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Focal therapy for prostate cancer with irreversible electroporation: Oncological and functional results of a single institution study

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Purpose: Focal irreversible electroporation (IRE) for prostate cancer aims to reduce quality of life complications, however outcomes data remains limited. We aimed to evaluate histological in-field clearance of prostate cancer at ≥12 months post-IRE.

Materials and Methods: Retrospective review of prospectively acquired data of consecutive patients treated between August 2018 and August 2021. Significant recurrence was defined as a ≥6 mm core Gleason 3+3, or ≥Gleason 3+4 with ≥4 mm tumour length. A second definition of any focus of International Society of Urological Pathology (ISUP) ≥2 was also analysed.

Results: The median follow-up of the entire cohort is 23 months (range 3–39 mo). For 64 primary IRE procedures, surveillance biopsy was performed in 40/50 (80.0%) with ≥12 months follow-up. Significant in-field recurrence occurred in 3/40 (7.5%), or 4/40 (10.0%) with any focus of ISUP >2. Significant out-of-field recurrence occurred in 5/40 (12.5%). In salvage IRE, three patients (3/6, 50.0%) have undetectable prostate-specific antigen levels, two have no residual cancer on biopsy and one patient had out-of-field recurrence. For sexually active men, erectile function was maintained in 24/28 (85.7%) of primary IRE. No incontinence developed in primary IRE (0/64).

Conclusions: Focal primary IRE for prostate cancer is associated with 90% infield ablation of any ISUP grade >2 cancer with a low risk of urinary incontinence or impotence. Surveillance prostate biopsies are required to exclude progression despite a normal post-IRE multiparametric magnetic resonance imaging (mpMRI). Salvage IRE is a promising option for localised recurrence after prostate radiotherapy with low morbidity.

Keywords: Focal therapy; Irreversible electroporation; Prostate cancer; Surveillance biopsy; Urinary incontinence

INTRODUCTION

Significant prostate cancer (PCa) is traditionally treated by whole gland therapy with a radical prostatectomy, or radiation treatments, including brachytherapy. Whole gland treatment of PCa is associated with potential quality of life side effects including, but not limited to, urinary incontinence, impotence and radiation toxicity to the bowel/bladder.

Management of PCa with focal therapy aims to minimise the quality of life complications while simultaneously decreasing the risk of PCa progression. The initial focal therapy programs have concentrated on management of low

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and intermediate risk PCa, as this cohort has a low probability of PCa specific mortality within a decade of diagnosis, even when treated with an initial approach of active surveillance [1-3].

There are many different focal therapy technologies, including high intensity focused ultrasound ablation, focal cryotherapy, focal brachytherapy and focal laser ablation. However, there are no prospective direct comparative trials between focal therapy technologies and no existing data to support any technology as superior [4,5]. Irreversible electroporation (IRE) is a focal therapy treatment that uses pulsatile electrical currents between needle electrodes to cause ablation of tissue due to non-thermal apoptotic death rather than coagulative necrosis [6,7]. IRE alters the cell membrane, irreversibly increases permeability of cells that results in osmotic disequilibrium and apoptosis. Importantly structures such as blood vessels and smooth muscle cells appear more resistant to damage using IRE technology [8]. Early clinical data shows promising in-field clearance of PCa with minimal side-effect toxicity, including a low risk of urinary incontinence [9-12]. Furthermore, IRE complications are uncommon and are usually Clavien–Dindo Classification grade 1–2 [4,13].

The aim of this study is to evaluate the oncological outcome of PCa focal IRE as defined by histological in-field clearance of cancer at biopsy ≥12 months post-IRE. Secondary aims included a review of postoperative complications, urinary incontinence and erectile dysfunction.

MATERIALS AND METHODS

A retrospective review was performed on prospectively acquired data from a single institution multi-surgeon cohort of consecutive patients treated with IRE between August 2018 and August 2021. Ethics approval was obtained from the Uniting Care Health Human Research Ethics Committee (approval number: 2021.21.359). Patients with localised PCa based on staging prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) scan were considered for inclusion. All patients required a pre-operative multiparametric magnetic resonance imaging (mpMRI), with radiological evidence of extraprostatic extension or seminal vesicle invasion (stage T3a/T3b) an exclusion for IRE. Tumours with a maximum diameter of ≥25 mm on mpMRI were considered unsuitable for IRE. Patients were not excluded based solely on prostate-specific antigen (PSA) levels, or any specific anatomical tumour location within the prostate. The IRE treatment zone was based on the significant cancer biopsy location on transperineal prostate biopsy +/- concordance with either a mpMRI Prostate Imaging Reporting and Data System (PI-RADS) 3–5 lesion, or an avid prostate lesion on pre-treatment staging ^{68}Ga-PSMA PET/CT scan. Prior to the IRE procedure all patients met the criteria for significant PCa based on a definition of "a ≥6 mm core International Society of Urological Pathology (ISUP) grade 1 (Gleason 3+3), or ISUP grade 2 (Gleason 3+4) with ≥4 mm tumour length, or any focus of ISUP grade 3–5".

In the primary IRE setting bilateral tumours were performed at surgeon discretion, but single ablations only were performed in the salvage setting after previous radiotherapy. Pre-IRE template prostate biopsies were required to exclude significant volume or Gleason grade cancer outside the IRE treatment zone. Patients were also excluded if they had prior IRE at another centre.

The IRE procedure was performed under a general anaesthetic with the patient in lithotomy position and a urethral catheter *in situ*. The treatment field was based on cognitive placement of transperineal IRE needles around the MRI lesion with a minimal margin of 5 mm (Fig. 1). The position of the IRE needles was confirmed in both the axial and sagittal sections via transrectal ultrasound probe imaging. The number of IRE electrode needles inserted depended upon the size and shape of the lesion. The IRE needles were positioned ≥4 mm off critical structures (rectal wall/urethra) and polarity changed to positive to avoid any potential thermal damage. Initially Magnetic Resonance Imaging - Transrectal Ultrasound (MRI-TRUS) fusion was used to help with precise needle placement, but due to the experience of the urological surgeons with transperineal biopsy

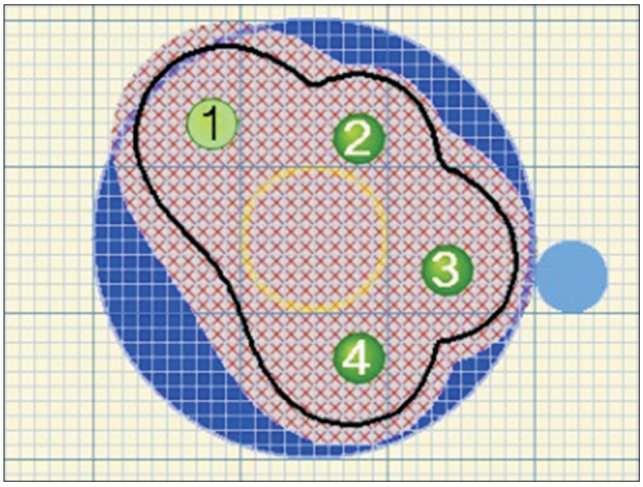

Fig. 1. Four IRE needles (labelled 1 to 4) placed via a transperineal approach around the tumour in the prostate (marked as the inner circle) with the aim of a minimal ablation margin of 5 mm. IRE, irreversible electroporation.

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and brachytherapy techniques, cognitive needle placement replaced MRI-TRUS fusion. The IRE needles were then connected to a NanoKnife (Angiodynamics PTL, Latham, NY, USA) computer- based treatment planning software machine that controls the current. A set of 10 pulses was initially applied to determine conductivity of the tissue followed by a therapeutic train of 80 pulses. Machine parameters were adjusted, with an aim to achieve a minimum change of current >nine amperes (Amps) between probe pairs where possible. In general, we aimed for the distance between IRE needles of 15 mm (10–22 mm), a current of 25 Amp (20–35 Amp), a voltage of 2,500 volts (1,500–3,000 volts) and a needle exposure length of 15 to 20 mm.

The timing of the indwelling catheter removal was dependent on individual surgeon preference, although initially at our institution patients remained overnight with the indwelling catheter (IDC) *in situ* for observation. Post-operative complications were based on Clavien–Dindo Classification system. Incontinence of urine was defined as any requirement for a pad in the post-operative period. Erectile function was defined as moderate (or greater) confidence to obtain and keep an erection based on question 1 of the International Index of Erectile Function (IIEF-5) score, or as small or no problem obtaining an erection based on the Expanded Prostate Cancer Index Composite (EPIC) questionnaire. Where patients had not completed pre and post treatment EPIC questionnaire or IIEF-5 forms, the patients were contacted via an investigator independent of the surgeons to confirm continence and erectile function.

The treating urologists recommended that all patients were investigated with a mpMRI six months after IRE and routine surveillance template transperineal biopsies of the infield treatment zone and also out of field prostate tissue at a minimum of 12 months post operatively. The histopathology was reviewed in a specialised uropathology department. The mpMRI images were reported by an institution which performs >200 prostate mpMRI procedures each month. Only surgeons who performed a minimum of ten IRE procedures were included for analysis.

Significant tumour recurrence on surveillance prostate biopsy was defined as a ≥6 mm core ISUP grade 1 (Gleason 3+3), or ISUP grade 2 (Gleason 3+4) with ≥4 mm tumour length, or any focus of ISUP grade ≥3. Lesions with a positive core length of <4 mm are associated with tumour volume <0.2 mL on whole mount histopathology [14]. A second definition using any focus length of Gleason score 3+4 (ISUP grade 2) as significant cancer was also evaluated.

RESULTS

Seventy men were treated with focal IRE between August 2018 and August 2021. All patients had significant cancer in the IRE treatment zone. Primary IRE was performed on 64/70 of whom four had bilateral lesions ablated. Salvage IRE for local recurrence after radiotherapy was performed in six patients. The characteristics of the cohort at diagnosis is outlined in Tables 1 and 2. The median follow-up is 23 months (range 3–39 mo). The median age was 72 years (range 51–87 y). Of the 70 patients in the study, 64 were discharged either on the day of the IRE, or day one post-operatively (64/70, 91.43%). The maximum length of stay was two days. No patient required re-admission within 30 days for post-treatment complications.

1. Primary IRE

Of the 64 men treated with primary IRE, 50 have been followed-up for more than 12 months (median 23 mo, range 3–39 mo). The median PSA is 6.10 ug/L (range 0.77–25.00 ug/L). The median ISUP grade was 2, with 12 patients treated with high risk ISUP grade 4–5 malignancy. Most patients had a PI-RADS 4 mpMRI (44/64) at diagnosis, with a low risk PI-RADS 2 mpMRI in only 4 patients. There was no contralateral tumour in 42/64 patients, out-of-field ISUP grade 1 in 17/64, ISUP grade 2 in 4/64 and one patient had a 1 mm focus of ISUP grade 3 in the contralateral lobe. Of the men with ≥12 months follow-up the median pre-treatment PSA density was 0.13 (range 0.02–0.55). The median PSA nadir in this cohort was 1.3 ug/L (range 0.07–7.20 ug/L). The PSA nadir ranged from 1.10% to 114.55% of the original pre-IRE PSA level, with a median of 26.5%.

1) Follow-up biopsy data for primary IRE

Surveillance biopsies were performed in 40/50 (80.0%) of patients usually 12 months follow-up post-primary IRE, although four biopsies were performed at year 2 and three biopsies three years post IRE. The remainder either declined biopsies due to low PSA levels and/or complete ablation on post IRE mpMRI (PI-RADS ≤2).

Complete ablation of all in-field cancer was identified in 35/40 (87.5%) of the surveillance biopsies. Significant in-field recurrence was identified in 3/40 (7.5%) of surveillance biopsies, or 4/40 (10.0%) using definition 2 of any ISUP 2 or greater (Tables 3, 4). One patient had a small focus of insignificant in-field ISUP grade 1 malignancy. Two patients with significant in-field recurrence have since proceeded to robot assisted laparoscopic radical prostatectomy (RALP), demonstrating Gleason 3+4 and 4+3 respectively. Both pa-

Table 1. Patient characteristics at baseline (primary IRE only)

Characteristic	Men undergoing primary IRE (n=64)
Age (y)	72 (51–87)
PSA (ug/L)	6.10 (0.77–25.00)
Prostate volume on mpMRI (cc)	40 (15–82)
Baseline prostate mpMRI PI-RADS score	
≤2	4
3	4
4	44
5	12
Size of primary target lesion on mpMRI (mm)	
No lesion (PI-RADS 2)	4
<10	17
10–20	40
>20	3
Lesion location on initial mpMRI	
Peripheral zone	
Apex	8
Mid-apex	3
Mid	21
Mid-base	3
Base	4
Transitional zone	
Apex	0
Mid-apex	0
Mid	3
Mid-base	1
Base	0
Anterior/anterior-transitional zone	
Apex	2
Mid-apex	1
Mid	13
Mid-base	1
Base	0
No MRI	4
Number of cores taken on initial biopsy	19.50 (2–55)
Number of positive cores on initial biopsy	5 (1–28)
Initial biopsy ISUP score	
1	4
2	33
3	15
4	6
5	6

Values are presented as median (range) or number only.
IRE, irreversible electroporation; PSA, prostate-specific antigen; mpMRI, multiparametric magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; ISUP, International Society of Urological Pathology.

Table 2. Patient characteristics at baseline (salvage IRE only)

Characteristic	Men undergoing salvage IRE (n=6)
Age (y)	70 (66–76)
PSA (ug/L)	2.20 (0.24–8.40)
Prostate volume on mpMRI (cc)	14.50 (11–41)
Baseline prostate mpMRI PI-RADS score	
≤2	0
3	0
4	4
5	2
Size of primary target lesion on mpMRI (mm)	
No lesion (PI-RADS 2)	0
<10	1
10–20	5
>20	0
Lesion location on initial mpMRI	
Peripheral zone	
Apex	0
Mid-apex	1
Mid	2
Mid-base	1
Base	2
Transitional zone	
Apex, mid, or base	0
Anterior/anterior-transitional zone	
Apex, mid, or base	0
Number of cores taken on initial biopsy	14.50 (4–28)
Number of positive cores on initial biopsy	4 (2–8)
Initial biopsy ISUP score	
1	1
2	2
3	2
4	0
5	1

Values are presented as median (range) or number only.
IRE, irreversible electroporation; PSA, prostate-specific antigen; mpMRI, multiparametric magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; ISUP, International Society of Urological Pathology.

tients were staged as pT2 with negative margins from their RALP histopathology. The third is awaiting a RALP and the fourth has elected on a conservative approach, due to a minimal component of ISUP grade 2 malignancy. Of the four in-field recurrences with ISUP ≥2, the pre-IRE PSA density was 0.12 (0.08–0.14), the median PSA nadir was 3.2 ug/L (1.4–4.2 ug/L) and the median PSA nadir level in comparison to the initial PSA was 58.00% (23.73%–91.43%).

Significant out-of-field recurrence occurred in 5/40 (12.5%) on surveillance transperineal biopsies, or 11/40 (27.5%) with any ISUP grade 2 focus (definition 2). Of the patients with

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Table 3. Patterns of recurrence after primary IRE on follow-up prostate biopsy

Recurrence	Significant cancer	Insignificant cancer
In-field	3 (7.5)	2 (5.0)
Out of field	5 (12.5)	12 (30.0)

Values are presented as number (%).
IRE, irreversible electroporation; ISUP, International Society of Urological Pathology.
NB - Definition of significant cancer: ≥6 mm core ISUP grade 1 (Gleason 3+3), or ISUP grade 2 (Gleason 3+4) with ≥4 mm tumour length, or any focus of ISUP grade 3–5.

Table 4. Patterns of recurrence after primary IRE with any volume ISUP ≥2 graded as significant recurrence

Recurrence	Significant cancer	Insignificant cancer
In-field	4 (10.0)	1 (2.5)
Out of field	11 (27.5)	6 (15.0)

Values are presented as number (%).
IRE, irreversible electroporation; ISUP, International Society of Urological Pathology.
Definition of significant cancer: ≥6 mm core ISUP grade 1 (Gleason 3+3), or ISUP grade 2 (Gleason 3+4) with ≥4 mm tumour length, or any focus of ISUP grade 3–5.

no contralateral tumour at diagnosis, 25/42 had a biopsy after IRE. Out-of-field ISUP grade 2 cancer was identified in 5/25 on surveillance biopsy, but only one patient had a tumour core length ≥4 mm. Of the 17 patients with contralateral lobe ISUP grade 1 at diagnosis, 11 had surveillance biopsies, of which four progressed to ISUP grade 2, with ≥4 mm core length in two patients. Three of the four men with contralateral ISUP 2 had similar malignancy at surveillance biopsy and the other had clear systematic cores. The patient with a focus of out-of-field ISUP grade 3 is not yet due for surveillance biopsy. Of the four patients treated for bilateral IRE lesions, one had a salvage RALP for in-field recurrence, two had significant out-of-field recurrence with both definitions and only one had a negative post-IRE biopsy.

2) MRI primary cohort data

The baseline mpMRI findings are shown in Table 1. PI-RADS 4 was the most common lesion (44/64, 68.8%) identified on pre-IRE mpMRI. A post-IRE mpMRI was performed on 52/59 men who were more than six months post primary-IRE. The mpMRI was usually performed 6 months post-IRE, although in three patients the mpMRI was performed 10 to 18 months after IRE and three men had the mpMRI within the first 3 months. Low risk PI-RADS 2 findings were identified in 46/52 (88.46%) with PI-RADS 3 in three, PI-RADS 4 in one and PI-RADS 5 in two patients. Of the post-IRE PI-RADS 2 cohort 33/46 have surveillance biopsy data, with significant in-field cancer identified in 2/46 based on both definitions of significance. On the template biopsies, significant out-of-field cancer was identified in 3/33 (9.09%) or 8/33 (24.24%) with any volume ISUP grade 2. For significant PCa the negative predictive value was 73.7% (28/38) for any focus of ISUP grade 2 malignancy. Five of the six men with PI-RADS 3–5 abnormal mpMRI 12 months post-IRE proceeded to surveillance biopsy. All had cancer, but significant cancer using both definitions was identified in three patients for a positive predictive value of 60% for mpMRI.

3) Outcomes of high-risk cohort (ISUP grades 4 & 5)

There were 12 men with high-risk PCa (six patients each for ISUP 4 and ISUP 5) who received primary IRE. The post-IRE mpMRI was low risk PI-RADS 2 in ten men and two declined follow-up mpMRI. Seven patients in this cohort proceeded to biopsy (one at two years posy-IRE and one at year three), three patients are not due for biopsy due to <12 months follow-up, one refused due to low PSA levels and one declined due to developing Wernicke's encephalopathy not related to the IRE. There was no in-field recurrence (0/7, 0%) in the high-risk group, however significant out-of-field recurrence occurred in one patient and 3/7 (42.86%) had insignificant out-of-field recurrence.

4) Complications of primary-IRE

All 64 men treated with primary IRE remain continent, with an incontinence rate of 0%. One patient subsequently developed incontinence after a repeat contralateral IRE procedure was performed. Of the 50 men with ≥12 months follow-up, 28 were potent pre-operatively with 24/28 (85.71%) remaining potent after primary IRE. There was only one Clavien–Dindo grade >2 complication, a patient who required dilation of a urethral stricture at three months unrelated to IRE of a left mid-anterior horn peripheral zone tumour.

2. Salvage IRE for radiotherapy failure

Of the six salvage IRE procedures for radiotherapy failure the median follow-up is 22 months (range 13–30 mo). The baseline median PSA at salvage IRE was 2.20 ug/L (range 0.24–8.4 ug/L). The post-radiotherapy, pre-IRE biopsy results showed ISUP grade <4 in five patients and ISUP grade 5 in one patient. Prior to salvage IRE there was no out-of-field cancer in 4 patients, one had a small focus of contralateral lobe ISUP grade 2 and another a small focus of ISUP grade 3. Following the salvage IRE, three patients (3/6, 50.0%) have undetectable PSA levels, and all patients have a PSA <0.55

ug/L (range 0–0.53 ug/L) at last follow-up.

1) Follow-up mpMRI and biopsy data for salvage IRE

Three patients had surveillance mpMRI scans after salvage IRE and all were low risk PI-RADS 2. The other three patients declined mpMRI follow-up due to low/undetectable PSA levels. Two patients proceeded with transperineal surveillance biopsies after salvage IRE, both with benign results and no residual in-field or out-of-field PCa. One patient had Gleason score 3+4 in 10% of the TURP chips performed seven months post-IRE for bladder outflow obstruction. The other three patients refused surveillance biopsy due to undetectable PSA levels. One patient had high-risk ISUP grade 5 on biopsy before salvage IRE. His post-IRE mpMRI was PI-RADS 2 and the patient declined biopsy as the PSA was <0.008 ug/L after IRE.

2) Complications of salvage IRE for radiotherapy failure

There was no Clavien–Dindo grade >2 complications. Incontinence developed in 2/6 salvage IRE procedures for radiotherapy failure, although incontinence only occurred after both patients subsequently underwent a TURP for bladder outflow obstruction. Only two of the six patients were potent before salvage IRE and one (50%) maintains post IRE erectile function.

DISCUSSION

The aim of focal therapy is to obtain oncological clearance of tumour, whilst at the same time avoiding significant treatment complications and maintaining quality of life. In the systematic reviews [4,13] on focal IRE there are only two series with larger patient numbers than our study, with the largest study a heterogeneous cohort that did not distinguish the outcomes of focal IRE from hemi-ablation or whole gland IRE [11]. Therefore, this manuscript adds important information on focal IRE outcomes. Complete histological in-field clearance of all cancer in our primary IRE series occurred in 87.5%, with significant in-field recurrence in 7.5%, or 10.0% if including any small core length of ISUP 2. However, significant out-of-field cancer in the template surveillance biopsies cores was identified in 5/40 (12.5%). When including any core length of ISUP grade 2 as significant, the out-of-field significant disease increased from 5/40 (12.5%) pre-IRE to 11/40 (27.5%) at surveillance biopsy. Out-of-field tumour progression is not a failure of the focal IRE technology, but more the failure of patient selection. If there was no out-of-field cancer on template biopsy prior to IRE, 5/25 developed ISUP grade 2 out-of-field progression on surveillance biopsy, but only one patient (4.0%) had a cancer core length of ≥4 mm. Our results indicate continued biopsy surveillance of the prostate is essential as part of a post-IRE active surveillance protocol, as potentially significant PCa can occur despite a low risk mpMRI in the early post-IRE follow-up.

Our results confirm the pleasing published early functional outcomes following IRE for primary PCa. In our series, no incontinence of urine developed in the primary IRE setting. However, a patient who was initially continent after IRE developed incontinence after a second IRE ablation for a new lesion in the opposite lobe. This is consistent with other published series, with between 88% to 100% of patient's continent of urine at 12 months post treatment [13]. However, the incontinence risk increased following IRE for salvage of localised recurrence after primary prostate radiotherapy. Six men received IRE for treatment of local recurrence post external beam radiotherapy. There was no initial post IRE incontinence, however two of these patients subsequently proceeded with a TURP for bladder outflow obstruction and both developed post TURP incontinence, requiring one incontinence pad per day.

Of the men with more than 12 months follow-up, 28/50 were potent prior to primary IRE and 24/28 (85.7%) maintained sexual function suitable for intercourse, with or without a PDE inhibitor. In other published series, erectile function is maintained in between 50% and 100%, including preserved potency in 77% when evaluated with EPIC questionnaire in the salvage setting [15]. Only two of the six patients in our cohort were potent before salvage IRE, of which one patient (50%) maintained satisfactory erectile function after salvage IRE.

The international Delphi consensus recommended oncological outcomes after focal therapy be reported with serum PSA, mpMRI, and systematic/targeted prostate biopsy results [16]. In our opinion, the use of post-IRE PSA as a marker of success remains controversial and unreliable, due to variability in PSA levels from different prostate volumes, the amount of tissue ablated with IRE and prostate inflammation. In the series of 123 men with intermediate (91%) or low risk cancer by Blazevski et al. [12], the median PSA fell from 5.725 ng/mL to 3.48 ng/mL (interquartile range 1.43–5.67) post-IRE. The PSA decreased by 71% in the series of 50 patients treated with IRE to the apical tumour [17]. This is almost identical to our median PSA nadir of 26.5% of the initial PSA level. There was a lower PSA percent decline in the four men in our study with primary treatment in-field recurrence, but the small numbers prevent statistical analy-

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sis. mpMRI has been used as a surrogate marker to identify recurrence after focal therapy, including IRE, but evidence-based evaluation of the accuracy of mpMRI post IRE in detecting local recurrence is not robust. In the Scheltema et al. [18] series 10/33 men who had a negative mpMRI 6 months post-IRE had cancer detected on the post-IRE prostate biopsy histology at 12 months, with a negative predictive value for in-field recurrence of 88% high because of the low probability of persistent cancer. In our cohort the negative predictive value of mpMRI to exclude any in-field or out-of-field ISUP grade 2 on surveillance biopsy was only 73.7% and therefore clinicians should not rely on mpMRI alone for long term surveillance after focal therapy.

Histological biopsy outcomes have previously been evaluated by Collettini et al. [2], who analysed 28 patients at 6 months post-IRE prostate. Two of the 28 (7.1%) men had clinically significant in-field recurrence. Of interest is the analysis of Ting et al. [10] who analysed 25 men with Gleason score <8 and PI-RADS 3–5 lesion/s visible on MRI. On prostate biopsy 7-months post-IRE there was no infield recurrence (0%), however, 4/21 (19%) had cancer recurrence adjacent to the treatment zone. This outcome is similar to the biopsy results in the diagnostic setting of PCa by Franklin et al. [19], who identified significant cancer in the near-target zone in 77% of cases when the target zone was positive, with 17% of participants upgraded through the addition of near-target cores. These findings outline the importance of a minimal IRE margin treatment zone of 5 mm, as mpMRI can underestimate histological tumour volume compared to radical prostatectomy histology [20]. The international Delphi consensus has only recommended focal therapy in D'Amico low-/intermediate-risk cancer including ISUP grade 3 [21]. In contrast, we identified in-field ablation in all high-risk ISUP grade 4–5 malignancy on surveillance biopsy following primary IRE. Long term outcomes of this cohort will be closely monitored.

The definition of success of IRE should be assessed by infield histological clearance of cancer. Post-IRE biopsy data remains the gold standard to evaluate tumour ablation. Despite expert (panel) recommendations regarding consensus on the follow-up biopsies after focal therapy, not all patients are willing to comply with these recommendations [22,23]. The international rate of post-IRE biopsies after focal therapy trials varies from 17 to 100% [4]. In our series, 76% of men beyond 12 months follow-up agreed to proceed with a surveillance prostate biopsy. The remainder were disinclined due to low PSA levels associated with low risk PI-RADS 2 mpMRI findings. Following primary IRE, in our cohort 35/40 (87.50%) are free of any infield malignancy. This confirms the encouraging early data on IRE as a reliable technology for PCa control, within the treatment field. An upgrade in significant out-of-field cancer on surveillance systematic biopsies is not necessarily a failure of focal therapy, but failure of the selection process, or failure to identify significant a volume malignancy at initial evaluation. In view of the lack of long-term overall and metastasis free survival from focal therapy, it is essential to minimise the risk of undiagnosed significant out of field tumour prior to focal therapy.

There is very little data available on the outcome of salvage IRE for radio-recurrent PCa. Scheltema et al. [15] analysed 18 men with localised radiorecurrent PCa and three men had biochemical failure based on the Phoenix definition. However, the Phoenix definition grossly underestimates the probability of recurrence cancer after radiotherapy, which is increasingly identified on PSMA PET/CT once a post-radiotherapy PSA level elevates above 0.5 [24]. In our cohort, three of the six patients treated with salvage IRE for radiotherapy local recurrence had a PSA <0.01 ng/L with a median follow-up of 22 months (range 13–30 mo) and the other three patients all had a PSA of <0.55 ug/L. The salvage IRE procedure was well tolerated with minimal side-effects and no initial incontinence of urine, in contrast to other treatments such as salvage radical prostatectomy. However, based on our results, caution is recommended when performing a TURP after salvage IRE in the post radiation therapy cohort, in view of an increased risk of urinary incontinence.

Limitations of our study include the relatively short follow-up and the retrospective review of a prospective database. Complications can be underestimated in retrospective studies; however, apart from two patients who have relocated overseas after IRE and were censored at last follow-up, we have complete follow-up on all patients.

CONCLUSIONS

Focal IRE for primary PCa is associated with complete in-field ablation of all cancer in 87.5% based on post-IRE biopsy, or 90% of any core length of ISUP grade 2. There was minimal postoperative complications and a low risk of post treatment urinary incontinence or impotence. Surveillance prostate biopsies are required to exclude in or out-of-treatment zone progression despite a normal post-IRE mpMRI. Salvage IRE is a promising option for localised recurrence after prostate radiotherapy with low morbidity.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: William John Yaxley, Troy Gianduzzo, Boon Kua, and John William Yaxley. Data acquisition: all authors. Statistical analysis: None. Data analysis and interpretation: William John Yaxley, Troy Gianduzzo, Boon Kua, and John William Yaxley. Drafting of the manuscript: William John Yaxley and John William Yaxley. Critical revision of the manuscript: all authors. Obtaining funding: None. Administrative, technical, or material support: None. Supervision: Troy Gianduzzo, Boon Kua, and John William Yaxley. Approval of the final manuscript: all authors.

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