POINT/COUNTERPOINT

Gel dosimetry provides the optimal end-to-end quality assurance dosimetry for MR-linacs

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OVERVIEW

Major advances in external beam radiation therapy in the last decade have provided technologies for planning and delivering highly conformal radiation dose distributions made available by refined beam targeting methods, including intensity-modulated radiation therapy using tomotherapy, volumetric-modulated arc therapy and many other auspicious tools for three-dimensional (3D) dose painting. The emergence of magnetic resonance imaging (MRI) systems integrated with linear accelerators (linacs), commonly known as an MR-linacs, has realized MR image-guided radiation therapy (MRgRT) systems. Such progress in technology imposes in turn additional constraints on quality assurance procedures for verifying that the delivered dose to the patient matches the planned dose distribution. In this regard, the advantages of gel dosimetry compared to conventional quality assurance dosimetry systems on MR-linacs are being debated within the medical physics community. While some think that gel dosimetry provides the optimal end-to-end quality assurance dosimetry for MR-linacs, others think that the technology is still technically challenging and not sufficiently developed in radiation oncology centers for wide adoption in clinical routine. This is the topic addressed in this month's Point/Counterpoint debate.

Arguing for the proposition is Clive Baldock, Ph.D. Dr. Baldock received his Ph.D. from King's College, London, with research undertaken in the field of gel dosimetry for improved 3D radiation therapy dosimetry. He subsequently moved to Queensland University of Technology, Brisbane, Australia in 1997 in the Centre for Medical, Health and Environmental Physics. In 2003, he moved to the University of Sydney as the Director of the Institute of Medical Physics and later as Head of the School of Physics. In 2012, he was appointed the Executive Dean of Science at Macquarie University, Sydney. In 2014, he joined the University of Tasmania as Deputy Dean of the Faculty of Science, Engineering and Technology followed in 2016 by his appointment as the Pro Vice-Chancellor for Research 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 Fellowship status by 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 Christian P Karger, Ph.D. Dr. Karger has been affiliated with the German Cancer Research Center (DKFZ) since 1993 and obtained his Ph.D. in Physics from the University of Heidelberg (Germany) in 1996. As a certified medical physicist, he participated in the clinical operation of the GSI heavy ion therapy research project from the very beginning, and since 2004, Dr. Karger has headed a

research group in DKFZ's Dept. of Medical Physics in Radiation Oncology. His research activities focus on ion beam and MR-guided radiotherapy, dosimetry, experimental radiobiology, as well as radiobiological modeling, where he serves as PI of various research projects. In 2007, he became an Associate Professor of Medical Physics at the Medical Faculty at the Heidelberg University. Dr. Karger published more than 100 peer-reviewed papers and acts as a reviewer for many international journals. Dr. Karger co-edited a textbook on medical physics and for more than two decades, has participated in several educational medical physics programs as coordinator and lecturer.

FOR THE PROPOSITION: CLIVE BALDOCK, PH.D

Opening Statement

Complex radiation dose distributions produced by advanced radiation therapies necessitate advanced dosimetry systems to provide the confidence that the delivered dose distribution is consistent with that planned clinically. With the introductions of MR-linacs, MRgRT treatments became feasible, offering evident unique advantages over treatment deliveries using conventional IGRT systems.[1] Such advantages include improved target definition and localization due to the high soft tissue contrast of MR imaging.

The clinical introduction of this novel MR-linac technology poses substantial technical challenges. In this technology, the B_0 magnetic field produces Lorentz forces which act on the secondary electrons arising from photon interactions by altering their path of travel and subsequent dose deposition.[2] Further, low-density regions induce the electron return effect (ERE) resulting in additional variations in the 3D dose distribution. These B_0 field induced effects potentially compromise accurate and precise dosimetry measurements highlighting the need for advanced 3D dosimetry tools.

Conventional quality assurance (QA) procedures in radiation therapy generally rely on point zero-dimensional (0D) and planar dosimeters two-dimensional (2D) to compare the measured dose to the planned dose at a number of points and planes of interest. These QA tools can provide, at best, discrete point measurements in a quasi-3D array.[3] Although 0D, 2D, and quasi-3D §radiation detectors have been evaluated in magnetic fields, a number of studies have exhibited behavioral differences due to the presence of the magnetic field.[4]

Gel dosimetry has been used as an alternative QA dosimetry system due to its ability to measure continuous volumetric dose distributions with high spatial resolution in 3D.[5] The applied radiation field induces physical changes in these 3D dosimetry media which can be imaged in 3D using MRI, x-ray, or optical CT techniques. A number of studies have utilized tissue-equivalent polymer gel dosimeters to map doses delivered by MRgRT.[6,7] Further, by using the on-board MR imaging capability, the gel dosimeter can be irradiated and readout in situ without removal from the MR-linac.[8] The advantage of such 3D measurements is that they enable end-

to-end tests such that the simulation, planning, and delivery process can be verified for each step of the treatment chain.[6]

AGAINST THE PROPOSITION: CHRISTIAN P KARGER, PH.D

Opening Statement

It is commonly agreed that MRgRT requires end-to-end tests to assure geometric and dosimetric accuracy of the treatment. For this, the employed radiation detectors should ideally

1. capture as much information of the dose distribution as possible,
2. be easy and flexible to handle,
3. allow fast and straightforward evaluation, and
4. enable accurate and robust dose measurements.

Dosimetry gels (DGs) undoubtedly fulfill the first condition: the possibility to measure 3D dose distributions with high spatial resolution is considered to be the main reason for the high present interest.

However, conditions 2 to 4 remain problematic. DGs are based on carrier materials (e.g., gelatin or silicone) with embedded active components, such as monomers, leucodyes, or ions, that react upon irradiation.[5] Already the production of DGs is challenging and requires thorough training. Strict protocols have to be followed[9] that require a well-equipped laboratory. Furthermore, some DG media can be inactivated by oxygen or other contaminants, for example, from the container material.[10] For this reason, only a few container materials may be used, which limits dosimeter size and shape, although some progress has been made recently by identifying a DG-compatible 3D printing material.[11] So overall, gel dosimeters are neither easy nor flexible to handle.

Although some DGs are evaluated by x-ray or optical CTs,[5] it seems attractive for MRgRT to perform the evaluation directly on the MR-linac, further raising the interest in polymer gels. Although these DGs can be evaluated directly after irradiation when only geometric parameters are of interest,[12] the radiation-induced polymerization process continues up to ~48 h after irradiation, which prevents dosimetric evaluation immediately after irradiation. Furthermore, MRI is still costly, may have limited access and its complexity requires special training. In addition, MRI evaluation may strongly depend on temperature. Thus, to achieve accurate and reproducible results, the gel temperature has to be strictly controlled during MRI, for example, by a water-flow phantom.[13] Further problems arise from the long acquisition times to achieve high spatial resolution and signal-to-noise ratios. Therefore, DG evaluation is neither fast nor straightforward.

Finally, as DGs are chemical dosimeters, thorough calibration against a dose standard is required for each batch. For accurate and reproducible results, measurement and calibration containers have to run through the same temperature history but even in this case, the obtained accuracy is less than

that of ionization chambers. Only with additional renormalization of the calibration curve to independently measured or calculated doses, an accuracy at the 1% level is achievable.[14] For end-to-end tests dealing with intrafractional motion, however, this renormalization may be limited by the reproducibility of the experimental setup or by the necessity of performing an arithmetical dose accumulation. Thus, DGs require high efforts to achieve accurate and robust results.

Gel dosimetry can certainly be used for end-to-end tests in adaptive MRgRT and admittedly, promising results have been obtained.[15] However, whether gel dosimetry is the *optimal tool* for this as claimed by the proposition will depend on the responsible medical physicist who will strongly deny this question, if gel dosimetry is not established at his/her institution.

REBUTTAL: CLIVE BALDOCK, PH.D

With studies indicating that up to 20%–30% of institutions participating in credentialing activities failed to deliver treatments that matched their own treatment plans, the need for improved 3D clinical dosimetry and inadequacy of conventional dosimeters has been clearly demonstrated.[3] Further, with MR-IGRT treatments, where the magnetic field is expected to change the delivered dose distribution in a complicated fashion over the irradiated volume, the need for a more thorough means of measuring the dose in 3D is apparent.[3]

Since Gore's seminal gel dosimetry paper,[16] much has been published advancing the field to the point where the capability of 3D gel dosimetry to answer challenging 3D clinical dosimetry questions[5] has been clinically demonstrated.

A number of reasons are often given for the lack of introduction of gel dosimetry into the clinic and these limitations have been highlighted by Dr Karger in his opening statement including in the manufacture, irradiation, and evaluation of the gel dosimeters.

Although the manufacture of gel dosimeters requires specialized facilities, gel dosimeters have been made commercially available. Further, commercially available optical CT scanners enable the evaluation of gel dosimeters in a not too dissimilar fashion to that of the evaluation of TLDs in the clinic. Radiation oncology physicists and dosimetrists currently undergo training as part of their accreditation. Adding gel dosimetry to such advanced training is both possible and achievable.

An advantage of the MR-linac is that irradiation and readout imaging without removing the gel dosimeter from the MR-linac can be achieved[17] in end-to-end evaluation of online adaptive treatment procedures.[15] For polymer gel dosimeters specifically, it has been shown that with the newly developed dosimeter formulations with much shorter time constant of the chemical reactions (~80 s) potentially overcomes the limitations of post-irradiation polymerization and temperature and temporal instability. Further, MRI pulse sequence developments enable fast imaging of the dosimeters with clinically appropriate accuracy, precision, and dose resolution.[18]

Although 3D gel dosimetry will not likely replace 0D and 2D dosimeters for non 3D applications, there are clear advantages in using 3D gel dosimeters when measuring combined spatial and temporal dose delivery for evaluating complex clinical dose distributions as part of the entire radiation therapy treatment process. As the use of MR-linacs becomes more widespread, and with recent developments in new gel formulations and evaluation techniques, gel dosimetry has every possibility of becoming the dosimeter of choice for end-to-end QA dosimetry.

REBUTTAL: CHRISTIAN P KARGER, PH.D

While I fully agree on the necessity of 3D dose validation in MRgRT and on the potential of dosimetry gels, I doubt that this method is sufficiently mature with respect to accuracy, robustness, and practicability.

Indeed comparable results have been obtained for film and polymer gel measurements;[7] however, gel-based dose distributions are still normalized and thus dependent on planning. Obviously, gel evaluation directly after irradiation at the MR-linac would present the optimal scenario being time-efficient and avoiding uncertainties from phantom repositioning in separate evaluation devices. In a recent comparison of different 3D dosimeters and evaluation techniques,[8] however, only the iron(II) oxide-based radiochromic gel was evaluated directly after irradiation and optical rather than MRI-readout was performed for accuracy reasons. While this gel type is susceptible to diffusion-related uncertainties,[5] polymer gels need time for stabilization and in this study,[8] a 3 T MRI was used for readout. While this improves the signal-to-noise ratio, MR-linacs employ lower field strengths down to 0.35 T.[19] Also the available sequences at MR-linacs may lag behind the possibilities of diagnostic MRI systems. The feasibility of evaluating polymer gels directly after irradiation in terms of absolute dose remains to be shown and up to now, this has only be demonstrated for geometric parameters.[12] Besides this, gel production, its temperature dependence and chemical reactivity compromises robustness and thus practicability of gel dosimetry in clinical practice.

Regarding the proposition, gel dosimetry may definitely be employed for end-to-end QA dosimetry in MRgRT and acquiring full 3D dose distributions opens up new opportunities for treatment validation. However, the above issues suggest that gel dosimetry is a tool for specialists with access to chemical laboratories and knowledge in MRI. Simplified gel production and evaluation protocols combined with an increased robustness would surely lead to wider application of gel dosimetry — not only in MRgRT.

CONFLICT OF INTEREST

Dr. Clive Baldock and Dr. Christian P Karger have no relevant conflict of interest.

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