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MRI-based sector analysis enhances prostate palladium-103 brachytherapy quality assurance in a phase II prospective trial of men with intermediate-risk localized prostate cancer

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ABSTRACT

PURPOSE: Palladium-103 (^{103}Pd) may be superior to other isotopes in brachytherapy for localized intermediate-risk prostate cancer because of its relatively short half-life, higher initial dose rate, and greater dose heterogeneity within the target volume; these properties also underscore the need for accurate target delineation and postimplant quality assurance. We assessed the use of prostate sector analysis based on MRI for quality assurance after ^{103}Pd monotherapy.

METHODS AND MATERIALS: Fifty men with intermediate-risk prostate cancer underwent ^{103}Pd monotherapy in a prospective phase II trial at MD Anderson Cancer Center. Dosimetric analyses on day 30 after the implant were done using both CT and fused CT/MRI scans. Dosimetric variables were assessed for the entire prostate and for each of three or six sectors. Volumes and dosimetric variables were compared with paired *t* tests.

RESULTS: Postimplant dosimetric variables for the entire prostate were significantly different on CT vs. CT/MRI ($p = 0.019$ for V_{100} and $p < 0.01$ for D_{90}). Prostate volumes were smaller on the CT/MRI scans ($p < 0.00001$). The base sector contributed the greatest difference, with doses based on CT/MRI lower than those based on CT ($p < 0.01$ for V_{100} and D_{90}). To date, these lower base doses have not affected biochemical outcomes for patients with disease in prostate base biopsy samples.

CONCLUSIONS: CT/MRI is more precise than CT for prostate volume delineation and dosimetric quality assessment and thus provides superior heterogeneity control assessment after ^{103}Pd monotherapy implants.

Keywords: Brachytherapy; Prostate cancer; Sector analysis; Palladium

Introduction

Intermediate-risk prostate cancer is defined by the National Comprehensive Cancer Network as that with a Gleason score (GS) of 7, a prostate-specific antigen (PSA) level of 10–20 ng/mL, or clinical T2b–T2c disease (www.nccn.org). Although radical prostatectomy and external-beam radiation therapy with short-course hormone therapy have been the mainstay of treatment for men with intermediate-risk disease, transrectal ultrasound–guided brachytherapy has also been used in combination with external-beam radiation therapy (1, 2) and is currently being investigated as monotherapy (3–5). Iodine-125 (^{125}I), the most commonly used radioisotope for prostate brachytherapy, has a half-life of 59.4 days and a relatively low dose rate of 7–10 cGy/h. Palladium-103 (^{103}Pd), introduced in 1986 as an alternative radioisotope for permanent interstitial therapy, emits low-energy photons similar to ^{125}I (average energy of 28.5 KeV for ^{125}I and 20.8 KeV for ^{103}Pd). However, ^{103}Pd may have advantages over ^{125}I and other isotopes because of its shorter half-life (17 days),

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higher initial dose rate (20–24 cGy/h), and increased dose heterogeneity within the target volume. A ^{103}Pd implant delivers 90% of its dose in 56 days as opposed to 197 days for ^{125}I. Notably, investigators in Seattle have published excellent biochemical and clinical outcomes in a series of 233 men with low-, intermediate-, or high-risk prostate cancer treated exclusively with ^{103}Pd (6). Excellent outcomes with ^{103}Pd have been reproduced and reported from several other high-quality centers as well (7, 8).

The shorter half-life, higher initial dose rate, and improved dose heterogeneity of ^{103}Pd underscore the need for accurate target delineation and postimplant quality assurance. The postimplant quality assurance process is essential both for assessing the quality of the implant and for evaluating subsequent toxicity and long-term outcomes to allow continued feedback and improvement in the treatment planning process. Currently, postimplant dosimetry and quality assessment are based on CT scans obtained after treatment (9). However, CT-based imaging is suboptimal for visualizing the anatomic boundaries at the prostate base and apex relative to MRI (10). The quality of CT-based dosimetry is also compromised by imaging artifacts introduced by the implanted seeds. Because seeds appear as negative signal voids on MRI, CT/MRI fusion is considered the superior imaging choice for postimplant dosimetry (9).

Quantification of the dose delivered to the prostate can be estimated by isodose line analysis or by sector analysis (11). Sector analysis allows for evaluation of the entire prostate and its three component sectors, the apex, midgland, and base. These sectors can be further subdivided into right and left subsectors, thus dividing the prostate into the six regions often used to delineate the location of prostate biopsies. Unlike isodose line analysis, sector analysis allows the collection and comparison of data to be standardized across patients. This in turn allows disease burden (as assessed by biopsy) and dose distribution to be analyzed collectively and allows physicians and brachytherapists to ensure adequate dose delivery to all sectors of the prostate, especially to areas with the highest tumor burden. Use of sector analysis in postimplant dosimetry enhances quality assurance because the dose to the predefined sectors can be evaluated and compared with disease coverage, as indicated by pathologic and imaging findings, and with long-term toxicity and clinical outcomes.

Given the unique physical properties of ^{103}Pd relative to ^{125}I, we used sector analysis to evaluate prostate dosimetry for a group of men treated with ^{103}Pd as part of a phase II prospective clinical trial investigating the use of interstitial brachytherapy as monotherapy for intermediate-risk prostate cancer (12). Specifically, the purpose of this study is to compare and correlate dosimetric variables derived from CT scans and CT/MRI fusion scans with disease outcomes and evaluate the role of CT/MRI fusion–based sector analysis for quality assurance after ^{103}Pd monotherapy.

Methods and materials

Patient characteristics

This analysis was approved by the appropriate institutional review board at MD Anderson Cancer Center. We identified 50 patients who received ^{103}Pd brachytherapy as monotherapy for intermediate-risk prostate cancer in a prospective phase II trial at The University of Texas MD Anderson Cancer Center from 2009 to 2011. For this particular analysis, patients were required to have histologically confirmed adenocarcinoma of the prostate, with a GS of 7 and PSA level of less than 10 ng/mL, or a GS of 6 and a PSA level of 10–15 ng/mL. Patients with clinical T2b cancer were eligible, and all patients underwent MRI to confirm the absence of gross extracapsular disease. Clinical disease staging involved a complete history and physical examination, including digital rectal examination.

Treatment responses and toxicity were also assessed in all patients by interval history and physical examinations, including digital rectal examination, a prospective patient-reported quality of life survey (the Expanded Prostate Index Composite questionnaire), and PSA measurements every 4 months for the first year after the implant and every 6 months during years 2–5. Treatment failure was defined as pathologic, radiographic, or biochemical evidence of disease (PSA $>$ nadir $+$ 2 ng/mL) during routine followup.

Treatment planning

Treatment planning was performed as described elsewhere (12). Briefly, patients were evaluated for suitability for an interstitial implant by transrectal ultrasonography to determine prostate volume and CT to rule out pubic arch interference. If brachytherapy was being considered, the ultrasound images were subsequently transferred to the VariSeed treatment planning system (Varian Medical Systems, Palo Alto, CA), with which the prostate, urethra, rectum, bladder, and seminal vesicles were contoured. Implants were then planned by using a modified peripheral loading technique with stranded ^{103}Pd seeds to reduce the dose delivered to the urethra. The prescribed dose was 125 Gy to the planning target volume, which included the gland plus a 3-mm margin except for posteriorly, where no margin was used beyond the gland to minimize rectal dose. Customized treatment plans were created with seed number, and loading patterns optimized to meet the following dosimetric parameters: V_{100} (the prostate volume receiving 100% of the prescribed dose) was to be $>$95%; V_{150} (the prostate volume receiving at least 150% of the prescribed dose), $<$75%; and the V_{200} (the prostate volume receiving 200% of the prescribed dose), $<$40%. No portion (0%) of the urethra was to receive 200% of the prescribed dose, and the rectal volume receiving 100% of the prescribed dose was to be $<$1 cm^3.