatments for PBI.

In 2014, the Alberta Health Services[11] issued a report on referral of patients for proton beam therapy (PBT). In this report, they constructed a framework for determining which situations were most likely to benefit from a referral for treatment with protons, recognizing the premium placed on this expensive resource. They estimated the average cost of each referral to be

$200,000. Additionally, the report summarized national guidelines for England, Denmark, and the Netherlands, none of which lists breast irradiation as a standard indication for protons. Similarly in 2014, ASTRO released its model policy for PBT[12] detailing the indications for insurance coverage based upon medical necessity and adequate clinical data. They state that (1) it is necessary to understand and document the associated clinical benefits of PBT and (2) PBT should not be considered *in lieu* of a photon-based schema that delivers quality clinical care with low normal tissue toxicities. PBI did not meet their criteria. Recently, Loeffler[13] laid out the current and future landscape for particle beam therapy and reviewed sites of proven clinical benefit and sites of ongoing investigation such as breast. He reminds us that dosimetric advantage does not necessarily correlate with a clinical advantage and that a definitive advantage needs to be established for PBT to become common treatment. He lists sites with the highest priority, acknowledging that the data are not yet available to warrant inclusion for breast treatment.

There are a few published clinical trials with protons[6,7] supplemented with dosimetric studies.[2] An early Phase I trial testing the feasibility of proton PBI reported more late skin toxicities compared to photon-based PBI,[6] a consequence, they postulated, of limiting daily delivery to a single proton treatment field due to machine time availability. Five-year results for a proton PBI phase 2 trial were reported by Bush *et al.*[7] demonstrating very good results with 5-yr disease-free survival and overall survival rates of 94% and 95% and excellent cosmesis using 40 Gy over two weeks. In comparison, Formenti *et al.*[14] reported 5-yr results on 100 PBI patients treated with photons with one recurrence out of the 100 patients (1%) with 95% disease-free survival. Updated results (private communication) with 397 patients and median follow-up of 40 months indicate a predicted 5-yr recurrence rate of 0.4% and overall survival rate of 98.2% using daily fractions of 6 Gy over five consecutive days.

Of course, cost-effectiveness is not based solely on either the expense of a treatment or even a Medicare-based reimbursement analysis but also upon nonmedical costs, weighting factors for normal tissue toxicities, outcomes, and costs of salvage treatments. Shah *et al.*[15] reviewed the cost-effectiveness of accelerated PBI compared with WBI using 2011 Medicare schedules with costs ranging from $8500 (3D planning), $12,500 (IMRT), up to $18,400 for multilumen brachytherapy. Their analysis included estimates of incremental cost-effectiveness ratios and costs per quality adjusted life year. For protons to be considered cost-effective, we need to demonstrate low costs or improved outcomes.

Rebuttal: Valentina Ovalle, M.D.

Indeed, for protons to be considered cost-effective, they must be proven to be of lower cost than the alternatives, or to have improved outcomes, or both. In the absence of cost-effectiveness analysis, one can analyze these separately.

Costs. Costs of therapy can be classified as medical and indirect costs. As previously mentioned, there are two available reports on APBI costs in the USA. The first one used the 2006 Standard Medicare Payments Schedule for professional and technical charges to estimate costs of proton APBI and compare them to a mixed-modality 3D-conformal external APBI schedule and a six-week WBI technique. Protons had higher medical costs than the alternatives but the lowest

patient related costs. Today, many other treatment options are utilized for patients with early stage breast cancer. These include APBI with brachytherapy devices and partial- or whole breast irradiation with IMRT. Using current Medicare reimbursement rates, Ovalle *et al.* compared these treatments (amongst others) to proton APBI.[10] The cost of protons was lower than APBI with a brachytherapy device and whole breast IMRT, and very similar to a 6-week WBI schedule with a boost.

Effectiveness. One of the most common and probably the most relevant way of comparing treatment effects is survival. Other outcomes specifically significant to radiotherapy are local and local-regional recurrence. Published data on proton APBI on all these fronts are promising, with a 5-yr overall survival of up to 95% and an ipsilateral breast tumor recurrence-free survival of 97%. Assessments of toxicity have been erratic and will be a vital factor when determining the role of proton APBI. Ongoing trials will aid in answering these questions.

Finally, according to ASTRO's proton beam therapy model policy (2014),[12] coverage with evidence development is suggested for disease sites such as breast as long as the patient is enrolled in a clinical trial. Hopefully, this will facilitate generating more clinical data and cost-effectiveness analysis will likely follow.

Rebuttal: J. Keith DeWyngaert, Ph.D.

A driving principle for initiating APBI protocols and certainly one of the major justifications for exploring APBI was an expansion of women's access to breast conserving therapy (BCT). It was noted that access to BCT was particularly an issue in areas underserved by radiation oncology, where traveling long distances for up to 30 daily visits pushed women toward mastectomies and away from BCT. The number of proton facilities, although increasing, remains small and they are largely situated in high population areas, a situation that may not address this original motivation and may increase the costs for those women who feel a pressure to seek out proton therapy but who live very far from a proton center. Thus, although the use of protons provides an alternative for BCT, it may not expand access for the population pools seeking an alternative to mastectomy.

As noted in my opening statement, acute and late effects following proton treatment are dependent upon regimen and technique similar to photon-based treatments, suggesting that protons are not inherently superior. They demand attention to dose-fractionation regimens and planning and treatment specifics just as photon-based APBI.[6] The APBI toolbox is already crowded and confusing, at least for the patient. Perhaps, the addition of protons will trigger a review of available protocols to determine which techniques are competitive on both a cost and outcome basis since both of these vary substantially. Protons and multicatheter brachytherapy represent the high end of costs, and five-fraction external beam the simpler, low-cost alternative.[14]

ACKNOWLEDGMENT

Dr. Ovalle wishes to acknowledge the assistance of her mentor Eric A. Strom, M.D.

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2.14. Particle therapy is ideal for the treatment of ocular melanomas

Kavita K. Mishra and Sou-Tung Chiu-Tsao
Reproduced from *Medical Physics* **43**, 631–634 (2016)
(http:// dx.doi.org /10.1118/1.4939223)

OVERVIEW

Ocular melanomas (OMs) are commonly treated by either stereotactic external beam therapy, brachytherapy with plaques, or heavy particle therapy with protons, helium, or carbon ions. Because of their claimed superior dose distributions and high-LET advantages, some believe that particle therapy is ideal for these treatments. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Kavita K. Mishra, MD MPH. Dr. Mishra earned her undergraduate degree in biology at Harvard University and her medical degree at the University of California, San Francisco. She then completed a Masters degree at the Harvard School of Public Health and returned to UCSF for her residency in radiation oncology. She thereafter joined the UCSF faculty and serves now as Associate Professor in the Department of Radiation Oncology and Director of the UCSF Ocular Tumor Proton Therapy Program. Dr. Mishra's research interests include studying the clinical outcomes of ocular patients with benign and malignant tumors, as well as the clinical implications of particle beam physics. She has presented at multiple national and international meetings and serves on a number of institutional boards, including as Co-Chair of the international Particle Therapy Co-Operative Group Ocular Subcommittee.

Arguing against the Proposition is Sou-Tung Chiu-Tsao, Ph.D. Dr. Chiu-Tsao obtained her Ph.D. in Physics from the State University of New York, Stony Brook in 1974 and entered the field of Medical Physics in 1976. After faculty positions in several medical centers, she founded and directs Quality MediPhys LLC, Denville, NJ in 2006, which is her current position. She is certified in radiotherapy physics by both the ABR and ABMP and is a Fellow of the American Association of Physicists in Medicine (AAPM). She has served the AAPM in a number of capacities including Chair of Task Group #129, Eye Plaque Dosimetry and Task Group #235, Radiochromic Film Dosimetry. Dr. Chiu-Tsao's major research interests are eye plaque and radiochromic film dosimetry for which she has about 50 peer-reviewed publications.

FOR THE PROPOSITION: Kavita K. Mishra, MD

Opening Statement

Charged particle therapy (CPT) is an ideal treatment for ocular melanomas due to the high local control (LC) and relatively high eye preservation rates that have been maintained with long follow-up in multiple international studies. CPT is, of course, not the only therapy and can be difficult to access due to limited centers with the required capital equipment and expertise.

Plaque and stereotactic radiation are also potentially appropriate therapies for patients who are carefully selected, who are treated by experienced surgeons and radiation oncologists using current best practice techniques, who may not have access to particle treatment, and who may otherwise be treated with primary enucleation.

OM, the most common primary adult cancer of the eye, can significantly threaten vision, eye preservation, and survival. Primary radiation therapy has been the standard of care for decades, with the use of brachytherapy plaques, stereotactic RT, and particle therapy. The potential benefits of CPT include improved tumor dose delivery and decreased collateral damage due to its uniform dose distribution throughout the tumor volume, minimal scatter, significant dose rate, high linear energy transfer, and sharp dose falloff outside the target region.[1]

LC is a primary endpoint in evaluating the utility of radiation practices. As such, treatment with particles, including protons, helium, and carbon ions, has shown consistent, excellent LC results.[1–5] Retrospective data, prospective randomized studies, and meta-analyses have shown consistently high LC after particle treatment on the order of 95% or greater.

A recent meta-analysis reviewed patients undergoing brachytherapy (*n* = 3868 patients) and particle (*n* = 7043 patients) treatment for OM.[4] With an average of 5 yr follow-up and weighted by study sample size, brachytherapy studies showed a weighted average local failure rate of 9.5% vs 4.2% for the particle studies. Of note, the particle studies had better results overall, despite having somewhat larger tumors to treat on average. Similarly, the recent update of the historical UCSF-LBNL randomized trial of helium vs plaque treatment showed superior results for helium particles with long-term higher LC, eye preservation, and disease-free survival rates at 12 yr follow-up.[5]

Eye preservation and vision outcomes are important endpoints as well for radiation modality evaluation. The physical quality of a particle beam allows for reduced peripheral doses to critical structures.[6] Clinically, this can result in improved outcomes such as vision retention. A recent comparison of patients treated with stereotactic radiation versus proton beam showed improved visual outcomes in the proton cohort.[7] Particle treatment has developed tremendously over the past decades in terms of treatment planning, dose delivery, and post-RT care to maintain a high level of tumor control while reducing the incidence and/or severity of side effects.

Pioneering work by dedicated ocular oncology particle centers worldwide has led to excellent results with CPT for OM patients.[8] Though historically there have been a very limited number of particle facilities, in the future CPT will be more accessible to patients. As with all available radiation techniques, appropriate patient selection and education regarding the most contemporary and effective treatments are crucial.

AGAINST THE PROPOSITION: Sou-Tung Chiu-Tsao, Ph.D.

Opening Statement

Ocular melanoma is the most common eye cancer. Many modalities (brachytherapy and external beam techniques, including photon and particle (protons, helium, and carbon ions) beam

therapies) have been used to treat ocular melanomas.[9] Particle therapy is, however, not ideal for all ocular melanoma treatments because this modality does not meet all of the following criteria:

1.be readily available to the majority of ocular melanoma patients;
2.be cost effective;
3.be of proven efficacy for all ocular melanomas in both the anterior and posterior hemispheres, without excessive side effects.

Criterion #1

As of 2014, there were only 13 centers worldwide that could offer particle therapy for ocular melanomas.[9] The particle therapy modality is not readily available to the majority of ocular melanoma patients.

Criterion #2

The particle therapy modality for ocular melanomas is very expensive and not cost effective.[10]

Criterion #3

While it is recognized that there is dose sparing of tissues posterior and lateral to the particle beams, particle therapy and stereotactic radiosurgery (photons) all require anterior entry field(s), even when treating posterior tumors. Since the majority of ocular melanomas are in the posterior hemisphere, the doses from particle therapy to the exposed anterior normal tissues have been shown to result in more anterior segment complications compared to brachytherapy.[9,11] Hence, particle therapy is not ideal for the majority of ocular melanomas.

In contrast, brachytherapy is a viable modality for all ocular melanoma treatments. Brachytherapy of ocular melanomas is available for most patients from centers throughout the U.S., Canada, and around the world. The cost of brachytherapy is reasonably affordable. Brachytherapy utilizes radioactive materials (photon or β emitters) assembled in an eye plaque (or called an ophthalmic applicator) which is sutured onto the eye ball at the location of the ocular melanoma and maintained there for a specified period of time. It delivers doses to the ocular melanoma, whether in the posterior or anterior hemisphere.[9] Due to the dose gradient, the subjacent sclera and adjacent ocular structures receive more radiation.[12] Since the majority of ocular melanomas are in the posterior hemisphere, brachytherapy is associated with posterior segment complications, which are dose related, but there are fewer anterior segment complications compared with particle therapy.[9]

Brachytherapy has a long history of successful treatment of ocular melanomas, beginning in 1930 with the use of radon seeds and being gradually refined with the utilization of ^{60}Co, ^{192}Ir, ^{198}Au, ^{90}Sr, ^{106}Ru, ^{125}I, ^{103}Pd, or ^{131}Cs, along with various eye plaque designs.[9,13] In 1985, the Collaborative Ocular Melanoma Study (COMS) was launched by the National Eye Institute of the National Institutes of Health (Bethesda, MD). One COMS multi-institutional cooperative clinical trial was to compare the survival rate for enucleation against ^{125}I plaque brachytherapy for ocular melanomas of medium sizes.[14] No survival difference was found.[15] Brachytherapy

with eye plaques was established as an effective modality of ocular melanoma treatment while preserving the eye. The American Brachytherapy Society (ABS) published consensus guidelines for plaque brachytherapy in 2003 and 2014.[9,16] The AAPM and American Brachytherapy Society Task Group 129 published recommendations for improved dosimetry methods to account for material heterogeneities in the eye plaque.[12] All these improvements continue to contribute to the success of ocular melanoma brachytherapy. Even many patients with large size ocular melanomas seek brachytherapy treatment for eye preservation.[9]

Rebuttal: Kavita K. Mishra, MD

I appreciate Dr. Chiu-Tsao's well-written Opening Statement and have the following thoughts regarding her criteria for ideal treatment.

First, we both completely support the idea that ideal therapies should be available to all patients. Unfortunately, in our medical system, this is less a scientific issue and more a health economics and public health issue. Especially in rare tumors like OM, specialized centers often carry the weight of R&D for ideal treatments. By the first criterion, enucleation is the most "readily available" treatment; however, few would argue today that this is ideal.

Second, in terms of cost-effectiveness for OM patients, counterintuitive to many, the average current treatment cost is actually lower for a course of proton therapy than a course of plaque therapy. A recent study of ocular melanoma-specific treatment costs based on national inpatient and Medicare payments found that the *mean total treatment cost for plaques was higher than* for *proton beams* and that both were higher than enucleation.[17] The difference may be that particles require a single surgery and are given over only 4–5 fractions, whereas a plaque requires two surgeries and additional inpatient costs.

Finally, regarding proven efficacy, meta-analyses, retrospective, and prospective data cited earlier have shown particles to be as effective or more for equivalent OM tumors in terms of *LC, eye preservation, and vision*—the top criteria sought by most patients. Of note, changes in particle treatment planning and post-RT care have significantly reduced the more common anterior segment side effects.[18] Furthermore, the ABS paper quoted by Dr. Chiu-Tsao[9] states the example that "*patients with peripapillary and subfoveal (tumors) and those with exudative retinal detachments typically have poorer resultant vision and local control outcomes* (with plaques) *and should be accordingly counseled.*"

Overall, while cost-effectiveness and center availability are important health economics/public health issues, these do not change the clinical research showing excellent outcomes of particles that drive individual patient decisions. Existing proton/particle centers specializing in OM treatment offer an ideal effective treatment for a rare disease entity.

Rebuttal: Sou-Tung Chiu-Tsao, Ph.D.

Dr. Mishra's Opening Statement actually confirms my point that charged particle therapy is not ideal for ocular melanoma treatment. She admits that access to CPT can be difficult due to a

limited number of centers offering this modality. Since CPT is not readily available to the majority of ocular melanoma patients, it is not ideal (Criterion #1).

The CPT modality is very expensive and not cost effective. Hence, it is not ideal (Criterion #2).

She did not mention the higher anterior segment complication rates with CPT compared to brachytherapy. CPT requires anterior entry fields, even when treating posterior tumors. The exposed anterior normal tissues are not spared with CPT for the majority of posterior ocular melanomas, so CPT is not ideal (Criterion #3).

Dr. Mishra cites eye plaque brachytherapy as a viable modality for ocular melanoma treatment, in agreement with my opening statement against the Proposition. She mentions a meta-analysis reviewing patients receiving CPT or brachytherapy, with the comparison of local failure rates of 9.5% for brachytherapy and 4.2% for CPT. Given the margin of error in this retrospective analysis of nonrandomized studies, the local failure rates of these two modalities do not appear very different. Both modalities allow eye preservation with a high rate of local control.

In conclusion, CPT is *not* ideal for the majority of ocular melanomas. Eye plaque brachytherapy *is*.

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2.15. Photon radiotherapy has reached its limit in terms of catching up dosimetrically with proton therapy

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Reproduced from *Medical Physics* **43**, 4470–4472 (2016)
(http:// dx.doi.org /10.1118/1.4954790)

OVERVIEW

Supporters of proton therapy claim that, by their very nature, protons are bound to lead to dose distributions that are superior to any that are achievable with photons and that photon therapy has reached its limit in terms of catching up dosimetrically with protons. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Harald Paganetti, Ph.D. Dr. Paganetti obtained his masters and doctoral degrees from Rheinische-Friedrichs-Wilhelms University, Bonn, Germany and started his career in Medical Physics as a postdoctoral fellow at the Forschungszentrum Julich, Germany, working on computer simulations and experiments toward microdosimetric characterization of clinical proton beams. After several positions in Germany, he moved to Massachusetts General Hospital and Harvard Medical School to continue his work in proton radiotherapy, where he is currently Professor and Director of Physics Research in the Department of Radiation Oncology. Dr. Paganetti has served on numerous task groups and committees of the AAPM, ASTRO, and the NIH/NCI, including as Chair of the AAPM TG 256 on proton RBE, and is an elected member of the NCRP. He has published over 170 peer-reviewed papers and is Editor of the book “Proton Therapy Physics.”

Arguing against the Proposition is Cedric X. Yu, D.Sc. Dr. Yu received his M.S. and D.Sc. degrees from Washington University, St. Louis and, after working in industry for three years, moved to William Beaumont Hospital, Royal Oak, MI, as a medical physicist and Assistant Professor at Oakland University. In 1997 he moved to the Department of Radiation Oncology, University of Maryland as Director of Medical Physics and became the endowed Carl M. Mansfield, M.D. Professor. Dr. Yu has served on many task groups and committees of the AAPM, including the Board of Directors, as well as President of the Mid-Atlantic Chapter. His major research interest is conformal radiotherapy such as intensity modulated photon therapy (IMRT) and intensity modulated arc therapy, which he invented in 1995. He holds 20 patents and has published over 100 peer-reviewed papers, and is certified in Radiation Oncology Physics by the ABMP. Dr. Yu is the founder and CEO of Xcision Medical Systems, LLC, and declares that he is a shareholder in the company.

FOR THE PROPOSITION: Harald Paganetti, Ph.D.

Opening Statement

Radiation therapy has undergone significant improvement in the last decades. For instance, advances have been made in planning and delivery techniques such as robust optimization[1] and image guidance.[2] When proton therapy was introduced, it offered a substantial dosimetric advantage over photon therapy due to the improved dose conformity and advanced in-room imaging (2D orthogonal radiography), which was first introduced in proton therapy because of the sharp dose gradients and the lack in exit dose for guidance.[3] Subsequently, photon therapy has decreased the gap in terms of dose conformity as new planning and delivery techniques were introduced, e.g., IMRT, tomotherapy, and volumetric arc therapy. At the same time, proton therapy started to lag behind, particularly in in-room imaging technology. Thus, today the achievable target dose conformity is often not significantly different between photon and proton techniques[4] and in-room imaging technology is more advanced on the photon side. It thus seems as if photon therapy has slowly closed the gap on proton therapy and is increasingly doing so. This is deceiving since it can be expected that the dosimetric gap between proton therapy and photon therapy will tilt toward a proton advantage in the next decade for the following reasons:

1.We see an increase in multimodality treatments such as combinations of radiation with targeted therapies or immunotherapy. These strategies will benefit from advanced control of the dose to organs at risk, tumor dose escalation, or dose painting. While a prescribed target dose can be often achieved with protons as well as photons, proton therapy will always deliver a factor of 2–7 less overall dose to critical structures, independent of photon delivery or optimization techniques.[5] This adds leverage when optimizing multimodality treatment strategies.

2.Most proton therapy patients are still treated with passive scattering. In the next few years, the majority of patients will be treated with proton beam scanning allowing treatment optimization with protons that is far superior to what is achievable with photons. Intensity modulated proton therapy (IMPT, which due to energy modulation offers one additional degree of freedom compared to IMRT) and robust optimization offer unprecedented dose shaping capabilities.[6]

3.Proton therapy is expected to catch up with photon therapy as far as in-room imaging is concerned. Even proton-MR systems are being designed. Most importantly though, there are novel imaging techniques for adaptive radiation therapy and dose delivery verification that are unique to proton beams (such as prompt gamma imaging) thus offering proton specific advancements in dose confirmation and image-guidance.[7]

Compared to these, further improvements in photon therapy are either marginal or can be utilized on the proton side as well.

In summary, both photon as well as proton therapy technology will continue to improve but the ceiling for proton therapy is significantly higher. Consequently, in the future we will see an even bigger dosimetric advantage for protons. Although clinical significance has to be shown in clinical trials, it is likely that this will have a profound impact on treatment outcomes.

AGAINST THE PROPOSITION: Cedric X. Yu, D.Sc.

Opening Statement

In the two decades since the advent of IMRT, we have seen tremendous improvements in delivery efficiency with rotational IMRT and in targeting accuracy with on-line and on-board image guidance. However, the dose distributions have not shown much improvement in spite of the intense efforts spent on optimization methods. This fact has misled many in the field to think that photon radiotherapy has reached its limits set by the physics of dose deposition and the future of radiotherapy is in protons and heavy ions. In a review paper on IMRT published eight years ago,[8] the authors concluded the following: "*Based on 10 years of experience with IMRT, we have learned that the opportunities in improving plan quality are limited within the constraint of present linac/MLC delivery*."

It is important to note that these conclusions were based on the (then) current designs of the linear accelerator (linac) and multileaf collimator (MLC) and current delivery methods. If a new system design or new treatment method injects new degrees of freedom into plan optimization, better treatment plans can be realized. An example of exploring additional freedom is the 4πRT proposed by Ke Sheng and his colleagues. They have demonstrated that significant improvements in dose distribution can be achieved for liver,[9] lung,[10] head and neck,[11] and prostate[12] by extensive use of noncoplanar IMRT fields.

Photons should also include gamma rays emitted from radionuclides. The small source sizes allow design of less compromising, site-specific solutions. A prime example is the Gamma Knife for intracranial radiosurgery. With the possibility of focusing hundreds of beams to a single spot, convenient and effective treatments can be delivered. The relative smaller sizes of teletherapy machines and linacs also allow simpler integration with imaging. The MRIdian system developed by ViewRay and the Atlantic system developed by Elekta exemplify the advantages of smaller photon machines.

While the dosimetric characteristics of protons have certain advantages over those of photons, we must also recognize their disadvantages. In addition to high cost, some of these disadvantages include broader penumbra, proton beam range uncertainties, dose calculation uncertainties (e.g., CT artifacts), distal-end RBE uncertainties, high dosimetric sensitivity to anatomical changes (e.g., nasal cavity filling), and the limitations in spot size. The argument that proton therapy is still in its infancy and, therefore, it will have more room to advance is both untrue and invalid. Generally, the more complex the technology, the more restricted and difficult it is to advance. For example, intensity modulated proton arcs would be harder, if not impossible, to achieve with the current spot scanning technology.

While the available freedom given by the current photon machine design and treatment methods has largely been exhausted, new designs and treatment techniques can inject new freedom and drastically improve the quality of plans. These dosimetry improvements can be achieved without losing the benefits of efficiency and image guidance. It would be shortsighted to think that radiotherapy with photons has reached its limits.

Rebuttal: Harald Paganetti, Ph.D.

Photon therapy has advanced leading to improved dose conformity. But these advances, instead of reducing the integral dose, mainly re-distribute the dose. This certainly has clinical merits. New techniques (e.g. 4π-RT) will increase dose conformity further. Yet, except at depths greater than about 15 cm (e.g., for lateral prostate fields), where scattering of protons causes the penumbra to be worse than with photons, the dose conformity can never reach that of a proton plan (which can be proven mathematically). Clinical significance is another matter.

This is not the argument we are trying to settle. This debate is whether the gap between photons and protons is likely to narrow or to widen. Protons offer more potential in improvements compared to photons as outlined in my opening statement.

Range and RBE uncertainties as well as sensitivity to anatomical changes are indeed proton-specific obstacles. Range uncertainties are currently reduced by advanced dose calculation and imaging, while RBE uncertainties are currently being assessed experimentally and clinically. This research will increase the current dosimetric gap between protons and photons, not decrease it. Anatomical changes are addressed with on-board imaging and adaptive therapy (for both photon and proton therapy). The lack of intensity modulated proton arcs is not a limitation because the technique is not even necessary for protons given the advanced dose shaping capabilities and small spot sizes.

Photon machines are significantly smaller than proton machines (even single-room solutions). Whether efforts to make proton delivery systems more compact will result in machines with the same size as a photon system is debatable. But size is related to cost, not to treatment quality.

I find my opponents' statement that "*new designs and treatment techniques can inject new freedom and drastically improve the quality of plans*" unconvincing. While I agree that photon radiation therapy can be improved, it does have a lower ceiling than proton therapy.

Rebuttal: Cedric X. Yu, D.Sc.

There is a consensus that the utmost goal in radiotherapy is delivering the best possible dose distribution to achieve the highest therapeutic ratio. The disagreement is which radiation type, photon and proton, will have a better long-term prospect to reliably deliver a more conformal dose distribution to the target while providing better sparing of the surrounding structures? Photon radiotherapy will more likely be the long-term winner based on the following facts.

Most of the known drawbacks of proton beams as listed in my Opening Statement are rooted in the physics of particle transport in the medium and, therefore, are not easily overcome with technology. These drawbacks, coupled with the complexity and size of proton accelerators, will set the ceiling on the quality of plans and on the reliability in realizing such plans in the patient. There are many advanced treatment delivery and image guidance techniques being practiced today or emerging in practice for photons that will be hard for protons to follow. These include tracking tumor motion, rotational intensity modulation, and MRI imaging during treatment delivery. Prompt gamma imaging is unique to protons, but it merely overcomes one of the dosimetric uncertainties unique to proton beam delivery. Therefore, it should not be viewed as an

advantage but rather an additional, required, imaging procedure that may further reduce patient throughput.

Although proton beam therapy produces better dose distributions than photon beams today, it would be premature to assume that photon beam radiotherapy will not catch up or even surpass protons in dosimetric conformity. For example, 4π radiotherapy has shown dose distributions that rival IMPT for many sites.[10,11] There is no reason that "the ceiling for proton therapy is significantly higher" than photons. It is often true that the more complex and cumbersome the technology, the harder it is to advance. Economic reasons aside, the relative reliability associated with photon beam treatment delivery and the associated treatment efficiency make advancing photon beam radiotherapy a better investment.

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2.16. In the era of IGRT and small and focal field external beam radiotherapy, brachytherapy is a dying modality

E. Ishmael Parsai, Zoubir Ouhib
Reproduced from *Medical Physics* **44**, 351–354 (2017)
(http:// dx.doi.org /10.1002/mp.12016)

OVERVIEW

The use of brachytherapy has steadily declined over the past decade, at least in the United States. Much of this is possibly due to significant technological advances in external-beam radiotherapy, whereby higher doses can be delivered with smaller margins, significantly mimicking highly conformal brachytherapy. Some are even claiming that in this era of Image Guided Radiation Therapy (IGRT) and small- and focal-field external beam radiotherapy, brachytherapy is a dying modality. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is E. Ishmael Parsai, Ph.D. Dr. Parsai obtained his Medical Physics M.Sc. from the University of Missouri, Columbia in 1985, and his Radiation Oncology Physics Ph.D. from the Medical College of Ohio in 1995. He is currently Chief Medical Physicist in the Radiation Oncology Department at the University of Toledo Health Sciences Campus, where he is the director of the graduate medical physics program. He is also Adjunct Professor in the Department of Physics and Astronomy in the University of Toledo, Toledo, Ohio, Adjunct Professor of Nuclear Medicine in the University of Findlay, Ohio, and Adjunct Professor at Wenzhou University, P.R. of China. Dr. Parsai is certified by the American Board of Medical Physics and the American Board of Radiology (ABR) in Radiation Oncology Physics and Therapeutic Radiologic Physics, respectively. He has authored or co-authored five patents and has published about 60 articles in peer-reviewed journals and six book chapters. Dr. Parsai has served as the major advisor to 16 Ph.D. students and 54 M.S.-level students in the past 10 years. He has also served as the Editor of *Medical Physics World*, Chairman of the ACRO Physics Commission, on the AAPM Board of Directors and many other AAPM committees, and as an oral examiner for the ABR.

Arguing against the Proposition is Zoubir Ouhib, M.S. Mr. Ouhib is the chief medical physicist at the Lynn Cancer Institute of Boca Raton Regional Hospital and Assistant Professor at the Florida Atlantic University in the Department of Medical Physics. He earned an M.S. from Georgia Tech in Nuclear Engineering and an M.S. in Medical Physics from the University of Cincinnati. He is board certified by the American Board of Radiology in Therapeutic Radiologic Physics and is a Fellow of the American College of Radiology (ACR). He has served as Chair of the American Brachytherapy Society (ABS) Physics Committee, Vice-Chair of the AAPM Brachytherapy Sub-Committee, and as a member of several AAPM Task Groups. Mr. Ouhib has published several peer-reviewed papers, and book chapters, and has presented at national and international meetings on topics such as patient safety, quality assurance, brachytherapy procedures, regulations, and medical events. He is the founder of the ABS Quality Assurance

School, and is a member of the ASTRO Accreditation Program (APEX) and the ACR Physics Committee. He served as President of the AAPM Florida Chapter.

For the proposition: E. Ishmael Parsai, Ph.D.

Opening Statement

With technological advances in small field Stereotactic Body Radiation Therapy (SBRT) with IGRT planning and delivery, similar dosimetric outcomes are achievable without the need for invasive surgery and its attendant complications or side effects; or the added uncertainty inherent in brachytherapy (BT) applications. This is well established for early stage prostate cancer.[1, 2] Today, despite the central role it continues to play in the management of several cancer types,[3, 4] there seems to be a trend in the US whereby the use of brachytherapy is in rapid decline.[1, 2, 5, 6] To illustrate this point, a recent article by Petereit, et al.[4] which examined changes in the management of prostate and uterine cervical cancers, found a significant decline of brachytherapy use and suggested some attributing reasons.

For cervical/uterine cancer treatments, in the last decade, when brachytherapy was mostly used as a boost, image-guided SBRT has replaced it simply because it achieved similar outcomes without the risks, and the fact that many patients do not select brachytherapy. Using the Surveillance, Epidemiology, and End Results (SEER) database to study 7359 patients who received EBRT for cervical cancer between 1988–2009, Han et al.[5] showed that there had been a 25% reduction in brachytherapy use. Gill et al.,[6] analyzing 7654 patients with cervical cancer using the National Cancer Data Base (NCDB) treated during the period of 2004–2011, reported a decrease in the use of brachytherapy from 96.7% to 86.1%, while IMRT and SBRT treatments showed an increase from 3.3% to 13.9%. Eifel, et al.,[7] in their report of patterns of radiation therapy practice, reviewed the records of 261 randomly selected patients from 45 institutions who received radiation for cervical cancer from 2005–2007 and compared them to patients treated in the period from 1996–1999. They found that 13% of patients treated from 2005–2007 did not receive brachytherapy, almost double the rate that was observed in the earlier cohort.

For prostate cancer, LDR brachytherapy is only an effective or feasible monotherapy treatment modality in patients who would be just as effectively treated with external beam IMRT.[8] In a mega study presented by Martin et al.[1] using the NCDB to look at approximately 1.5 million patients who were treated between 1998 and 2010, found that brachytherapy use reached a peak of 17% in 2002 and steadily declined to a low of 8% in 2010. The most dramatic decline in brachytherapy procedures between 2004 and 2010 was seen at academic centers (48%), although it was also significant at comprehensive community (41%) and community cancer centers (30%).[1] Similarly, Mahmood et al.[2] used the SEER database to study approximately 182,000 patients treated with radiation between 2004 and 2009. They found that prostate brachytherapy procedures decreased from 44.2% in 2004 to 38.0% in 2009. Concurrently, the difference in use of EBRT instead of brachytherapy grew from 11.6% in 2004 to 24.0% in 2009. Declining rates of brachytherapy use are not just because of physicians' reluctance to put patients through these invasive procedures, but from patients' strong desire to avoid these procedures because of invasiveness, discomfort, and operative risks. In many cases, these patients can even be managed with active surveillance rather than treatment.[6]

Against the proposition: Zoubir Ouhib, M.S.

Opening Statement

The addition of IGRT and small- and focal-field external beam radiotherapy over the past decade was a valuable step in the development of modern radiation therapy. In the same period, there has been a decrease in the use of brachytherapy in the last few years. These two facts are not directly inter-related. The reasons for such a change in the use of brachytherapy are associated with reimbursement and the risk of Medical Events, which have led to a decrease of interest and training in brachytherapy over the past few years. This is not to be interpreted that brachytherapy is a dying modality but simply going through a "pause mode." Brachytherapy is an immortal art that will never die. There is a renewal of interest in training (such as the ASTRO annual meeting Prostate Brachytherapy Simulation Workshop). In the US, the risk of clinical insignificant Medical Events in brachytherapy relative to EBRT is being mitigated by more reasonable rules proposed by the USNRC. Brachytherapy has been held to a higher standard. For example, radiation source location has to be documented and confirmed, whereas with IGRT we rely on an x-ray film or CBCT for target treatment, but there is no confirmation or documentation that the radiation itself was delivered to the intended location (…patient movement, breathing motion, machine malfunction, etc.) When evaluating IGRT treatment delivery, one relies on clinical outcome and untoward results. In brachytherapy, for the majority of the time the applicator and, therefore, the sources, will move with patient movement. The treatment site is still receiving the intended dose. It is worth mentioning that brachytherapy has been using image-guided technology for several decades, long before IGRT and, for the reasons stated above, is also a target-tracking modality. Other advantages of brachytherapy are reduced risk of radiation-induced cancer (less stray radiation and no neutrons), and better dose limitation to OARs.

On the reimbursement side in the US, brachytherapy has been treated unfairly. For similar treatment, brachytherapy has seen relatively unattractive low reimbursement. Because of its long and proud history of excellent outcomes, it is simply a matter of time before common sense and fairness will convince the decision makers to allocate the largest piece of the pie to the most deserving modality, brachytherapy. In a bundled system of reimbursement, brachytherapy is the obvious winner because it has provided better value as defined by parameters such as quality, patient experiences, and cost. When compared to other modalities, brachytherapy is a very cost-effective, medically efficacious, and efficient treatment. In a well-designed clinical trial, brachytherapy will undoubtedly surpass external beam with IGRT. The late Dr. Peter Grimm had an ongoing comparison for prostate treatment using all modalities that demonstrated the superiority of brachytherapy over EBRT and surgery for all groups (low, intermediate and high risk patients).[8] It also showed that spending more does not provide a better outcome. Treatment selection by healthcare providers is sometimes made, for obvious reasons, on a better reimbursement and not on best available evidence.

As healthcare policies become more scrutinized and the focus is on cost efficiency and proven outcome, brachytherapy will not only survive but will become the obvious choice of treatment for several body sites.

Rebuttal: E. Ishmael Parsai, Ph.D.

Brachytherapy has significantly declined for numerous reasons, but mainly due to the rise of SBRT and image guidance providing tangible benefits to the patients, delivering treatment with minimally invasive procedures, and no uncertainty typically inherent to brachytherapy applications.

Other reasons include high cost of maintaining radioactive materials licensing and material security, lack of training and/or time investment of professionals to maintain expertise and competency with brachytherapy technologies/techniques, and patient comfort.

My opponent argues that brachytherapy has been unfairly burdened with a higher standard for medical event reporting. He also argues that, for SBRT, pre-treatment imaging, and positioning verification is not sufficient to ensure dose delivery to the target, in light of patient motion or machine malfunction. I respectfully reject the suggestion that SBRT with on-board imaging is akin to a lottery in terms of delivery accuracy. The shift toward SBRT is due to its ability to effectively control tumors with minimal normal tissue complications, when delivered properly. However, this argument also neglects advancements in imaging technology, such as 4D CT, optical monitoring, active tumor tracking, and transit dosimetry, among others. While still relatively new, these technologies can alleviate concerns about patient motion (inter- and intra-fraction) and machine functionality. In many ways, these are better able to ensure accurate dose delivery than what is available for brachytherapy for which preliminary attempts to perform positioning verification during treatment are not being used clinically, although they are under development.

We also support the development of a well-designed, prospective, randomized trial to compare brachytherapy and SBRT outcomes for disease sites traditionally treated with brachytherapy. These data do not exist and should be a question that our community addresses to offer the utmost care with the least intrusion and discomfort to patients. We do not know which modality is best, or exactly how much better one is than the other. Debates such as this are useful in spurring thought but, ultimately, comparisons are only speculative until real clinical data can help guide the standard of care.

To conclude, the answer to the question of whether the use of brachytherapy is declining is an overwhelming yes. At this time, we have little prospective evidence that brachytherapy offers superior outcomes to IGRT. Establishing the relative efficacy between these two modalities should be an important goal of future research.

Rebuttal: Zoubir Ouhib, M.S.

My colleague stated in his first paragraph the reasons why brachytherapy is not as desirable as SBRT with IGRT. It is interesting that several of the references used for his argument happen to indicate the exact opposite. When describing brachytherapy treatment, the references support the following:

- It has comparable outcomes and favorable cost effectiveness.[1, 4]
- *"Without question, the inclusion of brachytherapy in the multimodality management of cervical cancer remains the standard of care for this disease*."[4]

- *"Brachytherapy not only works but is an irreplaceable component of contemporary cancer care*."[4]
- The one obvious advantage cited for EBRT was a better reimbursement but not outcome.[1, 2, 4]

For LDR prostate brachytherapy, I would urge my colleague to look more closely at the prostate radiotherapy paper by Grimm, et al.:[8] They concluded that "*brachytherapy approaches provide superior outcome in patients with low-risk disease*." Furthermore, Petereit et al.[4] had the following statements: "*…brachytherapy can be considered the ultimate form of conformal radiation therapy because it is unparalleled in its ability to direct a large dose of radiation to the tumor while minimizing exposure to surrounding sensitive normal structures*" and "*reimbursement for IMRT is markedly higher compared with that for brachytherapy*." Also, when looking at Mahmood's reference,[2] I could not help noticing the mention of higher reimbursement for EBRT compared with brachytherapy (a common theme!). Several arguments of my colleague seem to be based on perception and not facts. Frank et al.[9] addressed these items and concluded that brachytherapy provides the best value when evaluation of outcomes is based on sexual function, urinary problems, bowel function, biochemical relapse-free survival, and cost factors.

In summary, because of the superior outcomes and efficient treatments provided by brachytherapy, it is simply a matter of time and common sense before most practitioners will come back to the right choice. Those who have chosen to temporarily abandon it will have some catching up to do!

Acknowledgments

Dr. Parsai wishes to thank Drs. Changhu Chen and Krishna Reddy for helpful discussions.

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CHAPTER 3

Brachytherapy

3.1. Brachytherapy is better than external beam therapy for partial breast irradiation

Dorin Todor and Stewart Becker
Reproduced from *Medical Physics* **41**, 080601-1-4 (2013)
(http:// dx.doi.org /10.1118/1.4798227)

OVERVIEW

Partial breast irradiation (PBI) by either brachytherapy or external beam (EB) therapy is frequently used for the treatment of certain populations of breast cancer patients. Some claim that brachytherapy is better than external beam therapy, and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Dorin Todor, Ph.D. Dr. Todor obtained his Ph.D. degree in Physics from Old Dominion University, Norfolk, Virginia in 2000 and then completed a one-year Postdoctoral Research Fellowship at Memorial Sloan-Kettering Cancer Center, New York. Since then he has worked at the Virginia Commonwealth University where he is currently an Associate Professor in the Department of Radiation Oncology. His major research interests include image-guided adaptive radiation therapy, real-time 3D HDR source position detection and tracking, and dual fusion imaging for intraoperative planning, execution, and evaluation of brachytherapy implants, and he has published over 30 papers on these and other topics.

Arguing against the Proposition is Stewart Becker, Ph.D. Dr. Becker obtained his M.S. and Ph.D. degrees in Medical Physics from the University of Wisconsin, Madison after which he moved to the Department of Radiation Oncology, New York University Langone Medical Center, where he is currently a Senior Physicist and an Assistant Professor. He is certified in Therapeutic Radiological Physics by the American Board of Radiology. His major research interests include image-guided radiotherapy, and whole and accelerated partial breast radiotherapy. He currently serves as a member of the AAPM Radiation Oncology Medical Physics Education Subcommittee.

FOR THE PROPOSITION: Dorin Todor, Ph.D.

Opening Statement

The number of techniques and devices used to deliver breast radiotherapy has increased dramatically in recent years in an attempt to create more conformal, homogenous, and reproducible dose distributions as well as to provide shorter, more convenient treatment schedules. Brachytherapy and external beam radiotherapy for PBI offer equal convenience, but differ substantially in dose distribution and treatment delivery. Brachytherapy offers several advantages over EB-PBI. First, brachytherapy techniques are associated with smaller treatment volumes and integral doses as well as smaller normal tissue fraction doses, all of which contribute to a lower normal tissue toxicity. Next, the dosimetric parameters which affect toxicity have been thoroughly investigated for brachytherapy techniques.[1] In particular, the use of interstitial brachytherapy is supported by over ten years of follow-up data demonstrating excellent local control and minimal long-term toxicity when established dosimetric guidelines are used for planning.[2] Conversely, EB-PBI is the modality associated with the least available follow-up data, and no standardized, evidence-based treatment planning guidelines currently exist for this technique. The experience accumulated in accelerated partial breast irradiation (APBI) suggests a strong volume effect for late normal tissue toxicity.[3] There is compelling evidence for a steep dose response with external beam treatment, suggesting that 40 Gy/10 fractions/5 days may represent the maximum tolerance for EB-PBI.[4] Given that the current guidelines for the most widely used fractionation for photon EB-PBI (38.5 Gy/10 fractions/5 days) allows for inhomogeneity of up to 120% of the prescribed dose, depending on planning style and physicians' choice of prescription (from V90 ≥ 90% to V100 = 100%), a significant volume of tissue may receive upwards of 40 Gy in a typical plan. Schedules that may be safe when delivered with brachytherapy to small partial volumes with tightly controlled parameters cannot be assumed safe if delivered to larger partial volumes with external beam. In fact, the most recent evidence shows that APBI using 3D EBRT can increase the risk of moderate radiation side effects leading to poor cosmetic outcome for some patients.[5]

Finally, a recent analysis showed that incremental cost-effectiveness ratios for balloon-based brachytherapy compared with 3D-CRT were $519/$850 per percent improved excellent/good cosmesis based on reimbursement and $301/$647 based on facility costs, thus making brachytherapy a more cost-effective modality.[6]

Despite the differences in techniques, evidence currently suggests that treatment with both brachytherapy and EB-PBI have the potential for excellent clinical outcomes for patients. The sometimes conflicting results published by different institutions can likely be explained by differences in planning styles, a lack of proper radiobiological models allowing understanding of toxicity, and the lack of standardized dosimetric parameters.[7,8]

Debating the relative merits and drawbacks of the various PBI techniques encourages unnecessary partisanship and conflict, and distracts us from our real goal: achieving a better understanding of both techniques, optimizing patient selection and resource allocation, and customizing treatment for each individual patient. This goal will not be achieved until quality indicators for each modality can be established based on clinical data derived from an APBI registry rather than on inherent technical limitations of a method or device. While cost is

increasingly important, the ideal choice is not for all patients to get the least expensive treatment but for each patient to get the optimal treatment while minimizing costs at the population level.

AGAINST THE PROPOSITION: Stewart Becker, Ph.D.

Opening Statement

There are two main priorities in breast cancer treatment: survival and cosmetic outcomes. Partial breast irradiation has been established as a valid alternative to whole breast irradiation for a subset of early stage breast cancer patients based on 5–10 year data.[9] This is true whether PBI is administrated via brachytherapy or external beam x-ray therapy (XRT). While both techniques have been studied individually,[10–13] no definitive randomized study has been conducted to compare them. These studies have shown similar results in terms of survival outcomes for each technique. Cosmetic outcomes of PBI were discussed at a plenary session of the 2012 ASTRO Annual Meeting. The results varied widely between and among techniques.

Because cosmetic outcome studies have not produced definitive answers, we must rely on other measures to determine the most suitable treatment method.

There are several issues with delivering brachytherapy that make XRT more attractive.

(1) Every clinic has a linac, but not every clinic has a HDR unit or facilities to support LDR sources (i.e., free standing clinics).

(2) The success of brachytherapy is dependent on the skill and training of the radiation oncologist to achieve high quality implants.

(3) Brachytherapy treatments are invasive, whereas XRT is noninvasive and does not subject the patient to additional surgery or anesthesia.

(4) A brachytherapy program requires greater effort to commission and maintain due to training, equipment, and personnel coverage required.

(5) Brachytherapy is performed BID, which can be more difficult for patients than the once a day treatment schedules that XRT can offer.

(6) Some patients cannot be treated with brachytherapy due to their cavity shape or breast size, while these factors have no bearing on XRT.

(7) Brachytherapy can result in unnecessary procedures on patients with contraindicative pathology reports. This is not an issue for XRT patients since the pathology reports are available before treatment begins.

(8) Brachytherapy requires additional professional time to plan and image compared to XRT.

While none of these are as important as outcomes, they are real issues that clinics must assess and patients must endure.

Rebuttal: Dorin Todor, Ph.D.

My opponent offers a list of reasons for which 3D-CRT PBI is easier and maybe more convenient, but not necessarily better. He opens the list with the argument that "every clinic has a linac." Just as the availability of fast food does not make a frozen hamburger objectively better or healthier than a gourmet meal, the fact that all clinics theoretically possess the ability to deliver 3D-CRT PBI does not make this treatment better than brachytherapy. Although he appropriately indicates that none of his points "are as important as outcomes," he fails to acknowledge the paucity of long-term data on local control or the emerging reports describing unacceptable toxicity and cosmesis after 3D-CRT.[5] Some arguments are misleading: balloon or catheter placement do not require systemic anesthesia, 3D-CRT PBI is not more convenient as it is commonly delivered with exactly the same schedule as brachytherapy, and neither 3D-CRT nor brachytherapy treatments begin prior to final pathologic review. What is not debatable, however, is that the integral dose to the nontarget aspect of the breast is higher with 3D-CRT compared to brachytherapy. Larger volumes of nontarget breast tissue irradiated with current PBI fractionation schemes may lead to increased toxicity. The "triple-trouble" (high dose, dose/fraction, and volume) phenomenon associated with hot spots in hypofractionated treatment suggests a marked volume response for late effects such as breast size reduction, breast induration, and fat necrosis resulting from hot spots >110%. For these reasons, plan optimization for 3D-CRT might not be a trivial exercise and better plan evaluation guidelines might also be needed. Brachytherapy is a more conformal, better understood technique, which will continue to be a reliable and economical modality for APBI.

Rebuttal: Stewart Becker, Ph.D.

I agree with my opponent that currently brachytherapy and external beam both offer convenient treatments with comparable survival outcomes. However, we disagree when it comes to the importance of dosimetric differences such as integral dose, the interpretation of early XRT results, normal tissue toxicity outcomes, and the inherent costs of both procedures.

First, I want to address the issue of integral dose as a cause of normal tissue complications for XRT. There are many dosimetric issues that are not very well understood. Integral dose is one of them; very high dose regions close to the catheters in HDR is another. While both of these are academically interesting, neither is fully understood nor can they be blamed for toxicities… yet.

Interstitial brachytherapy now has ten-year follow-up data, but my opponent fails to mention the difficult start that the procedure had and how they adapted based on their own early data. Breast necrosis and infection were addressed for interstitial and skin toxicity was addressed for balloon systems. XRT-PBI may only have five-year follow-up data but has had a much smoother beginning. XRT will definitely benefit as standards are tightened for volumes and prescriptions based on these five-year studies, just as brachytherapy did. The RTOG and other groups are also helping to standardize planning techniques (i.e., prescriptions, dose constraints, and volumes treated). Our own five-year follow-up experience at New York University, shows a 1%

recurrence rate with 11% fair-to-poor cosmesis,[10] which is in line with many studies.[14,15] My opponent pointed out that the lack of defined prescription standards can result in large high dose regions which affect cosmesis.[4] This is the exact type of issue that is currently being studied and will eventually be solved.

Finally, my opponent points out that incremental cost-effectiveness ratios favor brachytherapy.[6] However, the initial startup and maintenance costs can be prohibitive. Larger clinics may have the patient numbers and staffing to fully schedule a HDR remote afterloader, but a smaller clinic may not be able to justify a new machine and the extra staff required. In addition, reimbursements are constantly being adjusted and clinics always have at least one linac. Finally, the study did not include IMRT, which would increase the reimbursement for XRT.

I want to share Dr. Todor's sentiment that both of these methods have shown promising results for PBI. He correctly states that no technique is perfect for all patients and these methods complement each other. My hope is that this debate stimulates thought and generates new and broader perspectives to trigger innovation in the field of PBI.

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3.2. Only a therapist should operate an HDR unit for patient treatments

Maria F. Chan and Chunli (Claus) Yang
Reproduced from *Medical Physics* **43**, 5581–5583 (2015)
(http:// dx.doi.org /10.1118/1.4929549)

OVERVIEW

A high dose rate (HDR) unit delivers high doses of radiation to patients in a short time, much like linear accelerators. Since it is a regulatory requirement that qualified therapists operate linacs for patient treatments, some believe that the same should apply for HDR treatments. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Maria F. Chan, Ph.D. Dr. Chan received her Ph.D. from the Medical College of Ohio in 1995 and was certified by the ABMP in 1998. She joined the faculty of the Department of Medical Physics at Memorial Sloan Kettering Cancer Center in 1999, where she currently works as Attending Physicist. Dr. Chan served as Chairperson of the Practice Guidelines Subcommittee of the AAPM for 6 years and has been an active member of many AAPM committees, work groups, task groups, as well as for the ACR, ACRO, and NACMPA. She has published over 50 peer-reviewed papers and book chapters, and has had 20 years' experience in HDR brachytherapy. Dr. Chan is a Fellow of the AAPM.

Arguing against the Proposition is Chunli (Claus) Yang, Ph.D. Dr. Yang obtained his Ph.D. in Physics from the University of Cologne, Germany and then, after working for two years as a Postdoctoral Fellow in the Institute for National Measurement and Standards, National Research Council, Ottawa, Canada, he undertook a Medical Physics residency at Toronto-Sunnybrook Regional Cancer Centre, Toronto. He then held physics positions in Albany, Detroit, and Sacramento before moving to his current position as Associate Professor and Chief Physicist, Department of Radiation Oncology, University of Mississippi Medical Center, Jackson, MS. He is certified by the American Board of Radiology in Therapeutic Radiologic Physics. Dr. Yang received the Teacher of the Year Award from the Association of Residents in Radiation Oncology in 2009.

FOR THE PROPOSITION: Maria F. Chan, Ph.D.

Opening Statement

HDR brachytherapy uses radionuclides such as iridium-192 at dose rates of 20 or more cGy/min to a designated target point or volume.[1] The US Nuclear Regulatory Commission (NRC) regulation requires an authorized user and an authorized medical physicist to be physically present during the initiation of all patient treatments involving the unit.[2] The rules and

regulations of most of the states in the US require that the licensee shall comply with the provisions and the requirements of NRC regulations (Subpart H of 10 CFR Part 35). For example, “A licensee shall ensure that operators, authorized medical physicists and authorized users participate in drills of the emergency procedures, initially and at least annually thereafter.” However, it does not specify “who” would be the “HDR operators.” Many physicists interpret the regulation as being fulfilled when physicists are operating the unit but with the physician pressing the treatment-delivery button on the HDR console. On the other hand, some states do specify that either an authorized user or a licensed radiation therapist must operate the HDR unit during the administration of radiation to cancer patients.[3–5] Based on my recent survey among physics colleagues, the operation of an HDR unit during treatment is still mainly done by physicists in many institutions. In my opinion, analogous to the regulations governing linac-based radiation treatments, the HDR unit, being a radiation-delivery device, should be operated by a licensed radiation therapist for patient treatments.

One of the clinical benefits of having therapists operate the HDR unit is to improve the communication in the radiation oncology team and also have extra sets of safeguards to crosscheck treatment plans before delivery to the patient. Plus, most therapists are enthusiastic and willing to learn, and are motivated to operate the HDR unit, which promotes and increases their communication and technical skills in the field. It also shows to administrators that HDR is a joint effort including radiation oncologists, nurses, physicists, and therapists. Furthermore, in some clinics, therapists also perform the HDR daily QAs under a physicist's supervision; this practice is supported by numerous official documents.[6–8] For example, in AAPM TG-59, it is clearly stated that the “radiation therapist executes daily QA protocol the morning of the procedure”;[6] similarly, in IAEA-TECDOC-1257, it is also stated that “daily tests can be performed by a technician.”[7]

The physicist's role is to define the organization and responsibilities of the treatment-delivery team members and to provide for their training.[6] In the past, since older models of HDR units were not directly interfaced and able to communicate with a Record and Verify (RV) system, physicists were heavily relied upon to ensure that treatment plans were being correctly transferred from the treatment planning system to the HDR unit. Currently, with many HDR units integrated into centralized information RV servers (i.e., ARIA or MOSAIQ), the chances of an HDR treatment plan being incorrectly transferred to a delivery unit is greatly minimized, and thus allows therapists to play more active roles in the operation of the HDR unit during treatments.

AGAINST THE PROPOSITION: Chunli (Claus) Yang, Ph.D.

Opening Statement

From both the regulatory and treatment safety points of view, a therapist should not be the only person to operate an HDR unit for patient treatments.

The U.S. Nuclear Regulatory Commission (USNRC) regulates the use of all reactor-produced materials (byproduct materials) including their medical use. The Code of Federal Regulations 10 CFR Part 35 requires, for HDR remote afterloader units, (i) an authorized user (AU) and an

authorized medical physicist (AMP) to be physically present during the initiation of all patient treatments involving the unit; and (ii) an AMP and either an AU or a physician, under the supervision of an AU, who has been trained in the operation and emergency response for the unit, to be physically present during continuation of all patient treatments involving the unit.[2] Currently, 37 states have entered into agreements with USNRC and assumed regulatory responsibility over most activities involving radioactive material within their states.[9]

Based on a survey of physicists working in different states, the current HDR treatment team can be a combination of the following professionals: AU, AMP, radiation therapist (RT), registered nurse (RN), and radiation safety officer (RSO). It varies across hospitals and from state to state. For instance, it can be AU + AMP + RN in Mississippi, AU + AMP + RT or AU + AMP + RN in California, AU + AMP + RN + RSO in Georgia, and AU + AMP + RT in Ohio. Who operates the console to administer HDR treatment also varies by state. Some states, such as Florida and New York, specify that only an AU or RT should administer an HDR treatment.[3,4] Some states do not specify who should operate an HDR unit for treatment, e.g., in Mississippi, where an AU or AMP or RT can push the treatment button.[10] In both agreement states and nonagreement states, the AU can execute an HDR treatment to meet the regulatory requirements.

Both AUs and AMPs play essential roles in HDR treatments as recommended by different professional associations such as the American College of Radiology (ACR), the American Society for Radiation Oncology (ASTRO), and the American Association of Physicists in Medicine (AAPM).[1,6] Although comprehensive pretreatment quality assurance is performed before an HDR treatment, the treatment process involves potentially high safety risks because it is given with a high activity source over a short duration. The AMP, who best understands the brachytherapy sources, risks, safety issues, machine delivery mechanism, and treatment planning, should take ownership of the treatment rather than simply act as a participant. When emergent situations appear, the AMP must take immediate action to minimize any potential risk.

The potential roles of the RT during an HDR treatment can be fulfilled by existing team members, e.g., AU, AMP, and RN. The AU operates the console to execute the treatment; the AMP monitors the machine performance; the RN monitors the patient; the AU oversees the process.

In conclusion, it is not necessary to have a therapist involved in an HDR patient treatment process, as it adds cost (of staff) and does not improve treatment quality or safety.

Rebuttal: Maria F. Chan, Ph.D.

I appreciate my colleague having listed all the different combinations of HDR treatment team members across the country, and I agree with his definitions of the essential roles of AUs and AMPs in the HDR process. However, I disagree with him that having a therapist in an HDR process adds extra cost and does not improve safety of HDR delivery.

First, Dr. Yang stated, “The potential roles of the RT during an HDR treatment can be fulfilled by existing team members.” I disagree with this statement. Currently, most HDR brachytherapy treatments require pretreatment imaging for verification purposes.[11] The RT plays very important

roles in the imaging process, and is there to operate an imager—either by C-arm (standalone HDR suite), O-arm (intraoperative brachytherapy), or OBI kV imager (linac room). This imaging role cannot be fulfilled by any existing team member because none of those members have the proper licensure to operate the imagers. Since RTs are already involved in the process, their operating the HDR unit really adds no additional cost.

Second, Dr. Yang stated that adding an RT does not improve safety. My view is that adding an RT would be definitely adding an additional layer of safety to the HDR process. On the other hand, having only a physicist operating the HDR unit may present a higher error probability due to lack of a self-checking mechanism. For HDR error prevention, the AAPM TG-100 has performed an FMEA for HDR brachytherapy, constructing fault trees and failure modes as a reminder of what could go wrong.[12] Also, we should provide ongoing training, including equipment usage, for all parties involved, in addition to mandatory annual training. With all the safety procedures in place, now is the time to make it a requirement that therapists should operate HDR units for patient treatments.

Rebuttal: Chunli (Claus) Yang, Ph.D.

When using the analogy between an HDR unit and a linac, one cannot ignore the fact that federal or state regulations do not require the physical presence of both an AU and the AMP for linac-based radiation therapy, but for HDR treatments, they do. For linac treatments, the AAPM only recommends the physicist's physical presence for special treatment procedures involving large fraction doses, such as for stereotactic body radiation therapy.[13] It is clear that during the initiation of all patient treatments involving HDR units, an AU can initiate treatment delivery while satisfying the regulations at both federal and state levels. The therapists do not have to be the only machine operators in radiation therapy.

Since treatment quality and patient safety are assured by the existing HDR team members of AU, AMP, and RN, adding unnecessary personnel (a therapist) could be a distraction and may potentially lead to confusion in an emergency situation. Having the therapist as the exclusive operator of the HDR unit improves neither quality nor safety and is unlikely to improve communication between the HDR team members. In addition, the physicist has to make sure that the therapist understands the treatment procedure and treatment plan, which will need extra effort and time. Furthermore, it is important to be able to demonstrate to administrators that the HDR program is cost-effective. Adding a therapist to the HDR team potentially increases personnel costs.

In summary, an HDR team of AU, AMP, and RN is effective in both cost and communication while satisfying regulations and maintaining optimal patient safety.

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3.3. Low dose rate brachytherapy for the treatment of cervix cancer is outdated and should be discontinued

Joey L. Meadows and Tewfik J. Bichay
Reproduced from *Medical Physics* **43**, 4963–4965 (2016)
(http:// dx.doi.org /10.1118/1.4959547)

OVERVIEW

Low dose-rate (LDR) brachytherapy for the treatment of cervix cancer dates back over a hundred years and, up until a few years ago, was still the dominant treatment modality for this disease. It has now been overtaken in popularity, at least in the USA, by high dose-rate (HDR) brachytherapy, and some would argue that LDR brachytherapy for the treatment of cervix cancer is now outdated and should be discontinued. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Joey L. Meadows, M.S. Mr. Meadows obtained his M.S. in Medical Physics from Wayne State University, Detroit, MI in 1990 after obtaining his B.S. degree in Radiation Therapy Technology, also from Wayne State University. He worked as a dosimetrist at the Karmanos Cancer Institute, Detroit as well as William Beaumont Hospital, Royal Oak, MI while obtaining his master's degree. Following his graduate studies, he worked as a medical physicist for several years at Radiation Oncology Services, Atlanta, GA. He then moved to Grand Rapids where he is a Senior Physicist at Spectrum Health. His clinical interests include high and low dose-rate brachytherapies, total body irradiation, and stereotactic radiation therapy. He is certified in Radiation Oncology Physics by the American Board of Medical Physics.

Arguing against the Proposition is Tewfik J. Bichay, Ph.D. Dr. Bichay obtained his B.Sc. degree in Human Physiology from McGill University, Montreal, his M.Sc. in Radiation Biology from Concordia University, Montreal, and his Ph.D. in Medical Biophysics from the University of Western Ontario, London, Canada. He is currently Director of Medical Physics, Radiation Oncology, The Lacks Cancer Center at Mercy Health, St. Mary's, Grand Rapids, MI. He started his career as a radiation biologist before transitioning into medical physicist with a residency at the Ottawa Regional Cancer Center. He is an accreditation surveyor for the ACR, served for a number of years as an ABR MOC examination committee member, and is the previous President of the Great Lakes Chapter of the AAPM, and holds a patent on a compact doorless radiation vault design. He is certified in Radiation Oncology Physics by the ABMP and his present research interests include SRS and SBRT.

FOR THE PROPOSITION: Joey L. Meadows, M.S.

Opening Statement

Over the past several decades, our profession has seen many changes which have greatly benefited patients. These new technologies allow us to deliver higher doses with increased probability of cure than would have been possible several years ago. We not only deliver higher doses to the disease but also improved spatial accuracy using modern image guidance technology. Continuing to use LDR brachytherapy to treat cervical cancer disparages our technical advancements and is a dis-service to our patients.

One of the hallmark attributes of LDR is the fixed geometry of the prescription point ("Point A")[1] relative to the applicator, where Point A is thought to be related to the internal anatomy. However, MRI has shown no correlation between the ICRU point doses and doses to organs at risk (OARs),[2] and it has been shown that in patients with large tumors, specifying the dose to Point A can result in decreased local control.[3] Today, image guidance is commonly used in HDR, which grants us the benefit of visualizing where the dose is delivered.

One of the limitations of LDR brachytherapy is its inherent inability to adapt to the environment of image guidance. Most LDR applicators are limited to 2D imaging due to their design. When we are forced to use 2D imaging, it is assumed that the points (e.g., Point A, rectum and bladder) being used for planning have specific patient anatomical significance. However, the DVH-evaluated bladder and rectal doses are often not consistent with the doses to ICRU points predicted from radiographs.[2] Continuing to use LDR results in treating the applicator instead of the patient, and it denies the clinician the benefit of using 3D imaging and planning. The LDR imaging limitation is further exemplified due to its incompatibility with multimodality imaging such as MRI and PET. Since MRI imaging has been shown to be advantageous in defining the extent of cervical cancer, it is important to use this capability for the patient's benefit.[4]

Dose optimization is also a weakness of LDR brachytherapy. The ability to optimize an LDR applicator is limited to only a few choices for distributing the source activity. Conversely, HDR brachytherapy has a wide range of choices achieved by changing dwell-time pattern, which allows the distribution of source activity to be almost limitless.[5] Even though poor implant geometry cannot be overcome entirely by optimization, HDR has the advantage of using inverse volumetric optimization rather than the trial and error approach for source activity used with LDR.[6] Inverse optimization allows for simultaneous consideration of tumor and OAR doses. This level of sophistication is impossible when using LDR-based brachytherapy.

Another limitation of LDR is applicator motion during the 24–72-h delivery time.[7] This problem can be exemplified even over the short time period between OR and simulation, where applicator motion is common. Conversely, the HDR applicator is amenable to stabilization since the delivery and planning can occur in a much shorter time frame compared to LDR. This should result in the more accurate HDR dose delivery compared to LDR.

AGAINST THE PROPOSITION: Tewfik J. Bichay, Ph.D.

Opening Statement

In North America and much of the developed world, the treatment of cervical carcinoma is typically managed by a combination of chemotherapy, external beam irradiation, and

intracavitary brachytherapy[8] by either LDR or HDR. At this point in time there is certainly sufficient clinical experience to be able to review the merits of both LDR, with about 100 yr of experience, and HDR, with about 30 yr. The questions that may be asked in comparing these two common modalities relate to clinical efficacy, safety, cost, and access to care.

Studies comparing treatment outcomes of LDR versus HDR have shown conflicting results, some indicating that LDR is superior,[3] some that HDR is superior,[9] and some, at least for nonbulky disease, that they are equivalent.[5] It appears reasonable to accept that there is no proven difference in clinical outcomes.

Remote application of sources in HDR therapy is sometimes presented as the safer modality since the exposure to medical staff is lower than that for sources placed manually in LDR.[10] This brings up two important points: first is that remote afterloading is available for LDR and, second, that serious overexposures to patients and personnel have occurred with HDR, despite the perceived improved safety.[11]

Various analyses have compared the cost of LDR versus HDR. In the case of LDR, the argument is that the cost of patient's overnight stay in a hospital is significant and can be eliminated by having HDR outpatient treatments.[12] Although this is certainly true, it is also important to note that HDR involves substantial capital costs; which include not only the HDR unit itself at about $300 K but also the cost of various sized applicators at about $50 K or more. There are also the recurring costs of sources and service that total about $75 K per year. These are real dollars that may be a challenge for smaller centers only treating a small number of patients. For the approximately 15% of radiation therapy centers in the United States that do not have access to HDR equipment,[8] the startup cost for such a program may be prohibitive. This will be even more of a challenge for developing countries with considerably lower healthcare budgets than developed countries. Being able to maintain an HDR program in an environment with limited funds would be difficult, while LDR would represent a much less expensive alternative.

Rebuttal: Joey L. Meadows, M.S.

I agree with Dr. Bichay's statement concerning LDR versus HDR: "*It appears reasonable to accept that there is no proven difference in clinical outcomes*." However, recent advances in image guidance with HDR, which allows volume optimization of the dose rather than using a fixed point dose (Point A) prescription, should allow higher doses to be delivered to more bulky tumors, while sparing organs at risk, with an expected improvement in clinical results. This potential benefit could be further enhanced as the adoption of HDR brachytherapy becomes more commonplace and the expertise is shared throughout the brachytherapy community.

Dr. Bichay asserts two other points: "*remote afterloading is available for LDR*" and "*serious overexposures… have occurred with HDR*." I agree that LDR afterloading "is available," but it is far from being commonplace. In my several decades of working in different departments, I have only encountered this technology once; this in a program well known for its brachytherapy expertise. Most institutions still utilizing LDR are doing so by manually loading sources, exposing medical staff, visitors, and patients in adjoining inpatient rooms. His second point refers to a higher likelihood of overexposures with HDR versus LDR. Granted, the consequences

of a malpositioned source are much more severe for HDR treatments. But I would also argue that this is the reason for emergency procedure training for all personnel involved in HDR. Mistakes can happen with LDR as well as HDR and we should not be reluctant to use new technology based singularly on this premise.

Finally, I agree that HDR technology is more expensive. However, the superior attributes of HDR (radiation safety, planning optimization) make it the best way to treat cervix cancer patients. To continue using LDR when a superior modality is available is unfair to patients.

Rebuttal: Tewfik J. Bichay, Ph.D.

I agree that we are in an age of image guidance and whenever possible the old "close enough" approach of dose placement should move into era of IGRT. However, I do not agree with the claim that LDR cannot adapt to image guidance. Several years ago we moved to a Henschke LDR applicator that is CT/MRI compatible. We did not invent it; it was purchased from a well-known brachytherapy supplier. The cost was less than one month of our service contract for our HDR unit. Interestingly, the ability to use MRI volumetric targeting does not seem to have caught on for either LDR or HDR. According to a recent poll of centers carrying out HDR, the vast majority relies on CT imaging, only about 3% on MRI, and the majority still used Points A for dose prescription.[13] Nevertheless, I would strongly agree that a move to volumetric imaging for brachytherapy should take place whether using HDR or LDR.

I agree that dose optimization is limited with traditional LDR using cesium pellets that are manually loaded into the applicator. There are cesium afterloader units, which allow for variable source positions and variable dwell times, essentially meeting distributions similar to those of HDR.[14] But cesium afterloaders are disappearing from use. The newer focus of pulsed dose rate (PDR) is perhaps a reasonable compromise, where pulsing can achieve dose distributions tailored to an individual patient's needs.[14–17]

The potential for applicator movement after LDR imaging is of real concern. Of course it is also a concern in the case of HDR. Any movement would negate the plan optimized for the patient. For guidance on this issue, we can look at the outcome data for both toxicity and cure rates. The data show no evidence that either approach results in increased toxicity or decreased cure.[10,18] In fact the reference given by my colleague on this topic also agrees that the outcome is the same for both techniques.[6]

In general, the assumed advantages of HDR presented by my colleague can be matched by using the latest LDR technology. Given the significant program cost for HDR, and similar clinical outcomes, it would be premature to completely discontinue LDR.

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3.4. Prostate brachytherapy should be MRI based

R. Jason Stafford and Ivan A. Brezovich
Reproduced from *Medical Physics* **43**, 6213–6216 (2016)
(http:// dx.doi.org /10.1118/1.4965810)

OVERVIEW

It is widely accepted that MRI is a useful diagnostic tool for staging and selection of appropriate therapies for prostate cancer but, for brachytherapy, it is not *widely* accepted that treatment planning and image-guided delivery ought to be MRI-based. This is the topic debated in this month's Point/Counterpoint.

Arguing for the Proposition is R. Jason Stafford, Ph.D. Dr. Stafford obtained his Ph.D. in Medical Physics from the University of Texas Health Science Center, Houston in 2001. He served as a Research Assistant at the M.D. Anderson Cancer Center from 1996 to 2001 and, since then, as a member of the faculty. Currently he is Associate Professor, Department of Imaging Physics, Division of Diagnostic Imaging, and Section Chief of MR and Ultrasound Physics. His current research interests include MRI/computed tomography (CT) markers for improved assessment of prostate cancer treatment with brachytherapy, MR-guided focused ultrasound (US), and nanoparticle mediated thermal therapy with MRI. Dr. Stafford has served on numerous AAPM committees and task groups including as Co-Chair of Task Group No. 241: MR-Guided Focused Ultrasound, on the Editorial Board of the *JACMP* and the Board of Editors of *Medical Physics*. He is certified in Diagnostic Radiological Physics by the ABR.

Arguing against the Proposition is Ivan A. Brezovich, Ph.D. Dr. Brezovich received his Ph.D. in Physics from the University of Alabama in 1977 and has since spent his entire career as a medical physicist at the UAB, initially in the Department of Diagnostic Radiology and, since 1977, in the Department of Radiation Oncology, where he has been a full professor since 1988. He is also a professor in the Department of Biomedical Engineering. He has served on many AAPM and ACMP professional and scientific committees and the AAPM Board of Directors, and as a member of the Radiological Devices Panel of the Medical Devices Advisory Committee, Food and Drug Administration. In 1994 he served as a president of the AAPM Southeastern Chapter. Dr. Brezovich is a Fellow of the AAPM, the ACMP, and ACRO, and a diplomate of the ABR in both Therapeutic and Diagnostic Radiological Physics.

FOR THE PROPOSITION: R. Jason Stafford, Ph.D.

Opening Statement

Prostate brachytherapy is an image-guided procedure that inserts radioactive sources inside the prostate to deliver high doses of radiation to the tumor and achieve a highly conformal dose distribution to ensure cancer cure with high quality of life for the patient. Multiparametric (mp)

MRI provides superior visualization of the prostate, dominant intraprostatic lesion (DIL), and surrounding organs at risk (OARs) compared to all competing imaging modalities for the delivery of radiation to this area.[1] The overall role of mp MRI in prostate cancer localization, staging, selection for therapy, response to therapy, and evaluation of recurrence with rising PSA continues to rapidly evolve.[2]

Current consensus recommendations for low dose rate (LDR)[3,4] and high dose rate (HDR)[5] brachytherapy include MRI alongside transrectal ultrasound (TRUS) and CT. Incorporating MRI into anatomical contouring can aid in reducing CT organ delineation error, OAR dose uncertainty, and user variation.[6] Postimplant dosimetry improvement strategies incorporating MRI have been actively encouraged.[3]

Prostate brachytherapy *should* be MRI-based in that, regardless of whether manual or software-based fusion of MR to US or MRI-guidance exclusively is used, the superior anatomic boundary visualization provided by MRI *should*, to the degree possible, be incorporated into critical procedure steps. These steps include pretreatment simulation, treatment planning, implant localization, and/or post-treatment implant assessment.

AGAINST THE PROPOSITION: Ivan A. Brezovich, Ph.D.

Opening Statement

Why do it the easy way if you can do it the hard way? This axiom from my native Austria was apparently written for MRI-based prostate brachytherapy long before the invention of this wasteful procedure. Brachytherapy, in conjunction with US and CT, is a well-established, efficient, and relatively inexpensive modality that has benefitted countless patients since its introduction in the mid-1980s.[7] There is no valid reason to replace it with an unproven, costly, and time consuming MRI-based procedure that may offer no further benefits for patients.

Once a patient opts for traditional transrectal ultrasound-based brachytherapy, the treatment is straightforward and fast. Physicians can take TRUS images in the comfort and patient-friendly atmosphere of their office. A treatment plan is generated and, in the case of a permanent implant, the necessary seeds are ordered. In the operating room, the position of the patient from imaging is easily reproduced, assuring a precise match between treatment plan and delivery. The needles are clearly displayed by US in real time while introducing the HDR catheters or the radioactive seeds, assuring an accurate implant. The treatment team can complete the procedure in typically less than an hour. A postimplant CT delineates seed and catheter positions with high spatial accuracy for final dosimetric evaluation.

MRI-based brachytherapy, on the other hand, requires a large machine for imaging and implantation that only a hospital can provide. Claustrophobia, pacemakers, and metallic prosthetics are show-stoppers, and patients are exposed to deafening noise and the infection hazards of a hospital. The relatively small bore of the MRI doughnut precludes the customary lithotomy position. The patient is forced into an awkward lateral decubitus position for implantation, which may alter the geometry of the implant when the patient assumes a more

normal position. The implant procedure takes hours[8] and is accompanied by the side effects of prolonged anesthesia.

Precise catheter implantation is hampered by the perturbation of the magnetic field by the needles and the ensuing uncertainty of their trajectories. Current research is studying a contrast agent that may produce MRI signals of seed positions similar to dummy seeds in conventional brachytherapy.[9,10] However, even if a new contrast becomes available, the scan would require a specific pulse sequence and be encumbered by the inherent geographic uncertainty of MRI.

Postimplant scans are equally burdened by spatial uncertainties. Seeds do not produce MRI signals and positions have to be deduced from the large signal voids they leave. Pinpointing actual locations is therefore subjective. Tanderup *et al.*[1] concluded that "*CT-based reconstruction remained superior to T1-based seed reconstruction due to manual interpretation of the seed signal voids …*" The fact that less contouring variability of the prostate gland was observed between individual physicians in MRI compared to CT (Ref. 11) does not mitigate the position ambiguity typical for MRI. No matter how many observers agree on a spatially distorted contour, any information derived from it is unreliable nevertheless.

Finally, the astronomical acquisition and operating cost make routine MRI-based brachytherapy prohibitively expensive and counterproductive. Low-income prostate cancer patients may have to forgo treatment altogether due to unaffordable insurance premiums or high deductibles. MRI-based prostate brachytherapy should therefore wait until clinical superiority is proven and small, practical, and quiet MRI scanners become available for the price of a rectal US system.

Rebuttal: R. Jason Stafford, Ph.D.

It might be best to respond with an admonition from Hillel, And if not now, when? There is a clear, valid reason to incorporate MRI in brachytherapy—to eliminate inherent uncertainties in ultrasound and CT-based dosimetry resulting in inadequate quality assurance, toxicities, and inconsistent outcomes, such as those revealed in the congressional investigation of veterans treated at the Philadelphia VA Medical Center.[12] MRI is demonstrably superior to ultrasound and CT for soft-tissue delineation, contouring, and post-treatment assessment. Time-driven activity-based costing analysis has recently demonstrated that MRI treatment planning can reduce costs by eliminating pretreatment office-based ultrasound procedures.[13] Additionally, MRI can assist in the intraoperative ultrasound-based deposition of LDR and HDR radiation therapy through low-cost fusion based strategies to ensure OAR preservation or DIL dose boosting. Postimplant assessment with CT-based dosimetry alone is inadequate as the prostate and OARs cannot be properly identified. Therefore, MRI for accurate visualization and identification of soft-tissue targets is critical.

MRI geometric and spatial uncertainties have been reduced with standardized protocols and sequences, and MRI prostate screening and postbiopsy staging have demonstrated improved detection of DIL, extracapsular extension, and seminal vesical invasion. Techniques for planning with MRI alone or fusing MRI to TRUS for delivery guidance have been incorporated into current treatment planning systems, which reduces uncertainty in radiation treatment delivery with brachytherapy.

For brachytherapy approaches requiring the levels of accuracy or verification of source placement with direct MRI-guidance, the time and costs need to be justified by improved outcomes. It should be noted that availability of wide bore systems relaxes patient selection and positioning concerns somewhat, but a true lithotomy position is not always attainable. Other factors such as MR compatible instrumentation and MR trained personnel must also be considered. With respect to guidance, however, transperineal applicator placements are axial to the field so suffer very little from the distortion issues due to susceptibility.

Additionally, prostate anatomy tends to be near magnet isocenter, minimizing gradient-induced geometric distortions, which vendors now address using 3D corrections. For calculating dose to the prostate, OAR and DIL, MRI anatomy provides the most robust delineation. Recent phantom studies indicate that inner pelvic organ distortion versus CT is <1 mm on 3T MRI using vendor distortion correction.[14] Precise localization of treatment delivery is critical for adequate postimplant dosimetry assessment. Delineation of seeds has been reported as less robust across observers, indicating the need to optimize MRI seed localization approaches,[15] although reports of MRI versus MRI/CT fused postimplant dosimetry demonstrate equivalence.[16] Further, MRI/CT fusion has been used to identify delineation errors in CT-only dosimetry evaluation.[17] Positive contrast MRI markers may further improve seed localization precision, supporting improved treatment assessment and quality assurance.

Current evidence demonstrates that MRI brings a substantial amount of critical information to the table for LDR and HDR prostate brachytherapy procedures. The VA incident has taught us that inherent uncertainties in ultrasound and CT-based brachytherapy lead to poor outcomes and inadequate quality assurance.[12] MRI in brachytherapy treatment planning, delivery, postimplant verification, and longitudinal assessment has optimized the quality assurance process and become a standard of care in the management of prostate cancer patients at MD Anderson. The future of MRI-based prostate brachytherapy has arrived! Why wait?

Rebuttal: Ivan A. Brezovich, Ph.D.

Dr. Stafford has not convinced me that prostate brachytherapy should be based on MRI. Neither the references he quotes nor his own arguments support this premise. Tanderup *et al.*[1] state that "*MRI simulation and treatment planning are emerging as active areas of investigation*." "*Emerging*" implies that the authors are not ready to call MRI an established tool for prostate brachytherapy. Turkbey *et al.*[2] see benefits of MRI for the diagnosis of prostate cancer, but do not advocate its use for treatment. They suggest fusing MRI to TRUS for real-time TRUS-based biopsies, while being aware of the technically complex MRI-guidance. In a consensus paper of the American Brachytherapy Society on prostate brachytherapy[3] "*postimplant computed tomography–magnetic resonance image fusion is viewed as useful, but not mandatory.*" References 4 and 5 are general practice guidelines that mention MRI as a 3D imaging modality, but make no recommendations on its use in brachytherapy or elaborate on its superiority over CT. Reference 6 explains how the prostate is more clearly visualized by MRI than CT and therefore contouring of the prostate is less likely burdened by errors. I therefore concede that MRI may have a place in prostate brachytherapy, but only as a diagnostic modality.

Furthermore, Dr. Stafford has not dispelled the concerns about the shortcomings of MRI. He has not mentioned the geometric uncertainties that may result in inaccurate placement of the radioactive sources and compromise the effectiveness of the entire treatment, nor the cost which could divert precious resources from other areas in prostate treatment where they could bring more benefits. Until these issues are resolved, I do not see any valid reasons for expanded use of MRI in brachytherapy beyond its general use for diagnosis.

ACKNOWLEDGMENT

Dr. Stafford thanks Steven Frank, M.D., Rajat Kudchadker, Ph.D., and John Hazle, Ph.D. for their helpful comments, insights, and contributions.

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CHAPTER 4

Imaging: mammography, CT, PET, molecular imaging, MRI

4.1. Resolution modeling enhances PET imaging

Adam M. Alessio and Arman Rahmim
Reproduced from *Medical Physics* **40**, 120601-1-4 (2013)
(http:// dx.doi.org /10.1118/1.4821088)

OVERVIEW

One of the methods frequently employed to enhance PET images is resolution modeling (RM). Resolution modeling is known to visually enhance images. Some argue, however, that such improvements are deceptive and that RM leads to degradations elsewhere, whereas others claim that the enhancements are real and overall beneficial. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Adam M. Alessio, Ph.D. Dr. Alessio is Research Associate Professor in the Department of Radiology, and Adjunct Associate Professor of Bioengineering and Mechanical Engineering, at the University of Washington, Seattle. He received his Ph.D. in Electrical Engineering from the University of Notre Dame and has been at UW since 2003. Dr. Alessio's research focuses on tomographic image reconstruction for PET and CT systems. He is involved in numerous translational research projects for topics including cardiac perfusion imaging, radiation dose optimization for PET and CT, accurate system modeling, and statistical estimation of parametric images.

Arguing against the Proposition is Arman Rahmim, Ph.D. Dr. Rahmim is Assistant Professor in the Department of Radiology and Radiological Science, and Chief Physicist in the Section of High Resolution Brain PET Imaging, Johns Hopkins University School of Medicine. He received his Ph.D. in Medical Physics from the University of British Columbia, British Columbia, Canada, in 2005 and has been at Johns Hopkins since. His research interests include resolution modeling, whole-body parametric imaging, and 4D image reconstruction in dynamic as well as cardiac- and/or respiratory-gated PET imaging. He is certified by the ABSNM in Nuclear Medicine Physics and Instrumentation.

FOR THE PROPOSITION: Adam M. Alessio, Ph.D.

Opening Statement

Image generation in a wide-variety of fields, from microscopy[1] to astronomy,[2] employs resolution modeling techniques to reduce the degradations inherent in their imperfect imaging systems. In all of these applications, resolution degradation is a consequence of many factors including the physics of the signal, the sensors, and the electronics. In PET, the physical degradations directly related to spatial resolution loss, in order of origination from signal to final measurement, include random positron range, photon pair noncollinearity, attenuation, intercrystal penetration, intercrystal scatter, detector inefficiencies, and electronics mispositioning. In total, a PET system has a spatially variant resolution loss. Resolution modeling and compensation techniques have been proposed for over two decades to account for the limitations in localization of radio-tracer distributions.[3]

To support the claim that "resolution modeling enhances PET imaging," it is important to clarify the term "enhances." In general, image restoration attempts to improve the image signal and/or reduce noise. In practice, restoration (or enhancement) needs to improve the task-based image quality (not simply signal or noise). It is well appreciated that two common tasks in clinical PET imaging include detection and quantification. In specific circumstances, resolution modeling in PET can genuinely improve hot-feature detection[4] and quantification.[5] Methods that enhance an image rarely provide improvement in all metrics and tasks—for example, detection may improve at the expense of quantitative accuracy. At the risk of oversimplifying the issue in the interest of a terse argument, my view is that most resolution modeling techniques provide some contrast enhancement with some apparent noise reduction (although true noise is minimally changed).[6] Both trends lead to demonstrably better detection performance,[4] leaving little room to question the assertion that resolution modeling enhances detection.

An interesting debate is whether resolution modeling enhances quantification. In PET quantification, we need both accurate and reproducible estimates of activity concentrations. The NEMA IEC phantom is commonly used to measure contrast recovery curves (CRC) for a system showing increasing partial volume errors for features below 2-3 cm. One holy grail in PET imaging is to develop a system and image generation method with a flat CRC curve (no partial volume effect errors with no size-dependent bias) with small error bars (reproducible). It has been shown that resolution modeling can cause unpredictable edge artifacts and these artifacts are generally exaggerated when the resolution model overestimates degradations.[7] Modest resolution models, which do not try to recover more frequency content that the sampling will support, have manageable edge artifacts and lead to genuine, albeit modest, contrast-to-noise improvements.[8] Current resolution modeling methodology is far from achieving the flat CRC curve. Future methods with better system modeling and convergent algorithms hold promise to improve the CRC further. These comments lead to a tempered statement that appropriate application of current resolution modeling techniques enhances, but does not solve all the challenges with, detection and quantification in PET imaging.

AGAINST THE PROPOSITION: Arman Rahmim, Ph.D.

Opening Statement

Resolution modeling in PET has attracted considerable interest especially in the past decade.[3] Unlike post-reconstruction partial volume correction (PVC) methods, RM models resolution-degrading phenomena within the reconstruction. It is a natural approach as one aims to design the system matrix to faithfully reproduce the true probabilities of detection, and is an attractive alternative to a range of PVC methods that make simplifying assumptions. In fact, RM produces images that are clearly enhanced visually, but it is my contention that RM is remarkable in its ability to deceive!

RM improves resolution (and contrast), and it is unfortunately not uncommon to see studies only characterizing this aspect. RM also reduces noise when defined as intensity variations within a region-of-interest (ROI), i.e., image roughness ($\sigma_{spatial}$). An alternative noise metric that assesses reproducibility is the ensemble standard deviation of ROI mean uptake ($\sigma_{ensemble}$). RM has been shown to reduce voxel variances but increase intervoxel correlations.[6,9] The first effect decreases both $\sigma_{spatial}$ and $\sigma_{ensemble}$, while the latter further decreases $\sigma_{spatial}$, but shifts $\sigma_{ensemble}$ in the opposite direction.[6] Subsequently, $\sigma_{spatial}$ is reduced in RM, but $\sigma_{ensemble}$ can increase especially for small ROIs.[10] This explains why RM can generate images assessed visually to be of higher quality, as it enhances contrast and reduces $\sigma_{spatial}$. However, it can degrade reproducibility and thus adversely impact quantitative imaging tasks as in pharmacokinetic imaging[10] or treatment response monitoring. RM may actually improve reproducibility for the Maximum Standardized Uptake Value (SUVmax) (Ref. 11) (which we attribute to reduced voxel variances) though increasing its range of values across the population (similar to PVC), and can degrade reproducibility for SUVmean, especially for small volumes (similar to PVC).[12]

In detection tasks, another note of caution is in order. Dual-metric resolution (contrast) vs. noise trade-off analyses commonly depict improved curves for RM whether noise is defined as $\sigma_{spatial}$ or $\sigma_{ensemble}$ (though to a lesser extent in the latter case, as explained above). Nonetheless, as demonstrated recently,[9] such simplified analyses do not properly capture the impact of the modified noise texture in PET images. In fact, detection task performance can be expressed as a function of the noise power spectrum (NPS), which is amplified at midfrequencies with RM and competes against the RM-enhanced modulation transfer function (MTF). One then must not make any conclusions of RM superiority based on dual-metric analysis and appropriate task-based performance assessment is required. A few detection studies have been performed for RM in PET,[13,14] and the results indicated *statistically significant* improvements for the designed studies, especially in the presence of time-of-flight. Whether or not RM will be *clinically significant* is another question. I believe that RM has the definitive potential to improve PET imaging in the context of diagnostic imaging, especially in oncology, but is likely to degrade performance in other contexts. By no means do I intend to discourage the application of RM, but wish to draw attention to its strengths and pitfalls, and to encourage research into its usage in a balanced and thoughtful manner.

Rebuttal: Adam M. Alessio, Ph.D.

My colleague raises valid concerns that resolution modeling (RM) can be deceptive. RM must be assessed with rigorous methods that analyze more than the simple metrics of: Resolution or quantification defined with hot features in a cold background; Noise defined as voxel-to-voxel

variance; and Detection defined as contrast to noise. Some papers employ these simple metrics and report overly optimistic performance with RM.

The concern about the *clinical significance* of RM improvements is valid. A detection performance evaluation by Kadrmas *et al*.[4] demonstrated, through observer studies on over 400 measured phantom images, that the area under the ROC increases by ~30% when using better RM. While this was a statistically significant improvement, the authors acknowledged that they could not conclude about the clinical significance of such a gain. In medical imaging, we rarely perform studies that prove real clinical improvements because these often require numerous patient exams, application in multiple sites, and knowledge of patient outcomes (all challenging!). We usually test our methods with much more limited evaluations. I would advocate that many of these limited evaluations, while not necessitating full clinical trials, should be improved.

In PET image generation, the customary approach for proving a method is to show improvement in a couple of reasonable metrics. This leads to the common expectation that performance on all other fronts stays consistent, i.e., the method only helps. For clinical acceptance, we need to quantify the good *and* bad performance of our methods to ensure they are applied in the appropriate context. In the future, I hope that clinical PET practice will use images tailored for the task at hand, as opposed to trying to garner all the necessary information from a single image. In the clinic, RM methods incorporated into convergent algorithms could provide more consistent, accurate quantification, but may not be appropriate for detection due to noise correlations. Conversely, RM methods designed to accentuate hot features of clinically relevant sizes could be used solely for tumor detection tasks. In this context, RM offers the potential to enhance clinical PET.

Rebuttal: Arman Rahmim, Ph.D.

Flattening the CRC curve is valuable but may incur other costs. What my esteemed colleague refers to as true noise [i.e., $\sigma_{ensemble}$, or the coefficient-of-variation (COV) when expressed as a percentage] may change little with RM,[2] or instead be amplified twofold[4] or even more[6] in small ROIs for some RM implementations. As such, the issue of reproducibility in quantitative imaging tasks merits special attention. This is a reason some sites with the HRRT scanner (including ours) pursuing quantitative pharmacokinetic imaging have discontinued usage of RM.

RM also results in increased mean uptake variability across the population,[15] attributed to true intersubject differences that are less suppressed in RM but may also be partly due to the degraded reproducibility.

Another issue is the impact of RM on the predictive and prognostic value of PET: PVC had no significant effect on the prediction of response following treatment[16] and in fact degraded performance in two studies.[17,18] This was attributed to the fact that PVC (similar to what RM does) removes the volume information implicit in SUVmean values, increasing them by greater amounts for complete-responders (which are associated with smaller tumors) than for partial-/nonresponders, thus actually diminishing intergroup differences. One could easily imagine that RM produces a similar detrimental effect on the discrimination power, though it is very

meaningful to investigate explicit usage of volume information in addition to corrected SUV values.

Finally, I note that I would have again taken the counterpoint position if the proposition was instead that "RM does *not* enhance PET imaging" (!) for these two statements are not logical complements, and there is a third real one, namely that RM may enhance PET imaging in certain tasks and degrade others. The community needs to achieve careful and comprehensive assessment of these issues and propose solutions appropriately sensitive to the various imaging tasks.

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4.2. ROC or FROC? It depends on the research question

Stephen L. Hillis and Dev P. Chakraborty
Reproduced from *Medical Physics* **44**, 1603–1606 (2017)
(http:// dx.doi.org /10.1002/mp.12151)

OVERVIEW

Receiver Operating Characteristic (ROC) and Free-Response Operating Characteristic (FROC) methods are used to assess the accuracy of radiological imaging systems. ROC methods analyze an observer's confidence that an abnormality is or is not present, whereas FROC methods additionally require the observer to locate abnormalities. Typically, ROC and FROC methods are applied to answer different research questions: sometimes ROC is the most appropriate and sometimes FROC. However, some believe that ROC is usually either equivalent or inferior and FROC is preferred over ROC for all research questions. This is the topic debated in this month's Point/Counterpoint.

Arguing for the Proposition is Stephen L. Hillis, Ph.D. Dr. Hillis is a research professor in the Departments of Radiology and Biostatistics at the University of Iowa. He earned a Ph.D. in statistics in 1987 and an MFA in music in 1978, both from the University of Iowa. Since 1999, when he first began working with Don Dorfman, Professor of Radiology and Psychology, his research at the University of Iowa has focused on methodology for multi-reader diagnostic radiologic imaging studies. He is the author of 90 articles from many diverse fields, many written when he was Director of the University of Iowa Statistical Consulting Center and Senior Statistician at the Iowa City VA Health Care System.

Arguing against the Proposition is Dev P. Chakraborty, Ph.D. Dr. Chakraborty earned his Ph.D. in solid-state physics from the University of Rochester, New York in 1977 then, in 1979, began his career in medical physics working with Ivan Brezovich in the Department of Radiology, University of Alabama at Birmingham, AL, where he worked until 1988 before moving to the Department of Radiology, University of Pennsylvania, Philadelphia. He subsequently moved to the University of Pittsburgh, Pittsburgh, PA, in 1997, where he was Professor in the Department of Bioengineering before assuming his current position at ExpertCAD Analytics, LLC in 2016. He has published over 75 papers in peer-reviewed journals, many in the field of observer performance analysis.

For the proposition: Stephen L. Hillis, Ph.D.

Opening Statement

When comparing imaging modalities in a diagnostic radiologic observer study, what type of data should a researcher collect? Receiver operating characteristic[1, 2] data consist of likelihood-of-disease ratings, one for each case (i.e., patient); free-response ROC[3, 4] data consist of localization (i.e., specification of location) of suspected diseased areas (e.g., malignant tumors),

referred to as *targets*, and target-specific likelihood-of-disease ratings; and localization ROC[5-7] (LROC) consists of both types of data. I argue that the appropriate data type and corresponding analysis combination is the one that best answers the research question.

In many medical centers, screening mammography recalled cases will undergo extensive further evaluation, making target location of minor importance.[8] Thus, for these centers a researcher might ask, "Which modality is best for classification of cases as diseased versus non-diseased?" Here, an ROC approach is appropriate. An ROC curve answers the question, "If a reader incorrectly classifies X% (e.g., X = 10) of nondiseased cases, what percent of diseased patients does the reader classify correctly?" The ROC area-under the curve (AUC) estimates the probability that a reader will correctly classify a randomly chosen pair of diseased and nondiseased cases.

In contrast, for diagnostic mammography for patients with suspicious screening mammograms, accurate localization of all actual targets is necessary to ensure appropriate treatment. Thus, a researcher might ask, "Which modality is best for classification when accurate localization of targets is needed?" Here, a modified LROC approach that requires a reader to accurately localize all of a patient's actual targets is appropriate. The resulting LROC curve answers the question, "If a reader incorrectly classifies X% of non-diseased cases, for what percent of diseased patients does this reader jointly provide correct classification *and* accurate target localization?" The LROC AUC estimates the probability that a reader will correctly classify a randomly chosen diseased/nondiseased pair of cases *and* provide accurate target localization.

Now consider the frequently used adjusted FROC[3] (AFROC) analysis. An estimated AFROC curve answers the question, "If a reader incorrectly classifies X% of non-diseased cases, what percent of actual targets (across patients) will the reader accurately localize?" This statement does not answer either of the two previous research questions. The corresponding jackknife AFROC (JAFROC)[4] summary statistic estimates the probability that a randomly selected actual target will be rated higher than the maximum rating given to a randomly selected normal image, which is not clinically relevant to the previous two research questions. On the other hand, AFROC seems more suitable than ROC or LROC for assessing performance of a computer algorithm used in computer-aided diagnosis (CAD) to suggest sites for a human reader to examine.

In conclusion, different approaches estimate different aspects of reader performance and hence answer different research questions. Furthermore, a researcher may want to estimate two or more aspects of reader performance. In the words of Charles E. Metz:[1] "*How effective is a particular diagnostic imaging procedure? … To address the question in a meaningful way, we must decide exactly what information is sought, and in answering we must state precisely what information we are giving*."

Against the proposition: Dev P. Chakraborty, Ph.D.

Opening Statement

The FROC-paradigm radiologist marks and rates suspicious regions. Based on a proximity criterion, marks close to lesions are credited as correct localizations. *ROC is a subset of FROC*: if the proximity criteria are large enough, and the radiologist knows it, the two paradigms are indistinguishable: specifically, the radiologist will make at most one mark/case and unmarked cases are "definite normals". A FROC model predicts ROC curves,[9] but one cannot go the other way. For interstitial lung disease, where location is implicit, ROC is appropriate, but then so is FROC. However, in clinical tasks which involve finding focal-disease, for example, screening mammography or lung nodules, if the radiologist suspects the patient is diseased, there is at least one associated suspicious location. For these tasks the ROC paradigm obtains a rating that there is disease "*somewhere"*, which begs the question: if disease is "*somewhere"*, why not point to it (Prof. Gary Barnes, private communication ca. 1985)? In fact they do—radiologists mark and annotate suspicious regions, but the ROC paradigm *ignores* this information, leading to loss of statistical power relative to FROC.[4] It is unethical to use a method with lower statistical power when one with greater power is available.[10] Over 104 publications, mostly non-US, have used JAFROC to analyze FROC studies. Clinicians have long recognized the importance of accounting for localization,[11] and a leading statistician[12] has recognized it. Yet there is opposition to JAFROC within the US. Here, is a recent reviewer comment: "*…the JAFROC statistic… does not yield a meaningful clinical interpretation*". I ask medical physicists: if the probability that lesions are rated higher than nondiseased cases (the JAFROC statistic) equals unity, is this a good thing? I hope your answer is a resounding "yes" because a unit value means *all* diseased patients are *correctly* recalled and *no* nondiseased patients are *incorrectly* recalled. (A zero value reverses correct/incorrect in the preceding sentence). This is the *clinical interpretation* the reviewer finds so elusive. The subject of this debate is not "rocket science", but it does require one to be open-minded and unbiased. Dirac[13] addressed an analogous then-existing criticism against quantum mechanics, namely, it did not provide a "*satisfying picture*" (translate "*satisfying picture*" to the reviewer's "*meaningful clinical interpretation*") as did classical mechanics. To paraphrase Dirac, the purpose of science is not to provide satisfying "*pictures*" but to explain phenomena. Since it allows zero or more mark-rating pairs per image, FROC is inherently more complex than ROC, no doubt about it. More importantly, it mirrors clinical practice, which is also more complex than the "*somewhere*" that the ROC paradigm accommodates. It is about time to stop using "*I don't understand*" as an excuse for impeding scientific progress and patient care. ROC methods should not be used to analyze localization tasks.

Rebuttal: Stephen L. Hillis, Ph.D.

An ROC analysis performed using FROC data by treating the highest target rating per case as the decision variable has been called an *inferred ROC* analysis.[14] This is different from a conventional ROC analysis of ROC data where the decision variable is a case-specific overall likelihood-of-disease rating. Although the two analyses are equivalent under the assumption that the two decision variables provide the same case rankings, this assumption has never been conclusively demonstrated empirically.[15] Furthermore, the assumption is intuitively not reasonable; for example, it implies that two cases are considered by a reader to have equal likelihood of disease if one case receives one mark and the other receives multiple marks, with each marked site rated as having 80% disease probability. Thus, inferred ROC answers a different question than conventional ROC. Although I disagree with Dr. Chakraborty's statement

that "*ROC is a subset of FROC*," I have no problem agreeing that *inferred* ROC is a subset of FROC."

Dr. Chakraborty has demonstrated through simulations that FROC (specifically, JAFROC) is more powerful than inferred ROC (conventional ROC is not included in these simulations). The problem with this kind of comparison is that JAFROC and inferred ROC have different hypotheses, and hence answer different research questions.

In conclusion, I agree that FROC data are required for assessing reader performance with respect to localization. However, this does not mean than one FROC analysis method (e.g., JAFROC) is suitable for all or most research questions. JAFROC is a statistically viable approach, but it should only be used if it answers the research question. A future area for research is development of FROC-ROC analysis methods designed to answer specific research questions. Before new analysis methods can be developed, however, there is a need for identifying important research questions and providing precise statements of them.

Rebuttal: Dev P. Chakraborty, Ph.D.

Let me address some of the statements made by my distinguished colleague, which I dispute:

- Location-specific methodologies (LROC/FROC/ROI) were developed not to address some abstract research question, but to better account for clinical reality.
- In my opinion, Dr. Hillis has the roles of screening and diagnostic mammography reversed. While screening mammography results in a binary decision (recall: yes/no?), radiologists also report locations of suspicious regions. Diagnostic mammograms are used to further investigate these suspicious regions.[16] There is an analogous difference between CADe (screening) and CADx (diagnostic).[16] The starting point for diagnostics is not that there are suspicious regions "somewhere in the breast", but that there are specific regions found at screening. Yet Dr. Hillis supports using ROC methodology, where location is ignored, to analyze screening mammography. As justification, he repeats an incorrect argument[8] that, because recalled cases will undergo "extensive evaluation", location is of "minor importance". The fallacy is that at the end of the extensive evaluation one is down to a few *localized regions*, whose truth is established by needle-biopsy, that is, *one is down to FROC data*.
- The issue is clinical, not statistical. Lesions are location-level manifestations of patient-level disease. A malignant lesion means the patient (not the lesion) has breast cancer. The lesion is not recalled—the patient is. If a lesion is rated higher than a nondiseased case, the patient who is attached to it is also being effectively rated higher, as accounted for in the weighted AFROC (wAFROC) figure-of-merit, which is a *case-level* figure-of-merit, where every diseased case effectively contributes exactly one lesion.[17] If the case is regarded as a random factor, results extrapolate to the population of cases. A "population of lesions", as Dr. Hillis' second-last paragraph seems to imply, is a contradiction in terms, as lesions have no independent existence.
- If an incorrect location is identified in a diseased case, then the recall is technically "correct" but for the wrong reason[18]—two canceling errors actually occurred, a missed lesion and a location-level false positive. A modality that minimizes "right for wrong

reason" outcomes would have an advantage when analyzed by wAFROC-AUC figure-of-merit[3] but not when analyzed by ROC-AUC, because in ROC the two canceling errors count as a perfect decision.

ACKNOWLEDGEMENTS

Dr. Hillis thanks Craig Abbey (U.C. Santa Barbara), Kevin Berbaum (U. Iowa), Patrick Brennan (U. Sydney), Leonel Vasquez (U. Iowa), and Tamara Miner Haygood (U. Texas) for their helpful discussions. This research was supported by the National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health under Award Number R01EB019967.

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4.3. The use of gadolinium-based contrast agents should be discontinued until proven safe

Stacy Matthews Branch and Michael F. Tweedle
Reproduced from *Medical Physics* **44**, 3371–3374 (2017)
(http:// dx.doi.org /10.1002/mp.12212)

OVERVIEW

Gadolinium-based contrast agents (GBCAs) are widely used in MRI to increase the visibility of tissues. Some believe, however, that due to their documented toxicity, clinical use of these agents should be discontinued until proven safe. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Stacy Matthews Branch, Ph.D. Dr. Branch is a biomedical consultant, medical writer, and veterinary medical doctor. She owns Djehuty Biomed Consulting and is a former faculty member in the Department of Toxicology at North Carolina State University and the Animal Science Department at North Carolina Agricultural and Technical State University. She has published research articles and book chapters in the areas of developmental, reproductive, forensic, and clinical toxicology. Dr. Branch received her DVM from Tuskegee University and Ph.D. from North Carolina State University. She is a Fellow of the American College of Forensic Examiners and Diplomate of the American College of Forensic Medicine.

Arguing against the Proposition is Michael F. Tweedle, Ph.D. Dr. Tweedle is the Stefanie Spielman Professor of Cancer Imaging and Professor of Radiology at The Ohio State University. He has researched and developed GBCAs in both industrial and academic settings for over 30 years. He sits on the editorial boards of *Magnetic Resonance Imaging*, *Investigative Radiology*, and *Radiology*, and has served on Expert Councils at the US Pharmacopeia, elected Boards and as Officer of four professional societies, and on Scientific Advisory Boards of public and private companies and universities. He has authored over 150 publications, including 13 book chapters. In 2005, he won The Harry Fischer Medal for Excellence in Contrast Media Research.

For the proposition: Stacy Matthews Branch, Ph.D.

Opening statement

Emerging research and clinical data are providing information that reveals links between gadolinium-based contrast agent administration and risk of toxicological endpoints. The development of nephrogenic systemic fibrosis (NSF) has been the primary toxicity endpoint of focus. The incidence of acute adverse events has also been considered when determining the overall safety of GBCA administration.[1] Published animal data and case reports are available that describe non-NSF adverse outcomes including hepatotoxicity, hematoxicity, nephrotoxicity, and neurotoxicity.[2-6]

The importance of further considering the effects of GBCA administration is demonstrated with the finding that gadolinium (Gd) is deposited in the brains of exposed patients who do not have renal pathology and have intact blood–brain barriers. A number of these studies have been published and reviewed in the literature.[7] For example, Gd deposition has been observed in normal post-mortem brain, bone, and skin tissue from human subjects that had normal renal function. Gadolinium tissue deposition is also dose-dependent as indicated by studies of post-mortem neuronal tissue from subjects who received four or more enhanced MRIs. In vivo studies showed Gd deposition in the skin, bone, and liver of rats exposed to linear and macrocyclic GBCAs.

Another important consideration in the potential toxicity of GBCA administration is the long-term persistence of Gd bone deposits,[8] which can serve as a supply of Gd that can be released over time and contribute to delayed or chronic toxicological effects. In the mentioned and other studies, linear GBCAs (which provide higher signal intensities) were found to be more strongly associated with tissue deposition than the macrocyclic GBCAs. This coincides with the known stability of the macrocyclic forms in comparison with the linear forms.

Retrospective and prospective studies are essential to better determine the long-term effects of GBCA exposure. Given the newly available information regarding long-term safety risks and body burden of GBCA-related Gd, revisions to the boxed warnings for GBCA products should be considered. Although it is not necessarily beneficial to completely eliminate all GBCA use at this time, modifications in the current use aimed to reduce exposure and adverse effects should be implemented. These modifications can include the development of protocols that determine when the benefits of use outweigh possible delayed or long-term effects based on the specific clinical cases in question.

Avoiding the use of linear GBCAs when possible and determining if the use of a macrocyclic form is sufficient can also provide an approach that can reduce or prevent toxicological outcomes. Further, eliminating routine or nonessential use of GBCAs and developing diagnostic planning strategies that limit multiple GBCA exposure in the same patient are paramount. Overall, the information regarding GBCA-related toxicity potential is significant and must be considered and applied when devising efforts to minimize exposure until alternative safer agents of equal or better effectiveness become available.

Against the proposition: Michael F. Tweedle, Ph.D.

Opening statement

The primary argument against this proposition is that the benefits of using GBCAs outweigh the known risks. GBCAs have accumulated 28 years of compellingly beneficial use in over 100 million patients. The risk/benefit consideration for acute reactions to GBCAs has remained positive, with serious adverse events in single digits per 100,000 administrations and < 1 death per million.[9]

Unlike most parenteral drugs, a metabolite of GBCA, Gd ion dissociated from the chelating agent, is far more slowly excreted than the parent agent.[10] This fact has been built into the

risk/benefit assessment for decades. The discovery that some, but not all GBCAs can trigger Nephrogenic Systemic Fibrosis (NSF), probably secondary to dissociated Gd, has led to use restriction on those GBCAs involved, and thus elimination of new cases of NSF since 2009.[11] But the finding that Gd could be chronically toxic in some patients has raised concern over undiscovered chronic toxicity. This concern has, and should, trigger further research into the chronic toxicity of GBCAs, and may result in further use restriction or even discontinuation of a subset of GBCAs. But there are certainly no data to support discontinuance of all GBCAs when toxicity appears to be associated with only a subset of the GBCAs. Indeed, multiple studies demonstrate that macrocyclic GBCAs are far superior (a hundredfold in human serum) as regards dissociation of Gd and elimination from deep compartments.[12, 13] The recent publication of retrospective accounts of MRI signal elevations in patients receiving multiple doses of GBCAs, followed by a few studies on human tissue samples, have documented, with tissue handling caveats,[14] dissociated Gd in human tissues at trace (ppm) levels. But not for the macrocyclic GBCAs.[15, 16] The trend is abundantly clear, despite the early and relatively crude forms of the existing human data: the macrocyclic GBCAs dissociate far less Gd, if any Gd, than the linear agents. Even if we assume the unproven hypothesis that dissociated Gd is a risk factor in patients with normal renal function, the risk/benefit for the macrocyclic GBCA is superior.

But is dissociated Gd a risk factor beyond NSF? At what level and for what? Research to better understand the risks of GBCAs should certainly continue. But discontinuation of all GBCAs would result in complete loss of their benefit, probably in loss of human life due to inaccurate or imprecise diagnosis, while we search for an hypothesized chronic toxicity of unknown seriousness that we, at this point, have no reason in evidence to anticipate. The reasonable response to the new findings is further research into chronic tolerance and more discriminating use of the available GBCAs.

Rebuttal: Stacy Matthews Branch, Ph.D.

There is agreement regarding the need to research the possible long-term effects of GBCA exposure. The consensus is also that complete discontinuation of GBCA use is not medically feasible at this time. Also agreed is that the differences in stability between linear and macrocyclic GBCAs is well documented and corresponds to differences in toxic potential. This information can be used to modify GBCA treatment protocols to reduce the risk of GBCA-related adverse health effects.

Although acute GBCA toxicity data indicate rare events, the risk of toxicological outcomes with multiple exposures is an important issue that needs examination. Also, the newest published data challenge the previous thoughts regarding the clearance of gadolinium (Gd) after GBCA administration. Delayed effects from single exposures must be considered given the new knowledge of Gd tissue deposition regardless of renal status. These are questions that need to be addressed to better determine the future use of GBCAs.

The data that have been published to date indicate the potential of serious long-term consequences of GBCA exposure. Various animal studies and human case reports have been reviewed[7] and demonstrate the potential of GBCA exposure to induce cellular and biochemical

abnormalities. For example, studies in pigs demonstrated a specific nephrotoxic endpoint (reduced glomerular filtration).[17] Effects of GBCA exposure in mice include decreases in white blood cell counts, elevation of serum cytokines, and hepatic cell damage.[3] Ataxia, tremors, and other neurotoxic endpoints were observed in exposed rats.[18]

Human case reports describe the development of pancreatitis (particularly after repeat GBCA exposure), tubular necrosis, and encephalopathy.[2, 4, 5] A group of patients reported a variety of health effects that started within a month after GBCA exposure.[19] Taken together, the growing body of biochemical, molecular, clinical, and post-mortem data is a strong indication of the need to design studies to better determine the GBCA toxicity potential and related effects on health and quality of life.

Rebuttal: Michael F. Tweedle, Ph.D.

This debate contemplates that GBCA use be discontinued until proven safe. But drugs cannot be proven safe; drugs can only be understood well enough to establish a risk/benefit ratio. I argued that drugs should be evaluated on that basis and concluded that the enormous benefits of GBCA used as indicated, outweigh the known risks, and that the macrocyclic GBCA agents had already a superior risk/benefit ratio compared to their linear GBCA counterparts.

My opponent's arguments are overall only subtly different from mine. I suggest that, after a quarter of a century of use, we are unlikely to discover important toxicology from the slow loss of ppm level Gd from bones, a phenomenon known and considered when the agents were first approved. Rather, it is the unexpected discovery of Gd in more sensitive neural tissue after repeated use of linear GBCA that has stimulated this debate. I agree that avoiding the linear agents when possible is a desirable first step, although it cannot happen overnight without creating drug shortages. The idea of testing macrocycles to explore whether they “can reduce or prevent toxicologic outcomes” is likewise laudable, but one must first identify genuinely toxic outcomes to study, which are exceedingly rare in this class of agent. The statement that “routine or nonessential use” should be avoided is obvious, true of any drug, and is thus not very helpful. But risk/benefit might indeed be improved by my opponent's suggestion that diagnostic planning strategies be developed that limit multiple exposures to GBCA in the same patient. But in the meantime, simply using the macrocyclic GBCA in such patients should be the preferred medical practice unless and until other less risky procedures are shown to have the same benefit.

Millions of patients each year derive positive, even lifesaving, benefit from MRI scans using GBCA. The macrocyclic GBCAs are already my opponent's desired “alternative safer agents” due to their lower risk *potential* with respect to metabolism. Inevitably they, like all drugs, will be superseded by innovation, but it is up to the innovations to yield superiority in risk/benefit terms. It does a disservice to patients in the meantime for their doctors to overreact to imagined threats.

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4.4. Physical characterization of the quality of medical images does not adequately reflect their clinical quality

Victor A. Gurvich and A. Kyle Jones
Reproduced from *Medical Physics* **44**, 4985–4988 (2017)
(http:// dx.doi.org /10.1002/mp.12376)

OVERVIEW

Quality assurance for radiological imaging equipment typically consists of analyzing data on images of physical phantoms and, if the results meet certain standards, it is assumed that clinical images obtained using the equipment will automatically be of good quality. Some claim, however, that such purely physical characterization of the quality of medical images does not adequately reflect their *clinical* quality. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Victor A. Gurvich, Ph.D. Dr. Gurvich earned his Ph.D. from the Russian Institute of Medical Technology, Moscow and then worked for Mosroentgen, Inc., Moscow, Russia, as a department manager and head of major projects, and later moved to Jerusalem, Israel, where he was cofounder and General Manager of ALVIM R&D, producing radiological phantoms and QA tools. Dr. Gurvich subsequently completed a Medical Physics residency in Ontario, Canada and was certified in Therapeutic Radiologic Physics by the ABR. He was then appointed Chief Physicist in the Radiological Institute, The Villages, FL. He is currently a Clinical Therapeutic Physicist in Fort Belvoir Community Hospital, Fort Belvoir, VA. Dr. Gurvich has worked as an IAEA expert, served on several AAPM committees, and is President of the Society of Euro-American Medical Physicists. He is the author of 20 patents and 34 scientific publications. His major research interests include IGRT, *in vivo* dosimetry, and tomotherapy.

Arguing against the Proposition is A. Kyle Jones, Ph.D. After earning his Ph.D. in Medical Physics from the University of Florida, he began his professional career at the University of Texas MD Anderson Cancer Center in the Radiological Physics Section, where he is currently an Associate Professor. He has co-chaired two AAPM Task Groups on digital radiography, was 1st author of AAPM Report No. 151 – Ongoing Quality Control in Digital Radiography and, in 2013, he and Louis K. Wagner, Ph.D., won the Farrington Daniels Award for the best scientific paper on radiation dosimetry in *Medical Physics*. Currently, most of his work is in interventional and intra-operative imaging, and he was recently the lead author on the *Best Practices Guidelines for CT-guided Interventional Procedures* as a member of the Health and Safety Committee of the Society of Interventional Radiology. Dr. Jones is certified by the ABR in Diagnostic Radiologic Physics.

For the proposition: Victor A. Gurvich, Ph.D.

Opening statement

Conventional physical characteristics of imaging modalities such as Modulation Transfer Function (MTF), Noise Power Spectrum (NPS), and Detective Quantum Efficiency (DQE), show potential diagnostic properties and fidelity of the evaluated system.[1-3] They are measured with special devices and calculated using computer programs. Such instrumental methods give quantitative and reproducible results. However, the data obtained with instruments alone often do not adequately take into consideration the characteristics of the human visual analyzer. Ultimately, it is humans who decide how well an image fulfills a diagnostic task.

Measuring spatial or contrast resolution by visually assessing detectability of test elements in phantoms is simple and fast but often subjective, because the response of an observer, who can predict the disposition of pathology simulators in the phantom image, may be biased. For example, the results of observers' evaluations depend on their experience with the phantom used. Noise in the image needs a statistical approach for quality evaluation and the four types of image-interpretation outcomes: true-positive (sensitivity), true negative (specificity), false-positive, and false negative, require psychophysical methods of analysis.[4, 5] Receiver operating characteristic analysis is considered the most comprehensive statistical methodology.[5] However, it is too complicated and inconvenient for daily clinical practice. Various other methods have been suggested[4] and, for example, a simple statistical method has been developed which defines diagnostic accuracy, sensitivity and specificity using phantoms within which the position of pathology simulators can be changed manually or with special software.[6-8] The method uses phantoms with several regions each containing different numbers of pathology simulators of various sizes and shapes. Within each region, the simulators are identical but spaced randomly. The observer locates simulators in each region and the results are compared with the real presence of the simulators in the selected locations in each region and the probabilities of true or false answers are calculated. It is assumed that the simulators in each region are correctly observed when the accuracy of their detection (probability of right answer) exceeds 0.9.[6, 7]

This method is visual, rapid, easy and, like other statistical techniques, removes observer's bias from image quality evaluation. However, it also has shortcomings. In patient images, the presence of anatomical noise may hide useful details. Test elements in phantoms do not adequately reproduce various pathologies and their anatomic contexts, so such parameters as signal-to-noise ratio, contrast, and spatial resolution, do not necessarily correlate well with lesion detectability, which depends upon shape, contrast, and size of surrounding organs. Anthropomorphic phantoms and clinical trials, therefore, remain important tools for quality assessment of clinical images.

Against the proposition: A. Kyle Jones, Ph.D.

Opening statement

If physical characterization referred only to the use of complex phantoms, often evaluated visually in a semi-quantitative fashion, to evaluate image quality, then I would certainly be for this proposition. Perhaps my favorite example of the shortcomings of the use of these phantoms to evaluate the performance of imaging systems designed to image the human body and tools used to intervene within is from Marsh and Silosky.[9] They presented an interesting example of

how an image from a modern angiographic fluoroscope showed zero contrast transfer from a periodic test pattern (a line pair phantom). There was, however, no defect in the detector, and in fact, this result indicated the image processing engine, which was designed to enhance the contrast of small guidewires, was functioning as intended.

In fact, certain defects can only be identified through physical characterization of imaging systems. Furthermore, if the goal is to identify a deficiency before it affects clinical images, then the only choice is to use physical characterization. Analysis of the noise power spectrum (NPS) can reveal interference occurring at specific frequencies,[10] and analysis of pixel variance can identify the dominant noise source (dark, quantum or fixed pattern) in an imaging system[11] and can be used to quantitate dead pixels and lines in detectors,[12] which degrade image quality.[13] Simple analysis of a flat field image with anatomical noise removed can identify most artifacts before they are noticed by a clinical observer.

Physical characterization can also be used to evaluate other aspects of image quality. For example, image segmentation can be used to assess positioning of body parts in radiography and centering of the patient for a computed tomography (CT) study. The same principles are currently used by some manufacturers of digital radiography systems to identify values of interest (VOI) for image processing.

Recent advances in physical characterization have used the correlation between machine calculated image quality metrics such as contrast and noise and ratings of specific aspects of image quality by trained human observers to build algorithms to automatically evaluate and score all clinical images as they are acquired.[14] Using these methods, image acceptability thresholds can be established and feedback provided to technical supervisors as each clinical image is evaluated and scored using these algorithms.

The latest advance in physical characterization is the use of actual clinical images to characterize the performance of the imaging system with each imaging study – patient-specific quality control.[15] These methods use specific regions of clinical images to calculate basic image quality metrics such as the modulation transfer function (MTF).

Rebuttal: Victor A. Gurvich, Ph.D.

I agree with Dr. Jones that methods of image quality measurement, which use various devices and mathematical algorithms but do not involve human observers, such as NPS and pixel variance analysis, can be useful for image quality optimization and eliminating some deficiencies and artefacts before they are visually distinguished. Ultimately, however, image quality is in the eye of the beholder (the clinician) so, in my opinion, such purely objective measures are incomplete and human intervention in the analysis of image quality is essential.

Dr. Jones refers to interesting papers where physical characteristics obtained from clinical imaging applying a computer algorithm demonstrated good correlation with perceptual image quality evaluated by radiologists.[14, 15] But he refers only to research conducted with the use of particular images and taking into account some physical parameters. At present, *visual assessments* of image quality are mandatory for each medical facility seeking ACR accreditation,

which must submit images of ACR-approved phantoms for visual review by experts. In addition, such visual methods with analogous phantoms are used for monthly QA in diagnostic and radiation oncology departments.[16]

Image viewing conditions play an important role in our ability to detect pathologies.[17] For example, contrast sensitivity depends on background brightness and glare, and resolution depends on viewing distance and background structure. The observer can adjust brightness and contrast of the image, and select optimal ambient illumination and viewing distance depending on the clinical task and personal perception. Physical characteristics of medical images received without human observers and only on the basis of instrumental methods do not take the viewing conditions into consideration.

Finally, I do concede that, for computer-aided diagnosis (CAD), where direct participation of human observers is not necessary, instrumental techniques can be successfully utilized. Development of CAD performance requirements, QA procedures, necessary software tools and phantoms, are topics of active interest.[18]

Rebuttal: A. Kyle Jones, Ph.D.

My opponent's argument ignores an important detail – the patient. He acknowledges this while understating the influence of anatomic noise, which is the limiting factor in detection of lung nodules on chest radiographs and varies by an order of magnitude among patients.[19] Furthermore, the signal-known-exactly task discussed by my opponent overestimates observer performance compared to the more realistic clinical task of detecting a lesion of unknown shape, size, and location. The phantoms referenced by my opponent do not adequately consider the human observer, e.g., a uniform phantom presents uniform background luminance to an observer whose contrast sensitivity varies with luminance.[20] In radiography, it is not even possible to use contrast-detail phantoms to implement statistical methods such as those described by my opponent, as values-of-interest (VOI) identification and subsequent image processing produces “clinical image quality” only when anatomic objects are imaged.

We should not forget that many imaging tasks are not binary, and therefore not suited for ROC analysis. Instead, tasks are diverse and involve pattern recognition, spatial reasoning, quantitative measurement of size or enhancement, and tracking fine structures, to name a few. To this end, my opponent suggests that “anthropomorphic phantoms and clinical trials remain important tools”, however, clinical trials are exceedingly expensive and anthropomorphic phantoms are limited in their ability to reproduce clinically accurate patterns, e.g., normal lung interstitial patterns.

In limiting his consideration of physical characteristics to MTF, NPS, and DQE, my opponent paints a distorted picture of image quality. Other important physical characteristics of images, such as size, shape, and texture, have long been used in computer aided detection to identify pathologic features. The use of physical metrics calculated from clinical images and calibrated to the human observer[14] is a natural extension of these methods.

The goal of quality assessment of medical images is to ensure consistent production of images of the quality necessary to perform the imaging task. The availability of standard physical metrics aids in the selection process of a system that is well-suited to the tasks to be performed, in the acceptance of the system as performing to specifications, and in ongoing acceptability evaluation. Optimization of the system for specific tasks adds knowledge of image processing and reconstruction options and is aided by the availability of metrics that are correlated with observer performance of the required tasks.

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CHAPTER 5

Ionizing Radiation Protection, Standards and Regulations

5.1. Exposure tracking for x ray imaging is a bad idea

James M. Kofler Jr. and David W. Jordan
Reproduced from *Medical Physics* **41**, 010601-1-3 (2014)
(http:// dx.doi.org /10.1118/1.4824059)

OVERVIEW

Tracking x-ray exposures of patients and submitting them to a central registry such as the ACR CT Dose Index Registry[1] where the data can be used for quality improvement, seems like a great idea. Unfortunately, such records of individual patient exposures are open to abuse since it is possible that they might be inappropriately used to limit future imaging procedures for these patients. This could be medically detrimental and far more life-threatening than the extra radiation exposure entailed. Some argue that such tracking is, therefore, a bad idea, and this is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is James M. Kofler, Jr., Ph.D. Dr. Kofler is an Assistant Professor in the Radiology Department, Mayo Clinic, Rochester, MN, where he has been since 1989. He obtained his Ph.D. degree in Medical Physics from the University of Wisconsin, Madison in 2000, and is certified by the American Board of Radiology in Diagnostic Radiological Physics. Dr. Kofler's main research interests have included exposure measurements in diagnostic radiology, and CT and ultrasound quality assurance. He has served on many ACR and AAPM committees, and is currently a member of the AAPM Working Group on Standardization of CT Nomenclature and Protocols.

Arguing against the Proposition is David W. Jordan, Ph.D. Dr. Jordan is Clinical Assistant Professor in the Department of Radiology, University Hospitals Case Medical Center, Cleveland, OH. He obtained his Ph.D. in Nuclear Engineering and Radiological Sciences from the University of Michigan in 2005, and is certified by the American Board of Radiology in Diagnostic Radiological Physics and Medical Nuclear Physics, by the American Board of Medical Physics in MRI Physics, and by the American Board of Science in Nuclear Medicine in NM Physics & Instrumentation. He has served on many AAPM committees and is currently Chairman of the Insurance Subcommittee.

FOR THE PROPOSITION: James M. Kofler, Jr., Ph.D.

Opening Statement

Exposure or dose metric tracking for x-ray imaging is a disservice to our patients. The information gathered is incomplete and meaningful interpretation is problematic, both in the imaging and broader medical community. Imaging decisions must be based on each individual patient's clinical needs, regardless of the amount of previously delivered medical exposure.

In regard to data available in DICOM image headers and structured reports, there is great potential for obtaining information that could benefit our patients and our practices. One example of beneficial use of such data collection is the ACR CT Dose Index Registry.[1] With over 800 facilities contributing over 10×10^6 scans, this registry has immediate value in terms of quality improvement initiatives, allowing sites to benchmark their dose levels against regional and national data.

One component of exposure tracking in x-ray imaging that is problematic, however, is tracking the exposure or dose metrics for specific patients for use in making clinical decisions about future medical exposures. Such tracking raises concerns regarding patient perception of radiation risk, and it does not provide meaningful data to health care providers.

Patients typically have little understanding of radiation units or effects, except generally that radiation is bad and more radiation is worse. Patients may compare their exposure, dose, or dose metric values to data available on the Internet while not understanding the important differences between radiological units (e.g., mrad vs mGy) or quantities (e.g., absorbed dose, effective dose, or CT dose index). Further, there is a wealth of misinformation on radiation risk on the Internet; I have counseled numerous patients who have read alarmist articles and were considering foregoing necessary exams. Others are emotionally distressed about dying from cancer. Not only is this not beneficial to our patients, it is harmful.

The effects of radiation at diagnostic levels on humans are not currently understood well enough to allow health care professionals to draw meaningful conclusions regarding radiation risks from diagnostic exams. Within the imaging community there is a renewed realization that we cannot speak with confidence regarding risk at diagnostic dose levels, even when relatively higher cumulative levels are delivered in small quantities over time.[2–4] Additionally, the quantities available for tracking (e.g., CTDI-vol and DLP in CT) are not measures of individual patient dose.[5] In particular, even though effective dose can be estimated from such quantities, effective dose is not defined for individuals.[6] This lack of patient-specific dose information, coupled with the uncertainties associated with risk estimates at diagnostic dose levels, makes any record of previous doses clinically meaningless. Knowledge of prior exams and imaging findings are extremely relevant for making current imaging decisions, but an estimate of the cumulative exposures associated with those exams is not. If a radiological procedure is medically justified, then it should be performed—regardless of prior exposure amounts.[7] What physician would withhold needed imaging of a trauma victim simply because the patient is a cancer survivor and has a high cumulative dose value? It is a very slippery slope to start applying dose thresholds to patient care, and in fact is counter to a basic premise of radiological protection in medicine.[8]

In conclusion, dose metric tracking for individual patients is a bad idea. It gives the illusion of providing meaningful data that can augment individual healthcare decisions. In fact, these data may lead to the withholding of needed imaging. Individual patient dose tracking simply attributes more significance to diagnostic dose levels than is scientifically justified.

AGAINST THE PROPOSITION: David W. Jordan, Ph.D.

Opening Statement

Medical physicists should understand that the use of radiation exposure tracking data is not appropriate for making prospective decisions about patient imaging.[9] It is easy to appreciate that many physicists are uncomfortable with the marketing of commercially available systems that promote such uses. Even more disconcerting are suggestions by radiation dose tracking vendors that imaging providers should give patients "score cards" to track their own personal exposure history, adding to the difficulty of confronting the sunk cost bias[10] in rational discussions of patient risk from imaging doses. Nevertheless, radiation exposure tracking in imaging has useful applications, and medical physicists currently have a fleeting opportunity to play a central and essential role in the inevitable deployment of the technology.

Patient radiation exposure tracking tools can be very powerful in the hands of a physicist or a quality control/improvement specialist or committee. Most imaging equipment produces and stores information about radiation exposure, but not always in a format that can be readily analyzed without manual data entry or formatting. Exposure tracking tools collect such data automatically for every study and provide various reporting and analysis tools that can be used to easily identify protocols, scanners, operators, and referring physicians or departments that deviate from institutional norms. While this function could be performed without exposure tracking software, much more time and effort would be required. Such reviews are a logical extension of protocol review and optimization committee efforts to evaluate whether protocol updates have achieved the desired dose reductions and been implemented correctly across departments and facilities. For researchers studying patient dose in imaging, exposure tracking provides an efficient method to collect large, accurate data sets without the time and expense of manually reviewing dose information embedded in image data. For retrospective studies, the exposure tracking databases are invaluable because in many cases, dose-related information is only stored locally on the imaging device and not transferred to archival storage with the images.

Commercial exposure tracking products have a head start in convincing physicians, administrators, and the popular media that cumulative patient exposure tracking is the right thing to do and that dose histories are of vital importance to patient care. The IAEA, in concert with several other prominent health and radiological organizations, has an initiative for individual patient dose histories using "smart card" technology.[11] It is tempting to dismiss exposure tracking as a bad idea, but that will not stop the technology from being deployed and misused by well-meaning individuals. Therefore, physicists should not eliminate themselves or discourage their colleagues from engaging with it, using it, and educating physicians and administrators about its proper and improper uses. There is an understandable concern about "scope creep" in the duties expected of the medical physicist, but exposure tracking is not the only contributor to this trend,[12] which will continue with or without electronic exposure databases and reporting.

Rebuttal: James M. Kofler, Jr., Ph.D.

Dr. Jordan and I agree on many of the valuable uses of radiation exposure tracking, particularly for population-based studies and quality improvement projects. However, for physicists to engage or embrace dose tracking for individual patients simply under the assumption that the use of the technology is inevitable is shortsighted. We are the experts regarding diagnostic radiation and to support individual dose tracking is equivalent to endorsing the concept as being meaningful to patient care. Allowing decisions on the use of individual patient radiation exposure tracking to be manipulated or dictated by those with commercial interests or by well-intentioned, yet uninformed, individuals—be they administrators, physicians, legislators, or media personnel—is neglecting our responsibilities as medical physicists. Dr. Jordan is correct in that physicists have a fleeting opportunity to play a central role in this technology, but a primary focus of that role should be to assure that it is used in a manner that is consistent with the scientific data and not let it inappropriately gain acceptance as a management tool for individual patients. This ball is already starting to roll down the hill—we cannot expect it will be easier to control once it gains more momentum. There are potentially very serious long term consequences regarding patient care if it continues unchecked. We must remain diligent in our responsibilities to our patients.

Rebuttal: David W. Jordan, Ph.D.

In considering the pros and cons of exposure tracking, we should not equate collection and analysis of data with use of that data to influence future imaging procedures. Dr. Kofler has correctly pointed out that such uses can be outright harmful. Also, there is clearly much work to do to educate patients and physicians and counter widespread misinformation about radiation. Exposure tracking did not create this problem, and eschewing exposure tracking will not fix it.

The ACR CT Dose Index Registry is an illustration of a beneficial application of exposure tracking in practice. Such a registry would not be possible without individual participants tracking and reporting their patients' exposures. This information is used appropriately for monitoring and quality improvement efforts. While the data reported are dose metrics and not true patient doses, they represent trends in patient dose that are useful to examine and analyze. Also, eventually we can expect scanners and dose tracking platforms to be able to report patient doses more accurately than they do today.

While it does not make sense to withhold beneficial imaging from patients in whom it is medically appropriate, there are scenarios where detailed knowledge of a patient's prior exposure could be useful to a clinician. First, consider a patient who has undergone a recent lengthy interventional fluoroscopy procedure. A tool that could automatically and accurately alert the physician could help them to be more aware of possible skin injury in a subsequent procedure. Second, consider the large amounts of repetitive imaging performed on radiation oncology patients during the course of treatment. Some physicists and radiation oncologists may feel that it is worth knowing how much dose these imaging procedures have delivered.

Exposure tracking is not a decision support tool, but used appropriately, it can provide many benefits. Medical physicists need to provide highly visible leadership to make sure that these tools and practices are not misused.

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5.2. Low-dose radiation is beneficial, not harmful

Mohan Doss, and Mark P. Little
Reproduced from *Medical Physics* **41**, 070601-1-4 (2014)
(http:// dx.doi.org /10.1118/1.4881095)

OVERVIEW

The recent rush to embrace the concept that diagnostic x-ray procedures are being overused, or that doses are too high and need to be reduced, is based upon the assumption that low doses of radiation are harmful and should be avoided as much as possible. On the other hand, some believe that such low doses of radiation are not harmful and might even be beneficial. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Mohan Doss, Ph.D. Dr. Doss obtained his Ph.D. in Physics in 1980 from Carnegie-Mellon University, Pittsburgh, PA and then spent the next ten years in research positions at the University of Washington, Seattle, Lawrence Berkeley Laboratory, Berkeley, CA, and the Saskatchewan Accelerator Laboratory, Saskatoon, Canada. He then began his career as a Diagnostic Physicist at Regina General Hospital in Regina, Canada. In 2001 he joined Fox Chase Cancer Center Philadelphia, where he is now Associate Professor. He is certified in Nuclear Medicine Physics by the Canadian College of Physicists in Medicine. Dr. Doss's major research interests include biodistribution and dosimetry of new PET imaging agents, small animal PET imaging, and health effects of low dose radiation, and he has published over 50 papers. He is the recipient of the 2014 Outstanding Leadership Award in the field of dose-response by the International Dose-Response Society.

Arguing against the Proposition is Mark P. Little, D.Phil. Dr. Little obtained his D.Phil. in Mathematics from New College, Oxford in 1985. He then worked for the next six years at British Coal, Harrow, London, and Berkeley Nuclear Laboratories, Nuclear Electric, Berkeley, UK. He then continued with his career in epidemiology first as Principal Scientific Officer, Epidemiology Group, NRPB, Chilton, UK, and then in the Department of Epidemiology and Biostatistics, Imperial College Faculty of Medicine, London, UK. In 2010 he moved to the USA as Senior Investigator at the Radiation Epidemiology Branch, National Cancer Institute, Rockville, MD. Dr. Little's major research interests have included models and epidemiological studies of cancer induction by radiation, risks associated with mobile phones, cancer risks of radiation exposure of children, and deleterious effects of occupational radiation exposures, on which he has published over 150 papers and supervised the work of 20 researchers and graduate students.

FOR THE PROPOSITION: Mohan Doss, Ph.D.

Opening Statement

The process of oxidative metabolism in living beings sometimes results in the production of free radicals which can cause oxidative damage. Our body has an elaborate system of antioxidants to neutralize these free radicals. This system is not perfect, and a small amount of damage does persist. There is evidence that accumulation of such damage contributes to causing many of the aging-related diseases.

When free radical production is increased, e.g., from low-dose radiation (LDR) exposure (or increased physical/mental activity), our body responds with increased defenses consisting of increased antioxidants, DNA repair enzymes, immune system response, etc. referred to as adaptive protection.[1] With enhanced protection, there would be reduced cumulative damage in the long term and reduced diseases. The disease-preventive effects of increased physical/mental activities are well known.

There is considerable evidence from animal studies supporting the hypothesis that LDR reduces the likelihood of cancer as well as nonmalignant diseases.[2] For humans, (i) epidemiological studies of irradiated populations exhibit reduced risk of cancer from LDR,[3–5] (ii) interspersed adjuvant LDR treatment has resulted in better tumor control and reduced metastases in radiation therapy of non-Hodgkin's lymphoma patients,[4] and (iii) tissues subjected to LDR have shown reduced second cancers per kg in radiation therapy patients.[4] For noncancer diseases in humans, LDR has been shown to control many such diseases.[2,6] Thus LDR is indeed beneficial, as it results in reducing cancer and noncancer diseases.

The present concerns over the carcinogenic potential of LDR are based on the concepts that LDR causes DNA damage resulting in increased mutations, and that the accumulation of mutations can transform a normal cell into an uncontrollably dividing cell, causing cancer.[7] This argument unjustifiably ignores LDR adaptive protective responses.[1] If the effect of LDR adaptive protection is included, there would be reduced DNA damage following LDR,[1] reducing the likelihood of transformation of normal cells into those with malignant phenotypes.

Also, the above mutation model of cancer cannot explain the more than 100% increase in cancers in organ transplant patients (and in AIDS patients), in whom the immune system is suppressed.[8] Hence there is little credibility in the prediction of a small percentage increase in cancer from LDR based on this model. On the other hand, using immune system deficiency as the cause of clinical cancer, many of the characteristics of cancer incidence can be explained.[2] Since LDR boosts the immune system, LDR would be expected to reduce rather than increase the risk of cancer.[1,2]

For both cancer and noncancer diseases, there is a threshold dose below which no increased risk of disease has been observed. The atomic bomb survivor data, considered to be the most important data for estimating radiation effects in humans, have traditionally been used to justify LDR carcinogenic concerns. Recent reanalysis has shown the data are more consistent with a threshold, or radiation hormesis, model than the linear nonthreshold (LNT) model.[4,5]

In view of the above, we can conclude confidently that low-dose radiation is beneficial, not harmful, from both mechanistic and epidemiological considerations.

AGAINST THE PROPOSITION: Mark P. Little, D.Phil.

Opening Statement

The detrimental tissue-reaction (deterministic) and stochastic effects associated with moderate and high dose ionizing radiation exposure are well known.[9] In contrast to tissue-reaction effects, for stochastic effects scientific committees generally assume that at sufficiently low doses there is a positive linear component to the dose response, i.e., that there is no threshold, or beneficial effect.[9] Moreover, there is accumulating direct evidence of excess risk of cancer and various other health endpoints in a large number of populations exposed at moderate and low doses. I review some of this evidence below.

There is evidence of excess cancer incidence of most types associated with radiation exposures of the order of 10–20 mGy from diagnostic x-ray exposure in the Oxford Survey of Childhood Cancers and in various other groups exposed *in utero*.[10] These data remain somewhat controversial, but as Wakeford and Little note "the consistency of the childhood cancer risk coefficients derived from the Oxford Survey and from the Japanese cohort irradiated *in utero* supports a causal explanation of the association between childhood cancer and an antenatal x-ray examination found in case-control studies. This implies that doses to the foetus *in utero* of the order of 10 mSv discernibly increase the risk of childhood cancer."[10] There is also evidence of excess risk of childhood leukemia associated with natural background radiation exposure, at doses above 5 mGy, in a large UK population-based case-control study.[11] At slightly higher doses, increased risks of leukemia and brain cancer have been observed in patients who were exposed as children to multiple computerized tomography examinations resulting in doses of about 60 mGy to the respective tissues (red bone marrow, brain).[12] The excess risks in all of these studies are consistent with those in the Japanese atomic bomb survivor data.[10–12]

The health risks of low-level exposure to ionizing radiation have been assumed to be related primarily to cancer.[9] Evidence has recently emerged of an association between lower doses (<0.5 Gy) and late circulatory disease. In particular, a recent systematic review and meta-analysis suggested an excess radiation-associated risk at occupational and environmental dose levels (<0.5 Gy).[13] However, the presence and magnitude of the excess circulatory disease risk at low doses is still relatively controversial, and much remains unknown as to the shape of the dose-response curve.[13] There is also accumulating evidence from the Japanese atomic bomb survivors and various other moderate- and low-dose exposed groups of excess risk of cataracts.[14]

There are data, reviewed in Ref. 15 suggesting an increase in stable chromosome aberrations and other markers of biological damage in the peripheral blood lymphocytes of nuclear workers and other groups with protracted radiation exposures. Chromosome changes play a major role in carcinogenesis and there is increasing evidence that the presence of increased frequencies of chromosome aberrations in peripheral blood lymphocytes in healthy individuals could be a surrogate for the specific changes associated with carcinogenesis and therefore indicative of risk.[15] Much other *in vitro* and *in vivo* radiobiological data suggest small adverse effects of moderate dose exposure—in particular there is little data to suggest a threshold in dose, or possible hormetic (beneficial) effects of low-dose radiation exposure.[9,15,16]

In summary, excess cancer risks have been seen in a number of (largely pediatrically- or *in utero*-exposed) groups. Excess risks of circulatory disease and cataracts have also been observed in a number of groups exposed to low or moderate doses. The available data on biological mechanisms do not provide general support for the idea of a low-dose threshold or hormesis for any of these endpoints. This large body of evidence does not suggest, indeed is not statistically compatible with, any large threshold in dose (>10 mGy), or with possible beneficial effects.

Rebuttal: Mohan Doss, Ph.D.

Dr. Little quotes the consistency of childhood cancer risk factors from Oxford and Japanese studies as evidence for carcinogenicity of *in utero* LDR.[10] However, for the Japanese cohort, leukemias were observed only following high dose radiation (HDR), and the risk coefficients were calculated using an assumed LNT model, creating the illusion of increased risk of leukemias from LDR whereas none was observed.[10] Also, cohort studies, which are superior to case-control studies, have not shown increased leukemia risk.[17]

The study of childhood leukemias correlated with background radiation[11] does not consider confounding factors such as breastfeeding. Small changes in the results from consideration of such factors could make the increased leukemias statistically insignificant. The study of childhood cancers following CT scans[12] has methodological issues including the lack of a control group, raising major doubts about its conclusion.[18]

With regard to heart disease, the meta-analysis[13] combined LDR and HDR data, effectively transferring HDR risk to LDR as described in a detailed critique.[19] Regarding cataracts, Chernobyl and atomic bomb survivor data do show a threshold dose for cataracts requiring surgery.[14]

Although Dr. Little expressed concerns regarding LDR-induced chromosome changes, mutation is not the primary determinant of clinical cancer, whereas deficiency in immune system is an important factor.[2] Since LDR *increases* immune system response,[20] it would *reduce* the cancer risk.[2]

Finally, Dr. Little quoted the UNSCEAR 1993 Report[16] as lack of evidence for the beneficial effects of LDR. However, Annex B of the UNSCEAR 1994 Report did discuss the beneficial effects of LDR. Also, many publications in recent years have demonstrated the disease-preventive effect of LDR for cancer and noncancer diseases.[2,4,21]

In conclusion, since the opposing arguments presented by Dr. Little are explainable as discussed above, considering the arguments and evidence presented in my Opening Statement, we can indeed conclude confidently that LDR is beneficial, not harmful.

Rebuttal: Mark P. Little, D.Phil.

Dr. Doss discusses the well-known involvement of the immune system in cancer, and more generally the role of adaptive response. The critical issue is whether the up-regulation of the immune system or other forms of adaptive response that may result from a radiation dose offsets

the undoubted carcinogenic damage that is caused. The available evidence, summarized in my Opening Statement, is that it does not, and that, given the similarities in risks per unit dose following exposures to very low doses of radiation and with those after moderate dose radiation exposure,[10–12,15] the nonlinearities induced by any adaptive response cannot be substantial. While adaptive response modulating the effect of relatively high challenge doses of radiation (of several Gy) following a smaller priming dose (of usually at least several tens of mGy) is well known experimentally (mostly *in vitro*), it is not universally observed in all experimental systems, nor does it last more than a few days, and there is little or no evidence for its involvement at low priming and challenge doses.[22,23]

Responding to the points relating to existence of a possible dose threshold, or hormetic effect, there is no evidence for these either for cancer[24,25] or for noncancer disease[26] in the Japanese atomic-bomb survivors. Naturally, thresholds below a certain size cannot be ruled out by the Japanese data, but the evidence suggests that thresholds cannot be larger than about 60 mSv for cancer[24,25] or larger than about 0.9 Sv for noncancer disease.[26] Taken together with the other data discussed above,[10–12] thresholds or hormetic effects much above 10 mGy can be largely discounted for cancer.

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5.3. Medical use of all high activity sources should be eliminated for security concerns

Jacek Capala and Steven J. Goetsch
Reproduced from *Medical Physics* **42**, 6773–6775 (2015)
(http:// dx.doi.org /10.1118/1.4934823)

OVERVIEW

The use and storage of high activity sources, as defined by IAEA categories 1 and 2,[1] present important security challenges in the hospital setting. Unlike nuclear and military facilities that are heavily guarded against intrusion, hospitals, by their very nature, are open to the public. It would be relatively easy for intruders to steal such sources and use them for nefarious activities such as to build a "dirty bomb." The problem is that these sources, which include those used for teletherapy, Gamma Knife stereotactic radiotherapy, HDR brachytherapy, and blood irradiation, are important for the care of patients. Nevertheless, some claim that use of such sources should be eliminated for security reasons, and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Jacek Capala, Ph.D. Dr. Capala received his M.Sc. in Medical Physics from Jagiellonian University, Krakow, Poland and his Ph.D. in Physical Biology from Uppsala University, Uppsala, Sweden. His Ph.D. thesis and postdoctoral work at Ohio State University, Columbus, OH, focused on targeting epidermal growth factor (EGF) receptors for molecular imaging and therapy, including potential application of tumor-targeted nanoparticles for drug delivery. In 1994, he moved to Brookhaven National Laboratory, Upton, NY, where he contributed to the design of clinical trials of Boron Neutron Capture Therapy (BNCT) for Glioblastoma Multiforme (GBM) and was subsequently recruited to start a new BNCT Research Program at the Studsvik Neutron Research Laboratory in Sweden. In 2004, he became the head of the Molecular Targeting Section, Radiation Oncology Branch of NCI Intramural Program. His research interests include nanotechnology, nuclear medicine, and image-guided, adaptive, and particle radiation therapy, on which he has published more than 80 papers and several book chapters. Since September 2011, Dr. Capala has been a Program Director for the Division of Cancer Treatment and Diagnosis, Radiation Research Program.

Arguing against the Proposition is Steven J. Goetsch, Ph.D. Dr. Goetsch is Chief Physicist at the San Diego Gamma Knife Center, La Jolla, California. He completed an M.S. in Health Physics at Northwestern in 1974, worked in industry and then completed a Ph.D. in Medical Physics at the University of Wisconsin where he served as Director of the Accredited Dosimetry Calibration Laboratory for seven years. He was later an Associate Clinical Professor in Radiation Oncology at UCLA Medical Center and has been director of physics at the San Diego Gamma Knife Center since its opening in 1994. He currently serves on the national Board of Directors of AAPM and

CAMPEP. He has served as Chair of the Education Committee of the Southern California Chapter of the AAPM since 2002.

FOR THE PROPOSITION: Jacek Capala, Ph.D.

Opening Statement

In medicine, radiation sources defined as category 1 or 2 safety concerns by the IAEA,[1] are used for radiation teletherapy (RT), radiosurgery, brachytherapy, blood irradiation prior to blood transfusions to prevent Graft-Versus-Host-Disease (GVHD), and sterilization of medical instruments. Alternative methodologies that do not employ high activity radioactive sources exist for each of these applications. RT and radiosurgery machines using radioactive sources are being replaced with linear accelerators (linacs).[2] Low activity sources can be used for brachytherapy. Furthermore, stereotactic RT combined with modern targeted therapies might soon make brachytherapy obsolete.[3,4] GVHD can be prevented by irradiation with x-ray or electron-beams, by photochemical methods using ultraviolet light,[5] or by filtration techniques. Medical devices can be sterilized by autoclave, dry heat, ethylene oxide, and x-ray or electron beam irradiation.

There are several reasons why these alternatives should replace high activity sources, recognizing that the phase out of high activity sources will take some time so as not to compromise cancer care in low-resource areas. The first and foremost reason is security. Radioactive sources pose a potential high risk to public health and safety in the event of loss of source control by an accident,[6] oversight,[7] or sabotage.[8] Concerns about the security of radiation sources escalated following the terrorist attacks of September 11, 2001. These sources might be used by terrorists to expose people to radiation by (i) placing a high radioactivity source in populated areas, (ii) mixing radioactive materials with food or water, or (iii) dispersing radioactive materials by radiological dispersal devices (dirty bombs) that would cause contamination preventing regular human access to an area.[9] These can have enormous health and economic consequences. In the Energy Policy Act of 2005, the U.S. Congress obligated the U.S. NRC to take several actions, including a study by the National Research Council to identify the uses of high-risk radiation sources and the feasibility of replacing them with lower risk alternatives. The resulting report provides a detailed description of this issue.[10] The second reason is that elimination of radioactive sources stimulates technological progress. For instance, introduction of linacs enabled significant improvement of RT techniques including intensity modulated RT and stereotactic RT, to name the most popular. The new devices represent state of the art technology on par with 21st century knowledge and will facilitate further development. The third reason is that promotion of alternative technologies will stimulate economic development. Currently, there are a limited number of companies providing radioactive sources and, thereby, controlling the market. Nonradioactive methods, like those used for reduction of pathogens, can be designed and produced by companies of any size. This will facilitate formation of start-ups, growth of small businesses, and creation of new jobs. Last but not least, the competition between many businesses of different sizes will benefit customers. The products will be constantly improved and the prices controlled by market mechanisms.

AGAINST THE PROPOSITION: Steven J. Goetsch, Ph.D.

Opening Statement

The subject of increased controls for radioactive materials has been much on the mind of everyone in the field of radiation therapy since the tragic events of September 11, 2001. However, I have been unable to find evidence that any terrorist group in history has ever successfully created a "radiological dispersal device" (aka, dirty bomb). Medical devices containing large amounts of radioactive material have been in widespread use since the "radium bomb" which dates back to 1917 at Memorial Hospital in New York City.[11] It is also clear that, for historic reasons, regulation of medical devices containing radioactive material has been subject to much higher levels of regulation (including training of personnel) than has been true of radiation producing medical devices.

As a clinical medical physicist, I have worked with both medical devices containing high level radioactive sources and x-ray producing devices since I entered the field in 1983. My experience, which others would probably agree with, is that medical devices containing radioactive sources are generally more reliable than radiation producing devices. Medical devices relying on decay of radioactive material are inherently simpler and therefore more reliable than far more complex devices. The beauty of cobalt-60 is that its decay rate is utterly predictable, and it is physically incapable of having an energy or output variation. In fact, cobalt-60 sources have been historically used by medical physicists to check the calibration of measuring instruments.

I have assisted a number of hospitals in implementing gamma stereotactic radiosurgery programs. The increased controls required since 2006 are generally not burdensome. Most hospitals can easily incorporate very high levels of security including locks, biometric readers, and security personnel.

Perhaps there is a danger of "throwing out the baby with the (radioactive) bath water" by eliminating all high level radioactive devices from hospitals.

Rebuttal: Jacek Capala, Ph.D.

Beauty is in the eye of beholder. Therefore, I will not dispute "the beauty of cobalt-60" experienced by my opponent during his 30+ year career. Instead, I will point out that the world is changing and, as the late Yogi Berra wisely noted, *the future ain't what it used to be.* The rise of the Middle East Islamic State (IS) and its followers, as well as other terrorist groups all over the world, has created an unprecedented threat of radiologic terrorism. In fact the IS fanatics already claim to have constructed a dirty bomb overseas.[12] One cannot quantify the risk of a dirty bomb being made and used in the US but we know that it might happen and, if it does, the consequences will be catastrophic. According to the report "Unthinkable—Radiological Dispersion Device using Cobalt 60" prepared by AristaTek, Inc., leading provider of hazardous materials planning and response solutions,[13] the detonation of a Co-60 RDD in Washington DC could result in significant cobalt-60 contamination of the White House and many federal buildings. Everyone in that area would be exposed to a "radioactive bath" delivering biologically effective doses of 50–100 mSv within the first day. The report also states that "The cleanup or decontamination process for this scenario is much more complicated, if even possible." Thus, due to the cobalt-60 half-life of about 5.3 years, this area could become uninhabitable for

decades. An even longer time would be needed if Cs-137 were used in an RDD. One can imagine the emotional and financial consequences of such an event in any major US city.

The levels of source security vary widely in different countries and, in hospitals, such security can be easily overrun with force. I leave to the readers of *Medical Physics* to ponder whether such an incident should be allowed to happen before we take the threat seriously enough to follow the proposition in question.

Rebuttal: Steven J. Goetsch, Ph.D.

The subject of dirty bombs has been on everyone's mind since 2001. I have personally attended two dirty bomb drills in San Diego County, including one at the University of San Diego in March 2015. A number of important national and international commissions have weighed in on this topic: the NCRP has issued statements (Commentary 19 and Reports 138, 165, and 175) describing the possible consequences of events ranging from contamination to a small scale fission bomb.[14–17] These reports often note the psychological nature (terrorism) of these threats, since the public image of radiation is strongly influenced by the horrific consequences of the atomic bombings, Chernobyl and, more recently, the Fukushima disaster. Yet, short of a stolen or amateur low yield nuclear weapon, none of these incidents appears to be capable of causing the same level of death and destruction as occurred on September 11, 2001 when terrorists used commercial aircraft as improvised weapons.

Is defending against hypothetical dirty bombs the wisest way to expend national resources? A recent estimate placed the global market for "homeland security" in 2018 at an estimated $544 billion per year. The United States agricultural output for 2011 was only $374 billion by comparison.

Sen. Dianne Feinstein (D, CA) introduced an appropriations bill in September 2015 that would have required the "phasing out" of radioactive materials in the practice of medicine over a period of years. No hearings were held and Washington observers were completely surprised at this proposal. A meeting was held under the auspices of the American Nuclear Society which was attended by dozens of medical associations, industry associations, and medical corporations. Ultimately letters were drafted in opposition to the bill and signed by AAPM, ABS, ANS, ACR, ACRO, ASTRO, MITA, and many others. The cost of phasing out radioactive material from medicine (if it is even possible) was estimated in the billions of dollars. For example, there are somewhat more than 125 Gamma Knife Centers in the U.S., which my distinguished opponent advocates phasing out. At a cost of $3–4 million each (not including a bunker) replacement of this small part of the medical radioactive market would cost hundreds of millions of dollars. And what about HDR units? Will federal money buy replacements for these facilities? The proposed phase out was removed from the Senate bill before it was passed but it is possible (likely!) that this will come up again.

The National Academy of Sciences, in the original Biological Effects of Ionizing Radiation manuscript[18] stated "… there should not be attempted the reduction of small risks even further at the cost of large sums of money, that spent otherwise, would clearly produce greater benefit." Would it not be better to extend medical care to those in this country (still in the tens of millions)

who do not have a health care plan? In the words of Pope Paul VI, “If you want peace, work for justice.” I could not say it better.

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5.4. Advocating for use of the ALARA principle in the context of medical imaging fails to recognize that the risk is hypothetical and so serves to reinforce patients' fears of radiation

Jeffry A. Siegel and Cynthia H. McCollough
Reproduced from *Medical Physics* **44**, 3–6 (2017)
(http:// dx.doi.org /10.1002/mp.12012)

OVERVIEW

The ALARA (As Low As Reasonably Achievable) principle is based upon the assumption that low doses of radiation might be harmful and, therefore, should be minimized for medical imaging procedures. Some consider, however, that such low doses are not only harmless but might also even be beneficial, and that advocating for use of the ALARA principle in the context of medical imaging fails to recognize that the risk is hypothetical and so serves to reinforce patients' fears of radiation. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Jeffry A. Siegel, Ph.D. Dr. Siegel obtained his M.S. degrees in Chemistry and Radiological Physics from the University of Cincinnati and his Ph.D. degree in Medical Physics from the University of California Los Angeles. After working for over 15 years as a medical physicist and Associate Professor, Diagnostic Imaging, at Temple University School of Medicine, as Director, Section of Nuclear Medicine Physics and Physics Research and Development at Cooper Hospital/University Medical Center, and as Clinical Professor of Radiology at the University of Medicine and Dentistry New Jersey – Robert Wood Johnson Medical School, Dr. Siegel assumed his current position as President and CEO, Nuclear Physics Enterprises, Marlton, NJ, USA. This is an international consulting firm specializing, among other things, in evaluation of new radioactive drug therapies and clinical trial design, translational research, biokinetic modeling, quantitative nuclear medicine/radiological imaging, internal and external dosimetry, radionuclide therapy patient release, radiation protection, and FDA and NRC regulatory issues, topics on which Dr. Siegel has published extensively. He has authored more than 350 publications, including two books providing guidance for compliance with NRC regulation of nuclear medicine.

Arguing against the Proposition is Cynthia H. McCollough, Ph.D. Dr. McCollough obtained her M.S. and Ph.D. degrees in Medical Physics from the University of Wisconsin, Madison. Upon graduation she began working in the Radiology Department at Mayo Clinic, Rochester, Minnesota, where she is currently Professor of Medical Physics and Biomedical Engineering. As Director of Mayo Clinic's CT Clinical Innovation Center, Dr. McCollough leads a multidisciplinary team of physicians, scientists, research fellows, and graduate students on projects seeking to detect and quantify disease using CT imaging. She has particular expertise in the use of CT for quantitative assessment of material composition, disease progression or regressions, and organ function, as well as methods to quantify and reduce radiation dose. Dr.

McCollough is internationally recognized for her contributions to the fields of CT imaging physics and technology, and radiation dosimetry and protection. She has served in numerous capacities in the AAPM including on the Board of Directors and the Editorial Board, and has been elected Fellow of the AAPM, the American College of Radiology, and the American Institute for Medical and Biological Engineering.

For the proposition: Jeffry A. Siegel, Ph.D.

Opening Statement

Medical imaging, particularly CT, is said to produce iatrogenic cancer risk from radiation exposure. Yet, credible evidence of imaging-related low-dose (< 100 mGy) carcinogenic risk is nonexistent; it is a *hypothetical* prediction derived from the demonstrably false linear no-threshold hypothesis (LNTH). On the contrary, low-dose radiation does not *cause*, but more likely helps *prevent*, cancer. Countless experimental and observational studies show this benefit.[1, 2] Epidemiological studies purporting to establish low-dose radiogenic risks fail to consider basic scientific research and employ circular reasoning, rendering their conclusions false and indefensible.[3]

The LNTH and its offspring ALARA are fatally flawed, focusing only on molecular damage, *while ignoring protective, organismal biological responses*. DNA double-strand break repair and other adaptive protections more than eliminate the low-dose radiogenic damage, *repairing or removing even the far greater damage from endogenous processes*.[4, 5]

Many radiologists and medical physicists grant that imaging's radiation-associated risks are minute, and may be nonexistent, with benefits far outweighing these putative risks, yet nevertheless, advocate the “prudence” of dose “optimization” (i.e., using doses that are ALARA); but this is a radiophobia-centered approach. For example, the goal of the Image Gently Alliance is to lower the potential risk of CT-caused cancer in children by providing information on dose management and “optimization” (based on notional LNTH-predicted risks) creating the false perception that some risk exists.

There is nothing prudent about ALARA dosing: radiophobia's far greater *actual* risks arise from patients' fear-driven imaging avoidance and physician-recommended use of alternative procedures, such as long-duration MRIs in children requiring anesthesia. *True* iatrogenic risk arises not only from such alternative procedures but also from *misdiagnoses* that are secondary either to patient *refusal* of medically indicated imaging or to *nondiagnostic* scans resulting from insufficient exposure.[6]

All medical procedures require the justification of medical indication, but such justification does not involve imaging's radiation levels. The problem is *radiophobia*, not radiation. Dose “optimization” efforts only multiply illnesses, injuries, and deaths without justification. Therefore, the ICRP-recommended fundamental principles of radiation protection – justification and optimization – are mutually contradictory and without merit for radiological imaging.

Moreover, imaging's *dual* benefits remain hidden: first, the valuable diagnostic information it provides, which either strengthens confidence in suspected diagnoses or leads to more accurate diagnoses and better treatments;[7] and second, the far more likely low-dose health benefits of reduced lifetime cancer risk and all-cause mortality.[8]

Medical imaging achieves a diagnostic purpose and should be governed by the highest science-based principles and policies (use of proper procedures, appropriately calibrated equipment, etc.). The LNTH is an invalidated anti-scientific hypothesis, spawning the ALARA policy: neither errs on the side of caution. Rather, LNTH and ALARA are responsible for misguided concerns and uninformed policies promoting radiophobia that leads to actual risks far greater than the hypothetical carcinogenic risk purportedly avoided, all while ignoring imaging's benefits. Therefore, these policies have no place in managing imaging's usage. Radiophobia can no longer be ignored: medical imaging's low-dose radiation exposure has no documented pathway to harm, while LNTH/ALARA most assuredly do.

Against the proposition: Cynthia H. McCollough, Ph.D.

Opening Statement

The fundamental principles of radiation protection in medicine require that two criteria are met.[9-11]The first is justification – any exposures to ionizing radiation must be justified by an anticipated medical benefit. The second is optimization – justified exposures should be applied using the lowest dose necessary to accomplish the required task. This latter principle is referred to as ALARA – As Low As Reasonably Achievable. The premise of Dr. Siegel is that this admonishment to keep doses as low as possible implicitly teaches that radiation is something dangerous, the obvious question being “why aim for low doses unless radiation is a bad thing?”

To address this question, I could discuss the topic of whether or not low doses of radiation are in fact dangerous. However, this is irrelevant to the need for the ALARA principle. Large doses of ionizing radiation are a known carcinogen. The evidence for this is unassailable and, because current biological and epidemiological evidence cannot *definitively* prove that low doses of radiation are safe, the precautionary principle of risk management must be invoked.[9-12]The precautionary principle is the precept that an action should be undertaken with great care if the consequences are uncertain and potentially dangerous.[4] Under the precautionary principle, it is the responsibility of a proponent (e.g., CT provider) to establish that the proposed activity (e.g., receiving a CT) will not result in significant harm (e.g., cancer induction).[12] Advising people to take the lowest effective dosage of a medicine (or receive the lowest appropriate dosage of radiation) is always the right thing to do if we know that at high doses, significant harm can occur. Medical imaging providers should not stop aiming to use the lowest radiation dosage that accomplishes the diagnostic task just because Dr. Siegel is concerned about the public perception of radiation.

Those who accept existing evidence that the low doses of radiation delivered by medical imaging are associated with risks too small to be definitively demonstrated, including the AAPM,[13] IOMP,[14] HPS,[15] and BEIR VII committee,[16] acknowledge that the linear nonthreshold (LNT) hypothesis is a reasonable ***model*** for radiation protection. This is absolutely not the same

thing as endorsing the hypothesis that risk actually exists from low doses of radiation. Neither does it mean that patient care should ever be compromised in the name of ALARA. ALARA simply means that we should treat radiation as the carcinogen that we know it is (at higher doses) and avoid unnecessary exposures. We should absolutely not abandon such common sense.

Rebuttal: Jeffry A. Siegel, Ph.D.

Dr. McCollough asserts that whether or not low-dose radiation is dangerous is irrelevant to ALARA dosing. *But that is precisely the **key** relevant point*.

She bases the *possibility* of low-dose harm, even if undetectable, on the undisputable fact that high doses are harmful, and advocates erring on the side of caution. However, she ignores voluminous scientific research demonstrating that the body repairs/eliminates low-dose radiation damage, and at the same time is stimulated to repair the much greater endogenous metabolic damage, resulting in a *net benefit*, through a variety of protective adaptive mechanisms. At high doses, repair is overwhelmed if not inhibited, indicating a different mechanism of action, thereby invalidating the LNTH. Without this evidence, Dr. McCollough's advocacy of ALARA would indeed, as she says, derive from common sense. Therefore, the question of low-dose danger could not be more relevant.

It is precisely the proven *benefit* of low-dose radiation that renders the ALARA principle a source of radiophobia. Furthermore, her invocation of the precautionary principle one-sidedly ignores the harms of *radiophobia*, including patient refusals of radiation-associated medical imaging and numerous deaths caused by unnecessary forced relocations of mass populations in the aftermath of the Fukushima nuclear accident.

She refers the reader to the ICRP and other organizations/committees that adhere to the LNTH. They all concede, with her concurrence, that low-dose medical imaging “risks [are] too small to be definitively demonstrated.” Like Dr. McCollough, they too ignore/dismiss the mountains of evidence that the LNTH-derived cancer risk is a *fiction*, and that benefit has been *proven* as presented in my Opening Statement.

ALARA-dosing fosters radiophobia because denials that low-dose radiation confers a net benefit, and averrals that it confers risk, are demonstrable falsehoods that neglect the sciences of biology, chemistry, and physics that demonstrate the falsity of the LNTH and the reality of the hazards caused by any policy based on the ALARA principle.

Rebuttal: Cynthia H. McCollough, Ph.D.

Dr. Siegel and I agree that “credible evidence of imaging-related low-dose (< 100 mGy) carcinogenic risk is nonexistent.” However, I challenge his claims that, instead, “low-dose radiation does not *cause*, but more likely helps *prevent*, cancer.” The effect of low doses of radiation – if they exist – are simply too small to demonstrate.[17] That holds true for hormetic effects just as it does for harmful effects. As much as biology adds to our understanding of radiation effects, epidemiological studies are the only way to take into account a whole organism's biological response to a radiation exposure. The protective and other adaptive

responses to which Dr. Siegel refers can only be shown in the context of the whole organism (i.e., epidemiology), and there it is just as difficult to prove hormesis as it is to prove carcinogenic risk.

I further disagree with Dr. Siegel's assertion that Image Gently, and other professional efforts that promote ALARA, are “creating the false perception that some risk exists.” The general public, and many medical professionals, *already* have the strong bias that radiation is bad. Images from Hiroshima and Nagaskaki, Chernobyl, and Fukushima, and hair loss from CT overexposures are what most people think of when radiation is mentioned. ALARA did not create a bias against radiation. Frightening events associated with *high doses* of radiation did. To disregard this public perception would be to ignore the beliefs and concerns of our patients.

Finally, there is irrefutable evidence that before the advent of Image Gently and other efforts like it, which seek to promote ALARA in medical imaging, children were being irradiated with adult doses. There was not universal attention to ***optimization*** of the exams, such as has evolved since these ALARA-focused campaigns. Without a focus on optimization, a cavalier approach to imaging – one that aims for the best pictures and not the best balance of overall care – would ensue. Such disregard of the actual dosage applied would erode the public's faith in imaging providers because of people's underlying belief that radiation is dangerous. Failure to acknowledge potential risks would ignore these beliefs and undermine trust, which is at the core of the patient–doctor relationship. Clear recognition of potential risks and demonstration of technical expertise to minimize risk and maximize benefit is essential in maintaining the trust of our patients.

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CHAPTER 6

Education

6.1. It is appropriate to deliver the didactic lecture components of Masters programs in Medical Physics completely online

C.-K. Chris Wang and Carmel J. Caruana
Reproduced from *Medical Physics* **43**, 5791–5793 (2016)
(http:// dx.doi.org /10.1118/1.4961013)

OVERVIEW

Distance-learning (DL) graduate programs have become common at universities worldwide, yet few such programs exist for medical physics. It has been suggested that, at least for the didactic curriculum, it is appropriate to deliver medical physics programs completely online. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is C.-K. Chris Wang, Ph.D. Dr. Wang earned his M.S. degree from Tuskegee Institute, AL and his Ph.D. from Ohio State University. He has over thirty years of combined industry and academic experience in nuclear engineering, radiation health physics, and medical physics. He is currently Full Professor of Medical Physics at the Georgia Institute of Technology and, since its inception in 2004, has been a key faculty member of the CAMPEP-accredited graduate Medical Physics program, which is available to distance-learning students. He has published extensively in nuclear physics, Monte Carlo methods in radiation dosimetry and shielding, nuclear criticality safety, micro/nanodosimetry, radiobiological modeling, and neutron-based radiotherapy modalities for cancer treatment.

Arguing against the Proposition is Carmel J. Caruana, Ph.D. Dr. Caruana has a B.Sc. in Physics and Mathematics and a PGCE from the University of Malta, an M.Sc. in Applied Radiation Physics from the University of Birmingham, U.K. and a Ph.D. from Charles University, Prague. He is Associate Professor and Head of the Medical Physics Department, Faculty of Health Sciences, University of Malta and Mater Dei Hospital, Msida, Malta. Dr. Caruana specializes in diagnostic and interventional radiology, protection from ionizing radiation and other physical agents, and legislative/professional/E&T issues in Medical Physics. He is past Chairperson of the E&T Committee of the European Federation of Organizations for Medical Physics and main author of the “Role” and “E&T” chapters of the EU sponsored document “European Guidelines on the Medical Physics Expert.” He is also the main author of the leadership in Medical Physics module of the EUTEMPE-RX project entitled “Development of the profession and the challenges for the Medical Physics Expert (D&IR) in Europe.”

FOR THE PROPOSITION: C.-K. Chris Wang, Ph.D.

Opening Statement

Recently, online education has become a popular alternative for a wide range of nontraditional students, and there should be no exception for the MS degree in Medical Physics (MSMP). To be clear, I am not for complete online delivery of the MSMP program because the program contains certain experimental and hands-on-based components that require the physical presence of the student, but I am very much for online delivery of the didactic lecture components of the program. In fact, Georgia Tech's MSMP program has been offered to both on-campus (OC) and DL students for more than a decade. All the didactic lectures are delivered to the DL students via a designated internet site. The admission and degree requirements for DL students are exactly the same as those for OC students. The sequence of courses offered to DL students, however, is designed for part-time students (who have full-time jobs) such that they can complete the MS degree in three years. DL students are required to travel to Georgia Tech's campus several times to complete the courses that encompass the experimental and hands-on-based components. These courses include radiation detection, radiation therapy physics, and clinical rotation. So far, Georgia Tech's DL program for MSMP has graduated 23 students. The follow-up record shows that, when compared with the graduates of the OC program, the graduates of the DL program are equally successful in terms of getting employed as junior/resident physicists and becoming ABR certified. We therefore consider the quality of the DL program at Georgia Tech to be the same as that of the OC program. This evaluation is supported by the fact that both the OC and the DL programs at Georgia Tech have received CAMPEP accreditation in 2010.

Online delivery of lectures, however, does require strong technical and administrative support in order to be successful. For example, the lectures must be recorded professionally and uploaded onto the course website in a timely manner, and homework assignments, exams, etc., need to be properly administered and documented. For a large institution this support can usually be provided by the Continuing Education Department (or equivalent), but only if it makes financial sense. A problem, therefore, arises when enrollment is too low to be financially feasible. For Georgia Tech, the minimum enrollment for delivering an online course is three. When enrollment is below three, one must take other options such as the use of recordings from the previous year, which degrades the quality of the program. The low-enrollment issue, however, is not unique to DL programs. It also applies to OC programs.

In summary, our experience with the DL MSMP program at Georgia Tech has been a positive one. All the didactic lecture components have been delivered successfully online, and the graduates of the program are equally successful in pursuing a career in medical physics when compared with their OC counterparts.

AGAINST THE PROPOSITION: Carmel J. Caruana, Ph.D.

Opening Statement

The objectives of the didactic lecture component of medical physics education are that participants:

(a) gain the theoretical knowledge underpinning medical physics,

(b) acquire the professional attitudes required of clinical scientists by direct interaction with role models,

(c) learn to problem solve and collaborate with other, and

(d) through their own presentations, learn to put forward and defend their perspectives for the consideration of peers and mentors.

I contend that e-learning is less effective in achieving these objectives than face-to-face teaching.

It is acknowledged that communicating difficult physics concepts is not easy during face-to-face learning notwithstanding the instant clarification of misconceptions and feedback from faculty and the opportunity of peer discussions. Such difficulties are magnified in e-learning when these instantaneous feedback mechanisms from faculty are not available and peer discussion is made harder, particularly when e-learning is carried out asynchronously with students partaking of online prerecorded lectures at different times and independently of each other. Feedback to faculty is also wanting. As a teacher, I scan students' eyes and body language to confirm understanding or otherwise—something not possible online. Uncertainties are easily eliminated through questioning, whilst improved understanding is achieved through an inflexion of the voice, use of facial expression, modified wording, or hand gestures.[1] In addition, as teachers we are not merely human knowledge communication devices but, above all, role models.[2,3] The attitudes we demonstrate during our teaching are those that our trainees need to emulate to help them transform themselves from fresh-faced physics graduates to expert professionals and future leaders. Such attitudes will not be acquired over a weekend retreat but are acquired through ongoing and sustained interactions with suitable mentors. Students also learn by bouncing ideas off their peers. During e-learning the stimulation of group interaction is lost; although one may attempt to create an online community it is simply not the same. Learning communities will not be built through a smattering of online meetings but through personal friendships and social moments when formal learning is put on hold and informal learning processes hold sway. Healthy competition and active mutual interaction with peers is what motivates many learners. In online learning the flow of the discussion is slower, the cut and thrust is dampened, and speedy questions and responses are lost. Student-led presentations are an integral part of the didactic component of our courses and need to be ongoing so that students may hone their own communication skills and learn to read their audience. One needs to create a community of learning, and the group seminar is what brings the community together.[4] Recently, the pace of placing entire didactic programs online has faltered and blended learning approaches are being adopted in which the advantages of face-to-face teaching are not lost. At the foundational Masters level, the nature of the blend should be in favor of face-to-face learning rather than the reverse. Even the best online program cannot replace the personal contact with a mentor or the intensity of learning arising from the human relationships that develop in a face-to-face group.

Rebuttal: C.-K. Chris Wang, Ph.D.

At the beginning of his opening statement, my opponent provided a list of four objectives of the didactic component of medical physics, and stated that e-learning is less effective in achieving these objectives than face-to-face teaching. I do not dispute the four objectives as they are consistent with those listed in the latest version of *CAMPEP Standards for Accreditation of Graduate Educational Programs in Medical Physics.*[5] However, I believe this debate is not about the appropriateness of delivering MSMP completely online; rather, it is about the appropriateness of delivering the "didactic lecture components" of MSMP completely online. As I mentioned in my opening statement, our experience with the DL program in MSMP at Georgia Tech does not show that online delivery of the didactic lecture components is any less effective than on-campus face-to-face delivery. In fact, many DL students at Georgia Tech felt that they learned better by watching the self-paced lecture recordings and that their questions regarding the lectures were effectively addressed via e-mail. The drawbacks of online delivery mentioned by my opponent, e.g., absence of peer interaction and teachers as role models, can be largely made up by requiring the DL students to come to campus a few times for the courses that involve hands-on and team work, including radiation detection, radiation therapy physics, and clinical rotation. Everyone would agree that, in medical physics training, there is no online replacement for face-to-face contact with experienced clinical physicists, but that should be the emphasis of the residency program rather than the MS program.

Rebuttal: Carmel J. Caruana, Ph.D.

I do agree with Prof. Wang that, for practical purposes, distance-learning is here to stay as many students are unwilling to put off employment and to dedicate themselves full-time to medical physics or most other postgraduate areas for that matter. Prof. Wang has compared the on-campus and distance-learning programs for the Masters in Medical Physics at Georgia Tech and asserted that graduates of both program are equally successful.

However, those of us who have experience of both methods of curricular delivery have noted differences in professional attitude and maturity between graduates from the two types of program. The reasons have already been outlined in my opening statement. I think that only in the case of bright, highly motivated students, is there no difference. In addition, there exists the problem of unfair practices in online only assessment, as effective proctoring is difficult.

I would like to describe one possible way forward. At the moment I am involved in the EUTEMPE-RX (www.eutempe-rx.eu) project for continuous professional development for medical physicists. We have taken the pragmatic view that what can be done online will be done online, but a face-to-face component is required for every module, and that this component should not only be limited to physics practical work but also to discussions on professional and legal issues. I lead the "Leadership" module.[6] Following several weeks of online work including online discussions, the participants meet for a week of face-to-face presentations and discussions with peers and European leaders. I have had the opportunity to compare the effectiveness and appeal of the presentations and discussions for both online and face-to-face components and the difference has been palpable. In addition, to ensure authentic and fair assessment, a written examination is held at the end of the face-to-face phase.

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6.2. Subjects such as strategic planning and communication and management have become crucial and should become an integral part of the medical physics curriculum

Carmel J. Caruana, J. Adam M. Cunha
Reproduced from *Medical Physics* **44**, 3885–3887 (2017)
(http:// dx.doi.org /10.1002/mp.12211)

OVERVIEW

In addition to their clinical duties, many medical physicists find themselves in a situation where they have to do managerial work such as strategic planning and communication within a hospital or with outside agencies. Typically, these skills are obtained on-the-job or by taking extra-curricular courses. However, some believe that such strategic planning and communication and management skills are so important that courses on these topics should become an integral part of the medical physics curriculum. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Carmel J. Caruana, Ph.D. Dr. Caruana has a B.Sc. in Physics and Mathematics and a PGCE from the University of Malta, an M.Sc. in Applied Radiation Physics from the University of Birmingham, U.K., and a Ph.D. from Charles University, Prague. He is Associate Professor and Head of the Medical Physics Department, Faculty of Health Sciences, University of Malta. Dr. Caruana specializes in diagnostic and interventional radiology, protection from ionizing radiation and other physical agents, and legislative/professional/education and training (E&T) issues in Medical Physics. He is past Chairperson of the E&T Committee of the European Federation of Organizations for Medical Physics and main author of the "Role" and "Education & Training" chapters of the EU sponsored document "European Guidelines on the Medical Physics Expert." He is also the main author of the leadership in Medical Physics module of the EUTEMPE-RX project entitled "Leadership in Medical Physics: Development of the profession and the challenges for the Medical Physics Expert (D&IR)."

Dr. Cunha received a Ph.D. in experimental particle physics from the University of California, Santa Barbara in 2006. He continued his experimental particle physics research with a post-doctoral position at the Brookhaven National Laboratory in New York working on code development for the ATLAS detector. In 2009, he moved to the University of California San Francisco, where he is currently working as an Assistant Professor in the Department of Radiation Oncology. His current research focus is on technological improvements for brachytherapy including dose optimization, robotics, additive manufacturing, and electromagnetic tracking. He has a strong interest in education and currently serves as the Vice Chair of the UCSF Academic Senate's Graduate Council. Dr. Cunha has served as President of the San Francisco Bay Area Chapter of the AAPM and is active on several AAPM committees including as Chairman of the Working Group on Medical Physics Graduate Education Program Curriculum.

For the proposition: Carmel J. Caruana, Ph.D.

Opening Statement

The clinical and wider economic and societal environment within which medical physicists exercise their profession has changed radically over the last years; indeed change is unrelenting and the ground seems to be constantly shifting under our feet.[1, 2] there was a time when being a good scientist was sufficient to thrive within the hospital environment; a time when good physicists were considered essential for the running and ongoing development of a quality clinical service. This is not true in general anymore; economic pressures and intra- and inter-professional turf wars now dominate many of our workplaces and have turned large hospitals into gargantuan malls selling health services. In such circumstances, the quality and safety values so dear to our profession are diluted as the profit motive dominates. For example, in diagnostic radiology reduction of population doses and the emphasis on diagnostic accuracy via high image quality tend to be looked upon as less important (read 'an unnecessary expense') provided they do not reach critical values detectable by patients or society at large (hence affecting profits). As we strive within this new milieu to reposition our profession, departments, and often our personal selves, ongoing formal, informal and instinctive professional, departmental and personal strategic planning via strengths, weaknesses, opportunities, and threats (SWOT) audits have become the order of the day.[3, 4] All healthcare professions are feeling the heat and the number of MBA programs with a specialization in healthcare management (all of which include a heavy dose of SWOT- based strategic planning) has mushroomed.

For many of us who were brought up in a world in which scientific excellence was our mantra, this has been a culturally shocking experience and it is even more bewildering to the unsuspecting physics graduate who transfers from the relatively 'safe' confines of a university physics department to the new economic-political healthcare minefield. It is therefore our duty as leaders and educators to acknowledge the new norm, negotiate a personal adaptation which does not compromise our core values, and prepare our students and trainees both academically and psychologically to perform well in such an alien environment based on a paradigm so distant from our scientific ethos. This training for the 'real world' out there, needs to be planned, structured, inbuilt into the curriculum, and start early since the 'real-world maturity' required to hold one's own in such an environment, cannot be acquired overnight. In particular, it requires a program to build up the psychology of our trainees and turn them into strong leaders. It is imperative that we introduce elements of strategic planning, medical sociology, management, leadership, economics, communication, office politics, and policy making into our curricula. In addition, the gradual elimination of the humanistic approach to healthcare and its replacement by a marketing paradigm lifted directly from the commercial world, has made a good knowledge of medical and professional ethics critical. We must help our trainees to adapt to the new order also through ongoing discussions with more experienced mentors based on real-world case studies and issues. I give examples of these in a Medical Physics leadership course I deliver which specifically targets these issues (in fact it is a 'mini-MBA' for medical physicists).[5, 6] We, as educators, must not shy away from this responsibility even if it requires a rethink of our own personal world-view and educational philosophy — the future professional success and personal happiness of our trainees depends on it.

Against the proposition: J. Adam M. Cunha, Ph.D.

Opening Statement

The proposition is comprised of three components: (a) the topics of study: *strategic planning, communication, and management*; (b) the claim of importance: "*…have become crucial…*"; and (c) the solution: "*…should become integral….*" The most contentious is the claim of importance.

As well established in the literature of education, communication skills in STEM fields (or in any career path) are highly correlated with career success. But while strategic planning and management may be beneficial skills for medical physicists, it is not clear these are *crucial skills* to have *upon graduating from a medical physics program*.

Early career positions do not involve management or strategic planning. The usual path for employment after graduation is as a junior medical physicist at a medical facility or in industry. A job including project management, let alone strategic planning, is not likely. And for large departments, it is absolutely feasible that these skills will never be necessary for a career medical physicist. Why should we teach these skills when there will be ample opportunities to acquire them after graduation as may be needed?

Jack of all trades; master of none. Technological advancement is always accelerating; therefore, medical physics programs must continuously evolve to incorporate new material. However, this cannot come at the expense of core medical physics coursework. Didactic training in many degree-granting programs entails two years of course work; and certificate programs, considerably less. The AAPM Reports 197 and 197S outline the *bare minimum* of topics that should be covered to ensure graduates have a core of medical physics knowledge, with the expectation that this minimum is supplemented by auxiliary course work to broaden or deepen students' didactic medical physics training.

It may be tempting to include strategic planning and management education to broaden our students' knowledge. Unfortunately, we play a zero-sum game with time: every addition requires a deletion. Do we want medical physics programs prolonged to accommodate more coursework? Possibly. But constantly advancing technology already causes a struggle to cover an expanded core of basic knowledge. In a choice between teaching new technologies or teaching management skills, I choose physics every time.

While communication skills are crucial to success in almost *every* occupation (medical physics or otherwise), communication training should be a constant, intrinsic, integral, and organic part of every academic curriculum, not necessarily a distinct course. Management skills and strategic planning, however, are *not* crucial for new graduates of medical physics programs; thus, they should not become integral parts of the medical physics curriculum.

While each program should evaluate the needs of their distinct student base, there is no demonstrable *need* for organizations such as AAPM and CAMPEP to advise or require inclusion of management and strategic planning. Nevertheless, each program must weigh allocating limited time and resources to additional physics courses, *or* to additional clinical experience, *or*

to managerial/planning education; they cannot do it all. A strong core of didactic physics courses is paramount. Students would not benefit from learning ancillary subjects at the expense of quality physics training.

Rebuttal: Carmel J. Caruana Ph.D.

I will focus on what I consider to be the strongest arguments of my opponent.

"*Early career positions do not involve management or strategic planning*": While formally this is true, in practice it is not. Today, young people are very job-oriented and the following questions are on their mind: "What shall I specialize/subspecialize in to ensure a good future for myself? What parts of the medical physicist's role will become obsolete? Conversely, what new techniques will become essential?"

"Why should we teach these skills when there will be ample opportunities to acquire them after graduation as may be needed?" Unfortunately, learning these skills when they become needed is invariably too late and the damage done. Strategic planning requires quality thinking time, a change of perspective and a strengthening of personal psychology — that takes time.

"Students would not benefit from learning ancillary subjects at the expense of quality physics training." I, of course, agree, but this need not be the case. Although our students can learn a lot of physics on their own as needed (having had a lot of experience in their undergraduate years), they have had little experience in these ancillary subjects. These skills are being taught to other healthcare professionals; if we defer to a later stage catching up will be difficult.

In essence, a vast amount of physics knowledge will be of little use if you end up without a job.

Rebuttal: J. Adam M. Cunha, Ph.D.

Change is inevitable; core science skills need to remain our focus; auxiliary training can be obtained as needed post hoc.

The younger generation is well connected and in touch. While constant change in our profession may seem "culturally shocking" to us in the old guard, for our students change is the norm. We must not project our generational experience onto our students; they are adept at operating in complex organizations.

Medical physics educators are responsible for teaching students the core skills of a scientist. Admittedly, our students need to learn how to function effectively within the larger healthcare milieu. However, are medical physics faculty the best teachers of management? Should the finite resources we have to teach science be diluted by allocating funds and time to teaching peripheral skills?

Dr. Caruana referenced Dr. Mills' comments[2] about the changing nature of the medical profession — insights obtained while earning a Ph.D. in Health Management. Students interested in health management *should* pursue such a degree. Dr. Caruana inadvertently argues this point

when he states: "*the number of MBA programs with a specialization in healthcare management… has mushroomed*." Our universities already have management classes taught by professional business educators. Is it not more efficient and productive to encourage students to pursue these subjects through other departments to the extent they are interested and motivated?

The optimum response to the potential need for strategic planning and management expertise in our profession is to: (a) leave the physics core intact, ensuring that our students have the rigor and confidence to argue the science in the face of bureaucracy; and, (b) allow/encourage interested students to take existing management coursework. A joint degree program, e.g. MS(PhD)/MBA/MPH, created by partnering with the business school within the university, could be an option offered to students willing to extend their tenure and pay the additional tuition. But extending the length/cost of our core programs to meet the needs of the interested few is misguided.

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CHAPTER 7

Professional Issues

7.1. Increasing dependence on industry-funded research creates higher risk of biased reporting in Medical Physics

Sonja Dieterich and Paul J. Keall
Reproduced from *Medical Physics* **41**, 100601-1-3 (2013)
(http:// dx.doi.org /10.1118/1.4812894)

OVERVIEW

When companies fund research they obviously hope that the research will demonstrate the superior effectiveness of their products. Consequently, publication of negative results might make companies less enthusiastic about supporting such research in the future. Since researchers who use industrial support are likely to be eager to continue with this funding, some believe that this might increase the risk biased reporting. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Sonja Dieterich, Ph.D. After completing her Ph.D. in Nuclear Physics at Rutgers University in 2002, Dr. Dieterich received training in Medical Physics at Georgetown University Hospital, Washington DC, from 2002 to 2003. In 2003, she accepted a faculty position at Georgetown. From 2007 to 2012, she worked at Stanford University Hospital as Clinical Associate Professor and Chief of Radiosurgery Physics. Currently she is an Associate Professor and Physics Residency Co-Director at the University of California Davis. Dr. Dieterich is Chair of the AAPM Task Group 135 "QA for Robotic Radiosurgery" and a member of the ASTRO Physics and Multi-Disciplinary QA Committees. Her current research interests are the development of QA/QM programs for new technologies, image-guided brachytherapy, and veterinary radiation oncology.

Arguing against the Proposition is Paul J. Keall, Ph.D. Dr. Keall is a Professor at the University of Sydney in Australia. His work is broadly supported by the NHMRC Australia Fellowship *Innovations in Medical Physics to Improve Human Health* with additional funding supporting individual projects from Australian and US government sources. Professor Keall's main scientific interests involve image-guided radiation therapy and accounting for anatomic and physiologic changes in healthy and pathologic tissue throughout a radiation treatment course. Additional areas of investigation include ventilation imaging, audiovisual biofeedback, and MRI-guided radiotherapy. These research activities have resulted in over 170 scientific articles and

several awards and honors. He has developed new methods for medical imaging and image-guided radiation therapy that have been translated into clinical practice. Relevant to this debate, and in the full disclosure spirit of TG109, to quote Rock Mackie "I am a poster-child for conflict-of-interest" having held over 20 research agreements with start-up, mid-size, and large companies along with awarded patents and commercial licenses.

FOR THE PROPOSITION: Sonja Dieterich, Ph.D.

Opening Statement

As humans, we are hard-wired toward implicit bias.[1] The Washington Post published on biased reporting in pharmaceutical research,[2] which triggers some self-examination about potential publication bias in medical physics. Let us assume that vendors and researchers have been able to avoid conscious bias exerted by pressures of market shares and up-or-out research faculty appointments which depend on securing ever scarcer grants. The issue of implicit bias still remains. To conduct good science, we must address all factors affecting the quality of science; publication bias is a major known factor to affect research quality, and with shrinking NIH budgets will only gain in influence.

A large body of research is available on publication bias. To summarize: (1) there is publication bias in medical journals toward positive outcomes,[3] (2) the incidence of editors or reviewers rejecting negative studies is small for JAMA,[4] but unknown for most other journals, and (3) published reports from industry-funded studies show a larger bias toward positive results.[5] Unless medical physics journals (e.g., *Medical Physics*, *PMB*, *JACMP*) publish data to the contrary, my working hypothesis is for an existing editorial/reviewer bias of unknown size toward rejecting papers which report negative study outcomes. No reviewer guideline, journal review submission websites, or our Code of Ethics[6] address implicit bias toward positive study outcomes.

One proposed way to remove positive publication bias is to require all federally funded-research to be published independent of the outcome, provided the scientific method and statistical analysis meet quality standards. It remains to be seen if industry would commit to this solution as well because, for such a commitment to be meaningful, vendors would need to provide means of independent verification such as a publicly accessible listing of all outside research contracts.

Increased reliance on industry funding also increases the risk for comparative effectiveness research on technology to remain unfunded. Few institutions can afford the cost and redundancy of operating two or more technologies designed to perform the same function. For vendor-funded research, there is no incentive to compare clinical effectiveness of competing technologies. Instead, the implicit bias is toward research on the new technology vs older technology. One clinical example is respiratory motion compensation. Several vendors provide solutions for each of the four techniques: compression, breath-hold, gating, and real-time tracking. Despite the widespread acceptance of these technologies and a large variation of cost to implement and use them, there is not a single prospective clinical trial which would provide data on patient outcomes based solely on the technology used for treatment.

AGAINST THE PROPOSITION: Paul J. Keall, Ph.D.

Opening Statement

As scientists we have a mandate to generate new scientific knowledge. As medical physicists we perform and publish work that can improve how we detect, image, diagnose, and treat disease. However, our academic integrity struggles against biased reporting for any publication independent of its funding source: we have an inherent self-interest in having articles published that help us get and keep grants, help with promotion and career prospects, help with invitations to give talks at interesting places, and many other benefits. As a result, for many reasons, a few of us "behave badly."[7]

Industry-funded research plays an important role in improving health outcomes, typically supporting medium-to-late stage research aligned with product roadmaps. Often late-stage research requires engineering support to allow clinical testing that otherwise would not be possible. The potential for conflicts-of-interest exists. Fortunately, to avoid any undue influence of industry pressure on the outcomes of research, there are a number of mechanisms to protect and isolate researchers from external influences and, therefore, reduce the risk of biased reporting. Three protection mechanisms reducing the risk of biased reporting are: (1) increased accountability from medical journals regarding ethics and conflicts of interest, (2) greater academic freedom in industrial-university agreements, and (3) stronger governmental regulation of commercially sponsored research.

Increased accountability from medical journals regarding ethics and conflicts of interest

All reputable medical journals now have conflict of interest policies. Many journals follow the ICMJE conflict-of-interest policy in which each author must submit a written signed disclosure. *Medical Physics* requires that "Each author of a paper is required to disclose any and all potential conflicts of interest that could be perceived to bias the results reported in the paper." This policy raises awareness for authors submitting the work, reviewers, and readers, and increases authors' accountability.

Greater academic freedom in industrial-university agreements

Over time, universities have taken a much stronger stance with respect to research conduct and publication control. An example from a University of Sydney agreement states: "As a matter of basic academic policy, the University retains the right to publish in it discretion material relating to the conduct and conclusions of the Research", meaning that the academic staff have the right to publish and interpret their own results without industry direction or oversight.

Stronger governmental regulation of commercially sponsored research

The US FDA, NIH, and other government bodies have a vested interest in ensuring that publications of studies represent the actual results. There is new and proposed regulation for conflicts of interest, assessing conflicts prior to the start of a study to potentially recuse investigators, avoid data falsification, and provide data storage and data access. An as example,

NIH policy states: “This complexity, as well as a need to strengthen accountability, led to changes that expand and add transparency to Investigators’ disclosure of Significant Financial Interests (SFIs), enhance regulatory compliance, and effective institutional oversight and management of Investigators’ financial conflicts of interests.”

In summary, medical journals, universities, and governments are actively working to protect investigators from external influences and, therefore, decrease the risk of biased reporting in journals such as *Medical Physics*.

Rebuttal: Sonja Dieterich, Ph.D.

Dr. Keall highlights the increased efforts to address biased reporting in science. The questions we need to evaluate are: How effective are we in enforcing these rules, and have we done enough to cause a change in our culture? To use an analogy, the posted speed limit is the rule, but the unwritten culture (on most highways in the USA, Germany, and Australia at least) is for traffic to proceed at 10 miles/h above the posted speed limit without fear of repercussion by the highway patrol.

Dr. Keall cited a very good paper published in 2005,[7] which I have examined for data pertaining to funding source influence on outcome reporting, i.e., violation of scientific integrity standards. Table I, entry 10 in this paper[7] lists the incidence of “Changing the design, methodology, or results of a study in response to pressure from a funding source” as 15.5% on average (9.5% for early career and 20.6% for mid-career scientists). Given that the study plausibly argues the under-reporting of results, these percentages hardly constitute just a few of us behaving badly, as my opponent states. I was unable to find data suggesting this percentage had decreased with the implementation of the three protection mechanisms Dr. Keall listed.

To be effective in making science less prone to bias, the interventions must (1) remove the motivation for biased behavior, (2) implement a means of identifying researchers who do not follow scientific standards, and (3) increase the stakes for being found in violation of scientific standards. None of the three interventions listed by Dr. Keall remove the motivation for biased behavior. Indeed, decreasing support through outcome-neutral funding sources has increased the pressure. The second intervention, greater freedom to publish, looks good on paper but in reality will not protect the researcher from losing continued industry sponsorship should negative outcome reporting be undesired by industry.

In summary, while gross scientific misconduct through fabrication, falsification, and plagiarism is indeed committed by very few of us, I (pessimistically) maintain that our scientific culture has not yet changed sufficiently to remove the significant pressure toward biased reporting. We neither have data to allow us to make a conclusive statement that biased reporting is not an issue, nor do we have any auditing procedures in place to raise the stakes for breaking the rules.

Rebuttal: Paul J. Keall, Ph.D.

Dr. Dieterich has some very good points and suggestions to improve the amount of negative-result research being published and the impact of declining Federal funding on clinically

important research, such as comparative effectiveness studies. She asserts that (1) humans are subject to bias, (2) there is evidence supporting publication bias, (3) federally funded (and ideally industry-funded) research be published regardless of positive/negative results, and (4) the impact of increased reliance on industry funding means that some important research areas are unfunded. These observations are all valid. However, they do not lead to the conclusion that *increasing dependence on industry-funded research creates higher risk of biased reporting in medical physics*. Moreover, several of the references used to support her statement pertain to the pharmaceutical world; none specifically address biased reporting in medical physics research.

To further the debate, the pathway to impacting patients on a large scale is necessarily through industry. Having ideas proceed from bench to bedside is one of the most rewarding professional accomplishments in our field. Academic/industrial interactions are essential for this translational research. AAPM TG109 (Ref. 6) states "*There is nothing inherently wrong with a conflict of interest, but it should be acknowledged to eliminate the perception of possible impropriety. The best protection against conflict of interest accusations is full disclosure and the acquisition, interpretation, and publication of research findings in a manner that is transparent and above suspicion*." To navigate these interactions, in addition to the three protections reducing the risk of biased reporting detailed in my Opening Statement, researchers receive ethics education throughout their lives, along with a growing ethics component of graduate[8] and residency[9] medical physics programs and in our profession.[6]

Prof. Keall wishes to acknowledge his lab group for lively discussion on this debate and particularly Brendan Whelan and Julie Baz for comments and suggestions.

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7.2. The future h-index is an excellent way to predict scientists' future impact

Daniel E. Acuna and Orion Penner
Reproduced from *Medical Physics* **41**, 110601-1-3 (2013)
(http:// dx.doi.org /10.1118/1.4816659)

OVERVIEW

Typically, when scientists are being considered for funding, appointment, or promotion, a committee reviews their publications and often estimates the importance of these using a metric such as the *h*-index.[1] This just represents *past* accomplishments, however, and not potential *future* impact, which is probably more important. A new metric, the future *h*-index,[2] has been introduced and is claimed to be an excellent way to predict scientists' future impact. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Daniel E. Acuna, Ph.D. Dr. Acuna received his Bachelor's and Master's Degrees from the University of Santiago, Chile and his Ph.D. from the University of Minnesota, Twin Cities, Minnesota. He is currently a Research Associate in the Sensory Motor Performance Program at the Rehabilitation Institute of Chicago and Northwestern University, specifically working in Dr. Konrad Kording's Bayesian Behavior Lab. He currently studies large data sets to make sense of the science itself—so called "science of science." Dr. Acuna and his colleagues try to find statistical regularities in large, unstructured data from heterogeneous sources to better understand publication, funding, and teaching activities. By using machine learning techniques, they hope to distill the rules that tell apart successful from less successful ways of doing science and predict quantities such as the *h*-index, yearly funding costs, and students' teaching evaluations.

Arguing against the Proposition is Orion Penner, Ph.D. Dr. Penner obtained his B.Sc. (Hons.) from the University of Manitoba, an M.A. from Boston University, and his Ph.D. from the University of Calgary, all in Physics. His thesis research focused on Complex Networks and information theoretic approaches to biological sequence alignment. He is currently an Assistant Professor at the IMT Institute for Advanced Studies, Lucca, Italy, and a member of the Laboratory of Innovation Management and Economics. His research now focuses on novel applications of data centric approaches to problems from Innovation Economics and the Science of Science.

FOR THE PROPOSITION: Daniel E. Acuna, Ph.D.

Opening Statement

Hiring, promotion, and funding decisions are to a large extent driven by predictions about scientists' future impact. A scientist's future impact can be defined with respect to many

different objectives, such as research publications, funding, teaching ability, and outreach.[3] Publications and their citations relate to a scientists ability to do research and are of great importance to decision makers in research focused institutions. This discussion focuses on a specific kind of impact estimation, the estimation of future publication impact.

The excellence of a prediction is defined by the quality of the decision that it supports. Indices like the future *h*-index are noisy: some aspects of excellence are not visible in the publication record. They may also be biased: some aspects of excellence, e.g., interdisciplinary training, may not be observable. However, estimates of committees are also noisy. For example, members may have highly individual favoritisms. They may be discriminatory: gender, race, and other types of prejudices may cloud judgments.[4] How useful each source of information is depends on the sizes of biases and noises, and these problems can be solved by predicting the future *h*-index.[2]

The *h*-index is one of the simplest and easiest metrics of publication impact,[1] making it attractive to use. It is robust and hard to manipulate.[5] However, the *h*-index does not account for the age of scientists and individual contributions of each co-author, and self-citation introduces biases in favor of authors with many co-authors.[6] Also, it varies substantially from field-to-field, making it hard to compare researchers across disciplines.[4] There are alternatives that fix these problems (e.g., Aziz and Rozing[6]) but they usually require access to more detailed information, making them impractical. However, both noise sources and biases can be addressed by statistics, and the future *h*-index is one such development.

Committees of peers and experts are the current standard for predicting future scientific success. These committees increasingly use metrics,[1] necessary because of the growing number of applicants per tenure-track job or funding opportunity.[7] Why should we not try to find the statistically optimal combination of multiple features to achieve better predictions? For example, we could have an index that combines many indices such as funding, teaching, and other metrics from social media (e.g., "Altmetrics"[8]) and maybe try to predict them in an optimal manner, similar to Acuna *et al.*[2] True excellence in future predictions comes from describing weaknesses of approaches, and then statistically finding ways of correcting them. The future *h*-index is just one small step in this direction.

AGAINST THE PROPOSITION: Orion Penner, Ph.D.

Opening Statement

This proposition can be parsed into three questions. First, assuming 100% prediction accuracy, is the future *h*-index a good measure of a scientist's future impact? Second, how accurate is the future *h*-index model proposed by Acuna *et al.*?[2] Third, how should its likely use as an evaluation tool shape the criteria we use to judge future *h*-index?

The first question appears to challenge the *h*-index as a measure of research impact, but it does not necessarily do so. What it does challenge is the logic of associating an increase in the *h*-index between years t and $t + \Delta t$ with research impact during those years. That increase is driven not only by citations to papers published between t and $t + \Delta t$ but also citations to papers published before t. In fact there is a good evidence that the increase is largely driven by citations to

previous work.[9] Indeed, even though the mathematician Paul Erdős passed away in 1996, his *h*-index increased by 9 between 2001 and 2010, one of the largest increases of any mathematician over that period.

Turning to the technical aspects of predicting the future *h*-index, the model of Acuna *et al.* is a good starting point but suffers a number of shortcomings. Collaborators and I discovered its predictive power depends heavily upon "career age."[10] In forthcoming work we further demonstrate much of the model's "predictive power" arises from the cumulative and increasing character of the *h*-index itself.[11] These challenges will likely be overcome by improving the model, but it is hard to overlook the fact that a sufficiently powerful model does not yet exist.

The third question is the one most often overlooked. To most practicing scientists these models and measures will be curiosities, but to people making decisions on tenure track hires, fellowships, institutional and national tenure, etc. they will be tools.[12,13] The true measure of the future *h*-index comes down to its suitability as a decision making tool. In that context a model must do more than simply fit the data, i.e., produce a high R^2, it must also produce accurate rankings. Further, for late career awards (e.g., election to the National Academy of Sciences) it is desirable to measure a scientist's future impact based on papers published before and after year *t*. But in the case of a tenure track hire it is critical to identify the scientist whose work after *t* will have the greatest impact. Again, the future *h*-index cannot discriminate between the future impact of previously published papers and the future impact of work yet to be published.

The future *h*-index is an excellent contribution to the scientific community and pushes the discourse in an important direction, but a great deal of technical and conceptual refinement is required before it is an excellent way to predict scientists' future impact.

Rebuttal: Daniel E. Acuna, Ph.D.

It seems that there is a deep level of agreement about the central issues that Dr. Penner so eloquently put into the three central questions.

The *h*-index is not perfect at measuring research productivity and it would be better to predict something more meaningful for decision makers—once such a measure has been properly defined. In fact, it would be useful to better understand the aims of the various players in the academic market. Methods related to utility elicitation[14] could help by allowing a scientific approach for measuring what we should predict.

The features that we used in the formulation of the future *h*-index were based only on the publication record, which is not overly indicative early on in the career.[10] Early career predictions could be significantly improved by adding other features such as courses taken, grades obtained, and text analysis of letters of recommendation. Since we did not have access to such information, we focused on the publication record only—which seems to work relatively well a few years into the scientific career, even in other scientific domains.[15] Our approach and feature set is just a first step on the path of providing useful predictions of impact.

Predictions are ultimately used for decision-making, rendering rank predictions or other model assessments more appropriate than simply demonstrating a high R^2. For example, granting tenure may be about future publication success, funding, and teaching abilities, whereas election to the National Academy of Sciences may be about career-length impact. Data-driven predictive tools offer an opportunity to impartially help during this process. The way we see our own approach is a starting point that can be improved by both better formulating what matters and by better predicting the variables that matter.

Finally, quantitative approaches need to be compared to the alternatives. Human experts are known to be biased in many ways and, just like any algorithm, might not optimize the variables that truly matter for the decision. A deeper analysis about how to improve these approaches would be an exciting topic for a future discussion.

Rebuttal: Orion Penner, Ph.D.

Indeed I agree with Dr. Acuna that the future *h*-index stands as a good first step towards the use of quantitative approaches in hiring and advancement decisions in academia. However, there is still a great deal more careful and rigorous work to be done before a mature suite of tools is devised. In my opening I highlighted several key flaws that must be addressed, but there are other factors that will play a role in determining whether or not quantitative approaches will be widely accepted. As Dr. Acuna points out, a good framework must be able to integrate information on many other facets of the academic career, including funding, teaching, communication and leadership skills. Any successful approach must also be flexible in how it integrates these data, such as being able to handle input that plays a nonlinear role in determining future impact. Perhaps most importantly it is critical that any framework explicitly produces easily interpreted confidence bounds for its predictions, clearly indicating to the user when it is being stretched beyond its "comfort zone." Satisfying these criteria in one modeling framework is a challenge to be certain, but it does not seem that any one piece is impossible.

If one huge challenge does lie on the path to an appropriate modeling framework, I speculate it is not a matter of the model at all but rather the availability of highly accurate career data for a huge number of scientists. Indeed, few quantitative studies of full and complete career trajectories have surpassed 5000 careers. Development of a suitably flexible and accurate prediction framework will require data sets that stretch, at the very least, into the hundreds of thousands and be spread across all academia. With such diverse data it may be possible to develop a model of academic careers capable of being fully validated, but at the moment the lack of such data represents a massive road block.

Dr. Acuna thanks Dr. Konrad Kording for helpful discussions.

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7.3. Future radiotherapy treatment practice will be based on evidence from retrospective interrogation of linked clinical data sources rather than prospective randomized controlled clinical trials

Andre L. A. J. Dekker and Sarah L. Gulliford
Reproduced from *Medical Physics* **42**, 030601-1-3 (2014)
(http:// dx.doi.org /10.1118/1.4832139)

OVERVIEW

Prospective randomized controlled clinical trials are often considered the only way to definitively compare different methods of treatment. Some believe, however, that future radiotherapy practice will be based on evidence from retrospective interrogation of linked clinical data sources rather than randomized clinical trials. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Andre L. A. J. Dekker, Ph.D. Dr. Dekker obtained his Ph.D. in Medicine from the University Hospital, Maastricht, The Netherlands, in 2003. After completing a Radiotherapy Medical Physics Residency at the MAASTRO Clinic, Maastricht in 2005, he stayed on as Medical Physics Head. He is currently Head of Information and Services and Member of the Management Team, Scientific Director, MAASTRO Innovations, and Research Head of MAASTRO Knowledge Engineering. Dr. Dekker's major research interests include transit dosimetry, adaptive radiotherapy, functional imaging, and predictive models for survival analysis.

Arguing against the Proposition is Sarah L. Gulliford, Ph.D. Dr. Gulliford obtained her Medical Physics Ph.D. in 2002 from The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sutton, Surrey, England. After spending three years as a Radiotherapy Physicist at Suffolk Oncology Centre, Ipswich Hospital, Suffolk, she returned to The Institute of Cancer Research, where she is currently a Staff Scientist. Dr. Gulliford's main research interest is the development of scientific methods to analyze the response of normal tissues to radiotherapy. Using her expertise on trials analysis, she is a member of the NCRI National Radiotherapy Trials QA group and associated Database and Information Technology sub group.

FOR THE PROPOSITION: Andre L. A. J. Dekker, Ph.D.

Opening Statement

If the past is anything to go by, future radiotherapy practice will need to consider increasingly available innovations and treatment options and greater processing of patient data (far exceeding human cognitive capacity).[1] A greater number of patient-specific decisions will need to be made, accommodating patient and tumor heterogeneity,[2] understanding of which is in constant evolution.[3]

To guide radiation oncologists and patients through this, evidence is needed. In an ideal world, this evidence would come from prospective randomized trials: Randomize into matched groups, control every aspect of the treatment, and collect data with perfect quality and with enough power to detect a change in outcome if one is present. Then do this for every decision you ever wanted to make, in every patient group you can think of and keep up with innovations in the field. Sounds impossible? That is because it is. Cancer research and innovations have created an explosion of things we know about a patient and an explosion of treatments we can give to a patient. We cannot possibly trial our way through every combination.

To make matters worse, in our technology-driven radiation oncology community the evidence is less vigorous than in many other disciplines because medical devices progress with incremental innovations and have a shorter development cycle compared with drugs. Furthermore, ethical considerations sometimes prevent the evaluation of medical devices in a randomized clinical trial.[4] The consequence of this evidence gap can be seen in current radiotherapy practice; when asked the question, "What will be the outcome of this treatment in this patient?", the answers radiation oncologists give are very close to a tossup.[5]

Where do we go from here? How do we close the evidence gap? We are sitting on a pile of retrospective patient data in our treatment planning systems, oncology information systems and electronic hospital records. Whenever we introduce something new, we generally collect data on this as well. What if we could supplement our clinical trial evidence base by learning something from this retrospective clinical data and use that knowledge to change our local practice. This is a concept now commonly called Rapid Learning?[6]

The only real obstacle standing in Rapid Learning's way (and retrospective analysis in general) is the amount and quality of the data to learn from. By linking clinical data sources across institutes these problems can be minimized. By linking data we can (a) learn from more patients, (b) identify data quality issues, and (c) learn from our differences in practice such as the use of different technologies. Together, we have the data to inform many of the decisions radiation oncologists face every day. Further, tools are on the way to learn unbiased, reliable evidence from the data in a privacy-preserving manner.[7]

Will future practice be based on evidence from retrospective linked clinical data sources rather than prospective randomized controlled trials? Yes, because we have no other choice. We need to learn from all patients we treat. Only then can we hope to help patients and oncologists make evidence-based choices for personalized radiotherapy treatment.

AGAINST THE PROPOSITION: Sarah L. Gulliford, Ph.D.

Opening Statement

Prospective randomized controlled clinical trials are the backbone of medical research. They provide a framework in which new treatments can be tested for safety and efficacy. Utilizing this framework reduces uncertainties by limiting the variation in patient characteristics; standardizing procedures and follow-up data for comparative studies of "experimental" vs "standard" treatment.[8] Evidence from a randomized controlled clinical trial is regarded as Level 1

Evidence,[9] the best available. Changes in radiotherapy treatment practice should be based on the best available evidence and as such should have their foundation in clinical trials. There are many benefits to clinical trials. Clearly, conducting a clinical trial ensures rigorous procedures and quality assurance to yield high quality, consistent data from both single- and multi-institutional studies. For each trial, the standardized case report forms ensure that the same validated questions and corresponding grading are collected for all patients. This facilitates true comparisons between patients regardless of where they are treated. There are also positive spin-offs from conducting clinical trials. In the case of multicenter trials, the audits and support given to participating centers often aid the safe introduction of new techniques into the clinic. Properly conducted randomized trials are costly both financially and in terms of resources, but the quality of information produced will drive changes in radiotherapy practice with confidence.

A classic example of the benefit of using clinical trial data is the Parotid Sparing trial PARSPORT,[10] one of the few fully randomized comparisons between conventional vs intensity modulated radiotherapy (IMRT). The subsequent analysis of the trial demonstrated clearly that IMRT was beneficial in terms of reducing xerostomia. In addition it was observed that acute fatigue was more prevalent in the IMRT cohort. Analysis of both dosimetric and clinical data has suggested that the explanation may be due to the dose to central nervous system (CNS) structures including the brainstem and cerebellum.[11] As with any scientific finding this result requires independent validation but is illustrative of what can be observed in the clinical trials context. I postulate that this particular needle would have been lost in the haystack of linked whole-institution databases. The PARSPORT trial is also credited with facilitating the implementation of IMRT for head and neck cancer in a number of centers in the UK. Indeed it is recommended in the Institute of Physics in Engineering and Medicine report "Guidance for the Clinical Implementation of Intensity Modulated Radiation Therapy"[12] that IMRT should, where possible, be implemented through participation in a phase III clinical trial. As radiotherapy practice continues to evolve the importance of clinical trials must not be underestimated.

Rebuttal: Andre L. A. J. Dekker, Ph.D.

Evidence based medicine is "*... integrating individual clinical expertise with the best available external clinical evidence from systematic research*"[9] and we should all strive for that in radiotherapy. So my esteemed opponent was right to state that "*changes in radiotherapy practice should be based on the best available evidence*." I have tried to point out the growing impracticality of obtaining this external evidence via randomized controlled clinical trials, as have others.[13] In this rebuttal I would like to focus on the integration of external evidence with clinical expertise and why that is a problem in trials.

Clinical expertise in a technology-intensive discipline such as radiotherapy is a concern. Staff need to be trained, QA programs are needed, etc. A case in point is the HeadSTART trial[14] which found that "*poor radiotherapy can greatly exceed the anticipated benefit of concurrent chemotherapy.*" I do not think these investigators would agree with my opponent's suggestion to use trials to gain clinical expertise, because they went on to recommend that "*to achieve quality radiotherapy, participation in trials should be limited to sites that can contribute a significant number of patients.*" This illustrates the dilemma that, to find the proverbial needle in the haystack (and my opponent mentions a very interesting one), one needs to apply a level of

radiotherapy in trials which is not representative of common clinical expertise. One cannot help but wonder if finding the needle has become more important than evidence based medicine.

Because our delivery process is technology and not drug-based, I believe that the evidence we generate should be tightly integrated with our clinical expertise. Linked clinical data sources allow early adopters to implement new technologies and create external evidence, and permit others to critically evaluate that evidence and use it to improve their local clinical expertise. For me, that is evidence-based radiotherapy.

Rebuttal: Sarah L. Gulliford, Ph.D.

My colleague suggests that it is impossible to conduct a prospective randomized trial for every improvement in radiotherapy practice and he is correct. However that does not mean that future radiotherapy practice will not be based on evidence from prospective randomized controlled clinical trials. The process of conducting a clinical trial allows issues of feasibility to be addressed; the resulting evidence provides confidence for centers to "join in" with a clearly stated methodology. If, for example, the intention of the study is to escalate to a higher prescription dose or a more extreme fractionation than has been implemented previously, no amount of data mining will accurately predict the outcome or toxicity profile of the affected patients.

The concept that it is "unethical" to perform clinical trials has a very weak foundation. Every new technique should be comprehensively audited before implementation in the clinic, with results compared to previous practice. My opponent cites a reference (4) which states that the use of randomized controlled trials to demonstrate superior efficacy "can be unethical if applied to many medical devices." The two examples given are a software development and an improvement in a beam model. Neither of these should ever be tested on patients, but instead should be evaluated using dosimetric verification and comparison. Clinical questions can be answered effectively using clinical trials. I do not believe that the timeline of clinical implementation is too short to conduct trials. There will always be a period of uptake of new technology[15] and, while it may seem obvious that a new technique is better, it is always prudent to check.

Randomized controlled trials do not match every variable possible (that is a case control study). Instead, clinical trials choose a cohort of patients who would likely benefit from a new technique. These are rich and varied datasets which can be mined with the best tools available to uncover hidden information that complements the validation of the best innovations in radiotherapy practice.

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7.4. Practicing and aspiring medical physicists can safely disregard university rankings at no peril to them

E. Ishmael Parsai and Clive Baldock
Reproduced from *Medical Physics* **42**, 050601-1-4 (2014)
(http:// dx.doi.org /10.1118/1.4866835)

OVERVIEW

Several organizations publish rankings of universities which attempt to identify the "best" undergraduate, graduate, and professional degree programs based upon academic reputation, selectivity, and many other factors.[1–3] Perceived benefits to potential students or faculty who are looking for a place to study or work are that, being from a high ranking university will help them to land future jobs, research grants, or national leadership positions. Whether this is appropriate for medical physicists is the topic of this month's Point/Counterpoint debate.

Arguing for the Proposition is E. Ishmael Parsai, Ph.D. Dr. Parsai graduated with an M.Sc. in Medical Physics from the University of Missouri, Columbia in 1985, and a Ph.D. in Medical Sciences from the Medical College of Ohio, in 1995. Since 1993 he has been a medical physicist at the University of Toledo where he is currently Professor and Chief Medical Physicist and Director of Graduate Medical Physics Programs. Dr. Parsai has served as major advisor to 11 Ph.D. and 46 M.S. students, while serving as committee member to many others. His research interests include mathematical modeling using Monte Carlo simulation, optimization of external beam therapy and brachytherapy, 3D dosimetry, and radiation detectors. He has two issued patents, seven other patent applications in progress, and has published 49 full paper articles and conference proceedings in refereed journals, and six book chapters. He has served on numerous committees in the AAPM, the ACMP, ACRO, ASTRO, and the IOMP, and was the Editor of Medical Physics World for 10 years. He is Board certified by the ABR and the ABMP, and serves as an oral examiner for the ABR.

Arguing against the Proposition is Clive Baldock, Ph.D. Dr. Baldock is the Executive Dean of the Faculty of Science at Macquarie University, Sydney, Australia which he joined in 2012 from the University of Sydney where he was previously Head of the School of Physics. He graduated from the University of Sussex, Brighton, United Kingdom with a B.Sc. (Hons) in Physics and was subsequently employed as a trainee medical physicist at Guy's Hospital, London while studying for his M.Sc. in Radiation Physics at St Bartholomew's Medical College, University of London. He subsequently worked in a number of UK hospitals providing scientific support to clinical nuclear medicine and MRI services. His main research interests were in the field of the MRI of radiation sensitive gels for improved three-dimensional radiotherapy dosimetry for which he received his Ph.D. from Kings College, University of London. Dr. Baldock moved to Queensland University of Technology, Brisbane, Australia in 1997 and subsequently worked at the University of Sydney from 2003 to 2012. In 2010, he completed a Master of Tertiary Education Management at the University of Melbourne, Australia. His current research interests

continue to be in the fields of radiation therapy, dosimetry, and medical imaging in which he has published over 140 research papers.

FOR THE PROPOSITION: E. Ishmael Parsai, Ph.D.

Opening Statement

Ranking organizations conduct an extraordinary amount of data collection, statistical analysis, and number crunching on such a wide variety of topics to boil down questions such as "Which institution has the best graduate program in a given area, or is the 'best' overall?" into a single numerical result. University level ranking systems frequently generalize across a large number of responses, rarely take into account posteducation performance, and inherently suffer from conflicts of interest.[1] Subject-specific rankings can help ameliorate some of these issues, but such an index does not presently exist for medical physics educational programs. Ideally, career decisions should involve a broad range of metrics focusing on the field, the location, and the desires of the individuals involved. Rankings are not an absolute indicator of performance or quality and can be disregarded safely.

The European University Association (EUA) has published two reports, one in 2011 and another in 2013, analyzing international university rankings and describing the benefits and pitfalls of each.[1,2] They conclude that rankings most accurately reflect research produced overall and not education quality. Metrics used to evaluate education quality vary drastically between the systems analyzed by the EUA, some metrics bearing little relevance to education. Rankings are typically done via surveys of the higher education deans and presidents of the universities being ranked, oftentimes asking only about the reputation of a university. We must also consider that none of these metrics evaluate such a small subspecialty as medical physics in any statistically relevant manner.

A more appropriate metric in North America for an initial evaluation of candidates or programs would be CAMPEP accreditation status, since applications for board certification are now contingent upon program accreditation. The accreditation process is a stringent and well-defined system to help standardize medical physics graduate education.[4] Accreditors consist of board-certified physicists reviewing the work of other physicists. Accredited programs ubiquitously adhere to the standards proposed by TG-197 defining the requirements for graduate education in medical physics.[4,5] Students coming from accredited programs have a proven higher passing rate for the ABR certification exams compared with students from nonaccredited programs.

For the sake of argument, let us assume that university rankings *do* reflect the relative quality of a medical physics program. If this were true, then we would expect to see a correlation between university ranking and CAMPEP accreditation.[6] As of July 2013, there were 44 CAMPEP accredited graduate programs. We binned these with U.S. News and World Report College Rankings[3] for undergraduate education, research achievements, and medical school and found that there is no distinct correlation with ranking quality. About half of schools with CAMPEP programs are listed as unranked or unpublished. Those that *are* ranked are relatively uniformly distributed across all subgroups.

The overall goal of any career or job search is to find the best match between employer and employee. While institutional rankings and educational acclaim are useful tools in evaluating the options, they should not be used as a method to filter out potential candidates.

AGAINST THE PROPOSITION: Clive Baldock, Ph.D.

Opening Statement

A number of metrics are used to assess the success and productivity of universities and their researchers therein.[7] Internationally, much emphasis is given to the rankings of universities and the production of associated league tables,[8,9] with much anticipation each year among university administrators, funding agencies, and students when a number of international ranking agencies publish their latest ranking lists.[10] Such rankings, now a standard feature, are playing a significant role in a changing higher education landscape internationally with implications for many, whether realized or not.

The practice of university rankings dates back to the beginning of the 20th Century with the publication of *Where We Get Our Best Men*. The backgrounds of "England's most prominent and successful men of the time" were evaluated with particular reference to where each studied. This resulted in a listing of universities ranked by the number of distinguished alumni that the universities could claim.[11]

Subsequently, graduate programs in United States universities were ranked on the basis of peer reputation.[12] More comprehensive rankings of universities began being published from 1983 when the US News and World Report initiated ranking college undergraduate education programs with this ranking being published annually from 1987.

Since 2003 numerous university rankings have been published with some now becoming particularly popular. Some of the most well known include the Academic Ranking of World Universities (ARWU) from Shanghai Jiao Tong University in China, the QS World University Rankings, the Times Higher Education World University Rankings, and more recently, the Leiden University Rankings.

Despite ongoing debates about the use and validity of university rankings, they enable students as consumers to compare institutions within a country and around the world as they make decisions regarding which university to potentially attend. Further, for many university presidents and administrators rankings influence organizational missions, strategies, personnel, recruitment, and public relations.[8,9] Furthermore, rankings often drive the allocation of resources with decision makers and administrators sensitive to the resulting prestige that may be associated with ranking performance.[13] Internationally, governments and funding agencies are also increasingly using rankings as policy instruments to assess the performance of higher education institutions.[14]

Students will potentially make future choices of what and where to study, whether it is a graduate program in medical physics or biomedical engineering, based on where a university lies

in a particular ranking. Such choices will not necessarily be based on which graduate programs are of higher "quality."

Rebuttal: E. Ishmael Parsai, Ph.D.

It would be unfortunate for prospective students to reference only rankings as an indication of program quality. As indicated in "The Role and Relevance of Rankings in Higher Education Policymaking,"[14] rankings should be used "only as part of overall system assessment efforts and not as a standalone evaluation of colleges." We should urge up-and-coming students to view rankings as a metric that does not necessarily guarantee program quality, student success, or eligibility for future career goals. Arguably, at least in North America, the best indicator to guide program decisions in medical physics is CAMPEP accreditation.

Our experience at the University of Toledo supports the idea that rankings can be safely ignored. The radiation oncology medical physics program was CAMPEP accredited in 2009, but has been in existence since 1979, producing highly successful medical physicists who are leaders in our community today. Since 2001 alone, we have produced 52 graduates with masters and 12 with doctoral degrees in medical physics. One hundred percent of these graduates have found employment in the field of medical physics. Our program has been involved in testing several emerging systems, such as the first MLC programs, compensator-based IMRT, and retrofitting a micro-MLC and IORT onto a linear accelerator. Our graduates have been directly involved in these efforts, exposing them to a broad range of clinical and research experience, more than the majority of graduate programs. However, the University of Toledo is one of many schools whose rank is not published in any of the three categories (undergraduate, research, or medical school). Our program, with a throughput of five students per year, and our specialty in general, are too small to be accurately sampled by a large rankings program.

Present experience and numerous reports from experts within higher education all point toward the ineptitude of large-scale ranking systems to adequately capture the true quality of a program dedicated to medical physics. Ignoring the overall rank of an institution can be done without any added peril to the student.

Rebuttal: Clive Baldock, Ph.D.

Over the past decade, the Council of Graduate Schools (CGS) has conducted a multiyear examination of international graduate application, admission, and enrollment trends from overseas students seeking masters and doctoral degrees from US colleges and universities.[15] With international students comprising 15% of all graduate students in the US,[16] the US has for many years been the destination of choice for students from overseas with the significant majority enrolling from China. Recently however, this trend has started to change, with the number of Indian students entering US graduate schools increasing remarkably while the share of new graduate students from China has increased only modestly. In 2013, graduate enrollments from India increased by 40% with, interestingly, those from Brazil rising significantly by 17% as a result of the Brazilian government funding large-scale scholarship programs to send students abroad, particularly in the sciences.[15] After seven consecutive years of double-digit growth, however, the number of Chinese students enrolling in US graduate programs in 2013 increased

by only 5%. This should be cause for concern for US graduate programs that have in recent years relied on student growth from China to offset weak domestic enrollments, particularly in the sciences and engineering. Without the significant number of new students from India, the second-largest source of overseas students, overall international enrollments would have increased only slightly.

University and clinic-based medical physicists often rely on graduate students to assist them as part of the normal practice and culture of undertaking research. As the number and profile of overseas students enrolling in graduate programs changes, there may be fewer students over time choosing to enroll in graduate programs in medical physics to pump-prime the pipeline of future graduate students undertaking research in this discipline.

Overseas students interested in enrolling in North American medical physics graduate programs will undoubtedly seek to be well informed as they consider and make their decisions. Inevitably university rankings will be a consideration for some.[17] Universities that are proactive in recruiting international students are potentially able to overcome, to some extent, a perceived low ranking in internationally recognized university league tables. To this end, it is valuable for medical physicists aspiring to have a research career to proactively avail themselves of university rankings as they develop their careers and research teams into the future.

If the trend of students using university rankings to inform and assist in the making of their choices, all who ignore this issue potentially do so at their peril.

ACKNOWLEDGMENTS

Dr. Parsai wishes to thank Sean Tanny and Nicholas Sperling, Ph.D. candidates in UT Medical Physics program, for helpful discussions.

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7.5. Medical physics residents should be placed using a matching program

Stephen Sapareto and X. Ronald Zhu
Reproduced from *Medical Physics* **42**, 060601-1-3 (2014)
(http:// dx.doi.org /10.1118/1.4871039)

OVERVIEW

Now that graduation from an accredited residency program is a requirement for Board certification in the USA, finding appropriate residency programs and recruiting the best applicants for these programs have become highly competitive and, some might claim, chaotic activities. This was the situation many years ago with physician residency programs, which ultimately led to the national matching programs for medical residents. Some argue that a similar matching program should be instituted for medical physics residencies, and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Stephen Sapareto, Ph.D. Dr. Sapareto obtained his Ph.D. in Radiation Biology from the Colorado State University, Fort Collins in 1978. Subsequently, for the next decade or so he held primarily research positions in Stanford University, Washington University, St. Louis, Wayne State University, Detroit, and City of Hope National Medical Center, Duarte, CA. He next moved to Arizona where he has held several senior medical physics appointments and is currently Professor and Director of Medical Physics, Division of Radiation Oncology, Banner MD Anderson Cancer Center, Gilbert, Arizona. Dr. Sapareto has served on numerous AAPM Committees and Task Groups, including as Chair of the Biological Effects Committee and as a member of the Board of Directors. Dr. Sapareto is Board certified by the American Boards of Radiology and Medical Physics in Radiation Oncology Physics, is a Fellow of the AAPM, and has authored or coauthored 55 peer-reviewed papers.

Arguing against the Proposition is X. Ronald Zhu, Ph.D. Dr. Zhu obtained his Ph.D. in Chemical Physics from the University of Utah in 1989 and completed a Radiation Oncology Physics Residency at Washington University, St. Louis in 1996. He is currently Professor of Radiation Physics, the University of Texas M. D. Anderson Cancer Center, Houston, and Director of the Radiation Oncology Physics Residency Program. He is a member of the CAMPEP Residency Education Program Review Committee, has chaired the AAPM Medical Physics Residency Training and Promotion Subcommittee, and has served on numerous AAPM Committees and Task Groups, including the Work Group on Coordination of Medical Physics Residency Programs. Dr. Zhu is Board certified by the American Board of Medical Physics in Radiation Oncology Physics, is a Fellow of the AAPM, and has authored or coauthored 100 peer-reviewed papers.

FOR THE PROPOSITION: Stephen Sapareto, Ph.D.

Opening Statement

In the 1920s the recruitment of interns by hospitals was in chaos. In order to fill their positions, hospitals were offering appointments to junior year medical students with little knowledge of their performance. This forced students to accept positions without knowing if better offers might be received from preferred hospitals. In the late 1940s, an attempt was made to establish a gentleman's agreement to have a uniform date for accepting offers, which failed miserably. Thus, in 1952, the National Resident Matching Program (NRMP) was created which has evolved into the current match.[1] The problems associated with the timing of this process are well described by Roth.[2] This matching process for medical residencies has been analyzed and refined over decades.[3,4] It takes into account the preferences of both the institutions and the applicants to provide a fair and equitable process.

The current residency situation for Medical Physicists is quite similar to that of the Medical residency programs in the 1940s. Beginning in 2014, in order to be eligible to become board certified by the American Board of Radiology, applicants must complete an accredited medical physics residency. Currently, about 250 medical physics graduates are produced each year to fill an estimated 200 needed radiation therapy physicist openings.[5] There are now nearly 70 accredited residency programs. For the most recent recruitment season, there were about 100 therapy residency positions available. From statistics of the Common Application Process (CAP), which is used by almost half of these residency programs for filling vacancies, the average number of applicants for each position was nearly 100 (range from about 57 to 157) (Presentation at the 2013 Annual AAPM meeting by John Antolak (with permission)). A gentleman's agreement was established between residency program directors using the CAP specifying the earliest dates that offers could be accepted but this has not been followed uniformly. This situation is exactly what happened with medical residencies prior to the NRMP. The problem is that every program feels it deserves the best applicants, but the programs do not consider the applicants' preferences. An applicant may prefer a particular program because of its content or location near to family, or even for health reasons. Unfortunately, with the current arrangement, applicants may be forced to accept positions that are not their preference or risk not being offered any program. Consequently, there are too many programs going after the same top applicants resulting in a recruiting race. What is proposed for the Medical Physics Residency Match is a simple match. A successful match guarantees the best and fairest possible pairing. Appropriate account is taken of both the applicants' and the programs' preferences. This is the only fair arrangement. It has been well tested and refined by the National Resident Matching Program for medical residents and there are numerous publications evaluating its methodology and fairness.[3,4]

AGAINST THE PROPOSITION: X. Ronald Zhu, Ph.D.

Opening Statement

Formal training for future clinical medical physicists has become increasingly standardized in recent years. In its 2010 initiative, the American Board of Radiology (ABR) began to require candidates taking the Part 1 examination in medical physics for the first time in 2012 and later to be enrolled in, or have graduated from, a CAMPEP-accredited education program.[6] In its 2014 initiative, the ABR further requires candidates to have completed a CAMPEP residency program in order to be eligible to take the Part 2 and 3 examinations starting 2014.[6] As a result,

CAMPEP-accredited residency programs have increased to a total of 77 (68 therapy physics and 9 diagnostic physics) as of January 2014.[7] One might argue that medical physics residencies should follow other specialties in medicine and have a national matching program.[8] After all, medical physics is a sub-specialty of medicine. The obvious advantage of a national matching program would be that institutions would get the residents they want, and residents would go where they would like to go. To have a matching program or not has been an intensely debated topic in the medical physics community in the past few years. I would argue for no matching program, or at least that we are not ready for a national matching program at this point of time.

Unlike medical schools normally having four years of a fixed curriculum, medical physics graduate students (PhDs or Masters) do not have such a fixed curriculum in the thesis or dissertation component of their graduate education. For example, some students take five years and other may take six years. For a given year, students may graduate at different times of the year, depending on their dissertation work and/or funds supporting their research. For a matching program with fixed start dates like other medical specialties, some of the residents may be unemployed for more than six months to a year before starting residency.

One could argue "why not standardize the medical physics graduate education like medical schools, for example, always four years?" Medical physicists contribute to medicine, especially in radiation oncology and radiology, through clinical service, innovative research, and education. A fixed curriculum would limit the amount of research that graduate students could accomplish during their tenure of graduate school. This approach is clearly not very good for care of our patients and the specialty.

In an attempt to combine didactic and clinical training, several Doctor of Medical Physics (DMP) programs are being established. Students in this type of program are guaranteed to have clinical training positions assuming they meet the academic requirements. Clearly these students would not be able to participate in the matching program. Also, diagnostic physics has too few programs to have a meaningful matching program.

One of the current problems with recruitment of residents each year is that some programs do not follow the AAPM gentleman's agreement when making offers to candidates. This happens because there are no consequences for not following the agreement. This problem can be relatively easily solved by establishing some disciplinary action criteria by accreditation bodies like CAMPEP.

In summary, while conceptually it is a good idea to have a matching program, at this time the entire medical physics community is not ready.

Rebuttal: Stephen Sapareto, Ph.D.

My colleague agrees that a match is a good idea but argues that we are not ready for a match program. The point of this debate is not when we should have a match but whether it should be implemented at all. The fact that different graduate programs may vary in the time of year a student graduates has little bearing on the need for a match, even though it will not be as uniform as for medical graduates and will mean that some may have to wait to enter the match. In order

for a match to be established, there must first be a common application process. We have the AAPM CAP, which now has 47 of the 74 CAMPEP accredited residency programs participating. This program has defined dates for application and acceptance. For the match to work, we will need nearly all programs participating. Presumably, participating programs would want to consider altering their graduate programs to coincide better with the CAP deadlines.

I agree with my colleague that the current voluntary nature of the AAPM CAP does not provide any consequence for violating the gentleman's agreement. Having all or most programs participating in the CAP and a match would provide more opportunity for creating disciplinary pressures for adherence.

While my colleague points out that Doctorate of Medical Physics programs include the equivalent of a residency and thus would not participate in a match, there will still be a need for a match for all other programs.

I agree with my colleague that the number of imaging residencies is too few to support a match, but clearly one is needed in therapy physics and we should be working toward implementation. And soon!

Rebuttal: X. Ronald Zhu, Ph.D.

In his opening statement, Dr. Sapareto presented some history of medical residency training in the 1940s and pointed out that the current residency situation for medical physicists is similar to that of medical residency programs at that time. However, he fails to recognize the key difference between the specialty of medical physics and more traditional medical specialties. Unlike medical school with a fixed curriculum and time, medical physics graduate education has a thesis/dissertation research component, which often consumes more than half the time of the entire graduate school career, with potentially large uncertainties depending on selection of research topic, funding supporting the student's research and other factors. Students will graduate at different times each year. That makes a matching program almost impossible.

Dr. Sapareto also argues that the current arrangement with a common application does not work because some institutes do not follow the established gentleman's agreement. The reason it does not work is not because of the agreement itself, but because no one enforces the agreement. The current agreement also allows both programs and candidates to select each other. In conclusion, while it will be ideal to have a matching program, it is not necessary and the community is also not ready for a matching program right now.

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7.6. The most suitable person to establish quality assurance guidelines for the generation and use of non-commercial clinical software is a medical physicist

Diane Kelly and Alan Wassyng
Reproduced from *Medical Physics* **42**, 090601-1-4 (2014)
(http:// dx.doi.org /10.1118/1.4883877)

OVERVIEW

Noncommercial software is widely used in radiation therapy, especially in academic centers. Such software can take many forms, ranging from MU-check spreadsheets; to in-house built treatment planning and plan-evaluation systems; or to public domain codes such as EGSnrc or MNCP that are interfaced to IMRT planning systems. This noncommercial software is usually written by in-house medical physicists and, thus, the question arises as to how to establish the integrity of the software they have written. One view has been that only software professionals are properly equipped to provide quality-assurance guidance on the generation and use of such software. An opposing view is that the medical physicists themselves are in the best position to determine effective practices to address software quality in their community, and this is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Diane Kelly, Ph.D. Dr. Kelly is an Associate Professor in the Department of Mathematics and Computer Science at the Royal Military College of Canada (RMC). She is cross appointed to RMC's Department of Electrical and Computer Engineering and to the School of Computing at Queen's University. Dr. Kelly's research focuses on ways to increase the trustworthiness of scientific software. She teaches a graduate seminar course to both RMC and Queen's students that critiques software development and quality assurance approaches popular in software engineering when specifically applied to scientific software. Dr. Kelly has a Ph.D. and M.Eng. in Software Engineering, both from RMC, and a B.Sc. in Pure Mathematics and B.Ed. in Mathematics and Computer Science, both from the University of Toronto. She worked in the nuclear industry for over 20 years as a scientific software developer, technical trainer, and QA advisor. She is a senior member of IEEE.

Arguing against the Proposition is Alan Wassyng, Ph.D. Dr. Wassyng earned his Ph.D. in Applied Mathematics from the University of the Witwatersrand, Johannesburg, South Africa in 1979. After spending 14 years as an academic, first at the University of Witwatersrand and then at the University of Minnesota, he incorporated a computer consulting company in Toronto, Canada. He returned to academia in 2002, joining the Department of Computing and Software at McMaster University, Hamilton, ON, Canada, where he is currently Associate Professor and Director of the Centre for Software Certification. Dr. Wassyng has published widely on software certification and the development of dependable embedded systems. He is cofounder of the Software Certification Consortium, and is Co-PI on the highly funded "Certification of Safety-Critical Software Intensive Systems" project led by McMaster University.

FOR THE PROPOSITION: Diane Kelly, Ph.D.

Opening Statement

Presentations at the Canadian Organization of Medical Physicists (COMP) Winter School[1] showed that medical physicists are deeply imbued in a safety culture. They react instinctively within this culture, pay attention to human-technology interaction, and exhibit due process in the light of safety concerns. I compare this to the environment of a software engineering colleague who specializes in testing: she lives in a volatile, market-driven, and cost-minimizing environment. Even though she has years of experience in testing different products, her instincts and her quality goals are different from those of a medical physicist.

The software engineering literature does not acknowledge the need for the conjunction of computational software design processes with a deep safety culture, which is required for deployment of software used to support clinical decision making. Instead, such software is confused with either control software, which directly operates a medical device, or commercial products where patient wellbeing is not directly affected by the correctness of the output. As a result, there are no guidelines in the software engineering literature that address the specific characteristics and needs of clinical software.

When advising on software quality guidelines, a typical software engineer takes a broad-spectrum approach. This approach suffers from two serious flaws. First, it encourages the perception that software is correct unless proven otherwise. This dangerous assumption has been a contributor to several fatal accidents in the safety-critical world.[2] A recent article[3] talks about problems "when a computer lulls us into a false sense of security". Second, this broad-spectrum approach does not use the knowledge of the people associated with the software, and does not acknowledge the specifics of the operational environment that these people understand.

Vessey and Glass[4] criticize the software engineering community for their broad, generic solutions, calling them weak solutions. They contend that the most effective and strong solutions are those that target the specific environment or situation. Medical physicists, with their knowledge, can provide this strong solution.

In a 2012 survey of software development and maintenance practices sent to medical physicists across Canada, the medical physics community demonstrated that it already has a level of understanding necessary to provide meaningful software quality guidance to its own community. The devil is in the details and the medical physicists who responded to the survey understood the details of their environment and the implications of problems. This understanding is far beyond what a software engineer outside the clinic can bring to the table.

Kendall and Post, after studying decades of development of nuclear arsenal simulation software at the Los Alamos National Laboratory, concluded that the best people to draw up a list of "best practices" for software development and maintenance are the members of the code project teams themselves, and that these practices are those "… *that the teams have judged useful for improving the way they do business*".[5] It is the same for medical physicists. They know the best ways to assess their software in order to safely do their business.

AGAINST THE PROPOSITION: Alan Wassyng, Ph.D.

Opening Statement

This proposition may make some sense if the guidelines are solely for the *use of the softwar*e. However, medical physicists (MPs) are experts in medical physics, not the software fundamentals necessary for establishing software quality assurance (SQA) guidelines for *software development*. A history of creating software is not necessarily a plus. There are lots of people writing software, many of whom are not really qualified to do so, and the dependability of software, in general, is dismal.[6] Software quality in the medical domain should be evaluated on the basis of safety, security, and dependability, and paraphrasing "official" definitions:[7]

- *Software safety* – under defined conditions, software should not contribute to unsafe behavior or generate results that can lead directly to harm;
- *Software security* – protection afforded the software to keep it from harm, and from causing harm through users maliciously bypassing the software's designed-in safety and dependability;
- *Software dependability* – in its intended environment, the software can be trusted to produce the outputs for which it was designed, with no adverse effects.

Anyone establishing SQA guidelines for the generation of software must fully understand fundamental principles of software that relate to safety, security, and dependability. Examples are:

- *Lack of continuity*[8] (Moderator: *in software engineering, continuity refers to a continuous function for which, intuitively, small changes in the input result in small changes in the output*) – If a bridge is built to withstand a force of 100 tonnes, because of the mostly continuous behavior of physical objects and our mathematical models, the bridge is likely to be safe for loads less than or equal to 100 tonnes. We do not expect it to collapse if a bicycle goes across it. In contrast, a simple error in software that finds a number within a list of n numbers could easily result in the software working only when n is even. This happens if the designer separates the behavior into two cases (n is even and n is odd) and forgets to deal with the one case (n is odd). Thus, in this case, the software will work when n = 1000, but not for all n < 1000 – it fails when n = 19, for example.
- *Information hiding*[9] (Moderator: *information hiding is a software development technique in which each module's interfaces reveal as little as possible about the module's inner workings and other modules are prevented from using information about the module that is not in the module's interface specification*)[7] – This is a specific way of performing modularization so that the resulting design significantly improves safety and dependability when changes are made. SQA monitors the development process of the software so that the resulting product is, and remains, safe, secure, and dependable. This should include ways of evaluating the information hiding aspects of the design.

Similar principles are *software testing*,[10,11] *hazard analysis*,[12] the absolute need for *requirements traceability*,[13] and *semantics* for *module interface specifications*,[14] and numerous others. How can medical physicists take these principles into account when they do not possess this

fundamental software knowledge? The person who does have this knowledge is a *software engineer* (or perhaps, a computer scientist). The *Professional Engineers Act of Ontario* ["Professional Engineers Act", *Professional Engineers Ontario*, http://www.e-laws.gov.on.ca/html/statutes/english/elaws_statutes_90p28_e.htm/] states that the mandate of an engineer is "*to ensure that the public interest may be served and protected*." A software engineer is tasked with developing software-dependent systems and protecting the public from harm caused by those systems. There are definite differences in SQA requirements in different domains – which is why some people think it is appropriate to have an MP establish SQA guidelines. However, there are more commonalities across different domains than there are differences, so software knowledge is of primary importance. SQA is a team effort, with domain expertise coming from the MP. However, the core knowledge and guidance must come from a software engineer.

Rebuttal: Diane Kelly, Ph.D.

My colleague built his argument around a software engineering list of software qualities: safety, security, dependability. Why not a list from scientists: accuracy, trustworthiness, readability, consistency with the physics, and simplicity? Apparently, scientists focus on simplicity far more than software engineers.[15]

For any set of qualities, we still need to achieve them. My colleague suggests, for example, information hiding and requirements traceability as fundamental principles for anyone. David Parnas, who first published the information hiding principle, complained in an invited talk[16] that most software engineers do not know how to properly apply the principle. Several Standish Group surveys reported that only 9%–16% of software projects are delivered successfully, largely because software engineers do not understand user requirements.[17] But medical physicists *do* understand their user requirements because they *are* the users.

How do we add quality to a piece of software? It is well understood[18] that there is a disconnect between the desire for the high-level quality and what low-level activities actually achieve it. There are no common activities or "silver bullets" such as "information hiding" to achieve, for example, "dependability". There is no research that demonstrates that particular code-level activities guarantee any high-level quality. The best we can do is to understand the particular software in front of us. In the case of clinical software, medical physicists have the best understanding of what is in front of them in terms of use and the physics embedded in it. By keeping the software code very simple (which scientists have a tendency to do[15]), medical physicists are in the best position to decide what further keeps them out of trouble. My colleague suggests that software engineers have a mandate to ensure that the public is served and protected. Software engineers do not always live in that culture. Medical physicists live in a safety culture and they have the capacity to fully understand what will best achieve quality software for their own work.

Rebuttal: Alan Wassyng, Ph.D.

I have been involved in the COMP Winter School[1] since its inception (I missed one year), and give a talk each year on medical device software. I have been told that the medical physicists

find this talk disturbing because they are surprised to find out how much they do not understand about software! Their safety culture is, indeed, admirable, but this does not make up for a lack of technical (software and system safety) knowledge. SQA needs a team of people, including domain experts and software experts. The SQA lead must have both the software expertise and the requisite safety knowledge. The fact that some software engineers are not immersed in the system safety world should not lead us astray. We see more and more software engineers who work in the medical domain, understand software, and have developed expertise in what is required in a regulated domain, in which safety is a primary concern. If there are not enough software engineers with this safety focus, we should be championing changes to the software engineering curriculum. There are conferences[19,20] targeted at software engineering in the medical domain. These conferences focus on medical devices and reporting/planning software. IEC standard 62304 focuses on safety of software used in medical devices.[21] Just because the standard applies to medical devices does not mean it is irrelevant for other clinical software. Software that can impact the health and safety of patients is deemed to be a medical device in most regulatory regimes. There is a (growing) body of software engineers who do have the specific software expertise required, as well as familiarity with basic safety concepts and regulatory guidelines. They are in a much better position to establish quality assurance guidelines for medical software than are medical physicists.

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7.7. Medical Physicist Assistants are a bad idea

Doracy P. Fontenla and Gary A. Ezzell
Reproduced from *Medical Physics* **43**, 1–3 (2016)
(http:// dx.doi.org /10.1118/1.4937596)

OVERVIEW

According to AAPM Policy PP-29A,[1] "*Some institutions may use the services of an individual who is not a qualified medical physicist (QMP) for certain clinical activities*." The document then goes on to confer the title "Medical Physicist Assistant" (MPA) to this individual. The duties of an MPA are somewhat similar to those that would otherwise be assigned to a "junior" medical physicist (a medical physics resident or a resident just out of training). This has led some to call the creation of the "medical physicist assistant" a bad idea and suggested that institutions might hire a "less expensive" MPA to do the work that a more qualified "junior" medical physicist could do better which, they claim, is bad for the patient and bad for the medical physics profession. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Doracy P. Fontenla, Ph.D. Dr. Fontenla obtained her Ph.D. in Physics from Instituto Balseiro, S. C. Bariloche, Argentina and came to the USA in 1982 as a postdoctoral fellow in the Department of Medical Physics at Memorial Sloan Kettering Cancer Center, NY, where she is currently an Associate Attending Physicist and Director of Education. Her research interests have been in *in vivo* dosimetry in radiation oncology, and analysis and implementation of new treatment methods. As Director of MSK's CAMPEP accredited residency program, she presently focuses on offering young medical physicists the opportunity to gain a high level of education, clinical experience, scientific research, leadership, and professional skills. She has served on dozens of AAPM committees and subcommittees, the AAPM Board of Directors, and as Secretary and President of the New York Chapter (RAMPS). Dr. Fontenla is certified in Therapeutic Radiological Physics by the American Board of Radiology.

Arguing against the Proposition is Gary A. Ezzell, Ph.D. Dr. Ezzell obtained his Ph.D. in Medical Physics from Wayne State University having previously been introduced to medical physics by Patton McGinley while doing his M.S. in Applied Nuclear Science at Georgia Institute of Technology. After working as a medical physicist at a community hospital in Cleveland for five years, he moved to Harper Hospital/Wayne State University in Detroit. He then moved to the Radiotherapy Department of Mayo Clinic Arizona in Phoenix, where he is currently Chief Physicist. Dr. Ezzell has served the AAPM in many capacities, including as Secretary, President, and Chair of numerous committees and Task Groups. He is certified in Therapy Physics by the American Board of Radiology and the American Board of Medical Physics.

FOR THE PROPOSITION: Doracy P. Fontenla, Ph.D.

Opening Statement

A profession is created and evolves to enhance its societal value and benefit. Although the medical physics profession has existed for over 100 years, its true value has not always been recognized or acknowledged; different times brought different professional issues.

There were always visionaries who recognized the need to formalize this new profession's priorities and values, recognizing that practicing medical physics should be entrusted only to those who are duly qualified. These people worked hard to elevate the profession to a level of recognition equivalent to other professions in the patient care field. Licensure for medical physicists was established in TX, FL, NY and HI by creating credentialing and training processes similar to those of physicians and other medical professionals. However, there were also members of this profession with different views about the effect of certain decisions on medical physicists' future. Recognizing that medical physics professionals were expensive, they reassigned associated duties of several medical physics positions to new groups such as experienced, computer-savvy radiation therapy technologists, with largely unintended consequences to medical physicists' job opportunities.

This first initiative was to create the medical dosimetrist to perform some medical physicist duties at lower salary. This led to job displacement of medical physicists. Presently, the American Association of Medical Dosimetrists has 3150 members,[2] an indirect measure of jobs lost for junior medical physicists over the years. Now, the idea to create the MPA has emerged; a move that will replace junior physicists with less qualified individuals, further reducing the number of available positions for qualified junior medical physicists. However, the loss of medical physicist positions is not the only issue: there is the unavoidable effect on the quality of services provided by our profession and the resulting detrimental effect on patient care.

Deeply troubling is the contrast between the MPA position's *educational requirements* and the associated *duties and responsibilities.* MPA advertisements list a Bachelor's degree in Physics as the minimum education requirement. Most *medical physicist* and MPA advertisements cite the *same* expected responsibilities. MPAs are expected to take on the duties previously assigned to QMPs,[3] including acquisition of data used in patient care.

The literature is full of examples of bad outcomes resulting from assigning clinical duties to inexperienced medical physics professionals. Confirming reports have been generated by international error reporting agencies, including NYPORTS,[4] IAEA,[5] ROSIS,[6] and ASTRO.[7] The AAPM created a Task Group[8,9] to address radiation therapy errors. Further, facilities seeking institutional funding to add or augment residency programs struggle ethically and pragmatically in a job market that could shrink as QMPs are replaced by MPAs.

Some decision-making senior medical physicists experience extreme pressure arising from administrative budget restrictions to convert junior medical physics positions to cheaper MPAs. I am not alone in my concern for the damage this may inflict on the younger members of our profession, if not to the entire membership. Accepting that we can replace a medical physicist by an MPA will certainly contribute to weakening the medical physicist position in the clinical field.

AGAINST THE PROPOSITION: Gary A. Ezzell, Ph.D.

Opening Statement

We need to live in the world as it exists, and it is a changing world. Our equipment and processes increase in complexity as do the demands for quality assurance. Simultaneously, the financial pressures on health care providers increase, and we are called upon to justify our value. A necessary consequence is that we need to allocate the proper resources to the proper tasks. My colleague, William Pavlicek, makes the useful distinction between work that is device-oriented and that which is patient-oriented. Only a board-certified medical physicist can provide patient-oriented judgments.[3,10] Device-oriented quality assurance tests that are prescriptive and objective, with defined procedures and established tolerance levels, can be done by well trained and supervised[10] assistants with fewer formal qualifications. The benefits from such a division of labor are multifold. First, there is the financial value of having less expensive staff do the work they are capable of doing. Second, the QMP can spend more time thoughtfully attending to tasks that require professional judgment. Third, the QMP can better keep up with technology changes and create and adapt QA processes instead of being buried under the burden of routine testing. Fourth, the QMP will be better recognized as a medical professional and not an expensive technician.

We need to live in the world as it exists, and the idea of physicist assistants is not a hypothetical construct. Many institutions already use them, either called by that name or another. John Hazle, chief imaging physicist at MD Anderson Cancer Center, reports that they have used assistants for about 15 years. In therapy departments, patient-specific QA measurements for IMRT are often taken by staff who are not QMPs; they may be assistants, residents, or therapists. In many proton centers, treatment hours run exceptionally late, and assistants do some machine- and patient-related testing. In the world as it exists, hiring, training, and supervising physicist assistants are happening, as it needs to, if we are to ensure that the professional abilities of QMPs are properly used and valued.

As with so much in life, there is a needed balance to be struck. Those of us who are responsible for technical quality assurance must not get too dissociated from the equipment and the staff who operate it. Many of the most useful interventions I have made were the result of observations or conversations not directly related to the task at hand. The “what is that doing here?” observation (e.g., eye shields for a superficial unit in a linac vault) cannot be made from your office. There is no substitute for physical presence and personal involvement, and I acknowledge that the use of assistants can dilute the physicist's hand's-on experience. However, it need not. Spending less time doing after-hours machine QA and more time in participating in clinical procedures can enhance the physicist's effectiveness.

We need to live in the world as it exists, and physicist assistants are part of it. Let us use them well so that we can bring as much value as possible to our colleagues and patients.

Rebuttal: Doracy P. Fontenla, Ph.D.

We need to live in the world as it exists. However, it is our responsibility to make changes to improve it, at least for our peers. So MPAs, must not be a part of it, be it a changing world or not.

In the world as it exists, the AAPM created CAMPEP-accredited residency programs to develop excellent junior medical physicists (JMPs). Institutions and caring senior medical physicist visionaries fight to finance these programs. Through formal education, these residency programs improve our profession's new members, if not the entire profession.

We need to live in the world as it exists and as it changes. CAMPEP-accredited residency graduates must compete for fading junior MP positions with lower salaried MPAs who lack medical physics knowledge.

In the world as it exists, it is unacceptable that MPAs should professionally replace these graduates. However this happens, thanks to the initiative of some senior MPs with no regard for our profession's future. These senior MPs do not realize that by providing high-level education and employment to our residents, we are building the future of the profession and earning our medical peers' respect.

As our equipment and processes increase in complexity along with quality assurance demands and financial pressure on healthcare providers, we must justify our value. Let us not forget: device-oriented work is patient-oriented work, if the devices are used to diagnose and treat patients.

We need to live in the world as it exists: *without* MPAs. Let us help CAMPEP-accredited residency graduates (who start their clinical careers in a world replete with job-displacing MPAs) bring more value to our constituency. We should not repeat past mistakes!

"The mission of the AAPM is to advance the science, education, and professional practice of Medical Physics;… the AAPM supports the Medical Physicist community with a focus on advancing patient care through education, improving safety and efficacy of radiation oncology and medical imaging procedures through research, and the maintenance of professional standards."

Hence, I request that AAPM publishes its position that MPAs *shall not* be used and that clinical services be curtailed when funding for more qualified junior medical physicists or QMPs are not available.

Rebuttal: Gary A. Ezzell, Ph.D.

I agree with Dr. Fontela's opening sentence: "*A profession is created and evolves to enhance its societal value and benefit*." Medical Physics is a profession, not a guild, and our primary mission is serve society; job opportunities are secondary. Dr. Fontela's example of how medical dosimetrists have replaced physicists as everyday treatment planners supports my side of the argument. Is there evidence that "*the quality of services provided*" to our patients has decreased as a result of this evolution? On the contrary, certified dosimetrists do exemplary work because they become expert at that task. There is no need for everyday treatment planning to be done by someone who is also qualified to do beam calibrations, shielding calculations, and failure mode analyses. The maturity of the medical dosimetry profession underscores the appropriateness of that evolution.

Dr. Fontela asserts that there are many "*examples of bad outcomes resulting from assigning clinical duties to inexperienced medical physics professionals*." Looking through the cited references, I do not find those examples and remain unconvinced that there is evidence to support the assertion that this is a failure pattern. That has not been a factor in the reports thus far submitted to RO-ILS (I am on the panel that reviews those reports).

The key question that Dr. Fontela raises, and it is a good one, is whether the MPAs will be used inappropriately and will be assigned to work that requires the professional expertise and judgment of a QMP. That is a concern, and some may feel pressure to give in. That is the world we live in, and we will need to be firm. The upcoming Medical Physics Practice Guideline on supervision will help. But let us be clear: MPAs can be used appropriately and in a manner that enhances our profession.

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7.8. Future qualification as a qualified clinical medical physicist (QMP) should be restricted to doctoral degree holders

John D. Hazle and David W. Jordan
Reproduced from *Medical Physics* **43**, 1585–1587 (2016)
(http:// dx.doi.org /10.1118/1.4942805)

OVERVIEW

According to the AAPM,[1] a qualified medical physicist (QMP) shall be board certified and have earned a master's degree (M.S.) or doctoral degree. Some, however, believe that future qualification as a QMP should be restricted to doctoral degree holders. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is John D. Hazle, Ph.D. Dr. Hazle is Professor and Chairman, Department of Imaging Physics, and Bernard W. Biedenharn Chair in Cancer Research, The University of Texas MD Anderson Cancer Center, Houston, TX. He obtained his M.S. Degree in Medical Physics from the University of Kentucky, Lexington, Lexington, KY, and his Ph.D. in Biophysics from The University of Texas Graduate School of Biomedical Sciences, Houston, TX. He is certified by the American Board of Radiology (ABR) in Therapeutic Radiological Physics and Diagnostic Radiological Physics, and in MRI Physics by the American Board of Medical Physics. Dr. Hazle has served the AAPM in numerous capacities, including Associate Editor of Medical Physics, President and Chairman of the Board. He also served as Chairman of the Commission for the Accreditation of Medical Physics Education Programs (CAMPEP).

Arguing against the Proposition is David W. Jordan, Ph.D. Dr. Jordan is Assistant Professor in the Department of Radiology, University Hospitals Case Medical Center, Cleveland, OH. He obtained his Ph.D. in Nuclear Engineering and Radiological Sciences from the University of Michigan in 2005 and is certified by the American Board of Radiology in Diagnostic Radiological Physics and Medical Nuclear Physics, by the American Board of Medical Physics in MRI Physics, and by the American Board of Science in Nuclear Medicine in NM Physics and Instrumentation. He has served on numerous AAPM committees and is currently Chairman of the Insurance Subcommittee.

FOR THE PROPOSITION: John D. Hazle, Ph.D.

Opening Statement

The qualifications for clinical practice are evolving for healthcare professionals. Historically, most physicians did not pursue residencies, and now it is a standard practice. When my father practiced as a pharmacist, they had Bachelor's degrees, now a Pharmacy Doctorate (PharmD) is the standard. In nursing, both research Ph.D. degrees and professional doctorate degrees (Doctorate of Nursing Practice or DNP) are becoming common. Other professions, like

veterinary medicine and dentistry, have traditionally required professional doctoral degrees (DVM and DDS, respectively) to practice. If medical physicists wish to maintain their status as professionals in the changing healthcare environment, they should address these degree expectations and require a terminal doctoral degree, either a Ph.D. or a Doctor of Medical Physics (DMP) for professional clinical practice.

Part of the motivation for recommending this now is because residency training for ABR eligibility and QMP status is now required. Currently, ABR eligibility and QMP status require at least a M.S. and a 2-yr residency. This opens M.S. graduates to the risk of not being accepted into a residency at the completion of their graduate degrees. While Ph.D. applicants face this too, they are typically stronger candidates because of their additional experience. The AAPM should be promoting the 4-yr DMP degree, where the didactic and clinical training are bundled, like other professional degrees, resulting in ABR eligibility at the end of the program. The AAPM also recognizes the need to reduce the numbers of graduate students (~250/yr) to better align with available residency slots (~125/yr) and manpower needs (~125/yr). Requiring a doctoral degree aligns those graduates (~150/yr) to residency slots.

Further, the DMP is the most financially sustainable model for professional education. It is financially competitive with other professional degrees when initial salary is considered. For example, in the USA, the average cost of veterinary school is about $35 000/yr, dental school about $40 000, and medical school about $50 000. Most DMP programs are in the $25 000–$30 000 range. In 2014, starting salaries for veterinarians were ~$70 000, for dentists ~$80 000, for pharmacists (with PharmD) ~$90 000, and for physicians ~$190 000. Starting salaries for clinical medical physicists with doctoral degrees were ~$120 000. For the investment made, DMP graduates are in a good financial situation compared to our healthcare professional peers. Further, the income for a 4-yr DMP (debt of $100 000–$120 000), followed by 3 yr of professional practice income at $118 000/yr, results in a 7-yr income of $254 000. During this same period, a Ph.D. student with an income of $25 000 for 5 yr and a 2-yr residency at $50 000 has a total income of $225 000. At the end of 7 yr, the financial status of the DMP and Ph.D. is approximately the same!

To summarize, in order to maintain our professional stature, the AAPM should be moving to require a doctoral degree to become a QMP. This in no way implies that current holders of M.S. degrees are any less qualified than their Ph.D. peers; it simply acknowledges that the requirements for medical physics clinical practice are changing and that we need to move forward and be consistent with our healthcare professional peers. This also brings us in line with the requirements for clinical practice of other American Board of Medical Specialties professionals, where doctoral level credentials are generally required for certification.

AGAINST THE PROPOSITION: David W. Jordan, Ph.D.

Opening Statement

The future pathway to becoming a QMP should not be restricted to individuals holding doctoral degrees. Today's QMP is defined by the AAPM as being board-certified; the pathway to qualify for the board exams is controlled by CAMPEP. To create such a restriction in the future would

likely require affirmative effort by AAPM to convince either the ABR or CAMPEP to disqualify individuals with master's degrees from the QMP pathway. Such effort is not justified by needs of the profession or the public nor by shortcomings of the Medical Physics M.S. degree as a foundation for clinical training and practice.

CAMPEP requirements reflect our profession's selfregulation of training pathways. To permit QMP status to a DMP but deny it to a residency-trained M.S. is illogical, since the CAMPEP requirements for both are identical. To state that QMPs of the future will require the training in research that differentiates the Ph.D. from the M.S. is also illogical, because the DMP does not contain this element either. The DMP and M.S./residency pathways differ in their typical funding structures, but one cannot credibly differentiate the content of the training. Based on the way we have defined our training via CAMPEP, there is no basis to require a doctoral degree for the QMP.

Employers and, by extension, patients and the public, are not looking for the QMP bar to rise. The October 2015 AAPM Placement Services listed 44 permanent positions, of which only two clinical jobs required a doctoral degree. The other 23 clinical jobs, including those in academic institutions, specified that a master's degree was acceptable. All of the clinical positions required candidates to be ABR-certified or -eligible, and only five clinical positions accepting M.S. candidates stated or implied preferences for doctoral-degreed individuals. Meanwhile, other jobs requiring doctoral degrees included duties such as research, teaching, or administrative roles in addition to clinical. This small snapshot of the clinical job market suggests that employers find the "M.S., DABR" suitable for their needs. This situation is virtually unchanged from a similar snapshot taken in 2011.[2]

Our physician colleagues do not seem to be clamoring for their clinical physicists to have doctoral degrees. On the contrary, a recent *ACR Bulletin* cover story discussed the clinical contributions of two prominent M.S. medical physicists, highlighting their strong working relationships with radiologists.[3]

There is no question that M.S. graduates face difficult competition for residency slots at present, but the situation is neither hopeless nor permanent. We would help no one at this time by creating additional artificial barriers to their attainment of clinical careers as QMPs.

Finally, such a change would risk damaging the reputation and credibility of our established M.S. QMP colleagues. We have a hard enough time keeping the public aware of who we are and what we do. We have not succeeded in convincing States to uniformly recognize and adopt the existing QMP definition and requirements. Creating more confusion and "grandfather clauses" will surely detract from our profession's public and government relations goals.

Rebuttal: John D. Hazle, Ph.D.

As I pointed out in my Opening Statement, my position is forward looking, not historical. There is no doubt that M.S. (and in fact some B.S.) medical physicists have made substantial contributions to our profession—and many do it every day! However, I will suggest that Dr. Jordan's last two paragraphs in *his* Opening Statement actually support the position that going

forward we should have a more uniform degree standard for QMP—a doctoral degree (Ph.D. or DMP). This is not about research, but about how the profession of "clinical medical physics" is valued by healthcare institutions in the future.

The risk of failure in maintaining medical physicists as "professional peers" to our physician colleagues is higher when trying to justify that several degree levels are equally acceptable. While the roles of some nondoctoral degree holders have been accepted for "professional status" in the past, the contrary trend dominates. The current standard in healthcare (academic and private practice) is that doctoral degree holders are "professional" and everyone else is "staff." Not setting the standard for medical physics practice at the doctoral level, consistent with the standards for professional status in other healthcare professions, will put us at risk of losing our current status as professionals.

Rebuttal: David W. Jordan, Ph.D.

Restricting medical physics practice to those with doctoral degrees is not necessary to maintain the status of our profession. We should not concern ourselves with trends in other health professions; our profession is selfregulating, and we have done plenty to improve education and training via CAMPEP oversight of graduate programs and residencies. The 2012–2014 ABR changes closed significant gaps between medical physicists and other ABR and ABMS diplomates; is it already time to declare that we have not yet done enough?

The current mismatch between graduates, residency slots, and jobs is a logistical issue, not one of professional practice. If there were more jobs (and residencies) for graduates, this concern would cease to exist. It would be unwise to impose strict new constraints on the training pipeline, as we would be unable to react to unforeseen future increases in demand for medical physicists. We probably have not seen our last "boom."

Nor are we likely to have seen our last "bust." Present tuition and salary figures suggest that a residency-trained Ph.D. and a DMP graduate will reach financial break, even after several years of practice, but we do not know the future trajectory for medical physics salaries or how DMP salaries will compare with residency-trained Ph.D. salaries. If all M.S. programs converted to DMP, we could end up with many DMP graduates unable to find clinical jobs, carrying significantly more debt than M.S. graduates.

The question remains whether it is truly fair to expect DMP students to come into the clinic and do the same work at the same level as medical physics residents, but to pay tuition for the privilege rather than being paid a modest salary. We owe those who will become the future of our profession better than a facile or oblique answer to this question.

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7.9. Due to potential concerns of bias and conflicts of interest, regulatory bodies should not do evaluation methodology research related to their regulatory missions

Dev P. Chakraborty and Robert M. Nishikawa
Reproduced from *Medical Physics* **44**, 4403–4406 (2017)
(http:// dx.doi.org /10.1002/mp.12373)

OVERVIEW

One of the major roles of regulatory bodies is to enforce rules and thus maintain standards. They also often do research related to their missions, some of which might be used to establish the standards they are regulating and how they should be evaluated. This has led some to believe that, due to potential concerns of bias and conflicts of interest, regulatory bodies should not do evaluation methodology research related to their regulatory missions. This is the claim that is debated in this month's Point/Counterpoint.

Arguing for the Proposition is Dev P. Chakraborty, Ph.D. Dr. Chakraborty earned his Ph.D. in solid state physics from the University of Rochester, New York in 1977 then, in 1979, began his career in medical physics working with Ivan Brezovich in the Department of Radiology, University of Alabama at Birmingham, AL, where he worked until 1988 before moving to the Department of Radiology, University of Pennsylvania, Philadelphia. He subsequently moved to the University of Pittsburgh, Pittsburgh, PA, in 1997, where he was Professor in the Department of Bioengineering before assuming his current position at ExpertCAD Analytics, LLC in 2016. He has published over 75 papers in peer-reviewed journals, many in the field of observer performance analysis.

Arguing against the Proposition is Robert M. Nishikawa, Ph.D. Dr. Nishikawa received his B.Sc. in physics in 1981 and his M.Sc. and Ph.D. in Medical Biophysics in 1984 and 1990, respectively, all from the University of Toronto. While at the University of Chicago, he developed computer-aided diagnosis systems for classifying and detecting clustered calcifications in mammograms. He has seven patents on CAD-related technologies and has over 200 publications in breast imaging. He is currently a Professor and Director of the Clinical Translational Medical Physics Laboratory in the Department of Radiology at the University of Pittsburgh. He has won 24 awards including two for “best” paper, two innovation awards, and one teaching award. He is a fellow of the American Association of Physicists in Medicine, the Society of Breast Imaging, the College of American Institute for Medical and Biological Engineering, and a Distinguished Investigator, Academy of Radiology Research. His research interests are in computer-aided diagnosis, breast imaging, image quality assessment, and evaluation of medical technologies.

For the proposition: Dev P. Chakraborty, Ph.D

Opening statement

The Food and Drug Administration (FDA) and the Center for Devices and Radiological Health (CDRH) both regulate imaging devices and claim leadership roles in how they are evaluated. To demonstrate that the CDRH leadership in imaging device evaluation research biases research in this area and results in suboptimal evaluation of new imaging devices, I will present a single extended example. CDRH scientists are leading proponents of FROC/ROC[1, 2] methods for analyzing observer outcome studies. An alternative and often more efficacious approach is the JAFROC method[3] pioneered in my laboratory. Does a computer-aided detection (CAD) manufacturer adopt evaluation methods developed by Chakraborty[3] or does the manufacturer feel pressure to adopt the FDA's methods?[1, 2] Chakraborty's methods/software (JAFROC) have been used in over 104 publications, *but only 24 are from the US* and *none* from the FDA. The chances that this low number is a fluke are astronomically small, especially given the much larger total numbers of published US studies relative to non-US studies. This is strong evidence the FDA has influenced US-researchers against using JAFROC. Most clinical trials, including the American College of Radiology Imaging Network (ACRIN) Digital Mammographic Imaging Screening Trial (DMIST),[4] have used the lower power ROC paradigm for localization tasks, which is inappropriate and unethical:[5] lower power means the study is either of dubious value or it is overly expensive. The location-specific method favored by the FDA[1, 2] is based on the FROC curve: *one can hardly do worse*. FROC data consist of *mark-rating* pairs; *marks* are locations of suspicious regions and the *rating* is the associated confidence level. Based on a proximity criterion, a mark close to a lesion is scored as *lesion localization* (LL) and otherwise, it is *non-lesion localization* (NL). Lesion localization fraction (LLF) is defined as the number of LLs $\geq$ threshold divided by the total number of lesions. The non-lesion localization fraction (NLF) is the number of NLs $\geq$ threshold rating divided by the total number of images. The FROC curve (plot of LLF (ordinate) vs. NLF) rises with infinite slope from (0,0). The slope then decreases monotonically and the curve ends abruptly at an unpredictable point. The FROC is not contained within the unit square. This makes it impossible to define a meaningful area measure. The FROC is defined by marks: *unmarked* nondiseased cases, which represent perfect decisions, do not contribute to the area under the curve (AUC) under the FROC. In screening mammography, about 995 cases out of 1000 are nondiseased. The perfect radiologist, who marks all lesions and does not mark any nondiseased case, yields zero FROC AUC, receiving no credit for the 995 correct decisions. JAFROC is based on the AFROC (alternative-FROC) curve. The *y*-axis is similar to LLF, but the *x*-axis is the ROC false-positive fraction defined by the highest ratings on nondiseased cases, and the AFROC plot includes a connection from the uppermost operating point to (1,1). Unlike the FROC AUC, the AFROC AUC for the perfect observer is *unity*, not zero. *JAFROC is ignored in FDA's Guidance Document*,[2] as are positive statements about JAFROC from the late Drs. Wagner and Metz,[6] and there is *not one* reference to Chakraborty's work. The FDA's bias has doomed progress in breast cancer CAD (40,000 deaths/yr). Besides using incorrect FROC methodology, it has set a low (second reader) bar for CAD to be considered a “success”. The end result: massive clinical trials[7] have shown that CAD is actually detrimental to the outcome and there has been a call to end CAD Medicare reimbursement.[8]

Against the proposition: Robert M. Nishikawa, Ph.D.

Opening statement

Regulation is necessary to balance the costs and benefits of implementing a product or activity. This raises two important issues. First, it is important to quantify costs and benefits accurately. Second, it is equally important for impartiality to acquire correct balances. The proposition directly addresses the second issue, but the first issue is necessary to discuss also. I will restrict my discussion to medical imaging devices for clarity.

There are many well-established methods to determine the benefits of medical imaging devices.[9] There are, however, situations where researchers need new evaluation methods, either for a new technology or to simplify tests for an existing type of technology. This requires research to develop and validate the new methodologies. The regulatory agencies need to understand the strengths and weaknesses of any tests presented to them as evidence for the effectiveness of a product. This would require regulatory agencies to either develop the expertise in-house or to rely on the scientific literature. That latter is insufficient for two reasons.

First, regulatory science is not a well-funded branch of science. Therefore, unless the regulatory bodies perform the research, a disconnect may occur between developing the technologies and measuring their benefits and costs. This will either slow down approval of new technologies or lead to unbalanced regulations, or both.

Second, reviewing the literature may be effective in understanding the basics of the evaluation methodology, but it is usually insufficient to understand the limitations of the method. Understanding the limitations is best done by applying the method, using simulations to a variety of situations, and evaluating the results. That is basically research and regulatory bodies benefit from conducting the studies themselves.

While we can quantify benefits and costs, it is often difficult to decide on the proper balance of the two, particularly in an unbiased manner. Part of the difficulty arises from benefit and cost estimates not having the same units. A prime example of this, while not exactly in the regulatory domain, is the United States Preventative Services Task Force (USPSTF) recommendations on mammographic screening.[10] We can evaluate the benefits of screening as lower mortality from breast cancer and costs as false-positive screens — recalling a woman for further imaging when, in fact, she does not have a breast cancer. It is not clear how to balance lives saved against more imaging and potentially an unnecessary biopsy. The USPSTF placed more weight on false-positive screens and chose not to recommend periodic screening for all women under the age of 50, compared to, for example, the American College of Radiology which supports annual screening of women 40 and older.[11] Some proponents of screening argue that the USPSTF was biased in making their recommendations.[12]

There is no clear solution for this potential bias, but I do not believe that researching evaluation methodology is the right place to start. On the contrary, I believe there is less potential for bias when people are more knowledgeable — unless they are predisposed to a bias to begin with. Which is to say a bias can exist whether knowledge is obtained first hand or from reviewing the literature.

Rebuttal: Dev P. Chakraborty, Ph.D

I agree with my colleague that the FDA/CDRH needs to be current on the science. If regulatory science is not a well-funded branch of science, that makes it even more important to be current on the *existing* science, both from a revered in-house predecessor[6] and from academia.[3]

I also agree that there is need for developing new evaluation methods, but then why is the new FDA/CRDH still wedded to the 1940s ROC paradigm; what is new about it? The "mechanistic" approach[13] that they are enamored with does not advance the state-of-the-art in general-paradigm multireader multicase (MRMC) analysis, rather it explains and generalizes the variance-component decomposition used in Dorfman/Berbaum/Metz analysis[14] in a mathematically appealing way. But, and this is the serious limitation, it applies only to the Wilcoxon ROC statistic; it is not even applicable to fitted ROC curves, let alone FROC methodology.

In my Opening Statement, I cited the "power" imbalance when it comes to reviewing/vetting the work of the FDA/CDRH, and examples of questionable work. I could go on, especially how they validate methodologies. It is a brave and knowledgeable researcher who can properly review a paper[15] listing as institution of origin: "*NIBIB/CDRH Laboratory for the Assessment of Medical Imaging Systems*". Any applicant for an NIH grant in methodology development, and I see there is a recent funding opportunity announcement (PAR-17-125), would be well advised to cite this paper, never mind that it is about ROC analysis, while CAD provides FROC data, so at the very least the title of the paper is misleading. The cited work remains true to model observer philosophy, which assumes the lesion location is known, ignoring the fact that if location were known, there would be no need for a radiologist to find it.

This entire debate would be of academic interest, but it was not for the implications for patient care: lives literally depend on the selection of proper imaging technology. Conducting ROC studies for search tasks is not only bad science but it is also unethical and a disservice to patients and taxpayers.

Rebuttal: Robert M. Nishikawa, Ph.D

My colleague Dev Chakraborty argues, I believe because it is not explicitly stated that the FDA, but principally the CDRH, is biased because it "forces" companies to use ROC analysis instead of JAFROC analysis, which Dev developed; and that this bias exists because members of the CDRH have done ROC research, but not FROC research. That is an interesting premise. Dev supports his assertion with statistics that are consistent with his view, but it does not constitute proof. Here is my prospective on Dev's claim of bias.

First, I know many of the people at the CDRH. In my view, they are among the leaders in the field, both in terms of their scientific rigor and in their vision. The CDRH has a long history of significant and cutting edge research and establishing methodology for evaluating screen-film systems, digital systems, computer-aided diagnosis systems, ultrasound, and others. I have not seen signs of bias in my interactions with members of the CDRH. Certainly, the members have preferences, but they remain open-minded and fair. It is important to note that just as there are

differences in approach between scientists in academia and industry, there are differences between scientists in the public service sector and academia (and industry). Scientists in the public are much more open to sharing data and ideas.

Second, companies applying for FDA approval are, in my experience working with them, very conservative in their approach, and they basically follow any FDA precedent or previous approved applications. This is because the approval process can be time-consuming and expensive. Companies usually overpower their observer studies to include more readers and cases than what is required by an 80% power calculation. They do not want to risk having a null result because the observer study was underpowered. Furthermore, and more importantly, it is much easier and less risky just to copy a previously approved application. This will result in the same methods being perpetuated over time. So, when a company develops a new method, even if there are some benefits to it over existing techniques, they are less likely to use the new method in FDA submissions. This is the company's choice, not an FDA edict.

So, while Dr. Chakraborty has presented evidence, it is all circumstantial and, until he produces a "smoking gun", I believe that his assertion of bias at the CDRH is false.

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CHAPTER 8

General Topics

8.1. Radiation oncology physicists, rather than diagnostic physicists, should lead the development and clinical implementation of image-guided nonionizing therapeutic modalities such as MR guided high-intensity ultrasound

Wolfgang A. Tomé and R. Jason Stafford
Reproduced from *Medical Physics* **41**, 030601-1-4 (2013)
(http:// dx.doi.org /10.1118/1.4789481)

OVERVIEW

Development and implementation of image guidance with conventional x-ray therapy has long been the purview of the therapeutic medical physicist and this is included in the educational and certification requirements for such physicists. This is not so obvious with image guidance for nonionizing therapeutic modalities such as MR-guided high-intensity ultrasound, however. Diagnostic physicists have often been leaders in the development and application of these newly emerging technologies but some believe that this is not appropriate and that therapeutic rather than diagnostic medical physicists should play this role. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Wolfgang A. Tomé, Ph.D. Dr. Tomé obtained his Ph.D. in Mathematical Physics in 1995 from the University of Florida and completed a postdoctoral and two-year residency in Radiation Oncology Physics at the Shands Cancer Center of the University of Florida in 1998. From 1998 to 2012, he served as faculty member in the Departments of Biomedical Engineering, Human Oncology, and Medical Physics of the University of Wisconsin, where he was promoted to Professor with tenure in 2009. He is currently the Director of Physics of the Oncophysics Institute at the Albert Einstein College of Medicine of Yeshiva University, Director of the Division of Medical Physics at Montefiore Hospital, and Professor of Radiation Oncology at the Albert Einstein College of Medicine. He is board certified by the American Board of Radiology in Therapeutic Radiological Physics and is a Fellow of the AAPM. Dr. Tomé's research interests are biomathematical modeling of cancer treatments, biologically guided radiation therapy, adaptive radiation therapy, deformable image registration, 4D patient management, image guided stereotactic body radiotherapy, image guided fractionated stereotactic radiotherapy, and radiosurgery. He has been a member of many AAPM Task Groups and Committees and currently serves on the ASTRO Radiation Oncology Institute Information

Technology Infrastructure Committee and the ASTRO Council on Health Policy: Evaluation Subcommittee of the Emerging Technologies.

Arguing against the Proposition is R. Jason Stafford, Ph.D. Dr. Stafford obtained his Ph.D. in Medical Physics from the University of Texas Health Science Center at Houston and M. D. Anderson Cancer Center Graduate School of Biomedical Sciences, Houston, TX in 2001, where he was subsequently appointed to the faculty and is currently Associate Professor in the Department of Imaging Physics. He is certified by the ABR in Diagnostic Radiological Physics. His major research interests include MR-guided interventions such as nanoparticle-directed photothermal ablation and MR thermal imaging. He serves on several AAPM committees and Task Groups and the Editorial Boards of both *Medical Physics* and the *JACMP*. He is Past-President of the AAPM Southwest Chapter.

FOR THE PROPOSITION: Wolfgang A. Tomé, Ph.D.

Opening Statement

Why should therapeutic medical physicists, rather than diagnostic physicists, lead the development and clinical implementation of image-guided nonionizing therapeutic modalities such as MR guided high-intensity ultrasound? Our diagnostic colleagues have had great success applying unfocused low intensity ultrasound in the field of oncology to detect and characterize tumors. The detection of breast tumors[1] and the quantification of liver tumors using dual frequency ultrasound[2] are two such examples. Clearly, as an imaging modality, unfocused low intensity ultrasound falls naturally into the domain of the diagnostic medical physicist. However, high intensity focused ultrasound (HIFU) is not an imaging but a therapeutic modality and hence its development as a therapeutic modality and its clinical implementation falls more naturally into the domain of the therapeutic medical physicist. Safe and efficient patient treatment using any therapeutic modality involves site-specific patient immobilization and virtual simulation of the treatment to choose the best treatment approach that allows for maximal sparing of normal tissue while allowing for adequate target coverage. This is followed by treatment planning, delivery verification, target localization using some form of imaging before and during treatment, and pretreatment delivery and treatment quality assurance. The aim of these processes is to mitigate normal tissue injury as far as possible and to maximize local tumor control through accurate and reproducible patient setup and adequate choice of treatment margins to deal with residual treatment uncertainties such as tumor motion and random setup errors. In fact, therapeutic medical physicists have spent the last decade and a half with great success perfecting these processes in radiation therapy through the development and implementation of image guided radiation therapy using ultrasound, CT, and MR imaging. These areas of patient care have not been traditionally part of the training of diagnostic medical physicists and, hence, only therapeutic medical physicists can assure the safe and effective delivery of HIFU, since the above areas of patient care are part of their clinical expertise and training. Moreover, HIFU is ablative therapy and hence is, by definition, a local therapy modality that can only be directed against the gross disease visible on imaging. Therefore, HIFU has to be combined with other regional therapies such as fractionated radiotherapy to treat microscopic disease extensions to afford patients the best chance for local/regional disease control. Currently, the American Board of Radiology defines therapeutic medical physics as the branch of medical physics that deals

with "(a) the physical aspects of therapeutic applications of x-rays, gamma rays, electrons and other charged particles beams, neutrons, and radiation from sealed radionuclide sources and (b) the equipment associated with their production and use…"[3] From the discussion above, it follows that this definition of therapeutic medical physics is unnecessarily narrow and should be broadened to include image-guided nonionizing therapeutic modalities such as MR guided high-intensity ultrasound and radiofrequency ablation, since only therapeutic medical physicists have the training and experience to safely and efficiently implement these technologies in the clinic for patient treatment.

AGAINST THE PROPOSITION: R. Jason Stafford, Ph.D.

Opening Statement

Image-guided nonionizing therapies encompass a broadening arsenal of approaches (e.g., cryoablation,[4] thermal ablation,[5] hyperthermia,[6] and irreversible electroporation[7]). Some of these modalities, such as HIFU,[8] as well as emerging techniques based on alternating magnetic field activation of nanoparticles,[9] incorporate extracorporeal delivery of nonionizing radiation. However, the majority in use today utilizes minimally invasive applicators which deliver energy locally. Together these approaches constitute a rapidly proliferating array of minimally invasive image-guided interventions aimed at achieving a variety of clinical goals reaching well beyond just cancer therapy and into applications in cardiology and neurology. Many of these modalities have matured over the last decade and are becoming commercially available to a wider variety of physicians, including surgeons, urologists, interventional radiologists, and radiation oncologists.

To directly address the verbiage of the proposition, the development and, in particular, clinical implementation, of these emerging therapeutic approaches should be led directly by physicians who are fully aware of the potential impact of the proposed nascent technologies in the management of their patients. Many of these procedures, such as cryoablation or radiofrequency ablation, are already delivered safely and effectively to a variety of anatomical sites under CT, ultrasound or MRI guidance.[10] In response to the proposition, the safety and efficacy of many of these procedures could benefit from the inclusion of physicists providing support and taking leadership roles in various aspects of these procedures, such as assisting in the design of techniques and protocols for treatment delivery as well as image-based planning, targeting, monitoring, and verification of treatment delivery, especially during the technical development and initial clinical implementation phase of research.

However, these procedures encompass a range of techniques using nonionizing energy which propagates and interacts with tissue in a fundamentally different manner than ionizing radiation. Some techniques, for example, HIFU in deep seated tissue,[8] rely heavily on the proper implementation and interpretation of nonstandard, advanced imaging techniques for real-time beam targeting and therapy monitoring. Very often it is the scientists who have helped shepherd these technologies through inception, preclinical, and early clinical trials who have developed the necessary expertise to lead clinical implementation efforts. Regarding the question of "therapeutic" or "diagnostic" medical physicist, at the current time, there is no distinction in the CAMPEP accredited didactic course work nor Medical Physics board certification processes to indicate that members of either of these professions possess the necessary expertise to advance,

let alone support, these approaches without substantial additional training. It would appear that the emergence of these therapies is an excellent opportunity to recruit scientists from these laboratories into medical physics in an effort to further diversify and enrich our research and clinical expertise portfolio.

Given this, and the fact that medical physicist participation and support is likely to be governed primarily by the clinical service performing the procedures, it seems the question that the Medical Physics community should focus on is not "who," but "how" we will accommodate emerging image-guided nonionizing therapies into our academic and professional programs as the traditional boundaries separating disciplines such as therapy and imaging physics continue to blur in an era of multidisciplinary patient care.

Rebuttal: Wolfgang A. Tomé, Ph.D.

I am in full agreement with my valued colleague that it should be a team of physicians and physicists trained in the safe application of these new therapeutic radiation modalities that should lead the clinical implementation of this "broadening arsenal of image-guided nonionizing therapy approaches" if they are to become successful. To that end, we tend to focus very much on the clinical subspecialty that tends to apply these new therapeutic modalities. However, clinical skills can only be helped by appropriate science to back it up. While basic scientists are investigating the biological mechanisms of HIFU, which are different from those of ionizing radiation, a medical physicist has the right experience and knowledge for appropriate clinical implementation of therapeutic ultrasound.

The clinical workflows for patient treatment for both ionizing and nonionizing radiation therapy are similar. As pointed out in my opening statement, safe and efficient patient treatment using any image-guided therapeutic delivery of physical energy would involve site-specific patient immobilization and virtual simulation of the treatment to choose the best approach that allows for maximal sparing of normal tissue while allowing for adequate target coverage. This would be followed by treatment planning to quantify the treatment dose to be delivered, treatment verification, image-guided real-time tumor/target localization, and pretreatment delivery and treatment quality assurance. The aim of these processes is to mitigate normal tissue injury as far as possible and to maximize local tumor control through accurate and reproducible patient setup and adequate choice of treatment margins to deal with residual treatment uncertainties such as tumor motion and random setup errors. Therapeutic medical physicists routinely perform these duties in the clinic. They have the appropriate training in respiratory gating, 4D simulation, and treatment planning for radiation. It is likely that some of the same techniques could accelerate the progress and success of clinical application of therapeutic ultrasound. Moreover, these newer nonionizing image-guided treatment modalities, just like surgery, are ablative and by definition local therapies that can only be directed against visible disease. Hence, they will need to be combined with some form of regional therapy such as radiation therapy. Therefore, these new nonionizing image-guided treatment modalities fall naturally into the purview of radiation oncology and therapeutic medical physics.

Rebuttal: R. Jason Stafford, Ph.D.

I sympathize with my colleague on the narrowness of ABR professional medical physics definitions. “Diagnostic medical physics” might be more appropriately called “imaging medical physics.” However, these definitions aim to concisely describe an expected minimum training scope for certificate holders. Broadening these definitions without concurrent changes in didactic and clinical training requirements, as well as examination content, is unwarranted, at best.

My colleague makes another excellent observation with respect to image-guided radiation therapy and the successful collaboration with imaging expertise. As nonionizing modalities proliferate in other services, collaboration with therapeutic medical physicists is likely to provide value. However, extension to all nonionizing therapeutic modalities, much less all MR-guided high-intensity focused ultrasound (MRgFUS) is not warranted. The recent FDA PMA of MRgFUS for treatment of painful bone metastases in patients who do not respond to, or cannot undergo, radiotherapy, exemplifies an application that may be performed within a radiology service, as other image-guided nonionizing modalities are now.

MRgFUS is unique in that imaging potentially provides a closed-loop mechanism for continuous periprocedural planning, localization, and quantitative monitoring of therapy delivery followed by post-treatment verification imaging, often in a single session. Prospective planning is unlikely to provide precise predictions of delivered dose, but rather serves as a tool for assessing feasibility of approach and likelihood of failure. Safety and efficacy, in most scenarios, is achieved via direct imaging feedback of heating or tissue changes at defined intervals during delivery to ensure proper localization of energy, heavily favoring imaging expertise in the design, implementation and interpretation of periprocedural imaging feedback and assessment. Such modalities will benefit from onsite scientists or physicists properly trained to support the equipment and procedures, and current focus should likely be aimed at defining what that training should encompass.

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8.2. Hybrid gold" is the most appropriate open-access modality for journals like *Medical Physics*

Samuel G. Armato III and Clive Baldock
Reproduced from *Medical Physics* **43**, 1–4 (2015)
(http:// dx.doi.org /10.1118/1.4895979)

OVERVIEW

The move to provide unrestricted free online access to articles published in peer-reviewed journals is progressing rapidly and is believed by most to be inevitable. There are essentially three methods to provide such access known as "green," "gold," and "hybrid gold" open access (OA). With green open access, authors self-archive their articles immediately upon publication in an open repository, whereas with gold, the journal itself provides free immediate access online to all articles it publishes. Both green and gold open access essentially make hard copy versions of journals superfluous. Thus, for journals like *Medical Physics* which are owned by scholarly societies (in this case the AAPM) that rely on print advertising revenue to support their activities, gold open access could jeopardize this income, leading some to propose an intermediate form of open access known as hybrid gold. With hybrid gold, authors may, if they wish, pay a fee to have their articles published free access immediately on the journal's website. That this is the most appropriate open-access modality for *Medical Physics* is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Samuel G. Armato III, Ph.D. Dr. Armato earned his B.A. in Physics and Ph.D. in Medical Physics from the University of Chicago. He has worked in the Department of Radiology at the University of Chicago since 1991 and is currently Associate Professor, Chair of the Committee on Medical Physics, and Director of the Graduate Program in Medical Physics. He is a Fellow of the AAPM and has been very active on AAPM committees, including Chair of the Journal Business Management Committee and member of the *Medical Physics* Editorial Board. His major research interests include computerized image analysis, especially for lung CT scans for mesothelioma and lung nodule detection, for which he has had a number of grants and patents and has published over 70 papers in peer-reviewed journals. Dr. Armato has been very active in teaching at the University of Chicago and has supervised the research of numerous undergraduate, graduate, and postgraduate students.

Arguing against the Proposition is Clive Baldock, Ph.D. Dr. Baldock graduated from the University of Sussex, Brighton, United Kingdom in 1987 with a B.Sc. (Hons.) in Physics and was subsequently employed as a trainee medical physicist at Guy's Hospital, London while studying for his M.Sc. in Radiation Physics at St Bartholomew's Medical College, University of London. He subsequently worked in a number of UK hospitals providing scientific support to clinical nuclear medicine and MRI services. His main research interests were in the field of the MRI of radiation sensitive gels for improved 3D radiotherapy dosimetry for which he received his Ph.D. from Kings College, University of London. Dr. Baldock moved to Queensland

University of Technology, Brisbane, Australia in 1997 and subsequently worked at the University of Sydney as Director of the Institute of Medical Physics and then as Head of the School of Physics. Until January 2014, he was Executive Dean of Science at Macquarie University in Sydney. His current research interests continue to be in the fields of radiation therapy, dosimetry, and medical imaging on which he has published over 140 research papers. He has been awarded Fellowships of the Australian Institute of Physics, the Australasian College of Physical Scientists and Engineers in Medicine, the Institute of Physics (UK), and the Institute of Physics and Engineering in Medicine (UK).

FOR THE PROPOSITION: Samuel G. Armato III, Ph.D.

Opening Statement

Open-access publishing is not new to *Medical Physics*. For the past several years, the Journal has made select categories of published articles available online without charge to the world.[1] The rationale behind this free content is simple: articles deemed to be high impact or to provide a special service to the medical physics community, draw readers to the Journal, which encourages an expanded reader base, exposure to potential future authors of submissions to the Journal, and possibly greater subscription revenue (or AAPM membership).

Beginning last year, research articles accepted for publication in *Medical Physics* also could become open access through authors voluntarily exercising the option to pay an article processing (or publication) charge (APC).[2] The APC was set at $2500, a figure that approximately represents the cost to publish a single article in the Journal under the current model that includes both online and print versions. This “author's choice” option to designate individual articles as open access transformed *Medical Physics* into what is known as a hybrid gold open-access journal and, in my opinion, moved the Journal forward in the scientific publishing world.

The open-access movement has evolved a number of variations to meet the needs of different journals, different groups of authors, and increasingly, different funding agencies, author institutions, and governmental bodies.[3] The approach that is most frequently associated with the term “open access” is the “gold open access” model, in which the entire content of a journal is online and freely available to anybody immediately upon publication/posting; the concept of journal subscriptions ceases to exist when a journal is gold open access. Recently, a series of open-access mandates has been enacted by, among others, the Wellcome Trust, the Harvard University system, and the United Kingdom.[4] This trend, combined with the growing success of open-access journals,[3,5] has transformed the open-access paradigm (once considered by some to be an interesting but unsustainable experiment) into a seemingly more permanent feature of the scientific publishing landscape.

So, existing subscription journals have a choice: either hold firm to the traditional in the hopes that a continued role for this model in science persists or consider adopting an open-access approach to provide a product that meets the changing needs, desires, and expectations of both producers (the authors) and consumers (the readers). By making *Medical Physics* hybrid gold open access (with individual articles being designated open access based on the author's

preference and APC payment), the AAPM's Journal Business Management Committee and the Editorial Board have more firmly established the Journal in the open-access world and have developed a publication model that can, without significant additional effort or risk, either actively follow the evolving landscape toward a full gold open-access journal or fully reinstate the traditional approach should the open-access movement wane. I believe that the prestige of *Medical Physics* will remain high and that authors will continue to desire to submit their best work to the Journal; however, economic forces and principles that reject the traditional subscription model for scientific communication may leave some authors no choice but to go elsewhere. Hybrid gold open access ensures that *Medical Physics* is in a position to withstand this complicated situation.

AGAINST THE PROPOSITION: Clive Baldock, Ph.D.

Opening Statement

From the time journals were first published in London and Paris in the seventeenth century,[6] scientists have been able to share their work with a wider audience. Over time, a particular business model developed in which interested readers would subscribe to commercially published journals either individually or via their institutions. Since the 1980s, journal subscription charges have risen significantly faster than inflation causing a so-called *serial pricing crisis* for many institutional libraries. Further, barriers erected by publishers have limited access to academic research that many thought should be freely available, particularly if financed via public funds.[7]

In 1994, cognitive scientist Stevan Harnad posted a *Subversive Proposal* to a mailing list calling on researchers to make copies of all their published papers freely available on the Internet. Subsequently the term *open access* was adopted at a meeting where the *Budapest Open Access Initiative* was initiated,[8] and the OA publishing movement was born. The OA movement has continued to grow significantly over the years with implications for scholarly research, for-profit publishers, and not-for-profit societies such as the AAPM that publish journals such as *Medical Physics*.[9]

The introduction of the hybrid-gold OA publishing model in which journals charge authors an APC to make individual published papers freely available in subscription-based toll-access journals was considered to be an intermediate publishing stage on the journey from the original toll-access form to that of full-gold OA.[10] It was assumed by many that, as more articles were published as hybrid-gold, the income from the associated APC would enable journals to move away from subscription-based toll-access with the cost being met by the author and not the reader/subscriber, thereby enabling members of the public and individuals in developing countries, among others, to have free access to published papers.

At the beginning of 2013, the Editorial Board of *Medical Physics* and the AAPM Journal Business Management Committee agreed to add the hybrid-gold OA feature to what had until then been a toll-access journal.[2]

There has been much debate regarding the success of hybrid-gold OA publishing with many considering it not to have fulfilled its potential. Hybrid-gold OA journals have consistently been accused of double-dipping, i.e., charging authors an APC for hybrid-gold OA whilst also continuing to charge a subscription fee for the same journal that the author or their institution/institutional library has to pay for toll-access.[11] Further, hybrid-gold OA journals are considered low risk for publishers because they still receive subscription income regardless of what has been a low uptake of hybrid-gold OA by authors.[12]

Rebuttal: Samuel G. Armato III, Ph.D.

The decision to begin a new gold open-access journal involves a thought process, business plan, and level of risk that are much different from those involved in the conversion of an existing subscription-based journal. For a highly regarded, financially sound journal such as *Medical Physics*, such a conversion, should it occur at all, must be undertaken prudently. My colleague is correct in stating that hybrid gold open access is considered an "intermediate publishing stage" in the transition from a subscription-based model to full gold open access: this statement precisely captures the motivation behind the decision to move *Medical Physics* in this direction.

The transition to gold open access is even more complicated for a journal that has a paper version, since gold open access only makes practical sense for an online-only journal. The conversion of *Medical Physics* to full gold open access first would require the elimination of the print version of the Journal, which would necessitate an overhaul of the advertising revenue stream—sponsors are not simply moving their advertising dollars from print to electronic when journals abandon paper. While the Journal is not in a position to absorb the burden of two major transitions at this time, the hybrid gold open-access approach allows the Journal to satisfy a need that has been expressed in various ways by a subset of authors and funders.

The Journal has an obligation to mitigate the impression of "double-dipping," as referenced by my colleague. Accordingly, the fraction of authors who opt to make their *Medical Physics* articles open access will factor into future subscription-rate decisions.

I agree that "the OA movement has continued to grow significantly over the years with implications for scholarly research, for-profit publishers, and not-for-profit societies such as the AAPM." The hybrid gold open-access model could be an important stepping stone for traditional journals that seek to become part of that movement.

Rebuttal: Clive Baldock, Ph.D.

The original intention of Tim Berners-Lee in introducing to CERN the information management system that went on to become the World Wide Web was to facilitate the sharing and updating of information among researchers at his institution. The Web has subsequently transformed our lives and revolutionized many industries such as banking, travel, publishing, and even pornography amongst others. Considering that the Web started as an information management system, it is perhaps ironic that the open sharing of information in the form of journal publications has not been transformed; the traditional journal publishing model is still very much in place in spite of the growth of OA.

It is far from clear how the OA phenomenon will develop and what eventually will be the steady-state destination of journal publishing. Some have argued that either full green and/or gold OA is the likely ultimate outcome with no long-term future for hybrid-gold OA publishing. Further, Stevan Harnad, author of the original *Subversive Proposal,* has referred to hybrid-gold OA as *fool's gold*, the rationale being that, if there is a subscription journal that offers hybrid-gold for a price, authors would be foolish to pay for hybrid gold when they can provide green OA for free (by self-archiving) with "no need for subscription publishers, who are already abundantly well paid via their subscriptions, to be double-paid for articles that authors foolishly pay to make Gold OA".[15]

Submissions to the United Kingdom Government Finch Review in 2012 into expanding access to published research findings[13] indicated that, should all journals end up as gold OA, a significant impact will likely be felt by learned and scholarly societies (such as AAPM) that rely on revenue from the publishing of journals for significant income to fund their societal activities for the benefit of their members and the wider community.[14]

Should the OA evolving landscape ultimately determine that *Medical Physics* reaches the full gold OA destination, then perhaps, to this end, the AAPM should proactively plan for a future in which this comes to pass, where there will be a reduction in a revenue stream with new sources of income needing to be developed within the framework of a new business model for the Journal.

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8.3. Spontaneous tumors in pets are an excellent translational model for human cancers

Stephen A. Sapareto and Andrew T. Vaughan
Reproduced from *Medical Physics* **43**, 6127–6129 (2015)
(http:// dx.doi.org /10.1118/1.4929980)

OVERVIEW

The vast majority of animal studies of human cancers involve using tumors induced in small animals such as rodents. Pets are relatively rarely used. It is claimed, however, that spontaneous tumors in pets are an excellent translational model for human cancers. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Stephen A. Sapareto, Ph.D. Dr. Sapareto earned his M.S. in Health Physics and Ph.D. in Radiation Biology and Cell and Molecular Biology from Colorado State University. After a Postdoctoral Fellowship at Stanford University Medical Center, he took his first faculty position at Washington University, St. Louis. He continued research in hyperthermia and tumor biology at Wayne State University and the City of Hope Medical Center. In 1992, he moved to Good Samaritan Medical Center, Department of Radiation Oncology in Phoenix as a Medical Physicist, and became Board Certified by the ABMP and ABR. After a position as Head of Medical Physics at the University of Arizona in Tucson, he became Director of Medical Physics at Banner Good Samaritan Medical Center, Phoenix, AZ and, in 2011, he moved to his current position as Director of Medical Physics in the Division of Radiation Oncology at the Banner MD Anderson Cancer Center. He has actively contributed to the AAPM and served as Chair of the Biological Effects Subcommittee and President of the Arizona Chapter.

Arguing against the Proposition is Andrew T. Vaughan, Ph.D. Dr. Vaughan earned his M.Sc. in Radiobiology and his Ph.D. in Applied Nuclear Physics from Birmingham University, England, after which he moved to the USA, first to Loyola University, Chicago and then to his current appointment as Professor in the Department of Radiation Oncology, University of California at Davis, Sacramento, CA where, in 2009, he was appointed as Director of Radiation Biology. Dr. Vaughan has published about 100 papers and his research has covered a wide range of topics that include both testing hypotheses in a clinical setting as well as basic biological processes, such as the lethality of DNA damage, its repair and modulation by transcriptional activators and, in particular, the use of apoptotic triggers as mediators of targeted DNA damage.

FOR THE PROPOSITION: Stephen A. Sapareto, Ph.D.

Opening Statement

Dogs and cats get cancer, just like people. Their tumors and incidence are quite similar to humans.[1–3] For example, spontaneous tumors in dogs are an excellent model for human breast cancer showing a remarkable number of similarities.[1] While the incidence of sarcomas is higher

in these animals, they develop similar incidences of nearly all kinds of malignancies seen in humans with the exception of lung cancer (they do not smoke!). It is quite reasonable to expect that pet animals should have similar incidences of cancer because they are exposed to all of the same environmental factors that humans face. Thus, they represent an excellent model for human malignancy with several important advantages over other models. First, unlike primates, they are in abundance and have their own health care system throughout the country (veterinary clinics). Murine tumors, while demonstrably useful in the study of malignancy, for the most part are induced rather than spontaneous and have many serious limitations in translation to human cancer. They lack, or are different in, a number of important features shown in human (and pet) tumors such as slow growth over long periods of time, genomic instability, immune response, heterogeneity of tumor cells, the tumor microenvironment, and stroma.[4,5] Taghian and Suit note that one of the most desirable characteristics lacking in models for human cancer is spontaneous development.[6]

Unlike murine tumors which require specialized imaging and delivery systems for radiation therapy studies, the relative size of dog and cat malignancies allow the use of standard human imaging and therapy equipment. Ironically, with the growth of animal rights activism, it is becoming increasingly difficult to perform clinical trials with laboratory animals. Because standards of care are not well established in pets, there is much less resistance to trials in pets, as long as proper and ethical studies are designed with informed owner consent. An important advantage of spontaneous tumors in dogs and cats is their more rapid response times compared to humans. While human clinical trials usually take five years to demonstrate durable response, tumors in dogs and cats usually respond in less than 2 years. Unfortunately, despite the growth of pet insurance, the alternative to animal clinical trials for malignancies is euthanasia due to economics.

Clinical studies of pet tumors of significance to human malignancies have been reported.[7] The clinical trials programs, while solidly established as shown by the Veterinary RTOG group of the American College of Veterinary Radiology,[8] are still in their infancy but are poised for rapid growth. There are nearly a dozen ACVR-approved radiation oncology programs at veterinary schools and nearly all show clinical trials opportunities on their websites.[9] Unfortunately until now, the use of spontaneous animal tumors for radiation therapy trials has been limited to mostly drug combination studies[4] in part due to the fact that animals are usually treated with relatively short-course (5–15 treatment) radiation protocols. This has not been comparable to the 25–35 treatment fractions traditionally used in human protocols. However, the rapid growth of hypofractionation for treatment of human malignancies has made these animal protocols far more relevant and useful. Thus, I predict spontaneous tumors in dogs and cats are poised to make significant contributions to radiation oncology for human malignancies.

AGAINST THE PROPOSITION: Andrew T. Vaughan, Ph.D.

Opening Statement

The development of pets (companion animals) is conditional on their close association with mankind, providing them a unique emotional and genetic place in society. The domestic dog, largest by number in current clinical trials using pets (www.VetCancerTrials.org), traces a

genetic lineage with the gray wolf and is the most phenotypically diverse animal on earth.[1,10] Such diversity is readily apparent when comparing breeds, such as the poodle and rottweiler, and is generated specifically from trait selection (hunting, temperament, etc.) controlled predominately by mankind and minimally through natural selection. It has been proposed that the rapid diversification of breeds has arisen from accelerated genetic changes directly attributable to the domestication process, avoiding the exercise of "fitness" to a changing environment that is a key element of Darwinian selection.[11] The practical reality of this can be observed in such breeds as the boxer or bulldog, bred for characteristics that can make it a struggle to both move and breathe efficiently, in addition to demonstrable biochemical differences between breeds as observed in hematological data.[12] Mankind has therefore bred these animals to specifically accentuate differences in their form, physiology, and behavior via unknown groups of genetic alterations. The question then arises, considering companion animals do develop tumors, does this matter in a translational test setting? At least part of the answer is linked to their genetic heritage. Genetic manipulation through breeding has generated widely variable attributes that directly, and in ways that remain unexplained, impact tumor development. A recent large survey of over 70 breeds found a greater than 3-fold difference in absolute tumor incidence, with the Irish water spaniel taking an unenviable first place with over half of recorded deaths being from cancer.[13] The key issue here is that the genetic underpinning to the phenotypic selection process intrinsic to companion animals has provided certain dog breeds with a predisposition to cancer and, by extension, likely different responses to experimental treatments for their disease. Thus, data obtained in a translational setting would always be biased by each animal's genetic makeup, manipulated and modified by generations of human selection. An appropriate parallel would be translational studies using random mixtures of different animal species, a process unlikely to find favor in any setting. This then highlights the alternative, and currently most common, animal systems used in testing, that of genetically matched animals. Such animals, usually mice, are bred to genetic uniformity such that each individual is genetically identical to the next. This allows replicate studies of treatment schedules within a fixed genetic background and can provide at least a guide to potential treatment efficacy. So, is the *status quo* of such isogenic animal strains the preferred option? It is clear that data generated from any animal experiment is essential to validate efficacy and safety of a novel treatment, but on its own is incapable of replacing human studies. But to make that key jump from animal testing to man, the most efficient and practical option remains the use of genetically defined mouse strains.

Rebuttal: Stephen A. Sapareto, Ph.D.

My colleague and opponent argues the point that because genetic traits have been bred in dogs, this is a reason for questioning their value in translational clinical trials. I believe that having greater heterogeneity than rodent models, but less heterogeneity than humans, the animal model strengthens the translational model, particularly for genetic studies where small numbers of genes are thought to account for the breed susceptibility. Each of the 175 canine breeds shares significant phenotypes. Most cancers that occur in people are observed in dogs and, as in humans, some tumor types are less common than others. My colleague feels that differences in incidence between breeds are a disadvantage. However, when a less common breed has a high incidence of an uncommon tumor, such as Scottish Terriers, which have a 30 times greater risk of bladder cancer than any other breed, this can be exploited. Using high throughput sequencing, subtle mutations that promote cancer susceptibility and progression can be detected. Canine

pedigrees, an important part of the dog breeding culture, also provide a unique tool that enhances association analysis and family linkage studies.[3] The genetic differences in breeds of dogs and their response to treatment may also provide important clues to the responses of human tumors.[3] The remarkable similarity in tumor characteristics and responses to treatment for osteosarcomas and melanomas,[2] and for mammary tumors,[14] between dogs and humans would also support the likelihood of their being a useful model. Furthermore, the dog is the only animal which develops spontaneous prostate cancer with clinical features, including relative age at onset and metastatic patterns, similar to humans,[3] although seen less commonly. The plethora of similarities in gene regulation between human and canine mammary tumors[1] also argues against my opponent's suggestion that they would not provide useful or reliable information for human therapies.

The failure of rat and mouse tumor models, including xenografts, to predict human response is well known in drug studies and, while useful in studying mechanisms of action, they are not very useful in predicting human clinical results of radiation treatment.[6] As stated by Professor Colin Garner, "*We have learned well how to treat cancer in mice and rats but we still cannot cure people*."[15] We need a more predictive model to investigate practical clinical questions in radiotherapy which clearly cannot be answered with murine models. Spontaneous tumors in dogs and cats are that model.

Rebuttal: Andrew T. Vaughan, Ph.D.

The argument for using companion animal models of cancer cites similarities with human disease including their spontaneous development, with genetic changes that parallel that in humans, such as the BRCA1/2 genes in breast cancer.[1] Comparisons of this type are perhaps predictable, considering the general compatibility between the biochemistry and physiology of humans and companion animals such as cats and dogs. However, a key difference lies in the genetic environment in which such genes operate, bred to near uniformity in specific animal breeds, but highly individualized in every patient. In contrast, translational studies using mice increasingly make use of human tumor tissue taken directly from the patient, without *in vitro* clonal selection, providing a robust snapshot of the tumor taken at the precise time therapy is to be applied.[16] This approach therefore retains the genetic uniqueness of individual patient tumors, representing the culmination of the tortuous genetic path the tumor has taken to presentation as a clinical problem.

The increasing sophistication of such mouse models of human cancer makes them, and not companion animals, ideal for translational studies of human disease. In particular, advances in sequencing technology can provide a full spectrum (personalized) genetic map for every tumor, providing an unparalleled level of detail to complement therapy-focused studies. In many ways, the key role of technology that drives these biology-based studies has an intriguing parallel with the applications of technology in the clinic, IGRT in facilitating the execution of SRS/SBRT, for example. In comparison, the use of companion animals in the same setting provides at best a blunt-edged tool to dissect questions of how to improve tumor treatment for human patients.

ACKNOWLEDGMENTS

Dr. Sapareto would like to acknowledge and thank Dr. Susan LaRue, DVM for her significant contribution to this debate.

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8.4. Open access journals benefit authors from more affluent institutions

Eduardo G. Moros and Per H. Halvorsen
Reproduced from *Medical Physics* **44**, 5265–5267 (2016)
(http:// dx.doi.org /10.1118/1.4959548)

OVERVIEW

At first sight it would appear that making published articles available for anyone to read worldwide at no cost (Open Access) would be an asset to all authors, but some claim that authors from less-affluent institutions would not benefit. This is the premise debated in this month's Point/Counterpoint.

Arguing for the Proposition is Eduardo G. Moros, Ph.D. Dr. Moros received his B.S., M.S., and Ph.D. degrees in Mechanical Engineering from the University of Arizona, Tucson, in 1984, 1987 and 1990, respectively. After receiving his Ph.D., he spent a year as an Associate Researcher at the University of Wisconsin, Madison, and then joined the Mallinckrodt Institute of Radiology at Washington University School of Medicine, where he eventually became Professor and Head of the Research Physics Section of the Department of Radiation Oncology. In 2005, Dr. Moros moved to the University of Arkansas for Medical Sciences, Little Rock, AR and, in 2011, moved to the H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL as Professor in the Department of Oncologic Sciences. He has served on numerous AAPM Committees including the Editorial Board, is the current Chairman of the Working Group on the Development of a Research Database, and is a Fellow of the AAPM. Dr. Moros is certified in Therapeutic Radiological Physics by the ABR.

Arguing against the Proposition is Per H. Halvorsen, M.S. Since receiving his M.S. degree in Radiological Medical Physics from the University of Kentucky in 1990, Mr. Halvorsen has worked in large academic medical centers and private community clinics and, currently, is the Chief Physicist in Radiation Oncology at Lahey Health in Burlington, MA. He has been very active in the AAPM and the ACR on professional practice issues with particular focus on practice standards and peer review, serving on the ACR's Radiation Oncology Accreditation Committee, as Chairman of the AAPM Professional Council, as an Associate Editor of the *JACMP*, on the AAPM Board of Directors, and as President of the AAPM Connecticut Chapter. Mr. Halvorsen is a Fellow of the AAPM and the ACR and is certified in Therapeutic Radiological Physics by the ABR.

FOR THE PROPOSITION: Eduardo G. Moros, Ph.D.

Opening Statement

Before defending the Proposition, I would like to make a statement of clarification and define a couple of terms. The statement is that Open Access (OA) publishing provides advantages to society, one of which is that it removes obstacles for the dissemination of science and does so at a lower overall cost.[1] The terms I would like to clarify are "Open Access" and "Affluent Institutions." For the purpose of this paper, I restrict my arguments to gold open access (GOA), which is the business model where the authors and/or their funders/institutions pay nonpredatory journals for the immediate freely accessible publication of their peer-reviewed work. By "affluent institutions" I mean institutions that enjoy healthy research budgets, whatever be the sources of funds.

With the above definitions in mind, the Proposition "*Open access journals benefit authors from the more affluent institutions*" is incontrovertibly true. In the GOA publishing model, authors or their institutions pay; it logically follows that the more affluent the institutions, the more GOA papers the authors from those institutions can afford to publish. In fact, many open-access journals make provisions for authors/institutions that cannot afford to pay such as those from third world countries,[2,3] thereby admitting that GOA represents an economic barrier to authors from less affluent institutions or countries. The cost to authors is a real problem that is beginning to affect junior investigators, especially those who do not yet enjoy extramural funding.[4,5] Ironically, while many funding agencies are calling for open science and many have agreed to pay for GOA publishing costs (and revenues), they obviously only pay for investigators (authors) that they support, therefore leaving nonfunded, less affluent authors, at a disadvantage.

As a nonscientific exercise in support of the Proposition, the reader is invited to check the list of open-access papers published in *Medical Physics* in 2015.[6] After excluding those papers which by journal policy are made freely available to the general public, it is quite obvious that all these author-sponsored papers come from affluent institutions. Moreover, a closer look reveals that about 80% of the papers acknowledged having been funded by grants or contracts. That authors want to make their papers freely available is not only logical but also commendable, and there is also an important incentive for authors—not only are their works more widely disseminated but they are also more highly cited.[3,7] That a relatively higher number of journal article citations benefit authors is also an incontrovertible fact.[8,9]

The cost of scientific publishing has traditionally been financed by institutional libraries, i.e., the readers, regardless of funding status. For most journal articles, there are more readers than authors, thus the cost per article was widely distributed among many payers. GAO publishing shifts the cost to authors/institutions. Today, on average, the cost per article is around $2500, which is not at all a small amount and is definitely burdensome for investigators without funding in less affluent institutions.

AGAINST THE PROPOSITION: Per H. Halvorsen, M.S.

Opening Statement

The rise of open access peer-reviewed scientific journals, beginning in the late 1990s, has caused a radical change in scientific publishing. This shift has significant impact on all three constituencies—the publishers, the readers, and the authors. The impact on publishers is

addressed in other venues and will not be repeated here. For readers, the shift is largely positive, enabling free and convenient access to quality peer-reviewed work. But does the shift benefit authors equally? While it is arguable whether open access journals are universally beneficial for authors, I posit that authors from more affluent institutions do not gain an inherent advantage over authors from less affluent institutions.

The transition away from closed, subscription- and print-based journals to open-access online journals is far from complete, and will inevitably encounter some bumps along the way, but the long-term trend is inevitable: scientific publishing will move online, and the benefits of open access are compelling.[10–12] Advertising models will adapt accordingly, and business models are evolving to ensure that authors continue to have fair access to publication of their work.[13] In the meantime, many reputable journals have procedures to grant full or partial waivers of article processing charges[14] (APCs) for authors from less affluent countries. Our own *Journal of Applied Clinical Medical Physics*, a "gold open access" journal,[15] imposes an APC equal to <0.3% of the average salary of US medical physicists[16]—resulting in an expense of <0.1% per author for a typical manuscript—and is implementing a fee waiver procedure for authors from less affluent countries. Experience with a wide range of open access journals shows that most article publication charges are not borne directly by the authors.[17]

While the direct cost to individual authors is quite manageable, the benefit to each author from open-access publication is distribution to a far larger audience than is possible with a closed, subscription-based model.[12] The fundamental purpose of submitting one's work for publication is to share knowledge— and open access journals provide a much more effective medium for sharing that knowledge than closed subscription-based journals. That benefit is just as strong for authors from less affluent institutions.

Rebuttal: Eduardo G. Moros, Ph.D.

My opponent supports the Proposition in his statement "*many reputable journals have procedures to grant full or partial waivers of article processing charges for authors from less affluent countries*," a point I made in my opening statement. While many GOA journals do give waivers, they also tend to target affluent authors and fields of study, as discussed below.

Perhaps in the long run publication cost will not be borne by authors, but that is not the case today. The available literature on this issue supports the Proposition. For example, Solomon and Björk[17] showed that the less affluent the country, the more the funds come from the authors and the less from their institutions. The reverse was also true, namely, the more affluent the country, the less the funds come from the authors and the more from their institutions.[17]

In 2013, Kozak and Hartley[18] reported that 28% of OA journals charged authors. This percentage is likely much higher today in affluent fields since they also reported that the more affluent a field, the higher the percentage of GAO journals. For instance, the figure was 47% in medicine and 0% in the arts.[18] In other words, GOA journals know where the affluent authors are. This has also resulted in the emergence of predatory journals.[19] Thinking along the line that the affluent authors can and should pay, my opponent argues that the cost to US medical physicists is highly affordable; however, his analysis would not hold true for medical physicists around the world.[4]

To add insult to injury, GAO journals also benefit greatly by the time and effort donated by reviewers and editors, who are typically authors themselves.

Authors need to be aware of the disparities introduced by GOA publishing and should exert influence so that the cost of OA publishing does not continue to adversely affect nonaffluent authors.[20]

Rebuttal: Per H. Halvorsen, M.S.

Performing quality research and publishing a high-quality journal are both resource-intensive endeavors. Unfortunately, individuals in under-resourced institutions face many challenges. In the subscription-based publication paradigm, both readers and authors from under-resourced institutions are disadvantaged through reduced access to publications and limited funding or equipment to support research. Hence, individuals working in affluent institutions derive many advantages. To hold up APCs as uniquely tilting the competitive landscape in favor of affluent institutions is naïve. Authors from more affluent institutions have enjoyed competitive advantages for decades, of a scale much larger than any impact from APCs.

Dr. Moros defines affluent institutions as "*institutions that enjoy healthy research budgets whatever the sources of funds*." This incorrectly assumes that research budgets finance the publication of articles. Funds to support the APC frequently come from the same money used to support professional development, books, and office computers. For medical physicists, for example, this money often comes from clinical revenue, not research budgets. Dr. Moros asserts that "*the more affluent the institutions, the more GOA papers authors from those institutions can afford*." This is not universally correct; most of the cost of the research leading to publishable work consists of the labor associated with doing the research and the equipment used in the research. Both of these are often covered through clinical revenue and clinical department equipment.

Dr. Moros used a nonscientific exercise (reviewing open access papers in *Medical Physics* in 2015) to support his Proposition that open access publishing benefits authors from affluent institutions. A similarly nonscientific exercise using the most recent (at the time of writing) issue of *Medical Physics* (Vol. 43, Issue 5) shows that *all* papers come from affluent institutions. Yes, all open-access papers published in *Medical Physics* appear to come from affluent institutions because that is entirely consistent with the pattern for all papers published in the journal. By contrast, authors publishing in the *JACMP* come from a more diverse range of institutions, including many lesser-resourced ones.

Dr. Moros states that open-access publishing "*shifts the cost to authors/institutions*." It is true that APCs shift some of the publication cost to authors and that can indeed be a hardship to some, which is why more than two-thirds of open-access journals have a fee-waiver policy for authors from under-resourced institutions.[21] APCs represent a very small part of the total resources required for high quality scientific investigations. Manpower, work environment, and availability of specialized equipment are all important in this regard, and the resources required to provide them far outweigh the cost of the APC. Individuals from less affluent institutions face disadvantages on several fronts; open access APCs are by no means a unique disadvantage.

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8.5. Famous medical physicists often get more credit for discoveries due to their fame than less prominent scientists who may have contributed as much or earlier to these developments

Clive Baldock and L. John Schreiner
Reproduced from *Medical Physics* **44**, 1209–1211 (2017)
(http:// dx.doi.org /10.1002/mp.12089)

OVERVIEW

Medical physics is a rapidly developing, technologically dependent field. New discoveries are being made almost daily, as demonstrated by papers in this and other similar journals. Many of the authors are early in their careers. Some are concerned, however, that more famous medical physicists often get credit for discoveries due to their fame rather than less prominent scientists who may have, in fact, contributed more to the development in question. This is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Clive Baldock, Ph.D. Dr. Baldock received his Ph.D. from King's College London with research in the field of gel dosimetry for improved three-dimensional radiotherapy dosimetry. He subsequently moved to Queensland University of Technology, Brisbane, Australia in 1997 as Lecturer and then Senior Lecturer in Medical Physics in the Centre for Medical, Health and Environmental Physics, School of Physical Sciences. In 2003, he moved to the University of Sydney as the Director of the Institute of Medical Physics and later as Professor and Head of the School of Physics. In 2012, he was appointed the Professor and Executive Dean of Science at Macquarie University, Sydney. In 2014, he joined the University of Tasmania as the Professor and Deputy Dean, and then as the acting Dean of the Faculty of Science, Engineering and Technology and, in 2016, he was appointed as the Pro Vice-Chancellor for Researcher Development and Dean of Graduate Research. His research interests continue to be in the fields of gel dosimetry, radiation therapy, dosimetry, and medical imaging in which he has published over 150 research journal papers. He has been awarded the Fellowships of the Australian Institute of Physics, the Australasian College of Physical Scientists and Engineers in Medicine, the Institute of Physics (UK), and the Institute of Physics and Engineering in Medicine (UK).

Arguing against the Proposition is L. John Schreiner, Ph.D. Dr. Schreiner obtained his Ph.D. from the University of Waterloo, Ontario, Canada in 1985 and has been the Chief Medical Physicist at the Kingston General Hospital since 1997 and Full Professor (Oncology and Physics) at Queen's University. He has been the Newsletter Editor for the Canadian Organization of Medical Physicists (COMP), and the examiner, board member, and President (1999–2002) of the Canadian College of Physicists in Medicine. He was a founder and organizer of the International Conferences on Three-Dimensional Dosimetry, and edited two conference proceedings. He has served on the *Medical Physics* Editorial Board and is currently a Senior

Associate Editor. Dr. Schreiner has supervised over 120 trainees at various levels; these trainees helped him publish research in about 100 peer-reviewed papers.

For the proposition: Clive Baldock, Ph.D.

Opening Statement

From the time that Henry Oldenburg created the *Philosophical Transactions* of the Royal Society of London in 1665, practitioners of science have endeavored to share the results of their research pursuits with a wider audience by way of publishing in scientific journals.[1] Since then, and up to the present day, many new journals have been founded giving authors a wide choice of avenues for publishing, particularly due to the current availability of online and open access journals.[2, 3] However, as well as reading previously published papers, a significant issue for active research scientists is in keeping up-to-date with the current journal literature due to the vast body of published papers, with the result that only a small proportion of the literature is read.[4] Due to many published papers going unnoticed or unread, many articles either never get cited or are only self-cited by the authors of the paper. This cultural aspect of scientific publishing has been explored in the discipline known as the sociology of science. In his seminal 1968 publication, the well-regarded sociologist, Robert K. Merton, discussed how eminent scientists get disproportionately greater credit for their scientific contributions when compared with less eminent and relatively unknown scientists, with the latter getting lesser credit for their comparable research contributions.[5] Merton went on to describe this phenomenon as the Matthew Effect derived from the Gospel according to Matthew in the Bible: "*For unto every one that hath shall be given, and he shall have abundance; but from him that hath not shall be taken even that which he hath*".[6] The phenomenon of the Matthew Effect is perhaps not surprising given that, as already mentioned, there is difficulty in keeping up-to-date with the vast body of scientific literature. When writing a paper, there may be a tendency to read and reference the work of the more well-known author without reading and referencing that of others. Further, the phenomenon, if indeed true, would potentially manifest itself in increased increments to the *h*-index of individuals.[7] The underlying open question, and topic of this Point-Counterpoint, is whether the Matthew Effect phenomenon is evident in the practice of medical physics research. It is the hypothesis of this author that this is indeed the case. Such behavior would not be a surprise as many active medical physics researchers also have significant routine clinical or teaching duties to perform. Even with the best of intentions, due to workloads and the constraints of time, there may be a tendency for researchers not to undertake a thorough survey and review of the literature for a particular topic.

Against the proposition: L. John Schreiner, Ph.D.

Opening Statement

The proposition ascribes to medical physics a well observed and analyzed characteristic of scientific advancement. It restates the "Matthew Effect"[5, 8] which can be summarized as: "if two scientists make the same discovery, either independently or as collaborators, the more eminent scientist will get the lion's share of the credit". In arguing against the proposition, it would be unreasonable to claim *a priori* that medical physics is 'purer' than other scientific

endeavors; so, the famous medical physicist may occasionally get unwarranted credit. But, I contend that conditions in our community regulate against influences that have been associated with the effect and proposition.

Various factors have been identified as possible grounds for the Matthew Effect. To start, multiple discoveries (in which many individuals develop ideas and research lines simultaneously) continue to increase and it can be difficult to identify the originator of ideas.[8] When measuring reputation by citations gained,[9] observations show that authors are inclined to cite the work of more famous scientists in order to secure preferential acceptance of their own work.[8, 10] Similarly, authors may consider it expedient to cite papers from journals with greater impact factor, or papers originating from more prestigious institutions, since these settings might be perceived,[10] perhaps incorrectly,[11] to select for work of the eminent. This of course assumes that scientists are able to find the relevant literature, which may not happen now that researchers more readily rely on computers and electronic databases to make the links.[12] The Matthew Effect may also extend to the commercialization of knowledge through licensing and patents.[13]

While the factors above apply somewhat to medical physics, our circumstances moderate the extent. Medical physics can be identified as a field in which empirical knowledge is consolidated into a succinct theoretical formulation. Young scientists can more easily make recognized significant discoveries in such "highly codified" fields.[14] Medical physicists also comprise a relatively small number of researchers who are more able to stay aware of all other contributors, in part because they are all publishing in, more or less, a small number of journals with similar impact factors. Also, commercialization is limited to a small pool of industrial partners. Thus, many of the conditions identified with the Matthew Effect are moderated in our field.

Finally, I will use an example from the north to challenge the proposition. The Canadian Organization of Medical Physicists recently established the Impact Publication Prize to recognize members who have had a major impact on the field through work in Canada. The impact is measured by authorship of a paper with the greatest number of citations for a set period in Web of Science databases.[15] The inaugural 2016 prize was awarded to Dr. Karl Otto for his seminal paper in *Medical Physics* introducing VMAT.[16] Dr. Otto wrote this influential paper building on the advent of tomotherapy[17] and attempts to advance arc therapies on conventional linear accelerators,[18] while he was a part-time medical physicist working in Vancouver.[19] This influential work had an extraordinary impact, changing the delivery of modern radiotherapy throughout the world, and credit was fully assigned to the young up-and-coming physicist who advanced the technique.

Rebuttal: Clive Baldock, Ph.D.

Without significant evidence to the contrary, a conclusion to be drawn is that the Matthew Effect is at work in medical physics. To many clinical medical physicists, this may not be of concern, particularly when their routine duties dominate. However, there are a number of what might be considered to be perverse consequences including, by way of example, the potential for decisions regarding research funding outcomes, for the research medical physicist to be influenced.

The Matthew Effect has a relationship with the *Matilda Effect*[20] whereby the work of female scientists is attributed to that of males whose publications get cited more for the same work. Often male scientists received more recognition and awards than their female contemporaries, including the awarding of the Nobel Prize. Interestingly, in 1903, the Royal Swedish Academy was initially going to award the Nobel Prize in Physics to Pierre Curie and Henri Becquerel. However, after intervention from an advocate for woman scientists, Marie Curie's name was added to the nomination, thereby making her the first woman to be awarded a Nobel Prize.[21] Further, the Stanford neurobiologist, Ben Barres, who transitioned to male from female and was the first openly transgender scientist in the US National Academy of Sciences, experienced differential bias for each gender.[22]

A concluding afterthought, as intimated in a footnote in Merton's 1988 paper,[8] is that the sentiments of the Matthew Effect were also articulated in the Gospels according to Mark and Luke, with all three writers quoting Jesus who, further, was using a saying from an earlier Jewish proverb, thereby making the Matthew Effect an interesting example of itself.

Rebuttal: L. John Schreiner, Ph.D.

Dr. Baldock and I have clearly approached the proposition from the same background citing the Matthew Effect and acknowledging the ample evidence supporting the premise in the general scientific enterprise. But we differ in how we handle any extension to medical physics. My colleague argues elegantly for the proposition in a primarily academic environment, where it may be difficult to keep up with the literature, and where researchers may be motivated primarily by personal *h*-indices. I accept that there will be some of this in medical physics. However, he does not seem to consider that there may be different circumstances in medical physics and his apologetics for the proposition are based solely on the observations of the academic condition. However, data from the 2015 AAPM Professional Survey Report[23] suggest that not all medical physicists can be assumed to be motivated by academic forces alone. Less than 45% of AAPM members with PhDs have an academic rank and less than 10% of Canadian AAPM members with PhDs consider themselves primarily academic. This may be because the majority of medical physicists are employed in radiation oncology. Also, as I noted in my opening comments, important discoveries in the field have originated from clinical physicists in the hospital. Thus, I will argue again, that some of the root causes for the proposition in general science do not necessarily carry over to medical physics. Furthermore, the case for the proposition will hopefully weaken even further after this short debate as readers, having been made aware of the Matthew Effect, strive to better give credit in the future to all those to whom it is due.

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8.6. The AAPM should significantly revise its current governance structure

Carri K. Glide-Hurst and John P. Gibbons Jr.
Reproduced from *Medical Physics* **44**, 5541–5543 (2017)
(http:// dx.doi.org /10.1002/mp.12456)

OVERVIEW

For the past twenty years, the AAPM has been actively considering ways to reduce the size of its Board of Directors, which now has reached a grand total of 49 members. Reduction in Board size is about to be put to members this Fall as part of a vote to "modernize" AAPM's organizational structure. Some believe that these changes are unnecessary and will do more harm than good, and this is the claim debated in this month's Point/Counterpoint.

Arguing for the Proposition is Carri K. Glide-Hurst, Ph.D. Dr. Glide-Hurst obtained her Ph.D. in Medical Physics from Wayne State University in 2007, focusing on breast ultrasound tomography and utilizing acoustic parameters for breast density evaluation. She then spent 2 years in postdoctoral training in the Department of Radiation Oncology at William Beaumont Hospital, with an emphasis on motion management techniques in lung cancer. She has since been at Henry Ford Health Systems in Detroit, where she currently holds the position of Director of Translational Research. Her primary clinical and research focus includes the implementation of CT and MR simulation into radiation oncology and treatment planning. Dr. Glide-Hurst is the co-chair of AAPM Task Group 284: Magnetic Resonance Imaging – Simulation in Radiotherapy: Considerations for Clinical Implementation, Optimization, and Quality Assurance. Dr. Glide-Hurst has over 35 peer-reviewed publications and about 100 abstracts related to imaging in radiation therapy. She is in her 3rd year of serving on the Board of Directors of the AAPM, and is a current member of the Strategic Planning Committee, three AAPM Working Groups, and serves on the *Medical Physics* Editorial Board.

Arguing against the Proposition is John P Gibbons Jr., Ph.D. Dr. Gibbons obtained his Ph.D. in Physics from the University of Tennessee-Knoxville in 1991 and completed a Post-Doc/Residency in Medical Physics at the University of Minnesota in 1993. He then worked for several years at various hospitals in Columbia, SC before moving to Mary Bird Perkins Cancer Center, Baton Rouge, LA, in 2004 as Chief of Clinical Physics. In 2014, he moved to his current position as Chief Medical Physicist, Ochsner Health System, New Orleans LA. Dr. Gibbons has served on close to 50 AAPM Committees, Task Groups, etc., several as Chairman. From 2009 to 2011, he served as AAPM Secretary and has represented two different Chapters as Board Representative. He was President of the Southeast Chapter from 2001 to 2002, served on the Board of Directors of the American Board of Medical Physics from 2006 to 2011, and is a Fellow of the AAPM and the ACMP.

For the proposition: Carri K. Glide-Hurst, Ph.D.

Opening statement

In 2016, as a result of an ongoing process improvement effort, a membership survey was conducted by an outside consultant, Quantum Governance, LLC, to query our full AAPM members to evaluate key areas of member satisfaction and potential opportunities for improvement. An astounding 2,536 out of 7,475 members responded. Many AAPM services were noted as "extremely valuable", including our vast library of AAPM Reports, Practice Guidelines, and access to professional resources. However, the survey revealed many potential areas of improvement. Notably, rising dues costs and expenses are chief concerns among members; ~26% of members rate their membership value to be less than membership costs. Increased engagement and improved strategic focus of the AAPM were identified as major opportunities for improvement. In fact, 64% of respondents agreed that an area of high strategic importance (score 7.1 out of 10, with 10 being "extremely important") is to "Improve the effectiveness of AAPM Leadership and Governance".

Thus, while it is clear that AAPM members value our organization and its benefits, the current, largely *legacy-based,* governance structure presents several major limitations. The current AAPM Board of Directors (BOD) consists of 49 (!!) members, 38 of which are voting members [21 Chapter-elected, 12 Nationally elected Board-members at Large, and five Executive Committee (EXCOM: Executive Director, Treasurer, Secretary, President, and President-Elect)]. The current BOD is so large that many key BOD tasks are currently outsourced to smaller sub-committees of the Board including the Strategic Planning Committee (SPC, tasked with developing and reviewing AAPM's strategic plan) while the majority of the day-to-day and high-level tasks are performed by EXCOM. This practice of creating ancillary committees is commonly reported with larger Board sizes.[1]

Having too large a BOD:

- *Is expensive*: Two BOD meetings have budgets of $112,500 with additional SPC and EXCOM budgets of $52,000 combined annually. For example, 37 out of 49 Board of Directors Members attended the BOD meeting at the 2017 Spring Clinical Meeting in New Orleans, LA, USA.
- *Results in communication breakdowns*: The need for ancillary committees (i.e., SPC, EXCOM) forms additional layers of communication barriers among chief stakeholders.
- *Makes attendance difficult*: Large board sizes have a "significant and negative effect" on attendance.[2]
- *Encourages "motivation decrement" and lack of individual effort*: Historical evidence suggests that individuals feel less responsibility in large groups,[3] often "hiding in the crowd" as group size increases.[4]
- *Is less effective*: Evidence suggests that corporations with smaller Board sizes outperform those with larger boards.[5]

Importantly, AAPM leaders and members have agreed that the BOD needs restructuring. In 2005, a By-laws amendment to reorganize the BOD went to a membership vote yielding 60% for and 40% against, but narrowly missing the 67% requirement to carry the amendment. To put this

into context: only *64* additional "ayes" out of 1003 votes would have carried the amendment and enabled the BOD restructuring *more than a decade* ago.

Thus, the time is now to revise the legacy-based BOD structure to yield a more cost-effective, integrated, proactive, and productive Board.

Against the proposition: John P. Gibbons Jr., Ph.D.

Opening statement

This Fall, AAPM membership will vote on a proposal to substantially revise our By-Laws. There are a number of changes in the proposal, but the primary difference is a reduction in the size of our Board of Directors by replacing chapter and at-large representatives with the council chairs. However, there are many disadvantages that far outweigh the potential advantages of such a dramatic change in our governance.

First, communication between the Board and the Chapters will almost certainly be reduced. Chapter representatives serve an important purpose of informing chapter membership of Board activities and updating the Board of chapter member concerns. With 21 chapters in the AAPM, this function would be difficult if not impossible to accomplish with the proposed Board structure.

Second, the proposal will reduce the opportunities for members who wish to serve on the Board. Service on the Board allows members to gain a better understanding of the issues facing the AAPM. It may also be beneficial to members professionally if, for example, their employer values service to their professional organization. Having more members on the Board is also beneficial for the AAPM, in that these members often rise to more important roles in the organization. For example, our two most recent Presidents began their service on the Board as representatives from local chapters.

Third, the proposal may effectively limit the type of members who have the ability to serve on the Board. It is already extremely difficult to find members who are willing and able to serve as officers, which requires a significant time commitment. As a result, these positions have traditionally been filled by members with faculty appointments from large, academic institutions. The current Board composition allows members with other degrees and from other areas of practice to participate in our governance. Having diversity in our Board membership should be better for the health of the organization.

Fourth, while proponents may argue that a smaller Board may allow more nimble decision making, it is not clear that that is always optimal for our professional organization. Our current structure allows for our Executive Committee to respond to any emergent issues when necessary, and to report such activities to the Board which meets 2–3 times per year. Most of the decisions made for our organization are better vetted through a larger group with time to consider all the issues involved, rather than a smaller Board which may not adequately represent the interests of all of the membership.

Finally, and perhaps most important is the unknown factor. The AAPM has been very successful and productive for over 50 years, and there have not been any significant problems that can be directly linked to our governance structure. The proposed change is a radical departure from our current operation which may cause problems which we have not yet considered.

Rebuttal: Carri K. Glide-Hurst, Ph.D.

My esteemed opponent has introduced several points against the BOD restructuring, but the overarching theme of all of them is to maintain the *status quo*, as evidenced by his last statement: "*the AAPM has been very successful and productive for over 50 years and there have not been any significant problems that can be directly linked to our governance structure*." Since its inception, the AAPM BOD has increased from 16 to 38 voting members. However, having more members does not equate to a better — and stronger — board composition. While having a larger BOD enables more people to participate in the AAPM, there are no minimum requirements of AAPM service for Board Members, with some current Chapter representatives having no prior history of service to the AAPM. This is likely secondary to Dr. Gibbons' statement that it is "*extremely difficult to find members who are willing and able to serve as officers*." While Board members may rise to "*more important roles in the organization*" in the future, there is a clear benefit of having *current* Board members who have sufficient experience to lead strategic initiatives and manage fiscal responsibilities. Indeed, boards require a "*high degree of specialized knowledge"* including an "*intimate understanding of operations*."[6] This domain knowledge will only come from serving within the organization before becoming a Board member.

There is a pressing need to assemble a strong, representative BOD with curated expertise to lead our national organization of over 8,000 members, much like our sister organizations. Consider that the RSNA, consisting of 54,000 members, has just eight Board members and ASTRO, with over 10,000 members, has only 15 Board members. In reducing the Board size, we must shift our focus toward more strategic recruiting to represent the diversity of the AAPM members serving on the Board. Diverse boards reduce the probability of complacency while producing a larger range of solutions for strategic decisions.[7]

Over the past 10 years, only 31.3 ± 5.0% of full members have participated in annual elections. Regardless of your position, we strongly encourage you to exercise your right to vote thoughtfully on this important initiative.

Rebuttal: John P. Gibbons Jr., Ph.D.

Although Dr. Glide-Hurst makes some good arguments why, in general, Boards should be smaller, many of these do not apply to the AAPM. The AAPM has a significant amount of involvement from its membership, with over 1500 (or an astonishing 25%) of our Full Members serving on at least one of almost 300 AAPM committees. With so many engaged members, a larger board can better represent the many stakeholders in our organization. Let me respond to each of her arguments individually:

1. *Is expensive*: First, the $112,500 figure quoted is overstated. This cost was for two special Board meetings, convened specifically to work on the governance proposal. Second, the $52,000 allocated to the SPC and EXCOM would presumably be moved to the new Board, which would assume the duties of these two committees. Finally, realize that this cost is relatively insignificant — less than 2% of the AAPM annual budget.
2. *Makes attendance difficult*: Actually, in contrast to the generic statement of Ref. [[2]], AAPM Board meetings are remarkably well attended. For example, at the two face-to-face meetings in 2016, 34 of 38 Board members attended each meeting. This fact itself demonstrates the uniqueness of our organization and why generic references to Board size do not necessarily apply to the AAPM.
3. *Encourages "motivation decrement"* and is *"less effective"*. Again, Dr. Glide-Hurst quotes generic references which do not apply to the AAPM. She provides no concrete examples of these effects, such as significant accomplishments which could have been achieved with a smaller Board. In fact, it would be easy to argue the opposite is true: AAPM is known among our sister societies as being extremely productive.

Finally, none of these arguments, even if true, are compelling enough to risk the significant changes within the AAPM governance reorganization proposal. The risks involved are too great to consider making such dramatic changes.

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