

Pathologic failure and salvage approaches following focal therapy for localized prostate cancer

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TREMBLAY S, Tabei SS, TAYEBI S, HINRICHS BH, LAZAROVICH A, KOEHLER J, HSU W-W, VERMA S, SIDANA A. Pathologic failure and salvage approaches following focal therapy for localized prostate cancer. *Can J Urol* 2026;33(4):799–810.

Background: Focal therapy (FT) is an emerging treatment modality for localized prostate cancer. However, limited data are available regarding the patterns of oncologic failure post-FT. This study aims to characterize the features of oncologic failure and salvage strategies following FT.

Methods: Patients presenting with pathologic failure (PF) after receiving FT (cryotherapy, High-intensity focused ultrasound, or irreversible electroporation) for intermediate-risk prostate cancer were selected from a prospective registry between 2018 and 2023. All patients underwent protocol-based follow-up, including PSA testing, multiparametric MRI, and mandatory biopsy. The primary outcome was PF, defined as biopsy-confirmed Grade Group ≥ 2 cancer post-treatment. Failures were classified as in-field or out-of-field based on lesion location relative to the ablation zone.

Results: This study included 101 patients who underwent primary FT, with a median follow-up of 16.5 months. PF occurred in 18 patients (17.8%). Failures included 7 in-field, 9 out-of-field, and 2 involving both locations. Notably, 50% of recurrences had no suspicious findings on MRI, and 67% occurred without meeting Phoenix PSA criteria for biochemical recurrence. Failures were typically low-volume (mean longest positive core length 4.8 mm), and 11 were detected within the first 12 months of follow-up. Among those with PF, definitive salvage treatments included repeat FT (55.6%), active surveillance (16.7%), radical prostatectomy (11.1%), whole-gland ablation (5.6%), and radiation therapy (11.1%).

Conclusions: Focal therapy is increasingly used for localized prostate cancer, but many failures occur without PSA rise or imaging abnormalities. These findings suggest that although PSA testing and imaging are valuable for surveillance after FT, biopsy remains essential.

Key Words: Prostate cancer, focal therapy, local recurrence, cryotherapy, irreversible electroporation, high-intensity focused ultrasound

Introduction

Radical prostatectomy and radiation therapy are the main options for clinically significant localized prostate cancer (PCa). These approaches carry a significant risk of genitourinary, sexual, and gastrointestinal side effects.^{1,2} Focal therapy (FT) has

Received date 08 November 2025

Accepted for publication 03 February 2026

Published online 21 August 2026

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emerged as an alternative approach for PCa with the goal of reducing treatment-related toxicities and improving quality of life.^{3–5} FT can be performed using a variety of energy modalities, such as high-intensity focused ultrasound (HIFU), irreversible electroporation (IRE), photodynamic therapy (PDT), radiofrequency ablation, and cryotherapy.^{6–8} These modalities have shown promising outcomes for carefully selected patients with intermediate-risk PCa.^{9,10}

Despite the promising oncologic outcomes of FT, treatment failures remain a concern.¹¹ A recent national survey indicated that almost half of responding urologists in the US offer FT, highlighting not only the growing adoption of this approach but also the need to better report its oncologic outcomes and failure patterns in real-world practice.¹² Comprehensive reporting of FT failure is essential to help define patient selection, optimize surveillance strategies, and guide salvage treatment strategies.

The objective of this study was to describe our experience regarding pathologic failures (PF) following FT treatment with IRE, cryotherapy, and HIFU. Additionally, we report our treatment strategy for patients who experience oncologic failure.

Materials and Methods

Study population and design

Demographic, clinical, imaging, and pathologic data were collected on patients who underwent FT ablation at the University of Cincinnati Medical Center between 2018 and 2023, using a prospective registry and database. This study was approved by the University of Cincinnati Institutional Review Board (IRB #20201245) with a waiver of informed consent. The full methodology and the functional and oncologic outcomes of the cohort have been previously published.¹¹

Briefly, patients underwent FT utilizing one of three energy modalities: cryotherapy (Cryocare[®] System, Endocare Inc., Austin, TX), HIFU (Sonablate[®] system, Sonacare Medical, Charlotte, NC, USA), or IRE (NanoKnife[®] System, AngioDynamics, Latham, NY). FT was offered to patients with NCCN intermediate-risk prostate cancer (Grade Group [GG] 2–3, PSA < 20 ng/mL) who had visible, localized disease on multiparametric MRI, including unifocal, unilateral, or anterior-only lesions.¹³ Patients with predominant intraductal carcinoma or cribriform pattern were excluded.

Follow-up

Patients were followed every 3 months in year 1, then every 6 months. PSA was measured at each visit. At 6 to 9 months post-FT, patients underwent mpMRI and a protocol biopsy, including 2–4 targeted cores from the ablation zone and any new lesions, along with a 12-core systematic biopsy. If the biopsy was negative, further mpMRIs were done at 24 months post-treatment and every two years or earlier if PSA trends suggested possible recurrence. Additional biopsies were only performed if necessary due to lesions on mpMRI or concerning PSA results. Patients with GG1 disease were monitored with active surveillance (AS). Those with GG2 or higher disease were given options for AS, salvage FT, or more aggressive treatments based on the severity of their condition and their preferences.

Study endpoints

The primary outcome was PF, defined as the presence of GG2 or higher prostate cancer on any follow-up biopsy. Low-volume disease was defined according to international consensus recommendation: <0.2 cc or 7 mm diameter GG2 disease.¹⁴ Recurrence was further categorized as in-field or out-of-field based on biopsy location relative to the treated zone. In-field failure was defined as recurrence occurring within the same sextant as the treated lesion and/or within a 1 cm margin of the intended ablation area. Sextants were defined using standard anatomical divisions of the prostate into six regions (left/right base, mid-gland, and apex), taking into account anterior vs. posterior location when applicable. To simplify the classification process and account for treatment margins and prostate shrinkage, we considered cancers in the same and/or adjacent sextant of the treated lesion as ‘in-field’ failures. Out-of-field failure referred to recurrence identified outside the ablation zone and not meeting the above criteria for in-field classification. Patients with clinically significant PCa identified on follow-up biopsy were considered to have reached the study endpoint and subsequently received additional treatment. We reported all types of additional treatments that patients received after PF.

Secondary outcomes were surveillance findings that triggered further investigation with PSA levels and imaging findings.¹⁵ Rising PSA meeting criteria for biochemical recurrence (BCR), defined as an increase in PSA level greater than 2 ng/mL above the nadir after treatment, was considered a trigger for further evaluation.¹⁶ Similarly, the identification of a new lesion with a PI-RADS score of 4 or higher in the non-ablated zone, the presence of residual restricted diffusion or new enhancement in the ablation zone on

TABLE 1. Baseline and preoperative characteristics by pathologic failure status

Characteristic	Failure (n = 18)	Non-Failure (n = 83)	Total (n = 101)	p-value†
Follow-up time, months (IQR)	12.9 (7.8–34.5)	17.0 (10.3–35.3)	16.5 (9.6–34.5)	0.437
Median age, years (IQR)	65.5 (63.0–72.0)	68.0 (62.0–72.0)	67 (62.0–72.0)	0.873
Median PSA, ng/mL (IQR)	5.4 (3.8–6.0)	6.5 (4.5–9.3)	6.0 (4.4–9.2)	0.189
Median mpMRI prostate volume, mL (IQR)	36.2 (29.0–55.7)	35.5 (27.2–44.8)	35.5 (27.6–48.3)	0.514
Highest PI-RADS score, n (%)				0.107
3	0 (0.0)	9 (10.8)	9 (8.9)	
4	9 (50.0)	20 (24.1)	29 (28.7)	
5	5 (27.8)	26 (31.3)	31 (30.7)	
Unassigned/missing	4 (22.2)	28 (33.7)	32 (31.7)	
Highest operative grade group, n (%)				0.214
GG2	14 (77.8)	60 (72.3)	74 (73.2)	
GG3	3 (16.7)	19 (22.9)	22 (21.8)	
GG4	0 (0.0)	2 (2.4)	2 (2.0)	
GG5	1 (5.6)	0 (0.0)	1 (1.0)	
Not Assigned	0 (0.0)	2 (2.4)	2 (2.0)	
Energy Modalities				0.552
Cryotherapy	11 (61.1)	39 (47.0)	50 (49.5)	
HIFU	4 (22.2)	26 (31.3)	30 (29.7)	
IRE	3 (16.7)	18 (21.7)	21 (20.8)	

Note: †: Wilcoxon Two-Sample Test or Chi-square test; IQR: interquartile range; GG: Grade Group; HIFU: high-intensity focused ultrasound; IRE: irreversible electroporation.

postoperative prostate mpMRI led to further investigation, including repeat biopsy. Regional or distant failure was defined as the presence of suspicious pelvic lymph nodes or distant metastases during the follow-up period.

Statistical analysis

Descriptive statistics were reported as medians with interquartile ranges (IQR) for continuous variables, and frequencies with proportions for categorical variables. Descriptive statistics were reported to characterize the study cohort. The non-parametric Wilcoxon two-sample test and the Chi-square test were used to assess differences between groups for continuous and categorical variables, respectively. Multivariable analyses were not performed due to the insufficient number of pathologic failures to support reliable modeling. All statistical analyses were performed using SAS software (V9.4, SAS Institute Inc., Cary, NC, USA). The significance level was set as $p < 0.05$.

Results

This study included 101 patients who underwent primary FT. Fifty patients underwent cryotherapy,

30 HIFU, and 21 IRE. Overall, 68.3% were treated for a single index lesion, while 26.7% were treated with a hemi-ablation template. The median follow-up time was 16.5 months. The cohort characteristics are summarized in Table 1. PF was observed in 18 patients (17.8%). Among these, 11 failures occurred after cryotherapy, 4 after HIFU, and 3 after IRE. Seven were classified as in-field failures, nine as out-of-field failures, and 2 as involving both locations. Of these failures, 12 (66.6%) were detected on the scheduled protocol biopsy, while 6 (33.3%) were detected on biopsies triggered outside the protocol due to PSA elevation or MRI findings.

Surveillance findings (Imaging and PSA)

Among the 18 patients with PF, only 9 (50%) had abnormalities on mpMRI prior to biopsy, including new enhancement, persistent restricted diffusion, or new PI-RADS 4–5 lesions outside the ablation zone. In contrast, the other 9 patients had unremarkable imaging at the time of recurrence, highlighting the limited sensitivity of mpMRI alone. Figure 1 illustrates a patient treated with IRE for a right lateral mid-apical lesion (pre-treatment PI-RADS 4). Pre-treatment PSA was 2.04 ng/mL, which decreased to 0.13 ng/mL at 3 months and 0.20 ng/mL at 6 months. A follow-up mpMRI at 1 year post-treatment

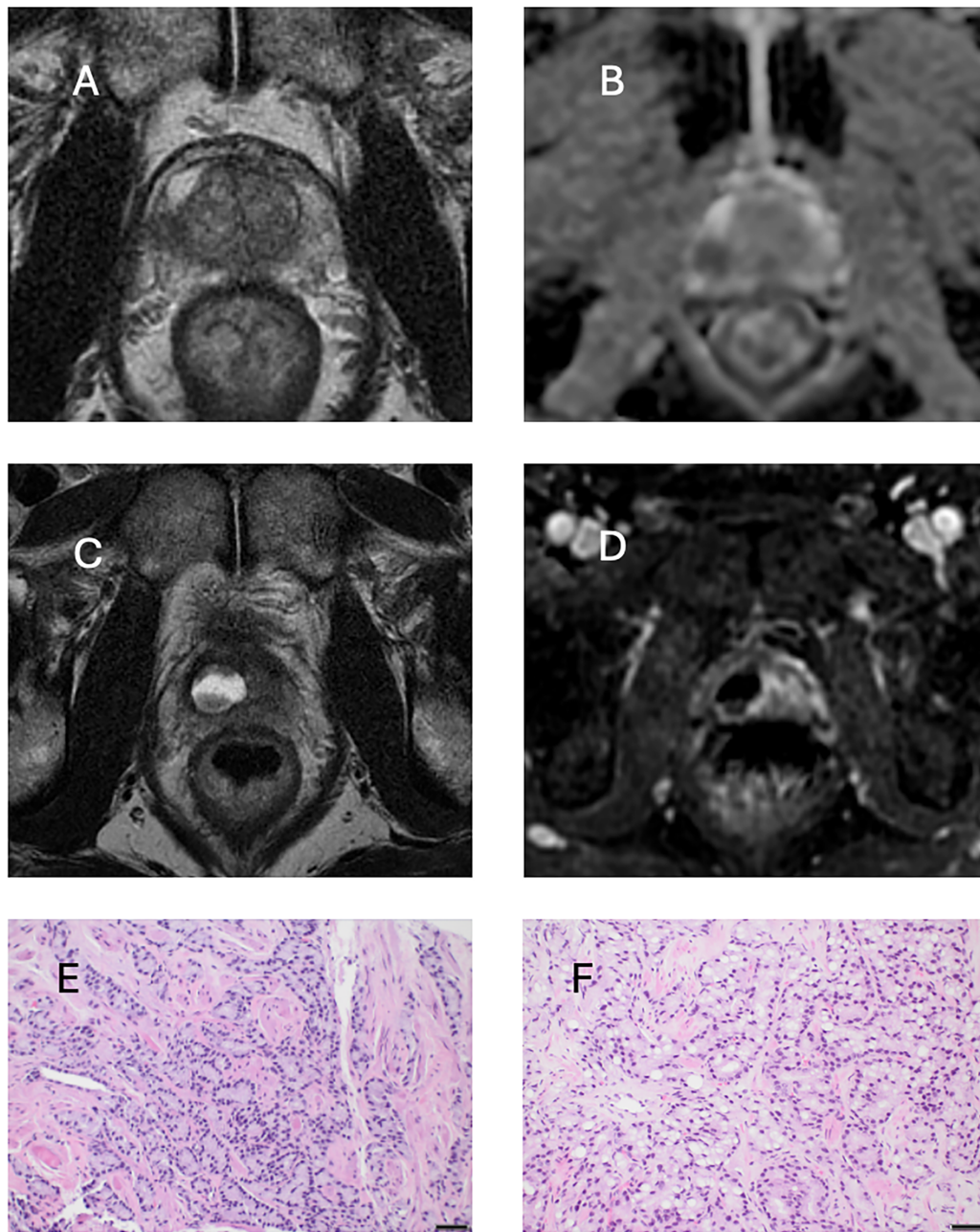


FIGURE 1. Pre- and post-treatment imaging and histopathology of a patient with biopsy-proven pathologic failure despite negative imaging findings. (A,B) Pre-treatment mpMRI showing a right lateral mid-apical PI-RADS 4 lesion. (C,D) One-year post-IRE mpMRI revealing treatment-related tissue changes and cavitation, with no radiologic evidence of recurrence. (E) Pre-IRE biopsy: Prostatic adenocarcinoma, Gleason pattern 4, right apex, anterior, 200x magnification, H&E staining, scale bar = 50 μ m. (F) Post-IRE biopsy at 13 mo follow-up: Prostatic adenocarcinoma, Gleason pattern 4, right apex, anterior, 200x magnification, H&E staining, scale bar = 50 μ m. mpMRI: multiparametric magnetic resonance imaging; PI-RADS: Prostate Imaging Reporting and Data System; IRE: irreversible electroporation; H&E: hematoxylin and eosin

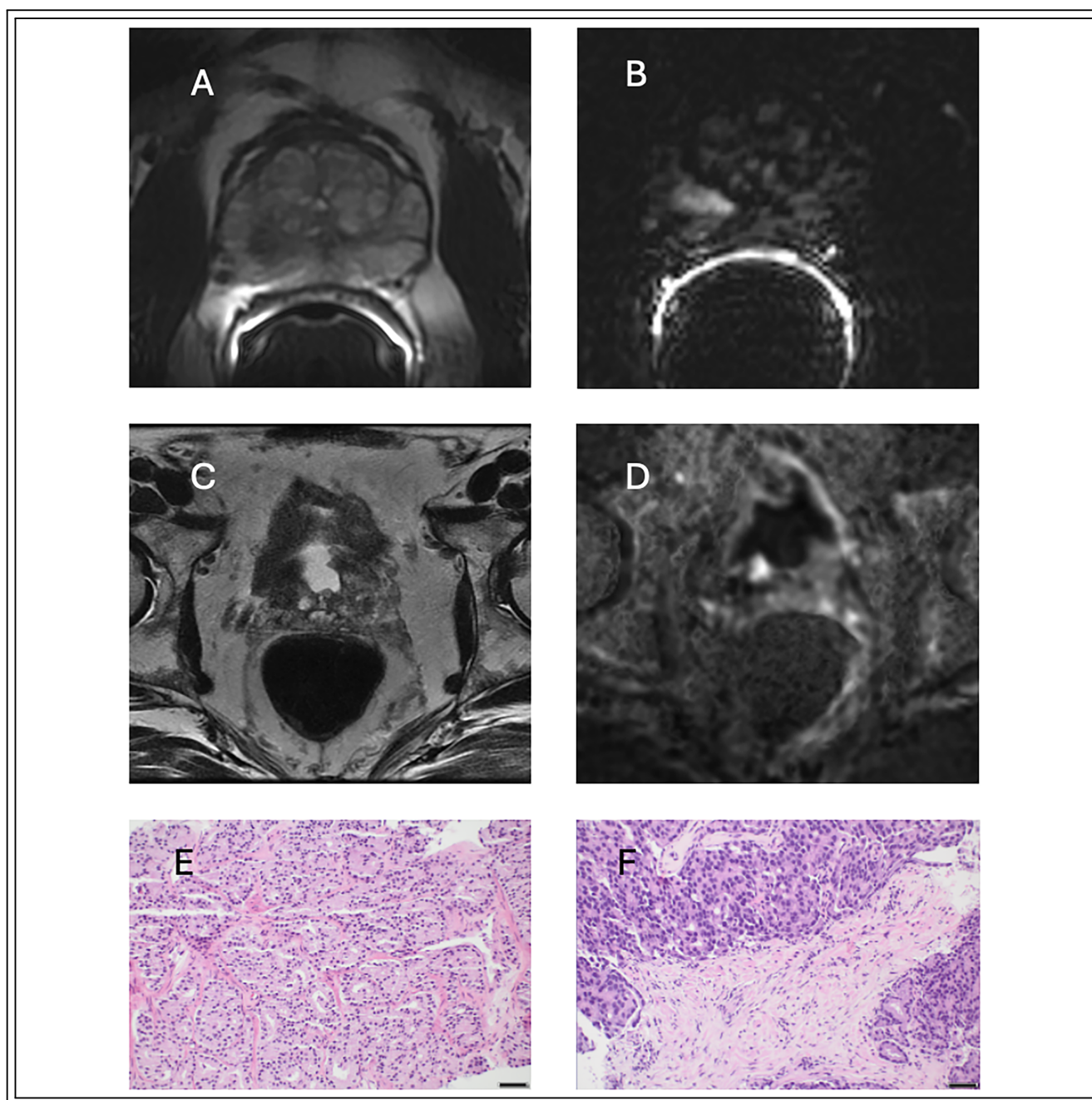


FIGURE 2. Pre-treatment and post-treatment radiological and pathologic findings of a patient with pathologic failure and imaging failure after cryotherapy. (A,B) Pre-treatment mpMRI showing a right mid-posterior peripheral zone PI-RADS 4 lesion. (C,D) mpMRI at 4 years post-cryotherapy showing a new hypointense lesion at the right base on T2 (C), with corresponding hyperintensity focus on DWI (D) consistent with a PI-RADS 4 lesion. (E) Pre-treatment biopsy: Prostatic adenocarcinoma, Gleason pattern 4, right medial apex, anterior, 200x magnification, H&E staining, scale bar = 50 μ m. (F) Post-treatment biopsy at 37 months follow-up: Prostatic adenocarcinoma, Gleason pattern 4, with adjacent cryotherapy-related stromal changes, right medial apex, anterior, 200x magnification, H&E staining, scale bar = 50 μ m. mpMRI: multiparametric magnetic resonance imaging; PI-RADS: Prostate Imaging Reporting and Data System; T2: T2-weighted imaging; DWI: diffusion-weighted imaging; H&E: hematoxylin and eosin

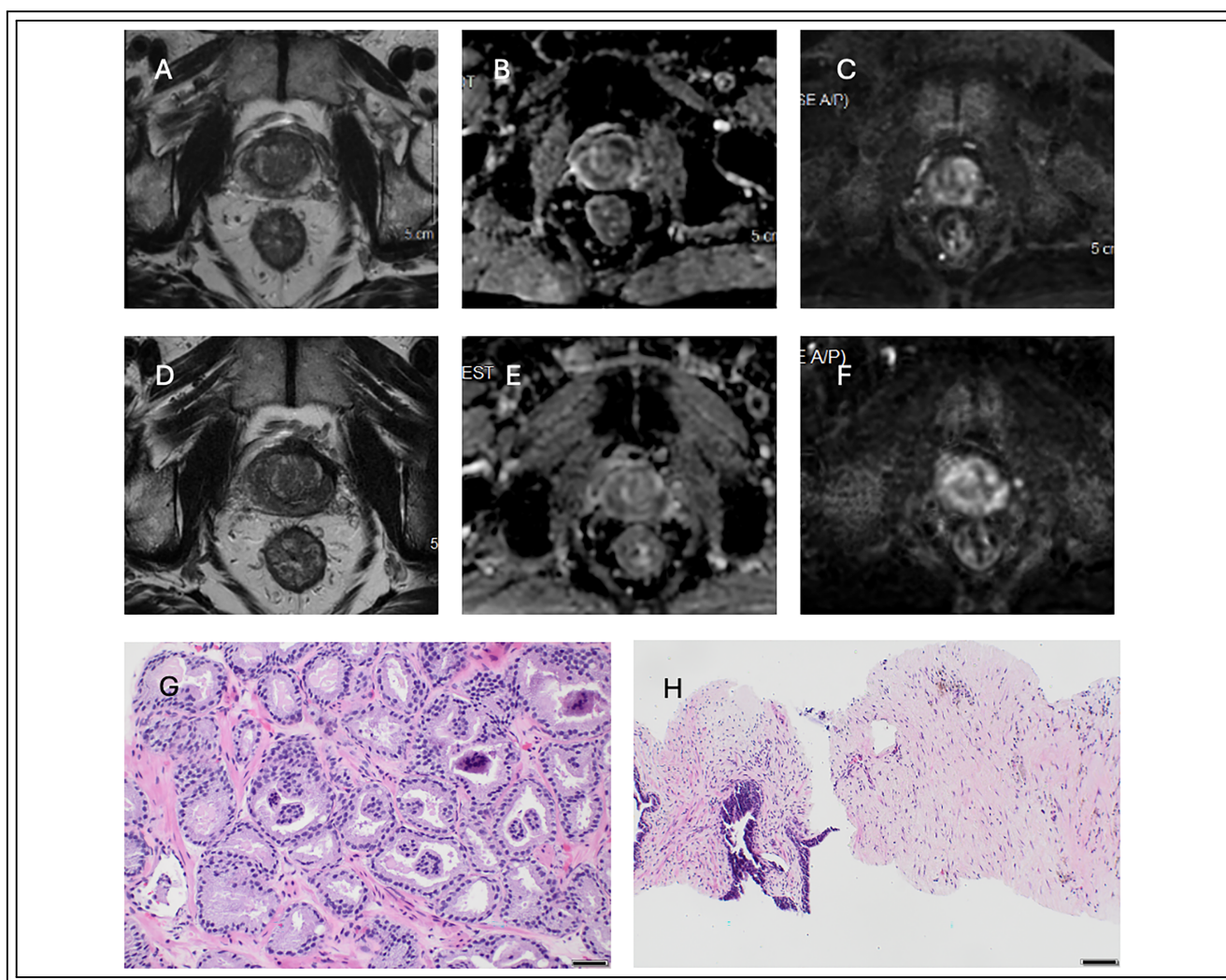


FIGURE 3. Pre-treatment and post-treatment radiological and pathologic findings of a patient without pathologic failure and imaging abnormality after cryotherapy. (A–C) Pre-treatment mpMRI showing a left anterior PI-RADS 4 lesion, demonstrating focal hypointensity on ADC (B) and corresponding hyperintensity on DWI (C). (D–F) Post-treatment MRI at 10 months follow-up revealing a new left posterior base PI-RADS 4 lesion without pathologic correlation. (G) Pre-treatment biopsy: Prostatic adenocarcinoma, Gleason pattern 3 + 4, left base of prostate, anterior, 200x magnification, H&E staining, scale bar = 50 μ m. (H) Post-treatment biopsy at 10 mo follow-up: Prostatic stroma showing fibrosis and occasional hemosiderin-laden macrophages, consistent with prior cryotherapy ablation site, left base of prostate, anterior, 100x magnification, H&E staining scale bar = 100 μ m. mpMRI: multiparametric magnetic resonance imaging; PI-RADS: Prostate Imaging Reporting and Data System; ADC: apparent diffusion coefficient; DWI: diffusion-weighted imaging; H&E: hematoxylin and eosin

revealed tissue changes and cavitation, with no suspicion of recurrent disease. A protocol biopsy at that time demonstrated a 5 mm focus of GG3 disease in the right apex. [Figure 2](#) presents a cryotherapy case treated for a right mid-posterior peripheral zone PI-RADS 4 lesion, in which a new lesion was clearly visualized on post-treatment imaging 37 months after FT. A follow-up mpMRI post-treatment showed a

new hypointense lesion at the right base on T2, with corresponding hyperintensity focus on DWI consistent with a PI-RADS 4 lesion. Biopsy demonstrated GG4 disease. In contrast, 7 patients with abnormal imaging had no evidence of recurrent disease. [Figure 3](#) is an example of a patient treated with cryotherapy, where imaging abnormalities are visible post-treatment, without pathologic correlation. The

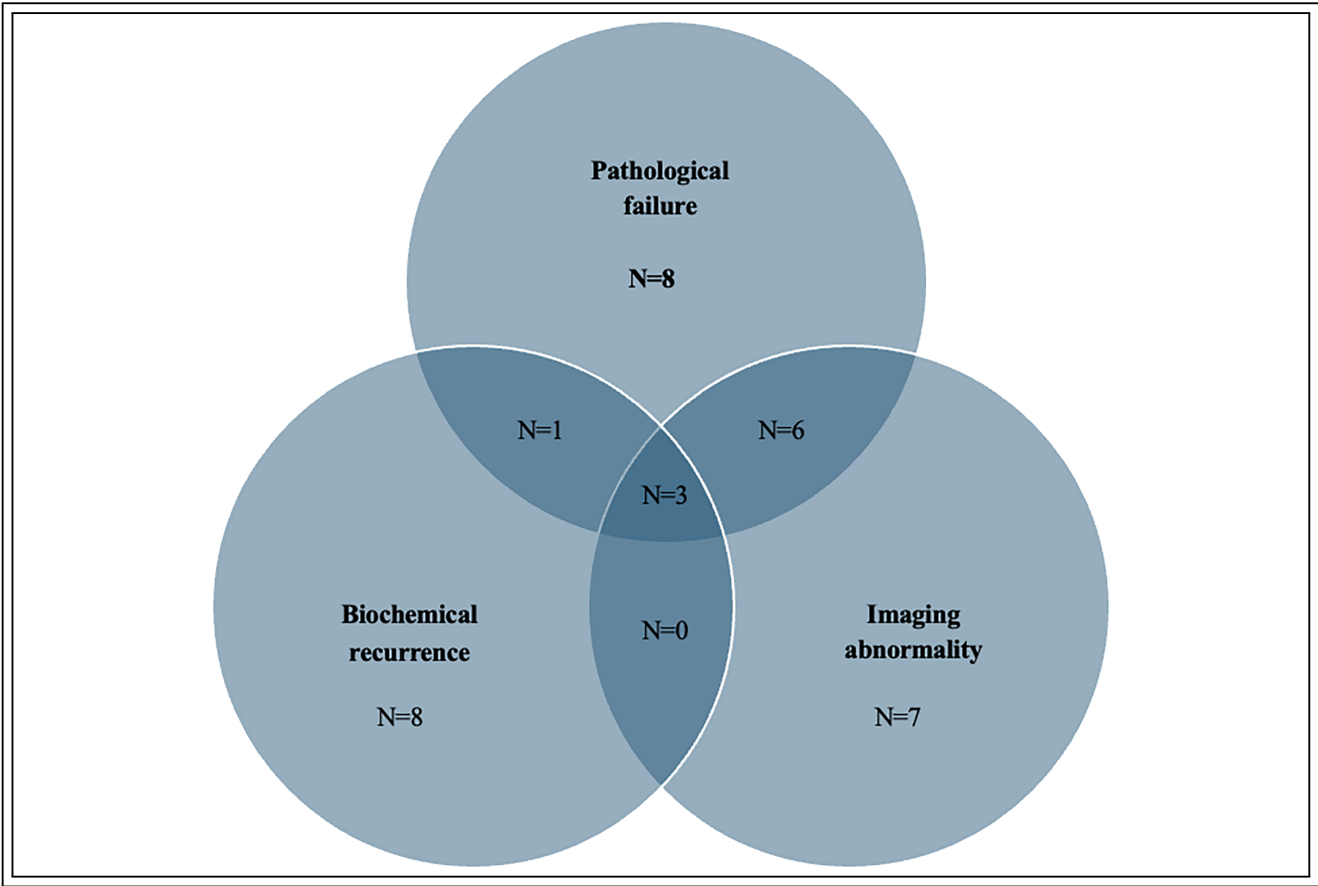


FIGURE 4. Venn diagram illustrating the overlap between biochemical recurrence (BCR), imaging abnormalities, and biopsy-proven pathologic failures following focal therapy. BCR was defined using the Phoenix criteria as a rise in PSA > 2 ng/mL above the post-treatment nadir. Imaging abnormalities were defined as the presence of new PI-RADS ≥ 4 lesions, residual restricted diffusion, or new enhancement within or outside the ablation zone on follow-up multiparametric MRI

imaging demonstrated a new PI-RADS 4 lesion at the left posterior base on 10-month follow-up, without histopathologic confirmation of residual disease.

Regarding PSA kinetics, 12 (11.8%) patients had a rising PSA who met the Phoenix criteria for BCR, but only 4 (3.9%) patients had a proven PF. 14 patients with PF did not meet the Phoenix criteria during follow-up, limiting the interpretation of PSA alone in detecting recurrence. Overall, neither mpMRI nor PSA reliably predicted PF, with 8 (44.4%) patients being missed without protocol biopsies. [Figure 4](#) demonstrates the overlap between PSA, imaging abnormalities, and PF.

Pathologic findings

Pathologic characteristics and failure varied by energy modality. [Figures 1–3](#) provide examples of pre- and post-treatment pathology slides, illustrating

the pathologic changes and failure patterns observed in this cohort. [Figure 1](#) presents a patient treated with IRE. Pretreatment biopsy showed infiltrative, poorly-formed and fused glands, consistent with Gleason pattern 4 prostatic adenocarcinoma. Post-treatment biopsy revealed adenocarcinoma with a similar growth pattern. Treatment-related changes were not conspicuous in the sampled tissue, suggesting a lack of energy delivery to the target area. This contrasts with radiation failure, where residual cancer typically coexists with extensive treatment-related alterations. [Figure 2](#) presents a patient treated with cryotherapy, who experienced PF. Pre-treatment biopsy demonstrated fused glands with slit-like lumina, consistent with Gleason pattern 4 prostatic adenocarcinoma. Post-treatment biopsy showed adenocarcinoma with a similar growth pattern and associated dense fibrosis with bluish-grey

TABLE 2. Characteristics of pathologic failure

Characteristic	Cryotherapy (n = 50)	HIFU (n = 30)	IRE (n = 21)	Total (n = 101)
Pathologic failure, n (%)	11 (22.0)	4 (13.3)	3 (14.3)	18 (17.8)
In-field, n (%)	3 (6.0)	1 (3.3)	3 (14.3)	7 (6.9)
Out-of-field, n (%)	7 (14.0)	2 (6.7)	0 (0.0)	9 (8.9)
In-field and Out-of-field, n (%)	1 (2.0)	1 (3.3)	–	2 (2.0)
Longest positive core length (mm)				–
Average	4.3	4.9	6.3	–
Max	9.0	7.0	9.0	–
Min	1.6	4.0	5.0	

Note: HIFU: high-intensity focused ultrasound; IRE: irreversible electroporation.

stromal changes consistent with cryotherapy-related changes. In contrast, [Figure 3](#) illustrates a case where a treatment response is observed after cryotherapy, with no evidence of recurrence. Pre-treatment biopsy revealed prostatic adenocarcinoma composed of closely packed, large glands of uniform size, consistent with Gleason pattern 3 + 4. Post-treatment biopsy showed prior cryotherapy-related changes consisting of bluish-grey stromal changes amongst fibroblasts and collagen, as well as hemosiderin-laden macrophages, without any evidence of recurrence.

To further characterize disease burden, the longest positive core length was measured in these patients. As expected, most of these recurrences were low-volume GG2 disease. The mean longest positive core length was 4.3 mm among patients treated with cryotherapy, 4.9 mm in those treated with HIFU, and 6.3 mm in those treated with IRE ([Table 2](#)).

Clinical course following failure

Following PF, a variety of treatment strategies were employed. Salvage FT was the most frequently used intervention, performed in 10 of the 18 patients (55.6%). Among these, 3 were treated with the same modality as their primary FT, while 7 received a different focal modality. No Grade 3 or higher complications were reported in any of the salvage FT patients. AS alone was used in 3 patients (16.6%), while 3 patients (16.6%) initially underwent AS before receiving definitive treatment. Salvage radical prostatectomy was performed in 2 patients (11.1%). One patient underwent whole-gland ablation, and one patient received external beam radiation therapy. One patient was lost to follow-up. A detailed patient-level summary of the clinical course following PF is presented in [Table A1](#).

Discussion

In this study, we evaluated PF in patients with intermediate-risk prostate cancer using HIFU, cryotherapy, and IRE, aiming to characterize failure patterns and surveillance challenges in a real-world setting. We found that nearly 18% of patients experienced PF, with careful selection and protocolized follow-up. Previous studies report a wide range of oncologic outcomes, but should be interpreted with caution, as reporting of clinically significant cancer post-FT remains inconsistent in the literature, follow-up durations are often limited, and the use of protocol-mandated biopsies varies significantly between studies.^{17–19}

Failure location was classified as in-field or out-of-field based on the relationship between biopsy site and the ablation zone, with in-field defined by recurrence within the treated sextant and/or adjacent sextant, or within 1 cm of the ablation margin. While we described the distribution of failures across these categories, we did not perform formal comparisons between modalities due to the limited number of failures and the influence of patient selection based on the treatment modality.

Among patients with PF, half had no suspicious findings on post-treatment mpMRI, underscoring the limitation of imaging alone. A recent systematic review by Séguier et al. similarly found that nearly half of recurrences after focal HIFU were missed by mpMRI, with a pooled sensitivity of 52% (95% CI: 36%–68%), and a specificity of 81% (95% CI: 68%–91%).²⁰ The poor performance of surveillance MRI may reflect the low tumor volume seen in many recurrences. In response to imaging limitations, efforts have been made to create new imaging reporting systems exclusively for FT surveillance,

such as the prostate imaging after focal ablation (PI-FAB) and the Transatlantic Recommendations for Prostate Gland Evaluation with Magnetic Resonance Imaging After Focal Therapy (TARGET).^{21–23} Early results of these emerging scoring systems indicate improvements in sensitivity and moderate inter-reader agreement. We also noted that 7 patients had abnormal imaging findings that did not correspond to recurrence on biopsy. These false-positive MRI findings may have led to additional biopsy, but did not result in any further treatment.

During the follow-up period, 12 patients met the Phoenix criteria for BCR, but only 4 of these were confirmed to have PF. Notably, 67% of all PF occurred within the first 12 months, thereby limiting the utility of the Phoenix criteria as a timely indicator of recurrence. Conversely, several patients with biopsy-proven clinically significant cancer did not exhibit a significant PSA rise. These discrepancies underscore the limitations of relying on PSA kinetics alone in the post-FT setting, where partial gland preservation and low-volume residual disease may mask recurrence. This aligns with prior findings showing that PSA thresholds after focal HIFU have variable accuracy and may require adjustment based on timing post-treatment.^{24–27}

The optimal next step in managing patients following PF remains uncertain, as robust data on long-term oncologic outcomes are lacking.^{28,29} Management strategies were tailored based on recurrence characteristics, prior treatment, and patient preference. In this cohort, salvage focal therapy was the most frequently selected option, followed by AS, salvage radical prostatectomy, external beam radiation therapy, and whole-gland ablation. For in-field failure where salvage focal therapy was appropriate, a different energy modality was generally selected. In cases with multifocal or more extensive recurrence, radical prostatectomy or external beam radiation therapy was usually considered the most suitable next treatment. In patients with prior HIFU failure, particular attention was given to the presence of calcifications or acoustic shadowing from dense residual tissue, as these findings suggest limited energy transmission and may render repeat HIFU less effective. These features were routinely assessed during protocol biopsy. Most patients had stable or undetectable PSA following salvage, suggesting reasonable short-term oncologic control.

This study has several limitations. Its small sample size, single-institution experience, and short-term median follow-up of 16.5 months limit our ability to assess long-term oncologic outcomes, particularly for out-of-field failures, which may emerge

later in the post-treatment course. While protocol biopsies were done in our cohort, this level of adherence may not reflect routine clinical practice, which could affect generalizability.^{9,30} Additionally, all mpMRI studies were interpreted by radiologists experienced in prostate imaging; however, the same reader did not always interpret both the pre- and post-treatment imaging, which may introduce inter-observer variability. Despite these limitations, reporting such data remains essential to better understand failure patterns after focal therapy and to guide future surveillance strategies.

Conclusion

As FT continues to gain interest as a treatment option for localized prostate cancer, understanding and reporting oncologic failures is critical. In this cohort, many failures occurred in the absence of PSA or imaging triggers, underscoring that biopsy remains an essential component of post-treatment surveillance.

Acknowledgement

None.

Funding Statement

The authors received no specific funding for this study.

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Availability of Data and Materials

The data that support the findings of this study are available from the corresponding

author, Samuel Tremblay, upon reasonable request.

Ethics Approval

This study was approved by the University of Cincinnati Institutional Review Board (IRB #20201245) with a waiver of informed consent.

Conflicts of Interest

The authors declare no conflicts of interest regarding the present study, except as noted. Abhinav Sidana reports relationships with Sonablate and AngioDynamics Inc., which include consulting or advisory roles.

Appendix A

TABLE A1. Clinical course of patients with pathologic failure

Patient	FT modality	GG (Pre)	GG at failure	Failure location	Salvage strategy	Time FT → PF (mo)	Time PF → Salvage (mo)	Time Salvage → Last FU (mo)
P01	IRE	3	3	In-field	HIFU	9.3	1	24.1
P02	IRE	2	2	In-field	Lost to follow-up	10.3	Lost to follow-up	Lost to follow-up
P03	HIFU	2	4	In-field		30.5		
P04	Cryo	2	2	Out-of-field	HIFU	25.5	23.4*	Lost to follow-up
P05	Cryo	5	4	In-field	Cryo	8.6	2.7	
P06	Cryo	3	4	Out-of-field	Cryo	34.5	3.1	42.8
P07	IRE	2	2	In-field	Cryo	11.5	1	13.3
P08	Cryo	2	2	Out-of-field	AS	7.1	0	56.8
P09	Cryo	2	2	Out-of-field	AS	7.4	0.5	46.2
P10	HIFU	2	3	Out-of-field	IRE	35.7	2	28.8
P11	HIFU	2	2	Out-of-field	Cryo	9.5	2.7	34.5
P12	HIFU	2	4	In-field And Out-of-field	RP	7.8	3.2	42.4
P13	Cryo	2	3	In-field	Cryo	26.6	2.5	43.3
P14	Cryo	2	3	Out-of-field	HIFU	36.7	2.1	20.4
P15	Cryo	3	2	Out-of-field	EBRT + ADT	7.3	12.3**	57.7
P16	Cryo	2	3	Out-of-field	HIFU	6.6	27.2***	33.3
P17	Cryo	2	2	In-field And Out-of-field	Cryo	5.7	2.3	57.9
P18	Cryo	2	2	In-field	AS	9.3	0	15.4

Note: AS = Active surveillance; EBRT = External beam radiotherapy; ADT = Androgen deprivation therapy; RP = Radical prostatectomy; FT = Focal therapy; IRE = Irreversible electroporation; HIFU = High-intensity focused ultrasound; Cryo = Cryotherapy; GG = Grade group; PF = Pathologic failure; FU = Follow-up. * P04 initially underwent 15.6 months of active surveillance before salvage therapy. ** P15 initially underwent 8.5 months of active surveillance before salvage therapy. *** P16 initially underwent 16.4 months of active surveillance before salvage therapy. Time PF → Salvage = 0 months indicates that patients were managed with active surveillance and did not undergo salvage therapy during the follow-up period.

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