Review Article

Focal therapy for localized prostate cancer – Current status

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ABSTRACT

Focal therapy (FT) has recently gained popularity for the treatment of localized prostate cancer (PCa). FT achieves cancer control by targeting the lesions or the regions of the cancer and avoids damage to the surrounding tissues thus minimizing side effects which are common to the radical treatment, such as urinary continence and sexual function, and bowel-related side effects. Various ablative methods are used to deliver energy to the cancerous tissue. We review the different modalities of treatment and the current state of FT for PCa.

INTRODUCTION

Prostate cancer (PCa) is the most common cancer in men.[1] Traditional management involves the treatment of the whole gland, in the forms of radical prostatectomy or radiation. Focal therapy (FT) has emerged as an alternative treatment to mitigate the adverse effects subsequent to the treatment of the whole gland, without jeopardizing cancer control.[2] FT is based on the concept that the index lesion drives the tumor growth and risk of metastasis.[3] By targeting the index lesion and avoiding the surrounding tissues responsible for urinary and sexual functions (neurovascular bundle, bladder neck, external sphincter, and rectum), FT is associated with fewer adverse effects which are more acceptable and are temporary and results in a better health-related quality of life.[2,3] However, treatment effectiveness is primarily dependent on patient selection. While several energy sources are available and new data is emerging on the novel therapies, most of the functional and oncological data is reported for high-intensity focused ultrasound (HIFU) and cryotherapy.

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METHODOLOGY

A literature search was performed for this narrative review. We reviewed PubMed database using mesh terms including but not limited to PCa, focal therapy (FT), focal ablation, focal HIFU, cryoablation, focal laser ablation (FLA), irreversible electroporation, photodynamic therapy (PDT), brachytherapy, radiofrequency ablation, and focal transurethral ultrasound ablation (TULSA). We focused on studies describing FT for the primary treatment of Pca and excluded those related to salvage focal therapies or whole gland treatments. The inclusion criteria was randomized controlled trials, systematic reviews and meta-analyses, ongoing trials, retrospective and prospective cohort studies, and single-arm studies related to the above terms. A full-text review of all the selected articles was performed.

PATIENT SELECTION FOR FOCAL THERAPY

Patient selection is the key for success of FT. Ideal requirements are the ability to predict and accurately map the clinically significant PCa, to deliver FT to the targeted area and to assess the efficacy of the treatment. The goal is

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to achieve these requirements by using a combination of imaging techniques and biopsy of the appropriately selected patients eligible for FT, with suitable energy sources.

Several studies have shown the superiority of magnetic resonance imaging (MRI) targeted biopsies for the detection of clinically significant cancers as compared to the standard biopsy technique.[4-7] A meta-analysis has shown that MRI targeted biopsies have a negative predictive value of 82.4% to rule out clinically significant PCa.[8] Ahdoot *et al*. demonstrated that combined MRI targeted and systematic biopsies lead to greater detection of clinically significant cancer (particularly the index lesion) and a lower chance of upgradation of the Gleason score on radical prostatectomy specimen.[9]

An international Delphi consensus project in 2017 provided insights on the consensus of the experts for selecting patients with clinically localized PCa for FT.[10] The consensus concluded that multiparametric MRI (mpMRI) should be considered a standard imaging tool for patient selection for FT. In the presence of an mpMRI-suspicious lesion, MRI targeted biopsies with systematic biopsy is necessary to evaluate mpMRI-negative areas. However, adequate criteria for systematic biopsy remained undetermined. In the absence of a lesion on MRI, the panel agreed that a 12 core transrectal ultrasound (TRUS) biopsy would be insufficient to select patients for FT but could not reach a consensus on the type and the extent of biopsy which would be adequate. The panel found that transperineal mapping biopsy is the standard of care in many centers (particularly in Europe) because of better sampling of the prostate. Furthermore, the panel recommended FT in D'Amico low-/intermediate-risk cancers including Gleason 4 + 3.[10] Tumor foci of <1.5 ml on mpMRI or <20% of the prostate, or those up to 3 ml or 25% of the prostate if localized to one hemi-gland, are suitable for FT. The panel recommended that Gleason 3 + 3 cancer on a single core upto 1mm in size is acceptable in the untreated area and should undergo surveillance. The other areas where consensus could not be reached were patients with high risk PCa, patients with PSA >10 ng/ml, cancer foci >3 ml or 25% or crossing the midline, and in patients with severe lower urinary tract symptoms (LUTS). However, there is a current trend against treating patients with low risk cancer who are eligible for active surveillance and the focus has shifted to the patients with intermediate risk PCa. We perform 12 core template biopsies of the prostate in addition to 2 core MRI targeted biopsy of the suspicious lesion and while selecting patients for FT we include all grade groups, except those with NCCN very low risk or high risk with high volume PCa, defined as more than 2 cores positive for any Gleason Grade 4 or greater, as these patients are better suited for active surveillance and radical treatment, respectively.[11]

The location of the tumor plays an important role while selecting the best treatment modality, hence, an "a la carte model" for FT was proposed based on the intraprostatic tumor location.[12] For posterior cancers, HIFU is recommended, considering the transrectal approach, shorter focal distance, and the precise contouring of the target area. However, for anterior tumors, HIFU might not be the ideal choice and a transperineal approach, such as cryotherapy, is preferred. Focal brachytherapy might be considered for apical cancers as other energy modalities have the potential to cause varying degrees of sphincter damage and brachytherapy is associated with superior continence rates.

Based on the available literature, it seems that patients with unilateral high volume low risk disease, intermediate risk disease, and those with low volume high risk disease (≤2 cores) are best suited for FT.

HIGH INTENSITY FOCUSED ULTRASOUND

HIFU is delivered via a transrectal ultrasound probe, which allows visualization as well as delivery of energy to the prostate. HIFU utilizes ultrasonic waves which are absorbed by the tissues and are converted into heat, usually heating the tissues above 80 degree Celsius, resulting in coagulative necrosis, while the rectal mucosa is protected with a coolant. HIFU is best suited for prostates with the anteroposterior diameter <40 mm and when there are no prostatic calcifications, however larger glands can be treated after transurethral resection of the prostate and cytoreduction. The focal length of most HIFU platforms is 4 cm.[13]

Guillaumier *et al*. in June 2018 published their results of 625 consecutive patients who underwent focal HIFU.[14] Five hundred five (84%) patients had intermediate risk or high-risk disease and the median follow up was 56 months. The primary endpoint was failure-free survival (FFS) defined as freedom from radical or systemic therapy, metastases, and cancer-specific mortality. The authors reported the FFS as 99%, 92%, and 88% at 1, 3, and 5 years, respectively. Ninety-eight percent of the patients achieved complete pad-free urinary continence and none required more than 1 pad/day. Within 6 months of the treatment, 8.5% developed urinary tract infection, 1.9% had epididymo-orchitis, 9.6% required endoscopic interventions for LUTS and 0.3% developed recto-urethral fistulae. We published the first series of focal HIFU from the United States, which included 52 patients with at least 1 year follow up. Eighty three percent of the patients had a negative in-field biopsy results and 13% had positive out of the field biopsy.[11] Urinary symptoms returned to the baseline at 3–6 months and the sexual function returned to the baseline at 12 months post treatment. Only 5 major complications (all grade III) were noted in 4 patients.[11] Similar results were reported by previous small sized studies.[15,16] Stabile *et al*. reported on the medium-term oncological outcomes of the largest published cohort of men who received primary focal treatment with

HIFU for PCa.[17] A total of 1032 patients were included and the majority had a Gleason 3 + 4 or higher disease (80.3%). The median follow-up was 36 months and the reported freedom from biopsy failure, defined as absence of Gleason 3 + 4 disease, was 84%, 64%, and 54% at 24, 60, and 96 months and the freedom from any further treatment was 85%, 59%, and 46% at 24, 60, and 96 months, respectively.

CRYOTHERAPY

Cryotherapy works on the principle of cooling the tissues to temperatures below minus 30 degree Celsius, which leads to cell death. Cryotherapy is delivered via argon-based cryoprobes that are placed transperineally into the tumor under TRUS guidance. When the freeze cycle is initiated, an ice ball forms at the tip of the needle which results in disruption of the cell membrane and cell lysis.[18]

Ward and Jones performed an analysis of the Cryo On-Line Database (COLD) registry and identified 1160 patients who underwent focal cryotherapy.[19] They reported a urinary continence rate of 98.4% and the rate of maintenance of spontaneous erections as 58.1%. Follow up prostate biopsy was performed in 14.1% of the patients, of which 26.3% were positive. Prolonged urinary retention (>30 days) occurred in 6 (1.1%) patients and 1 patient (0.1%) developed rectourethral fistula. Shah *et al*. prospectively evaluated 122 consecutive patients at five centers in the United Kingdom, of which 28.7% belonged to the high risk (majority were cT3a and only 1.6% were Gleason 4 + 4) and 71.3% belonged to the intermediate risk group. The inclusion of high and intermediate risk group patients was the major strength of this study, as the majority of the previous studies mainly included low risk PCa.[20] The median follow-up period was 27.8 months and the authors reported the FFS at 3 years as 90.5%. The urinary incontinence rate, defined as any pad use, was 0/69 (0%) and the erectile dysfunction rate (defined as erections insufficient for penetration) was 5/31 (16.1%).

The long-term outcomes of focal cryotherapy are lacking. Recently, Marra *et al*. performed a matched pair analysis of the patients with low to intermediate risk PCa who underwent either focal cryotherapy or active surveillance.[21] At a long-term median follow-up of 85 months, there were no differences in the 10-year radical therapy-free or ADT-free, any treatment free, metastasis free, and the overall survival between the groups. The only benefit of focal cryotherapy was the time to radical treatment or the time to ADT, which was shorter in the active surveillance group.

PHOTODYNAMIC THERAPY

PDT entails the intravenous administration of a photosensitizing agent, which when activated by the light delivered by the optical fibers inserted transperineally into the prostate under TRUS guidance, causes cellular destruction. The activation results in the production of reactive oxidative species, which cause direct cellular injury and vascular damage and lead to cell necrosis and apoptosis. Azzouzi *et al*. published a multicenter randomized controlled trial comparing PDT to AS in patients with low-risk PCa.[22] Interestingly, the PCa progressed in 28% (n = 206) of the patients in PDT group as compared to 58% (n = 207) of the patients in the AS group. However, the erectile dysfunction rates and the urinary complications were higher in the PDT group, 38% versus 11%, respectively.[23]

These results should be interpreted with caution as the patients did not undergo mpMRI and confirmatory or saturation biopsy prior to selection into treatment groups. This limitation could potentially explain the high rates of progression reported in the active surveillance group (nearly 60%).

FOCAL LASER ABLATION

FLA requires the placement of a laser fiber directly into the cancer tissues via the trans perineal or the transrectal route, thorough which the energy is transmitted which results in cell necrosis. FLA is found to be safe and feasible for the treatment of localized PC,[24,25] however most of the reported studies have small sample size and short follow-up. Lepor *et al*. published their results of 25 consecutive patients with low-intermediate risk PCa treated with MRI-guided FLA.[26] Post ablation biopsy at 3 months showed no evidence of cancer in 96% of the patients without a compromise in the functional outcomes.

IRREVERSIBLE ELECTROPORATION

IRE includes the placement of electro-needle probes through the perineum into the ablative target under ultrasound or MRI guidance. High voltage bursts of electric current are passed through the probes resulting in cellular disruption. Van den Bos *et al*. investigated 63 patients with low and intermediate risk PCa treated with IRE[27] and reported a16% in-field recurrence rate. The urinary symptom score remained unchanged at 6 months postoperatively and there was a mild decline in the sexual quality of life score from 66 to 54.

FOCAL BRACHYTHERAPY

Brachytherapy seeds can be placed transperineally into the prostate under TRUS guidance. King *et al*. evaluated 354 men with low and intermediate risk PCa who underwent partial prostate treatment with brachytherapy to the peripheral zone under 0.5 Tesla MRI guidance.[28] Twenty two patients developed metastases at a median follow up of 11 years. The 10-year biochemical progression–free survival rates was 77%, 51% and 28% for very low-risk,

low-risk, and intermediate risk disease, respectively. In another study which included 12 patients who underwent focal brachytherapy, all the patients maintained urinary continence however the authors reported a decline in the sexual function scores.[29] While these long-term oncologic outcomes are worrisome, the use of outdated MRI system in the study and the fact that <20% of the patients underwent a 12-core pretreatment biopsy, could have contributed to the poor patient selection.

FOLLOW UP

A standardized follow-up protocol post FT is not yet defined. To determine the oncological efficacy, a combination of biochemical, imaging, and histological results is recommended. The post FT PSA values are influenced by the remnant prostate tissue, proportion of pre-procedural PSA attributed to the cancer tissues versus benign prostate hyperplasia (BPH) tissues, the efficacy of the ablation therapy and the progression of BPH, and are difficult to interpret. Thus, it is impossible to define a cutoff nadir value of the PSA that can define biochemical recurrence. Nonetheless, Stabile *et al.* showed that the percentage of PSA reduction is a useful tool to assess men post FT[30] and was an independent predictor for the requirement of additional treatment. Huber *et al.* demonstrated that post HIFU PSA nadir of 1.0 ng/ml at 12 months and 1.5 ng/ml at 24–36 months might be used to select men for MRI and biopsy.[31] The first post-treatment PSA measurement is recommended within 3 months of treatment and the subsequent PSA measurements should be obtained every 3 months during the 1st year and then every 6 months thereafter.[32]

Imaging in the form of mpMRI is used to evaluate the treatment response.[32] Initial postoperative imaging should be obtained within 6 months after FT and subsequent mpMRI should be scheduled 12 months after the first post-procedural mpMRI and thereafter as clinically indicated. Early contrast enhancement in the treated lesion is suggestive of failure post FT.

Biopsy is recommended to confirm the presence or absence of disease after FT.[32] MRI targeted biopsy with systematic biopsy is preferred to evaluate the treated area and also the untreated areas to define in field and out of field recurrences, respectively. A scheduled biopsy should be preferably carried out 6–12 months after the procedure and as clinically indicated thereafter.

Patients should be followed to assess for functional outcomes and complications every 3–6 months until they achieve baseline or stability.[32] Satisfactory urinary control is achieved if no pads are required, however, a consensus has not been reached on the definition of success for erectile function.

COMPARISON WITH STANDARD TREATMENT OPTIONS

Bates *et al.* performed a systematic review to evaluate the evidence for FT as a treatment strategy in comparison with the standard treatment options for clinically localized PCa.[33] They included five comparative studies (1 randomized clinical trial and 4 retrospective nonrandomized clinical studies) and ten systematic reviews. Majority of the systematic reviews included were heterogeneous studies with low patient numbers, most were uncontrolled single-arm case series, with no data on long-term outcomes and with significant limitations. Due to the low quality of the evidence with significant uncertainties regarding the effectiveness of FT in terms of oncological outcomes in comparison to the standard treatment options, they recommend FT to be ideally undertaken in clinical trials or prospective cohort and comparative studies to gather robust evidence so that clinical recommendations could be made. Shah *et al.* compared oncological outcomes of FT to radical prostatectomy form a prospective multicenter database and performed propensity score matched analysis. After matching, 246 patients were identified in each arm, and they included patients with Gleason ≤4 + 3, PSA <20 ng/ml, and ≤T2c. Oncological outcomes over the follow up period of 8 years were similar between the FT and RP ((FFS for FT was 83% (76%–90%) and that for RP was 79% (73%–86%) $P = 0.12$)).[34] Table 1 includes primary studies comparing FT to standard treatment options such as radical prostatectomy, radiotherapy and active surveillance.

FOCAL THERAPY FAILURE

Management of localized recurrence after FT depends on the NCCN risk group, in field or out of field recurrence and the patient preference. The available treatment options are active surveillance, repeat FT, salvage prostatectomy and salvage radiation.[38] For the low-risk disease, active surveillance may be an appropriate strategy. For intermediate and high-risk recurrences active treatment should be pursued with a curative intent. The evidence on salvage ablation and salvage radiotherapy after FT failure, is low. Salvage radical prostatectomy after FT failure has been reported to have similar oncological and functional outcome as compared to the primary radical prostatectomy.[39,40]

EXPERIMENTAL TECHNOLOGIES

Transurethral ultrasound ablation

While MRI-guided TULSA is a novel technology which was initially used for whole gland ablation, ongoing studies are investigating TULSA's performance in the setting of FT. Klotz *et al.* published their 12-month results of 112 patients enrolled in prospective, single-arm multicenter trial using MRI-TULSA for whole-gland treatment of low-intermediate

Table 1: Primary comparative studies

Study	Design	Intervention	Patients	GS	Stage	FU	Conclusions
Azzouzi *et al*., 2016[22] and Gill *et al*., 2018 (EFU)[23]	Randomized trial	FT (VTP) versus AS	FT (VTP) 206 (147 EFU) AS 207 (119 EFU)	Gleason pattern 3 only	≤T2b	24 months (EFU 4 years)	At 24 months fewer FT patients progressed (28% vs. 58%; adjusted HR: 0.34, 95% CI: 0.24–0.46; *P*<0.0001) and needed less radical therapy (6% vs. 29%; *P*<0.0001). More FT patients had a negative biopsy (49% vs. 14%; adjusted risk ratio 3.67, 95% CI: 2.53–5.33; *P*<0.001). Updated results[13] showed that the differences were maintained after 4 years. Transient deterioration in erectile and urinary function with FT, with no difference between the groups by 24 months health-related QoL deteriorated transiently for the FT arm. The frequency and severity of adverse events were higher with FT, most of which were mild or moderate in severity
Albisinni *et al*., 2017[35]	Retrospective matched-pair analysis	FT (HIFU) versus RALP	FT 55 RALP 55	≤Gleason 4+3	≤T2	Median: 36 months (IQR: 16-56)	Focal HIFU was comparable to RALP in controlling localized unilateral PCa, with NSD observed in the need for salvage therapies (either EBRT or systemic androgen deprivation therapy: 12.7% vs. 10.9%; *P*=0.76), although 12.5% of focal HIFU patients required additional contralateral hemiablation owing to the development of contralateral cancer. Focal HIFU patients had better continence (82% fully continent at 1 month vs. 40%; *P*<0.001) but at 24 months it was 94.5% and 91%. Also, better erectile function (erectile dysfunction rate 20% vs. 44% at 24 months; *P*=0.03)
Zheng *et al*., 2019[36]	Retrospective PSM cohort	FT (FLA) versus RP	FT 321 RP 321	≤Gleason 4+3	≤T2a	Mean: 59.6 months	NSD in CSM between FLA and RP (HR: 0.82, 95% CI: 0.18–3.67; *P*=0.7936) but there was significantly higher ACM in the FLA arm (ACM: HR: 2.01, 95% CI 1.18-3.42; *P*=0.0103)
Zhou *et al*., 2020[37]	Retrospective PSM cohort study	FT (FLA) versus RT	FT 428 RT 2568	≤Gleason 4+3	≤T2b	Not stated	RT had better OS than FLA, (HR: 1.50, 95% CI: 1.17-1.93; *P*=0.001) but there NSD for CSM between RT and FLA
Shah *et al*., 2021[34]	Prospective PSM	FT (HIFU, cryotherapy) versus RP	FT 246 RP 246	≤Gleason 4+3	≤T2c	FT: Median 49 months (IQR 34-67) RP: Median 64 months (IQR 30-89)	Oncological outcomes over 8 years were similar between FT and RP, FFS for FT was 83% (76%-90%) and for RP was 79% (73%-86%) (*P*=0.12)

ACM=Any-cause mortality, AS=Active surveillance, CI=Confidence interval, CSM=Cancer-specific mortality, FLA=Focal laser ablation, FT=Focal therapy, FU=Follow up, EFU=Extended FU, GS=Gleason' score, HIFU=High-intensity focused ultrasound, HR=Hazard ratio, IQR=Interquartile range, NSD=No significant difference, OS=Overall survival, PCa=Prostate cancer, PSM=Propensity score matching, QoL=Quality of life, RALP=Robot-assisted laparoscopic prostatectomy, RP=Radical prostatectomy, RT=Radiotherapy, VTP=Padeliporfin vascular-targeted photodynamic therapy, EBRT=External-beam radiation therapy, CSS=Cancer-specific survival

risk localized PCa.[41] Their primary endpoint (>75% reduction in PSA) was achieved in 96% of the patients, and Grade 3 adverse events were seen in only 8%. Cancer was detected in 35% of the follow-up biopsies. The authors concluded that TULSA is safe, and effective in tissue ablation, and reduction of PSA.

Encage

Encage™ represents a bipolar radiofrequency system with a coil design utilized for focal ablation of clinically significant localized PCa visualized on mpMRI. Orczyk *et al*.[42] published their 6 months follow-up of 20 patients who underwent this novel procedure. Ninety percent of the patients had grade group 2 cancer. After the treatment, targeted biopsy at 6 months revealed absence of clinically significant PCa in 80% of the patients. Additionally, the authors reported relatively low genitourinary side effects. Although the long-term oncological control data are yet to be determined, this novel technology shows promising early efficacy in the treatment of visible clinically significant PCa lesions.

Gold nanoshells

Gold nanoparticles are designed to absorb and convert near-infrared light into heat, which can be utilized to induce tissue hyperthermia resulting in cancer cell death. Rastinehad *et al*. published a pilot device study of laser-excited gold sinica nanoshells used in combination with MRI-US fusion imaging for focal ablation of low-intermediate risk PCa.[43] This technology was successful in ablating clinically

Table 2: International guideline recommendation

Guideline	Recommendation
AUA guidelines 2017[45]	Clinicians should inform those localized prostate cancer patients considering focal therapy or HIFU that these treatment options lack robust evidence of efficacy (expert opinion) Clinicians should inform localized prostate cancer patients who are considering HIFU that even though HIFU is approved by the FDA for the destruction of prostate tissue, it is not approved explicitly for the treatment of prostate cancer (expert opinion) Clinicians should advise localized prostate cancer patients considering HIFU that tumor location may influence oncologic outcome. Limiting apical treatment to minimize morbidity increases the risk of cancer persistence (moderate recommendation; evidence level: Grade C) As prostate cancer is often multifocal, clinicians should inform localized prostate cancer patients considering focal therapy that focal therapy may not be curative and that further treatment for prostate cancer may be necessary (expert opinion)
EAU 2021 guidelines[46]	Only offer focal therapy within a clinical trial setting or well-designed prospective cohort study
NCCN guidelines Version 1 2022[47]	Only offer focal therapy within a clinical trial setting or well-designed prospective cohort study

HIFU=High-intensity focused ultrasound, FDA=Food and Drug Administration, AUA=American Urological Association, EAU=European Association of Urology, NCCN=National Comprehensive Cancer Network

significant PCa in 15 out of the 16 patients (94%) after 12 months without significant side effects.

ONGOING TRIALS

Multiple clinical trials comparing FT to the conventional therapies, such as active surveillance, radical prostatectomy, and radiation are ongoing. For example, CHRONOS is a parallel phase II-controlled trial in men with newly diagnosed localized intermediate-high risk PCa.[44] In CHRONOS arm A patients will be randomized to whole-gland treatment (radical prostatectomy, radiotherapy, and brachytherapy) versus focal cancer treatment (HIFU and cryotherapy). On the other hand, patients who enroll in CHRONOS arm B, will be randomized to FT alone versus FT with neoadjuvant treatment, e.g., finasteride or bicalutamide. This trial will primarily address the oncological outcomes between of the various therapies, in addition to the adverse events, health economics, and the functional outcomes. This promising trial, in addition to the other ongoing trials in Europe, will result in better understanding of patient selection criteria, biopsy criteria, and follow-up strategies as well as the definition of treatment success, and the management of residual or recurrent disease. However, there are limitations for conducting surgical RCTs such as poor patient accrual due to strong patient preference or denial to be included in the experimental arm, high cost, limited availability of FT, requirement of large sample size and longer follow up due to the inherent nature of localized PCa.

The current international guideline recommendations are summarized in Table 2.

CONCLUSION

FT aims at achieving cancer control with fewer side effects as compared to whole gland treatment, thus providing a better quality of life. A number of ablative techniques are available of which the highest quality data is available for HIFU and cryotherapy. By avoiding the surrounding noncancerous tissue (bladder neck, neurovascular bundle, and rectum), FT minimizes the side effects on the urinary and sexual function.

However, there are some limitations to FT. First, long-term oncological follow-up of the patients undergoing FT is lacking. Second, there is no consensus as for what defines the oncological control, like the presence of any cancer or clinically significant cancer and whether present in the treated or the untreated prostate. Furthermore, the role of PSA kinetics in the postprocedure follow-up has to be established. There is a consensus that PSA needs to be included in the follow-up, but the threshold which should trigger a biopsy is not yet known. Better imaging and navigational technologies and better mapping of the PCa are required to reduce both in-filed and out of filed recurrences. Modern imaging with novel agents such as PSMA PET in combination with MRI may better stratify the patients eligible for FT. It has been postulated that partial or incomplete treatment might result in resistant clones leading to locoregional recurrence.[39] However, data suggests that when FT fails, salvage prostatectomy and radiation therapy are viable alternative options.[39,48] This helps in patient counseling and reassurance, that they are not precluded from the standard multimodal whole gland treatment options, if FT fails.

In summary, FT is an alternative modality of treatment for localized PCa with a favorable side effect profile and comparable short to midterm oncological control as compared to the whole gland treatment. Nonetheless, FT should only be offered in clinical trials or prospective cohort or comparative studies until the results of the ongoing clinical trials are published which will provide robust data on the role of FT in the changing landscape of PCa treatment.

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