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Techniques in Vascular and Interventional Radiology

Focal Therapy of Prostate Cancer Using Irreversible Electroporation

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Focal therapy is a novel strategy that attempts to enhance the therapeutic ratio of standard radical treatment in prostate cancer. Irreversible electroporation (IRE) has some inherent characteristics that may be ideal for focal therapy. Precise confined ablation in the treatment area obtained via nonthermal damage with potential for minimal toxicity to surrounding structures may lead to optimal treatment with improved preservation of continence and erectile function. Initial data of focal IRE of the prostate are encouraging although further assessment is awaited to confirm these findings using robust methodology. In this article, we provide a comprehensive step-by-step description of our technique to deliver focal IRE in selected men with localized prostate cancer located in a discrete area of the prostate.

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Introduction

Prostate cancer therapy is being challenged in the light of recent evidence. The benefit of active treatment seems to be limited to those men with clinically significant disease having extended life expectancy[1]; however, even in this group the potential gain in survival comes with a high rate of genitourinary and bowel toxicity after treatment.[2] This unbalanced therapeutic ratio is mainly due to the current therapeutic strategies—both radiation therapy and radical prostatectomy—that target the whole gland, rather than the areas harboring the cancer. This indiscriminate therapeutic strategy has an effect on key surrounding structures that determine the functional outcome, namely neurovascular bundles, urethra, bladder neck, rhabdosphincter, and rectum.

The advent of imaging in the form of multiparametric magnetic resonance imaging (mpMRI) has allowed the possibility to use cancer location to guide treatment with a high degree of accuracy in ruling in and ruling out clinically significant disease.[3,4] In addition, although prostate cancer is usually multifocal, only the most aggressive clone seems to lead to biological, histological, and clinical progression, whereas secondary low-grade and low-volume lesions appear to have an indolent behavior.[5,6] The ablation of the disease harboring this clone—the index lesion—has been called focal therapy, and it represents the application of tissue-preserving principles to prostate cancer,[7] something we have seen in almost all other solid-organ malignancies.

Various sources of energy have been used to deliver focal therapy. Thermal energies leading to cell death by the creation of extreme temperatures less than −40° (cryotherapy) or more than +60° (high-intensity focused ultrasound) have been the most used.[7] The outcomes have been promising so far with cancer control in the short-term and midterm between 74% and 100%, continence preservation between 95% and 100%, and potency preservation between 54% and 100%.[7,8]

Irreversible electroporation (IRE) is a novel source of energy recently used in the treatment of prostate cancer. IRE leads to cell death by the formation of nanopores within the membrane cell, without causing a thermal

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effect. The nonthermal damage is a significant advantage as it may overcome the dissipation of energy that occurs when using thermal sources of energy, which may lead to undertreatment. In addition, preclinical studies have shown that IRE might be tissue selective with collageneous structures being able to recover after a short period from treatment.[9] If confirmed in clinical studies, there would be a positive effect on the functional outcome as the nerves, vessels, and muscles have large collageneous components.[10]

We have previously reported our registry case series with respect to focal IRE of the prostate in men with localized disease[11] and are currently undertaking prospective development study using patient-reported outcomes and mandatory biopsy after treatment.[12]

Clinical Evaluation of the Patient

Men with suspicious prostate cancer, based on digital rectal examination or blood test for prostate-specific antigen (PSA), or men with histologically confirmed localized disease need to undergo accurate risk and zonal diagnostic assessment before being considered for focal IRE. In our institution, a combination of imaging and precise sampling is required; mpMRI combining T2-weighted, dynamic contrast-enhanced and diffusion-weighted imaging sequences is performed and reported by experienced radiologists using a standardized 5-point Likert scale. This classification attributes a score to anatomical regions of the prostate ranging from 1 (extremely unlikely) to 5 (extremely likely) with respect to the likelihood of presence of clinically significant disease (Fig. 1).

Accurate sampling based on the mpMRI reports is then performed using a transperineal approach. In men with suspicious areas on mpMRI, targeted biopsy of this area plus a zonal sampling of the rest of the prostate is conducted according to the modified Barzell tamplate. In men with equivocal areas on mpMRI, systematic template prostate mapping biopsies are performed throughout the gland with a 5-mm sampling frame. Both these tests have been shown to have negative predictive values of 90%-95% for ruling out clinically significant disease (defined as lesion volume ≥ 0.2 ml or Gleason grade $\geq 3+4$ or both).[13,14]

Standard evaluation for general anesthesia including coagulation tests, renal function, electrolytes, and blood count is also performed. Of note, preanesthetic assessment is mandatory as deep muscle paralysis is required during the delivery of electricity to minimize unintended contractions of muscles.

Indications for the Procedure

A lesion visible on mpMRI concordant with histological parameters of clinically significant disease as verified by an accurate sampling strategy with absence of clinically insignificant disease elsewhere is the main indication for focal therapy. In our institution, we use a Gleason score $\geq 3+4$ or lesion volume ≥ 0.2 ml to define clinically significant disease.[15] Therefore, any Gleason score $\leq 3+3$ and maximum cancer core length on biopsy ≤ 3 mm is a considered clinically insignificant disease.

It is also critical to select those men with appropriate cancer location and lesion dimensions. As the surrounding margin of treatment around the needles has been estimated to be 5 mm, lesions too close to the rectum should be avoided to minimize rectal involvement. Consequently, we mainly use IRE for lesions in the transition zone, in the anterior fibromuscular stroma, or in the anterior reflection of the peripheral zone of the prostate.

Depending on the number of needles the operator wants to use, lesion volume is also a factor to consider. The distance between the needles should not exceed 2 cm and the maximum active needle exposure per ablation session is also 2 cm. If 3-4 needles are used—as usually performed in focal therapy—tumor volume should not exceed 3 cc, while also considering a treatment margin. However, in

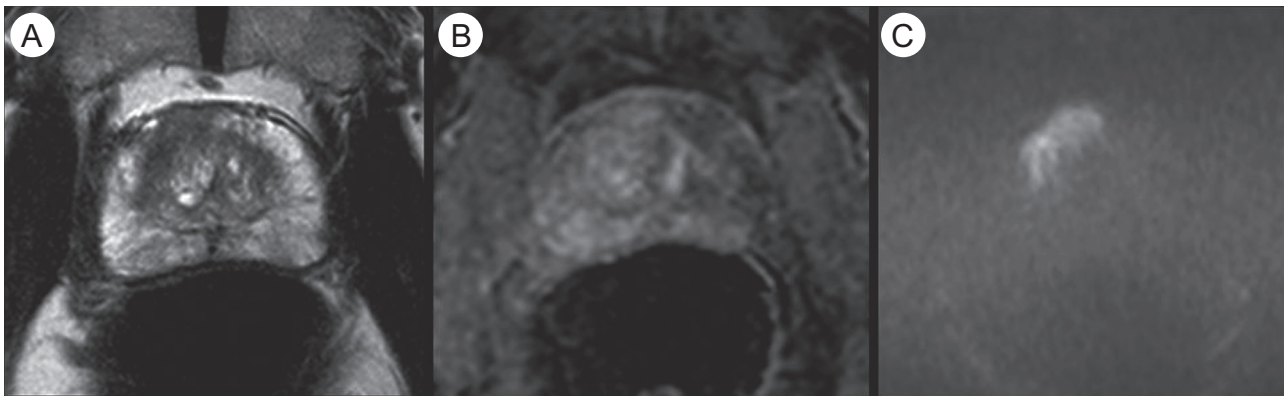

Figure 1 Preoperative mpMRI showing hypointense T2 signal (A), slight early contrast enhancement (B), and definitive high b-value on DWI (C) in the right anterior area of the prostate. Clinically significant disease in this area with no significant disease elsewhere was confirmed by template prostate mapping biopsy. DWI, diffusion-weighted imaging.