Image-guided prostate brachytherapy should be MRI-based

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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.\textsuperscript{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.\textsuperscript{2}

Current consensus recommendations for low dose rate (LDR)\textsuperscript{3,4} and high dose rate (HDR)\textsuperscript{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.\textsuperscript{6} Postimplant dosimetry improvement strategies incorporating MRI have been actively encouraged.\textsuperscript{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.\textsuperscript{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\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 vesicle 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.

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