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BRACHYTHERAPY

Brachytherapy 13 (2014) 433–441

Ultrasound-planned high-dose-rate prostate brachytherapy: Dose painting to the dominant intraprostatic lesion

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ABSTRACT

PURPOSE: To demonstrate the feasibility of using high-dose-rate (HDR) brachytherapy to deliver 125% of the prescription dose to the dominant intraprostatic lesion (DIL) as defined on multiparametric MRI while respecting critical organ dose constraints.

METHODS AND MATERIALS: Twenty-six patients with biopsy-proven predominantly unilateral prostate cancer consented to a university ethics–approved Phase 2 study of selective dose escalation. Combined information from endorectal T2 MRI sequences, dynamic contrast enhancement, and apparent diffusion coefficient maps was used to contour the DIL and prostate. Images were fused to intraoperative transrectal ultrasound for transposition of the DIL. Treatment consisted of two fractions of 10 Gy HDR brachytherapy to the entire prostate with 12.5 Gy to the DIL, combined with 46 Gy in 23 fractions of external beam radiotherapy.

RESULTS: All patients had intermediate- or high-risk disease; 25 of 26 had a visible DIL (mean volume, 2.9 cm^3; SD, 1.8). Mean percentage of prostate receiving prescription dose (V_{100}) was 98.1% (SD, 1.2). Mean dose to 90% of the DIL was 13.4 Gy (SD, 1.0). The coverage of the DIL was excellent with a mean of 95.7% (SD, 5.0) receiving the planned escalation of 25%. Established dose constraints to rectum and urethra were respected in all cases; where DIL coverage was limited by proximity to urethra or rectum, a mean dose to 90% of the DIL of 12.3 Gy was achieved.

CONCLUSIONS: Modest dose escalation to the DIL (25–30%) using ultrasound-planned HDR brachytherapy is feasible for selected intermediate- and high-risk patients while respecting critical organ constraints and is achievable within the practice setting of a community cancer center.

Keywords: Prostatic neoplasms; High-dose-rate brachytherapy; US planning; Multiparametric MRI; Dose painting

Introduction

There is ample evidence from multiple mature randomized trials that higher radiation doses are required to optimize local control and improve biochemical disease-free survival in men with localized prostate cancer (1–5). Although dose escalation has yet to show increased overall survival, the reduction in positive postradiotherapy biopsies is associated with improved cause-specific survival and distant metastasis-free survival (6, 7). Higher radiation doses require specialized techniques to avoid unacceptable toxicity.

High-dose-rate (HDR) brachytherapy has been shown to deliver a highly conformal radiation dose to the target safely and accurately using a stepping source of high activity ^{192}Ir. Hollow source-carrier needles (or catheters) are inserted in a defined pattern using transrectal ultrasound (TRUS) guidance under spinal or general anesthesia. By varying the source dwell times along the needles, isodoses can be elegantly contoured to avoid normal structures, cover the target with precision, and even maximize dose delivery to subvolumes of tumor infiltration within the prostate.

Local failures after external beam radiotherapy (EBRT) are frequently at the site of the original dominant lesion (8, 9).

Received 21 November 2013; received in revised form 7 March 2014; accepted 1 May 2014.

Financial disclosures: none.

Funding: British Columbia Cancer Agency Operating Grant.

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1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2014.05.006

Partial prostate dose escalation can potentially involve much higher doses than are possible for the whole prostate. The concept of dose painting was introduced by Ling *et al.* (10) in 2000 and requires advanced imaging techniques to identify the target (11, 12). Multiparametric MRI combines information from standard T1- and T2-weighted imaging with diffusion-weighted imaging to reflect cell density and dynamic contrast–enhancement (DCE) to image permeability of the microvasculature and blood flow (13, 14). When diffusion-weighted imaging is combined with DCE to image cancer within the prostate before radical prostatectomy, pathologic verification has shown excellent specificity. Identification of the dominant intraprostatic lesion (DIL) using DCE-MRI has been used for intensity-modulated radiation therapy planning (15) and other external radiotherapy techniques, such as helical tomotherapy (16, 17).

Magnetic resonance (MR) spectroscopy is also part of the multiparametric armamentarium and can be very useful in identifying regions of high-grade prostate cancer, especially in patients with elevated prostate-specific antigen (PSA) and negative TRUS-guided biopsies (18–21). However, the typical 7 mm-per-side voxel size lacks the geometric precision required for dose painting. Unless choline+citrate/citrate ratios are markedly elevated, a lesion volume of 15–20 voxels is required to predict high-grade cancer with an 80% probability of success (22). However, identifying unknown sites of tumor was not an end point of this study. For all subjects, imaging was confirmatory of known disease demonstrated in the transrectal biopsies performed before study entry.

We investigated the feasibility of visualization of the DIL on MRI, transposition of the DIL to TRUS intraoperatively, and subsequent dose escalation to deliver a 25% higher-than-prescription dose with HDR brachytherapy. In this trial, the shape and location of the 125% isodose was specifically controlled to cover the DIL region rather than having it randomly placed in the prostate gland. Target and critical organ dose parameters were compared with a prior cohort of 25 patients treated to standard dose (10 Gy fraction with no dose painting). Normal tissue dose constraints had priority in the planning algorithm. Patients who did not have a clearly identifiable DIL were treated with standard HDR planning.

Methods and materials

Eligibility criteria

Men with histologically confirmed prostatic adenocarcinoma were eligible if they had intermediate- or high-risk prostate cancer according to National Comprehensive Cancer Network criteria, with unilateral disease as indicated by either a histologically confirmed palpable nodule or a cluster of positive biopsies from a single region that would suggest the presence of dominant focus. Patients had to be medically suitable for general anesthetic, with an estimated life expectancy of at least 10 years, an Eastern Cooperative Oncology Group performance status of 0, and no contraindications to interstitial prostate brachytherapy or to MRI. Patients on anticoagulants had to be able to discontinue them safely for at least 7 days. Written informed consent was obtained from all patients according to local institutional review board requirements. All investigations required before study entry were standard for this grade and presentation of prostate cancer with the exception of multiparametric endorectal MRI. The workflow for imaging and treatment is shown in Table 1.

Imaging protocol

MRI was performed using a 1.5-T GE Signa MRI HD 8Channel Body MRI Scanner (GE Health Care, Waukesha, WI) with the patient supine. For each examination, an endorectal coil (HD eCoil Imaging System; Medrad Inc., Warrendale, PA) was inserted by the physician (J.C.) and the balloon inflated with 40–50 mL of air to provide adequate contact with the rectal wall without deforming the prostate. Peristalsis was suppressed by an intramuscular injection of 1 mL of buscopan. Localizing images were acquired to confirm coil positioning. If deformation was seen on the initial scout, air was withdrawn. For anatomic information, sequences using T2-weighted fast recovery fast spin echo were acquired in transverse, sagittal, and coronal planes (repetition time/echo time, 3200–5300/104–109 ms; field of view, 18 cm; echo train length, 21–23; 3-mm slice with 0 gap). These were followed by DCE obtaining 20 sequential 6- to 7-s axial scans initiated at the same time as rapid injection (3 mL/s) of gadolinium at a dose of 0.22 mg/kg (Fig. 1). Contrast-enhanced scans used Fast Spoiled Gradient Echo with a 4-mm slice thickness and −2-mm gap. Contouring of the prostate and DIL were performed by protocol physicians (J.C. or F.B.).

Next, a preoperative TRUS assessment was performed in the dorsal lithotomy position in the procedure room using

Table 1
Workflow sequence

1. Consult and eligibility
2. Staging
3. Endorectal MRI and contouring of prostate, urethra, and DIL
4. Pre-op TRUS with aerated gel in urethra and contouring of prostate and urethra
5. Fusion of eMRI and TRUS for transposition of DIL
6. HDR procedure: fusion of intraoperative TRUS with catheters in position to pre-op TRUS
7. Dose optimization
8. Treatment delivery
9. Placement of three fiducials for EBRT planning

DIL = dominant intraprostatic lesion; Pre-op = preoperative; TRUS = transrectal ultrasound; eMRI = endorectal MRI; HDR = high-dose rate; EBRT = external beam radiotherapy.