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Prostate Radiofrequency Focal Ablation (ProRAFT) Trial: A Prospective Development Study Evaluating a Bipolar Radiofrequency Device to Treat Prostate Cancer

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Abbreviations and Acronyms

AE = adverse event
bRFA = bipolar radiofrequency
CTC = Common Terminology Criteria
DCE = dynamic contrast enhanced
EPIC = Expanded Prostate Cancer Index Composite
EQ-5D = Euro Quality of Life 5 Domains
FACT-P = Functional Assessment of Cancer Therapy-Prostate
IIEF-15 = International Index of Erectile Function-15
IPSS = International Prostate Symptom Score
IPSS-QoL = IPSS-Quality of Life
MCCL = maximum cancer core length
mpMRI = multiparametric magnetic resonance imaging
MRI = magnetic resonance imaging
PSA = prostate specific antigen
UCL = University College London
US = ultrasound

Purpose: We determined the early efficacy of bipolar radiofrequency ablation with a coil design for focal ablation of clinically significant localized prostate cancer visible at multiparametric magnetic resonance imaging.

Materials and Methods: A prospective IDEAL phase 2 development study (Focal Prostate Radiofrequency Ablation, NCT02294903) recruited treatment-naïve patients with a single focus of significant localized prostate cancer (Gleason 7 or 4 mm or more of Gleason 6) concordant with a lesion visible on multiparametric magnetic resonance imaging. Intervention was a focal ablation with a bipolar radiofrequency system (Encage™) encompassing the lesion and a predefined margin using nonrigid magnetic resonance imaging-ultrasound fusion. Primary outcome was the proportion of men with absence of significant localized disease on biopsy at 6 months. Trial followup consisted of serum prostate specific antigen, multiparametric magnetic resonance imaging at 1 week, and 6 and 12 months post-ablation. Validated patient reported outcome measures for urinary, erectile and bowel functions, and adverse events monitoring system were used. Analyses were done on a per-protocol basis.

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Results: Of 21 patients recruited 20 received the intervention. Baseline characteristics were median age 66 years (IQR 63–69) and preoperative median prostate specific antigen 7.9 ng/ml (5.3–9.6). A total of 18 patients (90%) had Gleason 7 disease with median maximum cancer 7 mm (IQR 5–10), for a median of 2.8 cc multiparametric magnetic resonance imaging lesions (IQR 1.4–4.8). Targeted biopsy of the treated area (median number of cores 6, IQR 5–8) showed absence of significant localized prostate cancer in 16/20 men (80%), concordant with multiparametric magnetic resonance imaging. There was a low profile of side effects at patient reported outcome measures analysis and there were no serious adverse events.

Conclusions: Focal therapy of significant localized prostate cancer associated with a magnetic resonance imaging lesion using bipolar radiofrequency showed early efficacy to ablate cancer with low rates of genitourinary and rectal side effects.

Key Words: prostate, prostatic neoplasms, radiofrequency ablation

Focal therapy of localized prostate cancer is an emerging treatment that aims to limit the side effects of standard whole gland prostatectomy or radiotherapy[1–3] while retaining acceptable cancer control. The rationale is based on the current rather unfavorable therapeutic ratio when early prostate cancer is treated radically.[4,5] A recent systematic review and subsequent case series showed focal therapy using a number of different ablative modalities had low side effect profiles with encouraging short to medium-term oncologic results.[6–9]

There has been a shift in the last decade[10] to propose focal therapy as an alternative to men who would otherwise need radical therapy rather than it being an alternative to active surveillance.[11,12] Different ablative energies have been reported with some limitations in efficacy to ablate anterior and posterior disease, which has led to some proposing an "à la carte" approach to optimize either energy delivery or limit damage to critical anatomical structures like the rectum.[13]

Successful cancer ablation with radiofrequency has been already reported in many different organs, such as kidney[14] and liver,[15] as well as the prostate gland. Radiofrequency ablation using the coiled Encage device (bRFA) may be effective in safely and effectively ablating lesions in all locations in the prostate due to the coil design allowing a very sharp transition of up to 0.06 mm from ablated to non-ablated tissue.[16,17]

The primary objective of this study was to assess early efficacy of bRFA for cancer control in patients with clinically significant prostate cancer localized to the prostate. To our knowledge, this is the first report of an ethics committee approved, prospectively registered study evaluating the Encage device for focal ablation of prostate.

MATERIAL AND METHODS

Study Design

ProRAFT was a stage II prospective development study according IDEAL framework[18] for surgical innovation, which was registered prior to first patient recruited (NCT02294903) and underwent ethical approval (No. NRES London-Riverside 15/LO/009). Enrollment started in May 2015 and closed in March 2016 with followup until August 2017.

Cancer localization and risk stratification. Patients with clinically significant prostate cancer using UCL definition 2 (Gleason score 3+4 or Maximum Cancer Core Length $\geq$4 mm) on transperineal biopsy concordant with an mpMRI lesion were eligible. mpMRI followed a standardized acquisition protocol with T2-weighted imaging, diffusion-weighted imaging and DCE sequences and were interpreted by experienced radiologists. Only lesions with a Likert score $\geq$3 were eligible for ablation. The presence of insignificant foci was permitted outside of the planned treatment zone (Gleason score 6 and MCCL <4 mm). Men with multiple lesions at mpMRI were eligible for the study, provided all those locations were sampled and only 1 mpMRI harbored significant cancer.

Treatment planning: It was lesion based as the technology allowed the shaping of the treatment zone. Lesion amenability with the Encage technology was defined as a lesion accessible to complete ablation including a margin between 5 mm and 9 mm[19] and sparing critical anatomical structures using a combination of multiple coils and additional probes inserted around the coil if necessary as shown in figure 1. MRI lesions and margin were contoured manually from MRI sequence, which demonstrated the most extensive lesion volume (OsiriX®). An additional 5 mm to 9 mm intraprostatic margin was incorporated.[20,21]

Bipolar radiofrequency ablation: Focal ablation with the Encage device was performed either under general or spinal anesthesia in lithotomy position with antibiotic prophylaxis. The whole procedure is described in supplementary Appendix 1 (https://www.jurology.com). To summarize, we used a customized needle delivery system calibrated for use with the US-MRI nonrigid fusion device (customized version of the SmartTarget®). The procedure included acquisition of 3D ultrasound images which were then registered with the MRI contours, allowing overlay of the lesion and its margin. Treatment was delivered by a combination of coils and extra needles as depicted in figure 1. Coil bRFA is applied consecutively to the coils until complete coverage of the lesion and the margin were achieved. A urethral catheter was placed at the end of the procedure. The same procedure was conducted in case of re-treatment.

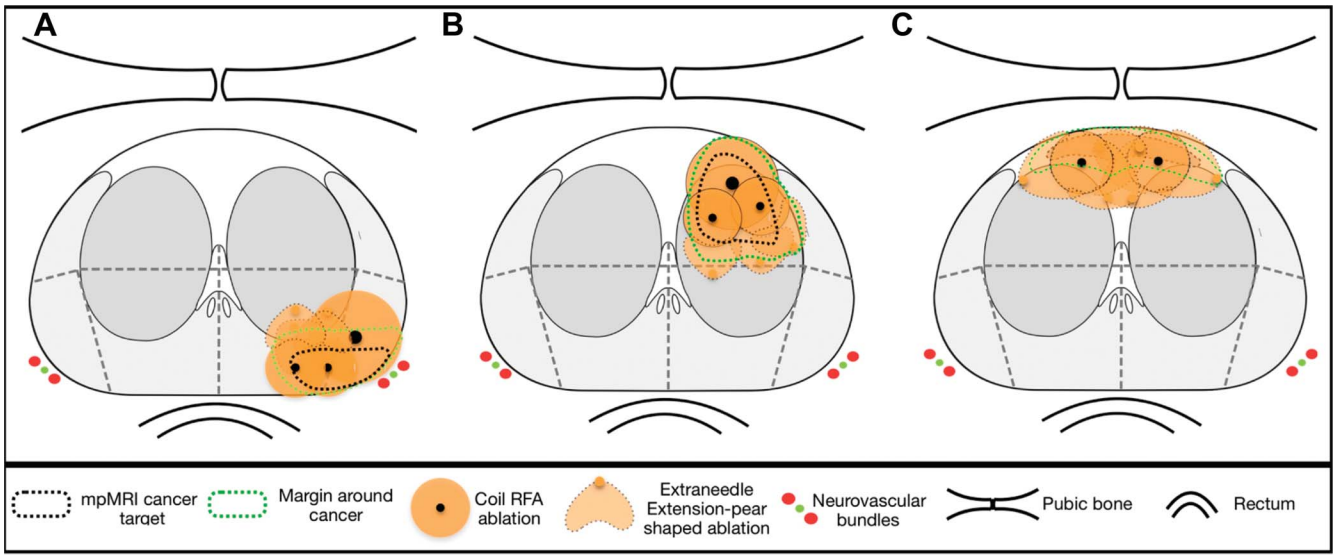

Figure 1. Focal treatment planning and delivery based on location of cancer focus using bipolar radiofrequency (*RFA*) and relationship to critical anatomical structures (pubic bone, rectum, neurovascular bundles and urethra). *A*, left peripheral zone cancer. *B*, left transition zone cancer. *C*, crossing midline cancer from anterior fibromuscular stroma.

Followup. A mpMRI was carried out between 3 and 10 days post-operatively after catheter removal. Early post-treatment MRI was performed to ensure absence of early complications and assess treatment coverage. Clinical reviews were organized at 6 weeks and 3, 6, 9 and 12 months concomitant with PSA measurements. At each followup visit, patients were asked to complete validated questionnaires, which included IIEF-15, EPIC (University of California–Los Angeles) Urinary Continence Questionnaire, EPIC Bowel Questionnaire, IPSS, IPSS-QoL, EQ-5D and FACT-P version 4.[22] Adverse events were graded using the National Cancer Institute CTC classification system (version 4). Use of a phosphodiesterase type 5 inhibitor for erectile function was recorded.

mpMRIs at 6 and 12 months were evaluated for residual cancer or emergence of new lesions. The 6-month mpMRI was used to guide targeted biopsies of the treated area with an approximate density of a minimum of 1 core per 1 ml tissue and any new lesions.

In case of re-treatment, another early post-treatment mpMRI was acquired after catheter removal. Biopsy of the re-treated area at 6 months from re-treatment also occurred (supplementary Appendix 2, https://www.jurology.com).

Objectives

The primary objective was treatment efficacy as assessed on histology from transperineal targeted biopsy of the treated area at 6 months. Treatment success was defined by histological absence of clinically significant prostate cancer in the treated area. Secondary objectives were to determine the achievement of trifecta status for patient with good baseline functions, side effect profile of bRFA, urinary, erectile and rectal toxicity, disease control in case of re-treatment, time to secondary prostate cancer intervention treating the whole gland, proportion of visible lesion at 1 week, 6 and 12 months, the role of mpMRI in followup and assessment of the US-MRI fusion workflow for treatment planning. Good baseline potency function was defined prior to analysis as score of 4 or 5 at question 2 of IIEF-15. Trifecta was defined as persistence of those functional features for continence and erectile function with absence of clinically significant prostate cancer on biopsy at trial completion.

Statistical Analysis

A sample size of 20 was chosen as this maximized the increase in precision to detect a proportion of 80% of patients with a successful ablation at 6 months. There was an increase in the precision estimate from n = 10 to n = 20 with little further gain in precision beyond 20 men, something that was consistent with previous studies.[23] With a sample size of 20 and an expected proportion of 80% achieving the primary outcome, the precision would be ±17.5 (95% CI).

A prespecified statistical analysis plan was written and approved prior to database lock and analyses (supplementary Appendix 3, https://www.jurology.com).

RESULTS

Baseline Demographics

Of the 21 recruited men, 20 received the procedure and these data were available for analysis of the primary outcome (table 1). One patient was withdrawn on the operating table because of combination of his perineal anatomy (thickness of fat layer) and length of the probe (too short to reach the base of the 33 cc gland). Two (10%) and 18 (90%) had D'Amico low and intermediate risk prostate cancer. All met criteria for UCL definition 2 clinical significance at minimum.

Median mpMRI cancer volume was 2.8 cc (IQR 1.4–4.8) for a median MCCL of 7 mm (IQR 5–10).

Table 1. *Baseline characteristics*

Pt demographics:		
Median yrs age (IQR)	66.5	(63–69)
Median ng/ml PSA (IQR)	7.9	(5.3–9.6)
Median ml prostate vol (IQR)	42.2	(30.5–50.9)
Biopsy mapping strategy:		
5 mm Transperineal:		
No. (%)	3	(15)
Median pos cores per lesion	9	
Transperineal systematic+targeted:		
No. (%)	4	(20)
Median pos cores per lesion	5	
Targeted only:		
No. (%)	13	(65)
Median pos cores per lesion	3	
Pre-treatment biopsy histology of lesion to treat:		
Median mm max Ca core length (IQR)	7	(5–10)
No. Gleason score (%):		
3+3=6	2	(10)
3+4=7	17	(85)
4+3=7	1	(5)
Untreated Ca focus outside treated area at baseline:		
No. (%)	6	(30)
Median mm max core length of Gleason 6	1	
No. D'Amico risk group (%):		
Low	2	(10)
Intermediate	18	(90)
High	0	(0)
No. threshold of significance of UCL definition (%):		
Insignificant	0	(0)
Matching only definition 2 (Gleason ≥3+4 or MCCL ≥4 mm)	13	(65)
Definition 1 (Gleason ≥4+3 or MCCL ≥10 mm)	7	(35)
MRI lesion characteristics:		
No. Likert score (%):		
3	3	(15)
4	10	(50)
5	7	(35)
Median ml vol (IQR)	2.7	(1.4–4.8)
Median mm width (IQR)	16	(13–19)
Median mm distance from apex (IQR)	3	(0–6)
No. abutting apex with distance equal to 0 mm to apex (%)	9	(45)
Median mm distance from base (IQR)	10	(2–12)
No. abutting base with distance equal to 0 mm to base (%)	5	(25)
No. MRI lesion location:		
Anterior Ca (%):		10 (50)
Mean mm distance from posterior capsule to most anterior part of Ca lesions (IQR)	35	(32–37)*
Mean mm distance from posterior capsule to most posterior part of Ca lesions (IQR)	13	(9–14)†
Posterior Ca (%):	10	(50)
Mean mm distance from posterior capsule to most anterior part of lesion (IQR)	19	(16–20)*
Mean mm distance from posterior capsule to most posterior part of lesion (IQR)	0	(0–0)†

* Significant difference (t-test, $p < 0.0001$; median 6.2 mm 95% CI 10.8569, 21.7431).
† Significant difference (t-test, $p < 0.0001$; median 5.1 mm, 95% CI 6.8251, 16.17490).

Ten (50%) patients had anterior and 10 (50%) posterior cancers. Mean distance of the cancer boundaries to apex of the gland was 3 mm (IQR 0–6). Anterior and posterior diseases presented significantly different morphometric characteristics at MRI analysis (table 1). This illustrates the different critical anatomical structures to avoid damage to, for instance, the rectum posteriorly or the pubic bone and bladder neck anteriorly (fig. 2) while delivering appropriate energy to pursue a complete ablation. A total of 11 patients (55%) were eligible at baseline for assessment of the trifecta status after patient reported outcome measures analysis using predetermined criteria. Those 11 patients eligible for assessment of trifecta status were continent (no leakage and no use of pad) before treatment, with good baseline erectile function defined as a score of 4 or 5 on question 2 of IIEF-15 (erection sufficient for intercourse reported as "always" or "most of the time"). No subject withdrew consent, died or was lost to followup.

Procedure

Characteristics of the procedure are presented in table 2. The development aspect of the technique is detailed in supplementary Appendix 4 (https://www.jurology.com), in compliance with the IDEAL framework for surgical innovations. The coils of 8 and 12 mm in diameter were found to be the more appropriate for prostate ablation. The median time to complete the fusion US-MRI using the SmartTarget® and treatment planning was 9 minutes (IQR 5.5–13.5). The median time to deliver the ablation was 89 minutes (IQR 66–118). Figure 3 shows preoperative, intraoperative and postoperative imaging.

Outcomes

Primary. There were 16 (80%) patients free of clinically significant prostate cancer on targeted transperineal biopsy of the treated area at 6 months. A median number of 6 (IQR 4–11) cores were taken from the ablated area, resulting in a sampling density of 3.3 cores per 1 ml (IQR 0.65–4.71) of lesion to treat at baseline. In all cases, the ablated zone and its inherent shrinkage was discernable in both mpMRI and ultrasound guiding the biopsy. Figure 4 depicts shrinkage of the gland, histology of coagulation necrosis and a sharp transition to undamaged tissue on a targeted biopsy of the ablated area at 6 months from treatment. Absence of any cancer was noted in 15 (75%) and 1 patient was considered clinically insignificant as per protocol due to MCCL of 1 mm and Gleason 6. Re-treatment as per protocol was delivered in 2 patients and 2 preferred active surveillance for 4 mm of Gleason 6 and 1 mm of Gleason 3+4=7 with a 5% component of grade 4. There was no difference in the proportion of patients failing the primary objective when stratified by location of the disease (anterior vs posterior, table 2). Serum PSA decreased from median 7.6 ng/ml (IQR 5.3–9.6) at baseline to 2.7 ng/ml (IQR 0.3–3.75; $p < 0.0001$; mean difference 4.41, IQR 2.98, 5.85).

Secondary. Per protocol analysis, 94% (16/17) of patients were free of significant cancer 6 months

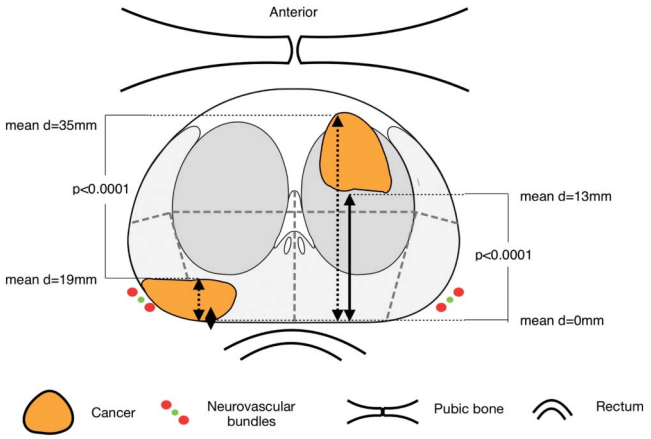

Figure 2. Differences in morphometric characteristics between anterior and posterior cancer based on mpMRI analysis. Distances (*d*) are measured from posterior edge of prostate in axial plan for most anterior and most posterior component of cancer to ablate. Ten anterior and 10 posterior cancers are compared using nonpaired 1-sided t-test.

after the last treatment, including re-treatment. Three patients did not fully comply with the protocol after visit 6 (biopsy), 2 entered into surveillance (no re-treatment) and 1 declined 6 months biopsy post re-treatment. No patient transitioned to another treatment within the timeframe of the study. No new significant cancer outside the treatment zone nor new lesion progression as expected in the time frame of the study (out-of-field recurrence) occurred during the trial. Performances of mpMRI in the postoperative are in supplementary Appendix 5 (https://www.jurology.com).

The absence of erectile dysfunction, defined by an inability to have erections sufficient for intercourse, at 12 months, as measured by the IIEF-15 questionnaire with or without the use of a phosphodiesterase type 5 inhibitor, in those with absence of erectile dysfunction at baseline, was seen in 91.7% (11/12, fig. 5). The return to baseline occurred by 6 weeks as assessed by patient reported outcome measures. There was no change in scores for intercourse satisfaction, in sexual desire, in overall sexual satisfaction and orgasmic function for patients with available data (fig. 5).

Absence of urinary incontinence (any pad usage plus any leakage of urine) as determined by the EPIC Urinary Continence Questionnaire at 12 months in those men with no urinary incontinence at baseline was seen in 89% (16/18). Two patients reported using 1 pad a day for bladder overactivity at 6 months from the procedure (supplementary Appendix 5, https://www.jurology.com). There was no change in scores measuring lower urinary tract symptoms, bowel habit, general health and prostate health related quality of life as determined by IPSS and IPSS-QoL, EPIC Bowel Questionnaire and EQ-5D and FACT-P scores at 12 months, compared to baseline, in men with data available (fig. 5). ANOVA testing only detected significant changes across the length of the study for IPSS ($p=0.017$) and EPIC urinary domain ($p=0.013$) even if at 12 months the change from baseline in score were respectively 0 (IQR −3 to 0) and 0 (IQR −6.6 to 5.2). Figure 5 shows that changes are captured at 6 weeks with a return to baseline by 3 months post treatment. Of the 11 patients eligible for assessment of the trifecta status, all of them (11/11; 100%) completed it at 1 year.

There were 40 AEs reported during the year of followup for the entire cohort. There were 11 (27.5%) CTC grade 1 AEs, 29 (72.5%) grade 2 and 0 grade 3, 4 or 5. The most reported AE was urinary tract obstruction reported 8 times. None of the 3 serious AEs were related to the intervention and were classified CTC AE 2. Presence of rectourethral fistula and severe (grade III type) or mild to moderate (grade I-II)

Table 2. *Procedure characteristics, histology and mpMRI results*

Procedure characteristics:		
No. general anesthesia (%)	15	(75)
No. spinal anesthesia (%)	5	(25)
Median mins SmartTarget US-MRI treatment planning (IQR)	9 (5.5—13.5)	
Median mins treatment delivery (IQR)	89 (66—118)	
Radiofrequency probe use:		
Median coils/pt (IQR)	2	(2—3)
Median pullbacks/pt (IQR)	2	(2—4)
Median extra needles/pt (IQR)	11	(7—14)
% Ultrasound changes detected during ablation*	100	
% Change in impedance superior to 10× pre-ablation impedance†	95	
Primary outcome (6-mo biopsy):		
No. cores/ablated zone (IQR)	6	(5—8)
Mean density of cores per ml ablated tissue (IQR)	0.9 (0.7—1.4)	
Mean density of cores per ml initial tumor vol (IQR)	3.3 (1.4—4.7)	
Neg for clinically significant Ca:		
No. (%)	16	(80)
No. neg for any Ca (%)	15	(75)
No. fibrosis-necrosis present (%)	20	(100)
Median mm max core length residual Ca (IQR)	4	(1—4)
Gleason score in residual cancer:		
No. Gleason 3+3=6	3	
No. Gleason 3+4=7	2	
No. failure with anterior disease/total No. (% anterior Cas)	2/10 (20)	
No. failure with posterior disease/total No. (% posterior Cas)	2/10 (20)	
mpMRI change:		
Median ml MRI necrosis vol	14.7 (11.1—21)	
No. complete coverage (%)	16	(80)
No. residual lesion (%)	4	(20)
Median ml residual lesion vol at 6-mo MRI (IQR)	0.7 (0.08—0.8)	
No. reduced MRI lesion size in pt with pos biopsy/total No. (%)	5/5 (100)	

* Ultrasound changes are hyperechogenic features seen within coil during ablation and shortly after completion.

† Increase in impedance of power between electrodes of bipolar system characterize dehydration of tissue and therefore coagulation necrosis. For patient 1, 1 ablation did not reach this threshold of 10 times start impedance.

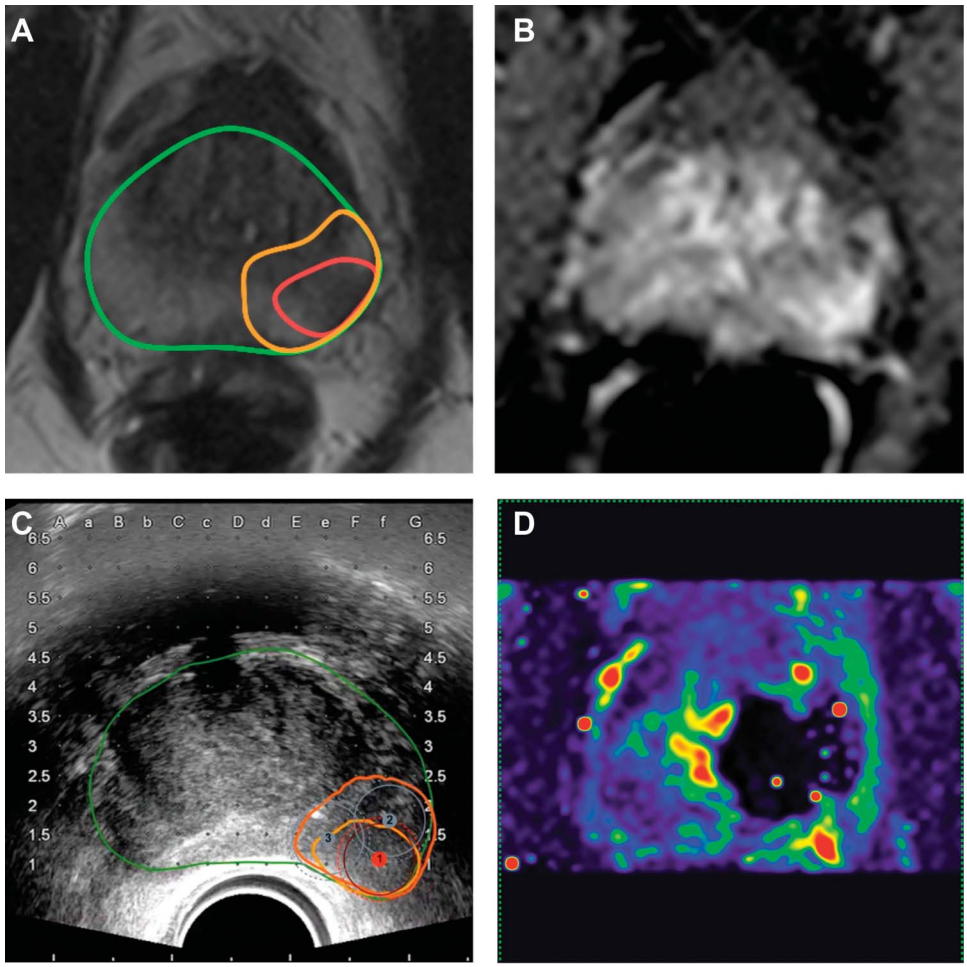

Figure 3. 68-Year-old enrolled patient presenting with localized prostate cancer Gleason 7 (3+4) with maximum core length of 11 mm of left peripheral zone. *A,* T2-weighted imaging with segmented prostate (green line) and lesion (red line) augmented by preplanned margin (orange line). *B,* DCE weighted imaging at matching level of *A. C,* intraoperative ultrasound with fused MRI derived lesion with compensation of deformation induced by endorectal probe. Circles 1, 2 and 3 represent treatment planning and coils to be inserted to perform complete ablation of cancer with margin. *D,* mpMRI DCE weighted imaging at 5 days post-treatment shows necrosis in location of targeted cancer and living tissue around it.

rectal toxicity were not reported in any men (0%). Two patients developed urethral strictures, which were managed successfully by endoscopic procedures and 1 man had a perineal skin tear which required immediate repair as a result of use of a larger 16 mm double coil, which we subsequently stopped using

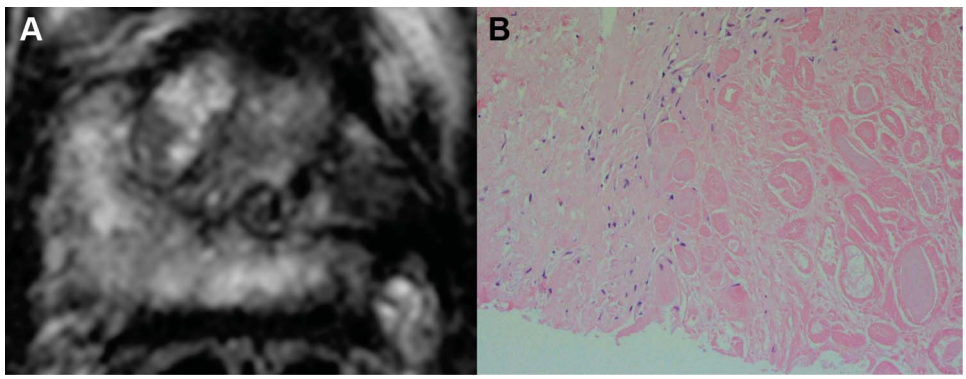

Figure 4. Example at 6 months of followup from treatment of enrolled patient. *A,* T2-weighted imaging demonstrates localized shrinkage in place of previous ablation *B,* biopsy core taken from ablated area and surroundings. H&E, reduced from ×40. Lesion of coagulation necrosis (at right) with sharp transition to healthy tissue shows persistent staining in nuclei (at left).

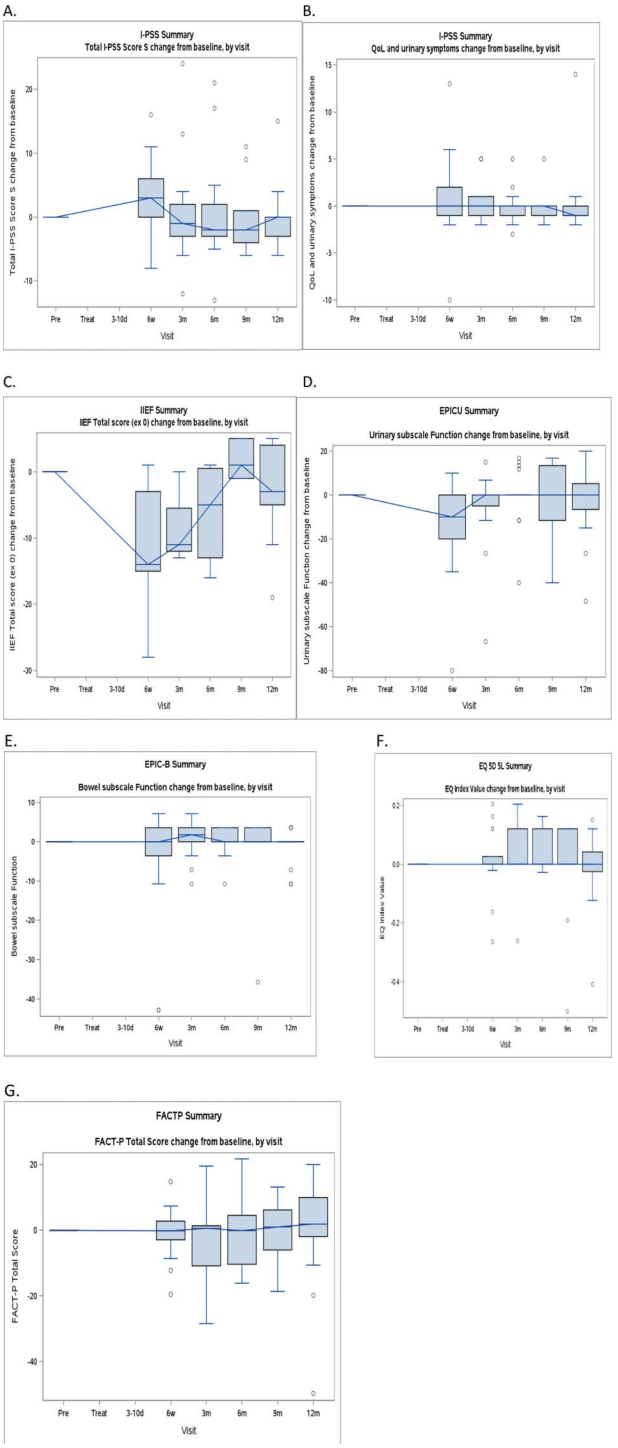

Figure 5. Functional outcomes after focal therapy using bipolar radiofrequency with coil design described as changes to baseline. Box and whisker plots indicate median with IQR (boxes) and range (whiskers). Dots represent outlier. *A*, total IPSS score. Median change from baseline to 12 months was 0 (IQR -3 to 0) in 17 patients (ANOVA, p=0.01707). *B*, IPSS-QoL. Median change from baseline to 12 months was -1 (IQR -1 to 0) in 20 patients (ANOVA, p=0.13067). *C*, IIEF total score. Median change from baseline to 12 months was -3 (IQR -5 to 4) in 20 patients (ANOVA, p=0.10376). *D*, EPICU (urinary domain). Median change from baseline to 12 months was 0 (IQR -6.6 to 5.2) in 19 patients (ANOVA, p=0.01303). *E*, EPIC-B (bowel domain). Median change from baseline to 12 months was 0.89 (IQR -1.79 to 1.79) in 14 patients (ANOVA, p=0.12909). *F*, 5-Level EQ- 5D tool. Median change from baseline to 12 months was 0 (IQR -0.02 to 0.04) in 19 patients (ANOVA, p=0.28635). *G*, FACT-P. Median change from baseline to 12 months was 1.9 (IQR -1.9 to 10) in 16 patients (ANOVA, p=0.69594). ANOVA was calculated using nonparametric analysis of longitudinal data method described by Brunner et al with SAS® 9.4 (Brunner E et al: Nonparametric Analysis of Longitudinal Data in Factorial Experiments. New York: Wiley 2002).

(supplementary Appendix 4, https://www.jurology.com). This AE resolved without complications.

The early post-treatment mpMRI depicted confluent necrosis in all cases with a mean volume of 16 cc.

As a development study, phase 2 according to IDEAL framework for surgical innovation,[18] iteration of the procedures was permitted to refine the surgical technique and workflow. This is documented in supplementary Appendix 4 (https://www.jurology.com).

DISCUSSION

In summary, we report the first successful study of coil bipolar radiofrequency ablation to deliver focal therapy to ablate clinically significant prostate cancer associated with a mpMRI lesion. This lends support to conducting an IDEAL therapeutic confirmatory study. The results show that not only can this technology destroy prostate cancer cells, but also can adapt to the challenging anatomical environment of the prostate gland and match the morphometry of significant cancers eligible for focal therapy. Most anterior and posterior lesions, including the necessary margin around an MRI lesion, can be ablated successfully with this device. While some strategies recommend the choice of energy by location of the disease,[13] the main limitation of this technology would refer to the detectability of the cancer as significant using a transperineal biopsy through a brachytherapy grid as a proxy to accessibility for ablation to this technology, potentially excluding anterior lesions in large glands (>100 cc) where the interference with the pubic arch could be problematic. We also confirm the low rate of side effects and complications that can occur from focal therapy, with no differences from baseline.

The specific design of an asymmetrical bipolar radiofrequency system using a coil, visible under ultrasound, permitted the delivery of a uniform zone of coagulative necrosis where it was planned. A previous phase 1 study using radiofrequency as an energy source but a different device design reported large variability in induced necrotic lesions, abortion of case due to concern of the rectal wall and the need for thermoprobes to control treatment.[24,25] We did not experience those limitations of the radiofrequency energy with the coil design and did not use thermoprobes. The sharpness of the transition zone between ablated and intact tissue (fig. 3) and its predictability limit the challenge of focal ablation to placement of the coils and delivery of the treatment planning.

The development of a stabilized technique required multiple refinements in this IDEAL phase 2 trial. Operators had significant experience in transperineal procedures under US guidance, which is a prerequisite to deliver the intervention. Otherwise, the learning curve would be considerable. Iterative changes were needed as detailed in supplementary Appendix 4 (https://www.jurology.com) to develop a new intervention specific for the prostate using this coil based design. One of the most significant findings was the use of the needle electrode outside the coil to create a bipolar system permitting extension of the margin outside the coil. Outside critical anatomical zones to be preserved, this was very useful to quickly perform an additional ablation in contiguity with the intra coil ablation to extend the margin by inserting a needle through an already positioned hole of the coil holder. Even going through those refinement steps and a learning curve, we achieved in this first use in men trial very good efficacy of 80% free of significant disease.

In this area of treatment guidance, the study benefited from the use of the nonrigid MRI-US fusion platform system adapted for the study to ensure lesion and margin coverage to overcome our limited experience with this device. In the 20% of cases with failure, there was more residual disease on the boundaries of the ablated area rather than within the centroid of the ablated zone. The urethral stricture rate should be carefully assessed in further larger exploratory study.

The design of this study follows the recommendations from focal therapy consensus panels to treat patients presenting with clinically significant prostate cancer, intermediate risk, and not those who would be eminently suitable for active surveillance. As a limitation, the current results cannot be generalized to this whole risk category. One of the main entry criteria was the presence of a single MRI visible lesion confirmed by transperineal sampling with significant cancer matching inclusion criteria. Lesion amenability with the device was assessed based on MRI, which could have impaired the morphometric characteristics of the ablated lesions. However, those characteristics match both in shape or volume what has been described in contemporary detailed analysis of cancer foci of radical prostatectomy series.[20,21] For example median index tumor volume of 2.8 ml was in the same range as the 2.2 ml described by Haffner et al.[20]

In comparison to other technologies tested in phase 2 studies for which systematic sampling was obtained, coil bRFA shows the same range of success with 80% of absence of disease in this first of its kind trial.[6] Previous lesion based focal ablation studies not including an appropriate margin failed to achieve similar results to those presented here with a higher failure rate of up to 75%.[26–28]

In conclusion, focal therapy of a MRI lesion associated with clinically significant prostate cancer

using bipolar radiofrequency ablation showed early efficacy to ablate cancer, and had low rates of genitourinary and rectal side effects.

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EDITORIAL COMMENT

Coil bRFA with the Encage device is a unique option for focal prostate ablation. With transperineal insertion, and ablation limited to the coil cage, treatments can be applied to both anterior and posterior lesions with minimal chance of ablating nearby vital structures. In this series of 20 men with intermediate risk prostate cancer, no grade 3-5 adverse events were reported and 15 men had complete absence of any cancer at the 6-month biopsy. This is impressive considering that it was a first of its kind experience and post-treatment biopsy was mandated and thorough, with a median of 6 cores from the treatment site, which is beyond the approach of most focal therapy series.

However, the success may in large part be due to the ingenious approach of adding extra needles to

pull the energy outside the coil. Even though keeping energy inside the coil provides safe gating of vital structures, I assume that it was almost too precise. Because lesions are typically larger than they appear on MRI, successful focal therapy requires wide margins (reference 19 in article), a dictum we follow carefully in our MRI guided transrectal high intensity focused US and transperineal laser trials. I imagine that having the ability to reshape and expand the ablation with additional needles in bRFA gives the freedom to tailor the shape to accommodate almost any tumor morphology.

Although intermediate term outcomes are unknown, these early results are quite promising. One major challenge will be generalizing bRFA because, as the authors explain, experience with US guided transperineal procedures is a prerequisite for successful bRFA. This is a skill that many urologists lack. Despite this, the results are encouraging, and I am excited to see the growth of this platform.

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