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Learning curve of MRI-based planning for high-dose-rate brachytherapy for prostate cancer

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ABSTRACT

PURPOSE: To evaluate introduction of MRI-based high-dose-rate brachytherapy (HDRBT), including procedure times, dose-volume parameters, and perioperative morbidity.

METHODS AND MATERIALS: Study included 42 high-risk prostate cancer patients enrolled in a clinical protocol, offering external beam radiotherapy + two HDRBT 8.5 Gy boosts. Time was recorded for initiation of anesthesia (A), fixation of needle implant (B), end of MR imaging (C), plan approval (D), and end of HDRBT delivery (E). We defined time A−E as total procedure time, A−B as operating room time, B−C as MRI procedure time, C−D as treatment planning time, and D to E as treatment delivery time. Dose-volume parameters were retrieved from the dose planning system. Results from the first 21 patients were compared with the last 21 patients.

RESULTS: Total procedure time, operating room time, MRI procedure time, and treatment planning time decreased significantly from average 7.6 to 5.3 hours ($p < 0.01$), 3.6 to 2.4 hours ($p < 0.01$), 1.6 to 0.8 hours ($p < 0.01$), and 2.0 to 1.3 hours ($p < 0.01$), respectively. HDRBT delivery time remained unchanged at 0.5 hours. Clinical target volume $_{\text{prostate+3mm}}$ D_{90} fulfilled planning aim in 92% of procedures and increased significantly from average 8.3 to 9.0 Gy ($p < 0.01$). Urethral $D_{0.1\ \text{cm}^3}$ and rectal $D_{2\ \text{cm}^3}$ fulfilled planning aim in 78% and 95% of procedures, respectively, and did not change significantly. Hematuria occurred in (95%), hematoma (80%), moderate to strong pain (35%), and urinary retention (5%) of procedures.

CONCLUSIONS: After introduction of MRI-based HDRBT, procedure times were significantly reduced. D_{90} Clinical target volume$_{\text{prostate+3mm}}$ fulfilled constraints in most patients and improved over time, but not at expense of an increased urethral or rectal dose.

Keywords: HDR; Workflow; Morbidity; MRI; Prostate cancer; Learning curve

Introduction

Brachytherapy (BT) either alone or in combination with external beam radiotherapy (EBRT) for localized prostate cancer has demonstrated a favorable relapse-free survival (1−3). BT, and high-dose-rate brachytherapy (HDRBT) in particular, has superior physical abilities for sparing the rectal and bladder wall in comparison with modern external beam techniques (4). BT for prostate cancer is an established treatment modality that has been used increasingly over the past decade (5, 6). Transrectal ultrasound−based BT has been the mainstay of prostate cancer BT since the pioneer work of Holm *et al.* (7). This may be changing as MRI-based HDRBT seems superior to US-based HDRBT with regard to target definition, needle reconstruction, and delineation of organs at risk (OAR). MRI can more accurately define the prostate gland especially at the apex and base, and it is useful for identifying the dominant intraprostatic lesion as well as extracapsular cancer extensions (8). MRI enables detailed definition of organs as risk such as the neurovascular bundles, external urinary sphincter, bladder neck, and intraprostatic ejaculatory ducts (9, 10). Arguments against MRI-based HDRBT is extra

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procedure time, a more complex workflow, and unavailability of MRI.

In 2012, HDRBT was introduced in our department as a new treatment modality for prostate cancer patients. HDRBT was performed in a newly built facility, housing contemporary imaging modalities including an MRI scanner dedicated for radiotherapy planning. The purpose of this study was to evaluate the introduction of MRI-based HDRBT, including procedure times, perioperative morbidity, and dose-volume parameters.

Methods and materials

Facility

Facility includes a patient room, operating room (OR), stepper system (Oncoselect tablemount stepper + ECRM endocavity rotation mover), MR compatible template (TPS 061 1.5 mm), ultrasound system (Prosius Integrated Ultrasound System + US transformer Logiscan 128 Model INT-2Z-Kit + BiopSee biplanar transrectal ultrasound probe), remote afterloader (Flexitron, Elekta + Flexisource Ir 191, 370 Bq), treatment planning system (OncentraProstate version 4.2.21, Nucletron), MRI scanner (Ingenia 1.5 T, Philips Healthcare, The Netherlands), PET/CT scanner (Philips Gemini TF Big Bore., The Netherlands), and a treatment delivery room. The patient-related procedures involved four different rooms located in the same building and on the same floor.

Training

A team of radiotherapists, physicists, radiologists, and nurses was trained to perform MRI-based HDRBT. Training included site visits to two departments with significant experience in MRI and US-guided prostate BT, respectively. The HDRBT procedure was simulated several times using a prostate phantom (CIRS 053A). During the first patient procedures, an HDRBT experienced technician and an urologist were present.

Patient selection

The study included 42 consecutive D'Amico high-risk prostate cancer patients (11) enrolled in a prospective clinical protocol in which patients were offered combined EBRT + HDRBT. In December 2014, we changed our procedure to include repeated MRI to assess the stability of the needle implant, and patients from this time on are not included in the study. Inclusion criteria beyond GEC ESTRO guidelines (12, 13) were biopsy-proven prostate adenocarcinoma, Stage T1−T3a, no lymph node metastases on lymph node dissection, negative bone scan, and planned 3 years of luteinizing hormone−releasing hormone agonist treatment initiated 3 months before radiotherapy. Exclusion criteria were maximal urinary flow <15 mL/s (later changed to <10 mL/s), inflammatory bowel disease, ileostomia, colostomia, prior pelvic radiotherapy, and comorbidity interfering with anesthesia.

External beam radiotherapy

Before HDRBT, patients received EBRT 46 Gy in 23 fractions, 5 weekly fractions. EBRT was delivered to the prostate gland and seminal vesicles using volumetric arc therapy technique based on planning CT and MRI. Clinical target volume $(CTV)_{prostate}$ was defined on planning MRI as prostate gland plus extracapsular extension. Planning target volume was generated from the $CTV_{prostate}$ + $CTV_{vesicles}$ added a margin of 7 mm axially and 9 mm craniocaudally. No elective lymph node irradiation was performed.

Patient preparation

Patients were instructed to discontinue anticoagulants 3−5 days before the first HDRBT procedure. Blood samples were taken 2−3 days before each HDRBT procedure for analysis of coagulation parameters, hematological parameters, pretransfusion compatibility, and electrolytes. Patients were fasting for at least 6 hours and received bisacodyl 10 mg × 2 orally and 2 mg rectally for bowel emptying. Venous thromboembolism prophylaxis included the use of antiembolism stockings during the HDRBT procedure, and subcutaneous dalteparin 5000 IU was administered two times postoperatively with a 12-hour interval. For microbial prophylaxis, a urine sample was examined with a urine test stick 2−3 days before each HDRBT for excluding urinary infection. Patients were advised to shave the perineum and scrotum, and 500-mg ciprofloxacin and 500-mg metronidazole were administered orally 3 hours before the HDRBT procedure.

Anesthesia

General anesthesia was used for the first 28 patients, but the procedure was changed to spinal anesthesia for subsequent patients. In patient number 31, general anesthesia was used for the second HDRBT due to a severe anaphylactic reaction during the first HDRBT. If general anesthesia was performed, patients received infiltration analgesia of the perineum with 10−12 cm^3 of bupivacaine 2.5 mg/cm^3. For postoperative pain and nausea, patients received 1-g paracetamol, 20-mg morphinesulphate, and 8-mg ondansetron 3−4 hours before HDRBT.

High-dose-rate brachytherapy

HDRBT was delivered twice with each procedure separated by 1 week after EBRT. Plastic needles were inserted US guided, but HDRBT dose plans were based on MRI reconstructed needles and MRI defined volumes ($CTV_{prostate}$, urethra, rectum, and bladder) (Table 1). The tip of each needle was resolved by the resulting signal loss artifact on MRI, and the first available dwell position was defined as