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A comparative dosimetric analysis of virtual stereotactic body radiotherapy to high-dose-rate monotherapy for intermediate-risk prostate cancer

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ABSTRACT

PURPOSE: Stereotactic body radiotherapy (SBRT) is being used with increasing frequency as definitive treatment of early stage prostate cancer. Much of the justification for its adoption was derived from earlier clinical results using high-dose-rate (HDR) brachytherapy. We determine whether HDR's dosimetry can be achieved by virtual SBRT.

METHODS AND MATERIALS: Patients with intermediate-risk prostate cancer on a prospective trial evaluating the efficacy of HDR monotherapy treated to dose of 9.5 Gy × 4 fractions were used for this study. A total of 5 patients were used in this analysis. Virtual SBRT plans were developed to reproduce the planning target volume (PTV) HDR dose distributions. Both *normal tissue−* and *PTV-prioritized* plans were generated.

RESULTS: From the normal tissue−prioritized plan, HDR and virtual SBRT achieved similar PTV V_{100} (93.8% vs. 93.1%, $p = 0.20$) and V_{150} (40.3% vs. 42.9%, $p = 0.69$) coverage. However, the PTV V_{200} was not attainable with SBRT (15.2% vs. 0.0%, $p < 0.001$). The rectal D_{max} was significantly lower with HDR (94.2% vs. 99.42%, $p = 0.05$). The rectal $D_{2\ cc}$ was also lower (60.8% vs. 71.1%, $p = 0.07$). Difference in $D_{1\ cc}$ urethral dose was not significantly different (87.7% vs. 75.2%, $p = 0.33$). Comparing the PTV-prioritized plans, the rectal D_{max} (94.2% vs. 111.1%, $p = 0.05$) and mean dose (27.1% vs. 33.3%, $p = 0.03$) were significantly higher using SBRT, and the rectal $D_{2\ cc}$ was higher using SBRT (60.8% vs. 81.8%, $p = 0.07$).

CONCLUSIONS: HDR achieves significantly higher intraprostatic doses while achieving a lower maximum rectal dose compared with our virtual SBRT treatment planning. Future studies should compare clinical outcomes and toxicity between these modalities.

Keywords: Prostate cancer; Brachytherapy; High-dose rate; Stereotactic body radiotherapy; Dosimetry

Introduction

Interstitial brachytherapy has been a standard treatment for localized prostate cancer for decades. It was not until the 1980s, owing to the advances in ultrasound technology, that brachytherapy became a common treatment for prostate cancer. In 2000, Yoshioka *et al.* (1) first reported the favorable results of high-dose-rate (HDR) brachytherapy as monotherapy for various risk groups of localized prostate cancer. Subsequently, five prospective Phase I/II trials of HDR monotherapy with promising results have been published (1−6).

Parallel advances in brachytherapy, CT-based imaging target localization, and linear accelerators (LINACs) have

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led to increased implementation of what was initially termed ''virtual HDR,'' now better known as stereotactic body radiotherapy (SBRT) (7). As the name implies, much of the justification for changes in standard external beam radiation therapy (EBRT) dose and fractionation (usually ≥35 fractions for prostate cancer) to fewer and higher doses administered as SBRT was derived from the HDR literature (8). Hypofractionated EBRT treatments have been proposed since the 1960s; however, it was not until contemporary advancements in technology that these treatments have been allowed to be safely performed (9, 10).

The radiobiologic rationale for the usage of high dose-per-fraction treatments relies on the low α/β ratio of prostate cancer (11–13). The techniques and dosimetry of SBRT and HDR differ greatly, which may impact their relative radiobiological effect. Fuller *et al.* (7) attempted to address these differences using CyberKnife (Accuray, Inc., Sunnyvale, CA) as the SBRT treatment delivery modality to compare with HDR. The comparison performed suggested that simulated HDR treatments may be able to mimic the dose distribution of SBRT. However, the converse has not been investigated, as this study did not answer the question of whether SBRT can replicate HDR. Furthermore, a simulated HDR plan in the absence of interstitial catheter implantation cannot legitimately be used as the standard because catheter placement alters the planned anatomy. If the hypothesis that SBRT can reproduce HDR is to be accurately tested, it requires comparison with actual HDR treatments to be valid. We present here a dosimetric analysis comparing virtual SBRT with actual HDR monotherapy plans from treated patients.

Methods and materials

Between August 2010 and December 2011, 20 consecutive patients were enrolled in our institutional HDR monotherapy prospective trial (NCT00573833). Enrollment eligibility for the study mandated the patients to be of intermediate risk according to the current National Comprehensive Center Network (NCCN) prognostic risk groupings (www.nccn.org) (14). Five of the 20 patients had CT scans that were suitable for entry into this study. All patients had histologic confirmation of prostate cancer from a transrectal biopsy confirmed by an expert urologic pathologist. Pretreatment diagnostic evaluations at our institution has been previously described (15).

Patients were treated with HDR ^{192}Ir temporary interstitial brachytherapy as previously described by Yamada *et al.* (16), with a dose of 9.5 Gy × 4 fractions as monotherapy. Implantation was performed under general anesthesia using transrectal ultrasound guidance and a transperineal approach. Treatment delivery was performed using flexible plastic catheters (FlexiGuide needles; Mick Radio-Nuclear Instruments, Inc., Mount Vernon, NY), held in place by a template locked and sutured to the perineum. An intraoperative CT scan using an O-arm scanner (Medtronic Inc, Minneapolis, MN) was performed for treatment planning purposes after application of bladder and rectal contrast.

Contours were designed and catheter positions were identified using BrachyVision (Varian Medical Systems, Inc., Palo Alto, CA). The organ at risk (OAR) were defined as follows; the rectum and bladder were contoured at the levels of the planning target volume (PTV), and the urethra was defined by the Foley catheter (16–18 French).

Optimization was performed to determine the dwell positions and dwell times required to achieve a dose of 9.5 Gy per fraction to the entire prostate for a total dose of 38 Gy in four fractions. In accordance with our institutional guidelines and the recommendations of the American Brachytherapy Society, dose parameters used in this optimization included a maximum urethra dose (D_{max} urethra) of 130%, with an institutional preferred constraint goal of 120%, a maximum rectal dose (D_{max} rectal) of 100% of the prescribed dose, dose to 2 cc of rectum (rectal $D_{2\ cc}$) less than 70%, and dose to 2 cc of bladder (bladder $D_{2\ cc}$) less than 75% (17). Additionally, at least 90% prescription dose coverage of the target volume was required. The patients received a total of four fractions, two the same day of the implant and two the following day.

Subsequently, using BrachyVision and our in-house treatment planning software, the intraoperative CT scan was fused to the preimplant CT scan. Isodose lines generated from the planning software were created for the prostate V_{100}, V_{150}, and V_{200} generated from the HDR plan. With the isodose lines displayed, using in-house software we were able to manually contour on the preimplant scan to ''trace'' the isodose distributions and convert them into target volumes. The isodose line for V_{100} for example became the PTV_{100} and encompassed the prostate. A second physician confirmed their accuracy. As prostate volumes were similar but not identical from the preimplant and intraoperative CT scans, manual adjustments were performed to ensure anatomic appropriateness of the new target volumes, so the PTV_{100}, PTV_{150}, and PTV_{200} respected the prostate gland and OAR contours. The OARs including the rectum, bladder, and urethra were recontoured on the preimplant CT scan. Using the PTV_{100}, PTV_{150}, and PTV_{200} volumes and OAR, an optimized SBRT plan was generated. To compare HDR dosimetry to ''virtual SBRT'' plans, two approaches were used. The first approach, referred to as the *normal tissue–prioritized* plan, was designed to maintain institutional OAR constraints while attempting to maximize target coverage. The second approach referred to as the *PTV-prioritized* plan required matching HDR target coverage and allowed OARs to exceed institutional constraints with optimization to limit dose to these structures as much as possible.

Statistical analysis performed using simple two-sided *t* tests with *p* values of 0.05 or lower was considered statistically significant. Statistical analysis was performed using SPSS version 19 (SPSS, Inc., Chicago, IL).