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Original article

Magnetic resonance imaging-transrectal ultrasound fusion focal cryotherapy of the prostate: A prospective development study

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Abstract

Objectives: The use of software-based magnetic resonance-transrectal ultrasound fusion to deliver focal therapy may increase the precision of treatment. This is a prospective development study assessing the feasibility of Magnetic resonance imaging-transrectal ultrasound (MRI-TRUS) fusion focal cryotherapy.

Methods and materials: Consecutive patients undergoing focal cryotherapy were included in an academic registry (December 2013–June 2014). MRI-TRUS fusion focal cryotherapy was offered to men with visible clinically significant prostate cancer (Galil SeedNet system). Eligibility was determined by multiparametric MRI (mpMRI), and transperineal template mapping or targeted biopsies. A rigid fusion platform (Biojet) was used with the operator ensuring the ice ball covered at least the lesion. Adverse events were scored using the NCICTC V4. Genitourinary toxicity was assessed using patient-reported outcome measures (IPSS, IIEF-15, and UCLA-EPIC). Early contrast-enhanced MRI and mpMRI at 6 to 12 months were used to assess extent of lesion ablation.

Results: Of 23 patients scheduled, 5 did not have image fusion owing to surgeon preference. Overall, 18 patients undergoing image-fusion cryotherapy had median age of 68 (interquartile range [IQR]: 65–73) years and median preoperative prostate-specific antigen = 9.54 (5.65–16) ng/ml. In all, 13 (72.2%) and 5 (27.8%) patients had intermediate and high-risk cancer, respectively. In total, 10 adverse events were reported with one of these as serious (grade 3) because of admission for hematuria requiring wash out only. There was no difference in the IIEF-15 between baseline and study end ($P = 0.24$). The IPSS remained stable ($P = 0.12$), whereas the UCLA-EPIC tended to improve ($P = 0.065$). The prostate-specific antigen level significantly decreased at 1.8 (1.04–2.93) ng/ml ($P < 0.001$). Both early and late mpMRI showed no residual disease in the treated area. In 2 men, radiological progression of known contralateral disease was observed; both underwent focal high intensity focused ultrasound.

Conclusion: MRI-TRUS fusion focal cryotherapy is feasible in most patients and seems to accurately guide ablation demonstrated by posttreatment imaging. Additional studies are needed to determine efficacy using postcryotherapy biopsy.

Keywords: Cryotherapy; Focal therapy; Image fusion; Prostate neoplasms

1. Introduction

The therapeutic ratio of current radical treatments for localized prostate cancer is being questioned by clinicians, authorities, and lately by patients themselves. Recent randomized trials have questioned the exact benefit from radical treatments across all localized prostate cancer, but do point to survival advantages in men with clinically significant disease who have a good life expectancy [1–3]. Nonetheless, the genitourinary toxicity of radical treatments

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can be significant with a rate of erectile dysfunction and urinary incontinence varying between 30%–60% and 15%–20%, respectively, and a high rate of serious complications in the long term, especially in older patients [4,5]. To rebalance the therapeutic ratio, a strategy that has been proposed is focal therapy [6].

This strategy aims to treat the area of the prostate harboring the largest volume, highest grade (index) lesion with a margin, while preserving the rest of the gland and reducing collateral tissue damage [7]. Concern and enthusiasm both exist regarding this novel approach [6,8]. Despite the open debate, there is consensus that although further robust research is required, focal therapy is an attractive strategy for patients and health care systems.

Focal therapy can be delivered using various sources of energy. A recent systematic review of the literature has shown variable results with urinary incontinence, erectile dysfunction, and disease control (using histological outcome measures) ranging between 0% and 5%, 0% and 46%, and 77% and 96.3%, respectively [9]. Focal therapy efficacy has been criticized in light of 2 issues: first, some novel sources of energy have not been tested in the clinical setting; therefore, treatment failure might be related to incomplete ablation, rather than failure of the focal strategy. Second, the inability of devices to deliver precise therapy in the area harboring the index lesion.

In this study, we sought to assess the feasibility of focal cryotherapy delivered to the index lesion using software-based magnetic resonance imaging-transrectal ultrasound (MRI-TRUS) fusion.

2. Materials and methods

2.1. Design

Consecutive patients undergoing software-based MRI-TRUS fusion focal cryotherapy were identified from a prospective academic registry (December 2013–June 2014). Signed informed consent was obtained. Internal review board approval was waived by the local joint research office. This report is adherent to the recommendations of the Idea Development Evaluation Assessment and Long-term guidelines for stage I to IIa prospective development studies assessing novel technologies in surgery [10].

2.2. Population

In our unit, men with primary localized prostate cancer and men with recurrent disease after initial radiation or ablative therapy underwent multiparametric MRI (mpMRI). Images were acquired in a 1.5 or 3 T scanner with a pelvic coil using a standard protocol including T2-weighted, diffusion-weighted, and dynamic contrast–enhanced sequences. Every scan was reported by an experienced radiologist reporting all zones with a Likert score between 3 (equivocal presence of clinically significant disease) and 5 (extremely likely presence of clinically significant disease) [11]. Histological characterization of the radiological phenotype was obtained according to the mpMRI report. Transperineal targeted biopsy with no additional sampling to zones scoring ≤ 2 were performed in men with a single lesion; however, template prostate mapping biopsies were offered to men with multiple lesions or diffuse equivocal findings (Fig. 1). Treatment-naïve men with Gleason pattern ≥ 4 or prostate-specific antigen (PSA) level ≥ 10 ng/ml or both and all men with radiorecurrent disease also underwent a radioisotope bone scan to rule out metastases.

MRI-TRUS software-based fusion focal cryotherapy was offered to men with 1 or 2 MR-visible lesions confirmed to be clinically significant, in whom, a standard focal strategy was deemed to be able to achieve complete ablation (hemifocal, quadrantfocal, focal, or bifocal ablation).

2.3. Procedure

Before the procedure, the full 3 mm thickness T2-weighted sequence was downloaded and imported onto the Biojet rigid image-fusion platform (D&K Technologies GmbH, Barum, Germany). The prostate and visible lesion(s) were contoured [12]. The cryotherapy procedure was performed in the lithotomy position. Antibiotic prophylaxis was administered intravenously at induction of general anesthesia. First, the prostate was scanned using a biplane transrectal ultrasound probe (Hitachi Preirus, Hitachi Aloka Medical America, Inc, Wallignford, USA) positioned on a stepper fixed to the operation table by a flexible arm (D&K Technologies GmbH, Barum, Germany). Second, the Biojet computer was connected to the ultrasound probe using sensors located on the stepper, one for tracking longitudinal movements and the other for rotation. MRI-TRUS fusion was obtained manually by aligning the contour of the prostate drawn on the MRI to the margins of the prostate visible on the TRUS by rigid registration. Third, cryotherapy needles were inserted transperineally using a brachytherapy grid to ensure a parallel position. The cryotherapy needles were placed using the Biojet platform for guidance to cover the area to ablate with a margin of 1 cm (Fig. 2). We used the cryotherapy SeedNet system (Galil Medical Inc., Arden Hills, MN) with 17-gauge (1.5 mm) needles. In total, 2 types of needle were chosen according to the dimensions of the lesion to ablate on the axial and the longitudinal MR/TRUS software. IceRod needles achieve a complete ablation of 41 mm longitudinally, whereas IceSeeds achieve 19 mm. Thermocouples were then placed within the ablation area, and in the Denovilliers' fascia in case of posterior or midgland lesions, or in the peripheral area in case of anterior lesions.

Fourth, a flexible cystoscopy was performed to rule out urethral perforation, and a urethral warmer was inserted. Finally, 2 freeze-thaw cycles were delivered to achieve a temperature less than $-40^{\circ}C$ in the ablation area, as measured by thermocouples. A temperature more than