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Image-guided high-dose-rate brachytherapy boost to the dominant intraprostatic lesion using multiparametric magnetic resonance imaging including spectroscopy: Results of a prospective study

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ABSTRACT

PURPOSE: To evaluate the long-term outcomes of image-guided high-dose-rate (HDR) brachytherapy boost to the dominant intraprostatic lesion (DIL) using multiparametric magnetic resonance imaging (MRI), including spectroscopy (MRI/magnetic resonance spectroscopy [MRS]).

METHODS AND MATERIALS: Between December 2009 and March 2011, 20 patients with intermediate-risk prostate cancer underwent multiparametric MRI/MRS protocol before treatment. All patients were treated with an external beam radiotherapy dose of 40 Gy, combined with an HDR brachytherapy boost of 15 Gy. Concurrently, the DIL received a boost of 18 Gy. Missing data during followup were handled with multiple imputations.

RESULTS: The median followup was 62 months (range, 23−71 months). Six patients (31%) were classified as favorable intermediate risk and 13 patients (69%) as unfavorable intermediate risk. One patient experienced a prostate-specific antigen biochemical failure, and the 5-year biochemical failure-free survival rate was of 94.7%. The mean International Prostate Symptom Score rose from 7, with respect to baseline, to 10.42 1 month after treatment, and rapidly decreased to 6.97 after 3 months. Grade 1, 2, and 3 acute genitourinary toxicities were reported in 13 (68%), 3 (16%), and 1 (5%) patients, respectively. Grade 1 and 2 late genitourinary toxicities were reported in 9 (53%) and 3 (18%) patients, respectively. Only grade 1 acute and late gastrointestinal toxicities were reported in 4 (21%) and 3 (18%) patients, respectively.

CONCLUSIONS: Delivering an HDR brachytherapy boost to the DIL using image-guided multiparametric MRI/MRS is feasible with good outcomes for biochemical control, acute and late toxicities, and dosimetric constraints for critical organs.

Keywords: Prostate cancer; HDR brachytherapy; Dominant intraprostatic lesion; MRI; Spectroscopy

Introduction

Intermediate-risk prostate cancer represents one-third of prostate cancer patients (about 8500 men annually in Canada) and has a high likelihood of cure. Localized therapies, such as radiation therapy, play a pivotal role in the management of prostate cancer. Although a great interest is found in focal therapy of prostate cancer, this type of cancer is often multifocal, and thus, a radiation dose should be given to the entire gland (1).

Historically, radical radiotherapy was aimed at treating the entire gland rather than individual cancer foci. However, delivering high radiation dose to the prostate with external beam radiotherapy (EBRT) is often limited by the increase in toxicity (2, 3). In comparison to EBRT, high-dose-rate (HDR) brachytherapy offers the possibility of targeting more selectively the cancer foci within the

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prostate by sparing surrounding normal tissues, with the potential of offering higher cancer control rates with similar or lesser side effects (4). HDR brachytherapy, alone (5, 6) or in combination with EBRT (7−10), has shown excellent outcomes with an improved tumor control, lower toxicity and an improved quality of life. On the other hand, few studies have evaluated focal targeting of the dominant intraprostatic lesion (DIL). These studies provided the proof of principle of the concept but did not report any longer-term outcomes (11, 12).

In this context, the purpose of this study was to evaluate the long-term outcomes of multiparametric magnetic resonance imaging [MRI]/magnetic resonance spectroscopy [MRS] imaging-guided HDR brachytherapy boost to the DIL, in terms of tumor control, dosimetric coverage, and toxicity.

Methods and materials

Patient eligibility

Between December 2009 and March 2011, 20 patients with intermediate-risk prostate cancer according to the National Comprehensive Cancer Network (NCCN) guidelines (13) and no contraindication for an MRI/MRS prostate examination were enrolled in this prospective image-guided brachytherapy study. The main ineligibility criteria were the previous use of Androgenic Deprivation Therapy (ADT) and the insertion of fiducial gold markers. The study was approved by the Ethical Committee of CHU de Québec−Université Laval, and all patients provided their written informed consent.

MRI/MRS protocol

In total, 20 patients underwent the multiparametric MRI/MRS protocol. All MRI/MRS examinations included T1W, T2W, and spectroscopy acquisitions. Seventeen examinations included a diffusion-weighted imaging sequence with apparent diffusion coefficient mapping. The entire prostate and seminal vesicles were imaged in each patient. A prostate coil (BPX Series disposable endorectal coils-MEDRAD) was used for acquisitions on a GE 1.5 T MR (GE Healthcare, Milwaukee, WI). The reconstructed slice thickness was 3−4 mm, depending on the sequence. The duration of the scan was approximately 25 min. For imaging analysis and tumor localization, each prostate was subdivided into the base, midgland, and apex. Each of these subdivisions was defined as being right or left according to a sagittal midplane line. In each case, six regions of interest, called sextants, were defined (14).

One radiologist reviewed all the MRI studies. MRI standard sequences (T1W and T2W), diffusion-weighted imaging, and MRS were analyzed independently. For each sextant, the reader identified the DIL area, if cancer was found in the regions of interest. The DILs identified in the prostates were of type 3 in 2 cases, type 4 in 7 cases, and type 5 in 11 cases according to the Prostate Imaging−Reporting and Data System (PI-RADS): 2015, version 2 (15).

Treatment

All patients were treated with 40 Gy of EBRT delivered in daily fractions of 2 Gy, 5 days per week. EBRT was followed by a single-fraction HDR brachytherapy boost of 15 Gy to the whole prostate gland within 3 weeks of EBRT. Using inverse planning with simulated annealing (16), the DIL defined on the multiparametric MRI findings was boosted to 18 Gy (120% isodose coverage). In the end, one patient was not eligible because he did not receive a DIL boost at the time of HDR. Data from 19 patients were thus available for analysis.

Followup and outcomes

All patients were followed prospectively. Prostate-specific antigen (PSA) progression and urinary symptoms measured with the International Prostate Symptom Score (IPSS) were evaluated at each patient visit (at 3, 6, 9, and 12 months during the first year, and every 6 months thereafter); the symptoms were categorized as mild (IPSS score 7 or less), moderate (IPSS score between 8 and 19), or severe (IPSS score 20 or more) (17). Biochemical failure-free survival rate was determined according to the Phoenix consensus definitions. The acute and late genitourinary (GU) and gastrointestinal (GI) toxicities were also evaluated at each patient visit and graded according to the Radiation Therapy Oncology Group (RTOG) criteria. Patients were also classified into favorable intermediate risk (FIR) or unfavorable intermediate risk (UIR), as suggested for intermediate-risk prostate cancer (18).

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation (SD) or median (range), while qualitative variables were expressed as numbers and percentages. The Kaplan−Meier method was used to determine the biochemical survival curve. Statistical analysis was performed using SPSS software version 23.0 (IBM Corporation, Armonk, NY). Patients with missing data for late toxicity score were excluded from the analysis, whereas missing data were handled with multiple imputations for IPSS score. The missing data were imputed 20 times and pooled according to Rubin's rules (19).

Results

Patient characteristics

Table 1 summarizes the baseline patient characteristics. The median patient age was 64 years (range, 53−80 years), and the median followup was 62 months (range,