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Clinical use of magnetic resonance imaging across the prostate brachytherapy workflow

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ABSTRACT MRI produces better soft tissue contrast than does ultrasonography or computed tomography for visualizing male pelvic anatomy and prostate cancer. Better visualization of the tumor and organs at risk could allow better conformation of the dose to the target volumes while at the same time minimizing the dose to critical structures and the associated toxicity. Although the use of MRI for prostate brachytherapy would theoretically result in an improved therapeutic ratio, its implementation been slow, mostly because of technical challenges. In this review, we describe the potential role of MRI at different steps in the treatment workflow for prostate brachytherapy: for patient selection, treatment planning, in the operating room, or for postimplant assessment. We further present the current clinical experience with MRI-guided prostate brachytherapy, both for permanent seed implantation and high−dose-rate brachytherapy.

Keywords: Prostate cancer; Brachytherapy; Low-dose rate; High-dose rate; MRI

Introduction

The improved soft tissue contrast with MRI relative to ultrasonography (US) and computed tomography (CT) has prompted the prostate cancer brachytherapy community to explore the potential benefits of using MRI in the management of prostate cancer. Postimplant dosimetry seems to be more accurate when evaluated with MRI vs. CT/transrectal ultrasonography (TRUS) for low−dose-rate (LDR) brachytherapy (1−3). These findings have prompted the American Brachytherapy Society to include in its 2012 guidelines the use of MRI for disease staging or treatment planning in ''clinically relevant circumstances'' by ''experienced teams'' and to encourage the use of MRI−CT image fusion for postimplant dosimetry to improve the reproducibility of contouring and the reliability of dosimetry (4). Using MRI for postimplant assessment allows organs at risk to be identified that cannot be seen on CT (e.g., the external urinary sphincter) that have been linked with increased toxicity when they receive excessive doses (5). If this enhanced accuracy could be implemented earlier during the treatment process, namely at the time of treatment planning and seed implantation for LDR or during the high−dose-rate (HDR) planning procedure in the operating room, that might translate into improved outcomes. The aim of this article was to describe the potential benefits of using MRI before, during, and after LDR or HDR prostate brachytherapy and to describe the clinical workflows currently in place or under evaluation at selected institutions.

Methods

Literature search

From a Pubmed search with the equation ''(MRI or ''magnetic resonance'') AND brachytherapy AND

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prostate," we retrieved 425 references, of which 57 were analyzed and 23 were eventually selected for consideration (see Supplementary Figure 1). These 23 reports included 12 clinical reports on LDR brachytherapy (including seven from a Dana–Farber study) (6–17) and 11 clinical reports on HDR (18–28). The 34 excluded reports consisted of 11 reports on contouring/registration, 12 planning studies, and 11 studies on postplanning dosimetry. We focused on the clinical reports that describe and analyze the clinical workflow used to implement MRI in routine practice as the aim of our review was to discuss potential clinical benefits of MRI-guided brachytherapy and to provide guidance regarding its implementation.

Clinical data

Clinical data from the MD Anderson cohort come from a prospectively maintained institutional database of all patients treated with prostate brachytherapy and a group from a prospective Phase 2 study of patients with intermediate-risk prostate cancer treated with brachytherapy as monotherapy.

Results

Use of MRI before brachytherapy: its role in disease staging

The usefulness of MRI in terms of its improved capability for tumor staging is of paramount importance and really is the first step to integrate MRI into the routine care of patients who underwent prostate brachytherapy. The European Association of Urology 2015 prostate cancer guidelines state that multiparametric (mp) MRI is indicated for standard initial disease staging for men with high-risk localized or high-risk locally advanced prostate cancer and for some men with low-risk disease who are candidates for brachytherapy (29). mpMRI is defined as the use of two different MRI sequences during the same examination, namely a T2-weighted sequence with a diffusion-weighted, a dynamic contrast-enhanced, or an H1-spectroscopy sequence. MRI facilitates visualization of intraprostatic primary tumors and rules out macroscopic posterolateral extracapsular extension (ECE) or seminal vesicle invasion. However, a meta-analysis has demonstrated that the sensitivity of mpMRI for detecting ECE remains low at around 0.6 because it cannot detect microscopic ECE (30). The sensitivity increases with the radius of ECE extension within the periprostatic fat (31). In another study, MRI scans showing no evidence of ECE in patients with T1c or T2a disease had a negative predictive value of 91% for ruling out ECE and 97% for ruling out ECE >3 mm (32). Patients with gross ECE visible on MRI are usually not candidates for LDR brachytherapy as monotherapy. The use of the Prostate Imaging Reporting and Data System scoring system is encouraged to reduce inter-reader variability and standardize MRI interpretation (33). MRI can also be used to evaluate the risk of pubic arch interference, measure prostate volume, rule out a prominent median lobe, or detect anteriorly located tumors that would require a specific implantation technique for appropriate tumor coverage (34). Although the frequency of anterior tumors has not been clearly established, it is probably underestimated; indeed, a large series from the Princess Margaret Hospital of 1112 men with prostate cancer suggested that up to 20% could have anterior tumors (35).

Use of MRI during LDR prostate brachytherapy

The initial experience with using MRI during LDR prostate brachytherapy was reported by the Dana–Farber Cancer Institute team, who from 1997 through 2007 has treated 318 men with cT1c, prostate-specific antigen (PSA) $<$ 15 ng/mL, and Gleason score 3 + 4 or less prostate cancer using an intraoperative real-time MRI-guided brachytherapy technique in which only the peripheral zone is targeted (11). The implantation took place using a peripheral loading technique and involved iodine-125 sources, an MR-compatible perineal template and catheters, and an intraoperative 0.5-T MRI scanner. Long-term biochemical control results were disappointing for patients with favorable intermediate disease (36, 37), with rates of 73.0% at 5 years and 66.4% at 8 years (12). The reasons for these results are unknown but could be related to patient selection, focal treatment of only the peripheral zone, or the reliability of the technical process used. Also, whether the quality of the coverage was evaluated with postimplant MRI-based dosimetry is unclear. However, this clinical trial paved the way for future research using advanced imaging techniques in prostate brachytherapy.

In addition to reports from the Dana–Farber Cancer Institute (11–17), we also evaluated five other reports, two on focal salvage brachytherapy (7, 8), two on MRI spectroscopy (9, 10), and one a preliminary report of the MD Anderson experience (6). The major drawback of these studies is that although they used MRI at the treatment-planning stage and three of them (7–9) involved adequate fusion with TRUS during the implantation, none seem to have confirmed the quality of the implant on MR images. Therefore, these reports cannot confirm that the seeds were actually implanted where they should have been and the clinical results cannot be fully attributed to the use of MRI guidance.

The treatment paradigm at MD Anderson is described subsequently and in Box 1. At 2–4 weeks before implantation, patients undergo diagnostic MRI, during which an endorectal coil is inserted and a planning MR image obtained for treatment simulation. For patients who have not undergone diagnostic MRI before their brachytherapy consultation, only one pretreatment MR image is obtained and used for both planning and diagnostic purposes. The prostate and organs at risk are delineated on the T2 3D sequence, including the