EDITORIAL

"Targeted microwave ablation: another way to kick the can(cer) down the road?"

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Interest in focal therapies for localized prostate cancer (PCa) has blossomed over the past decade, with an estimated 80% growth in utilization [1]. The goal of focal therapy is to selectively ablate the known areas of disease in the prostate while minimizing the known morbidity associated with radical prostatectomy or radiotherapy. As of 2022, focal therapy has not been compared to these standard whole-gland treatments in a published randomized trial in terms of oncological outcome. Much of the data in support of its use stem from registry studies and selected single- and multi-center single-arm studies. The evidence base has historically been deepest for high-intensity focused ultrasound (HIFU) and cryoablation.

In this issue of *Prostate Cancer and Prostatic Diseases*, Chiu et al. [2]. report on the preliminary result of the first phase II trial of transperineal Targeted Microwave Ablation (TMA), focusing on the first 15 patients enrolled in this study. All patients had low to intermediate risk localized PCa and underwent TMA under MRI-ultrasound fusion guidance and organ-based tracking. They showed that 91.3% (21/23) of the ablated areas had no evidence of cancer at 6-month targeted biopsy, while 13% (2/15) patients had in-field positivity and 33% (5/15) of patients had out-of-field positivity at 6 months. Among these 5 patients (all with out-of-field recurrence), one pursued radical prostatectomy although technically he remained a candidate for AS, and one pursued radiotherapy given newly discovered Gleason $3 + 4 = 7$ disease; the remaining three continued active surveillance. Importantly, urinary and bowel complications were limited to grade 1 only, including hematuria (33%), dysuria (7%) and perineal discomfort (13%). Among 5 patients with normal baseline erectile function, one had significant worsening of symptoms.

Although microwave ablation has a long track record of treating metastasis in the liver, lung, kidney, and bone, its application in the setting of localized PCa is still in its infancy, with only one other small trial with 10 patients having been reported [3]. Compared to other existing focal treatment modalities, TMA offers a few advantages. For example, it is less susceptible to the "heat sink" effect caused by adjacent vasculature compared to radiofrequency ablation and has the ability to penetrate deeper and heat faster in a larger volume [4]. A detailed comparison of TMA with two of the most commonly used focal treatment modalities (i.e. HIFU and cryotherapy) is shown in Table 1. In terms of toxicity, both studies [2, 3] reported 0% grade 3 toxicity with 100% urinary pad-free rate, which is similar to the corresponding < 2% and 95–100% rates seen with HIFU and cryoablation. Regarding short-term oncological outcomes, Chiu et al. reported an excellent rate of local control, with only 8.7% of the treated areas with biopsy-proven any grade cancer in 6 months, compared to a median of 28.6% and 22.1% in the literature for HIFU and cryoablation, respectively [5]. Cancer in untreated areas of the prostate was detected in 33% of the patients in the study by Chiu et al., compared to a median rate of 8.9% and 10.5% for HIFU and cryoablation, respectively. However, the study by Delongchamps showed insufficient local control at 6 months, with 5 out of 9 biopsied patients (55.6%) showing persistent disease in the targeted area. While 60% of the patients with recurrences in the Chiu et al. study have avoided radical therapy for now, follow-up is still limited.

We commend Chiu and colleagues for studying TMA in the appropriate forum—a prospective trial. It is notable that only 5 of the patients had erectile function at baseline; this is considerably lower than on the landmark ProtecT trial [6], in which the rate of men with erectile function at baseline was 67%, rendering comparisons hard to make. It is also notable that in-prostate recurrences were found in 1/3rd of patients in such a short median follow-up period. TMA, as with all focal therapy approaches, is inherently limited by the imaging modality, and MRI-invisible lesions harboring clinically significant disease have been demonstrated in this low-risk population [7]. Although MRI-invisible lesions detected on systematic biopsies were treated by Chiu et al., it is unclear how treatment volumes were defined for these lesions and what margins were used. Furthermore, since systematic biopsy samples <0.05% of the prostate and has a false-negative rate exceeding 20% [8], focal therapy will inevitably overlook a significant portion of cancer foci that could have been covered by radical treatments. While most men with such recurrences on this study are being managed with surveillance, the major question remains as to whether the toxicities of an unsuccessful focal therapy plus a salvage radical therapy outweigh the toxicities of upfront active surveillance followed by radical therapy on progression—the latter would have been an option for these men. Focal therapy may also make future interpretation of MRI, insertion of fiducial markers and performing radical prostatectomy more challenging. Further, it is notable that the vast majority of these men had non-aggressive disease. What would the outcome have been if more aggressive cancers were treated? Moreover, while toxicities of radical therapy certainly exist, it is important that men and their families are informed that this space too has seen significant advances over the years. For instance, in the context of radical radiotherapy, the use of hydrogel rectal spacers [9] and MRI-guidance [10] has been shown to significantly reduce bowel and urinary toxicity, respectively, in randomized trials. Overall, TMA represents a novel focal treatment strategy for localized PCa. However, for now, as with other focal therapies, it should be done on a prospective trial for fully informed patients who warrant intervention.

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Table 1. Comparison of targeted microwave ablation with HIFU and cryoablation.

	Targeted microwave ablation	HIFU	Cryoablation
Surgical approach	Transperineal [2]/ Transrectal [3]/	Transrectal	Transperineal
Patient position	Lithotomy [2]	Lithotomy or right lateral decubitus	Lithotomy
Anesthesia	General [2, 3]/ Spinal [2]	General/ Spinal	General/ Spinal
Ablation type	Thermic: heating	Thermic: heating	Thermic: freezing
Treatment setting	Outpatient	Outpatient	Outpatient
Lesion location preference	For Transrectal approach, not optimal for anterior lesions, or tumor oriented transversely; for transperineal approach, not optimal for posterior lesions	Not optimal for anterior lesions	Not optimal for posterior lesions
Urinary catheterization	Yes (for a median of 7 days) [2]/No [3]	Yes	Yes
Intraoperative visualization	TRUS with organ-based tracking	HIFU TRUS	Conventional TRUS guidance
Intraoperative monitoring	Hyperechoic ultrasound changes in treatment zone	Visualization of cavitations ("popcorn" phenomenon)	Visualization of the of the ice-ball
Treatment time (min)	75 [2], 82 [3]	~90	~90
Oncological outcomes [2, 3, 5]	Any cancer in treated area: 8.7% [2], 55.5% [3] CSC in treated area: 0% [2], 11.1% [3] Any cancer in untreated area: 33% [2], 66.6% [3] CSC in untreated area: 6.7% [2], 33.3% [3]	Any cancer in treated area: median 28.6% (0–65.4%) CSC in treated area: median 15.4% (0–30%) Any cancer in untreated area: median 14% (7–34.7%) CSC in untreated area: median 8.9% (2–20.5%)	Any cancer in treated area: median 22.1% (0–57%) CSC in treated area: median 18% (0–20%) Any cancer in untreated area: median 20% (19–43%) CSC in untreated area: median 10.5% (4–17%)
Grade 3 toxicity rate	0% [2], 0% [3]	2% (0–4.8%)	1.6% (0–9%)
Urinary pad-free (%)	100% [2], 100% [3]	95.3% (88.1–100%)	100% (83–100%)
Decrease in erectile function sufficient for penetration (%)	20% [2]	6.6% (4–16.5%)	0.5% (0–31.2%)
Re-treatment feasibility	Yes	Yes	Yes

HIFU high-intensity focused ultrasound, *TRUS* transrectal ultrasound, *CSC* clinically significant cancer.

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AUTHOR CONTRIBUTIONS

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ADDITIONAL INFORMATION

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