Focal therapy for localized prostate cancer: is there a “middle ground” between active surveillance and definitive treatment?

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In recent years, it has come a long way in the diagnosis, treatment, and follow-up of prostate cancer. Beside this, it was argued that definitive treatments could cause overtreatment, particularly in the very low, low, and favorable risk group. When alternative treatment and follow-up methods are being considered for this group of patients, active surveillance is seen as a good alternative for patients with very low and low-risk groups in this era. However, it has become necessary to find other alternatives for patients in the favorable risk group or patients who cannot adopt active follow-up. In the light of technological developments, the concept of focal therapy was introduced with the intensification of research to treat only the lesioned area instead of treating the entire organ for prostate lesions though there are not many publications about many of them yet. According to the initial results, it was understood that the results could be good if the appropriate focal therapy technique was applied to the appropriate patient. Thus, focal therapies have begun to find their “middle ground” place between definitive therapies and active follow-up.

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INTRODUCTION

Watchful waiting for prostate cancer (PCa) is an established concept that has been tested in clinical trials.1–3 However, the nomenclature was often used to refer to patients with shorter survival who could be observed and possibly treated with hormonal therapy at progression. Active surveillance (AS) then became the experimental concept and new nomenclature for observing patients with disease lacking progression and/or lethal characteristics.4,5 Active surveillance for low grade and selecting favorable intermediate risk cancers is now a more clinically established pathway.6,7 It can be functionally divided into three concepts as follows: who is a candidate, how to monitor them, and when to change to treatment.8 Despite the acceptance of AS, 15%–30% of candidates will eventually be reclassified to higher risk and treated at some point. Patients on AS maintain the very competitive quality-of-life survey scores9 compared to treated.10–12 However, they require repeat diagnostic testing—centered on imaging and repeat biopsy.

The broader picture of this pathway relates to prostate-specific antigen (PSA) screening over the past 30 years.13 However, this issue is still controversial in urology, for example, there is conflicting results about relationship between survival and PSA screening in broad-based randomized controlled trials (RCTs).14,15 Even in the European screening trial, the cautionary message is that it results in overdetection of disease.14 In many countries such as the USA, overdetection correlates with overtreatment, though the trends are more favorable in the past 5 years.16

What are the options for improving outcomes for men with the clinically localized disease in the low risk to favorable intermediate risk range?17,18 One option is to select the lowest risk patients for AS, and the rest are selected for standard definitive therapies.8 A wide body of literature centers on the narrative of improving technical features of treatment, i.e., open/lap/robotic technique, neurovascular bundle sparing surgery, incontinence improving reconstruction, proton radiation, etc. Prediction models can be used such as nomograms, or magnetic resonance imaging (MRI)-targeted biopsy, or clinical genomic platforms.19–22 Either way, the standard options vary from treating all of the prostate to treating none of the prostate with nothing in the middle as a standard option. Is there a safe and effective middle ground? If so, it would likely be characterized as effective in stopping progression to needing definitive treatment, requiring less intensive monitoring, and having the quality-of-life results more in line with surveillance as for surgery or radiation.

WHAT IS FOCAL THERAPY?

Whole-gland treatment is the standard when curative intervention is indicated. The act of treating the whole prostate makes sense; given it is a disease that has a high prevalence of being bilateral and multifocal.24 However, such treatments create functional loss due to the proximity of the neurovascular bundles, rectum, bladder, and urethra. If focal therapy (FT) is to work, it has to produce less tissue trauma and achieve accurate tissue ablation at the appropriate targets. Ward et al.,25 described three different possible treatment maps, true lesion-directed focal therapy, hemiablation, and a hockey stick, which are described in Figure 1. The former is more in line with the “index theory” (more to follow) of treatment. The latter is a combination of hemiablation and anterior contralateral–a plan that
eradicates the most clinically significant and less dominant tumors based on prostatectomy pathology comparisons.

FT has already been widely used in the treatment of solid organ tumors such as brain, liver, breast, thyroid, and lung, before it was used in urogenital system tumors. Therefore, FT is the potential middle ground (almost “adjuvant therapy”) between AS and definitive treatments. Perhaps, a new treatment corridor can standardize patients with PCa diagnosis in this middle ground.

PATIENT SELECTION

For patient selection, the risk stratification must be reliable. The ideal patient for FT should have unilateral, low volume, low-favorable/intermediate risk and completely targetable and destroyable lesion, and also life expectancy over 10 years. However, the situation is usually not so easy. Because over 90% of PCa is multifocal and only 20%–40% is settled in one site.

Several studies have described an “index lesion” where there is only one dominant lesion from which 90% of metastases originated from the same single cell clone—despite the multiple synchronous tumors in the whole prostate gland. Up to 80% of the prostate tumor volume can originate from the index lesion. Studies on synchronous lesions outside of the index lesion show that 80% of patients with index lesion have secondary insignificant cancer, and the total volume was <0.3–0.5 cm³ of these secondary lesions with Gleason score (GS) ≤3 + 3. Index lesions with local growth and metastatic potential are usually >0.5 cm³ and GS ≥4 tumors. As Klotz reviews the literature and hypothesizes: treatment of the index lesion alone may yield acceptable oncologic outcomes, even if satellite low grade lesions remain untreated.

Defining eligibility criteria for FT remains a challenge due to our limitations in diagnostic accuracy. Consensus type efforts have suggested that the appropriate patient would have a PSA <15 ng ml⁻¹, GS 3 + 3 or 3 + 4, clinical stage T1c or T2a, life expectancy >10 years, and any prostate volume. A more ambitious/controversial (and potentially dangerous) profile would include PSA <20 ng ml⁻¹, GS 4 + 3 or 4 + 4, and clinical stage ≤T2c. Again, the concept is not to select excellent candidates for AS such as no MRI target, small volume GS 3 + 3.

Patient selection should also include detailed counseling, including the need for follow-up testing (biopsy and PSA trending), and the possible need to repeat focal therapy or proceed to definitive surgery or radiation, and any treatment after FT will be difficult than treatment for therapy-naïve patients. Rare/emerging indications reported that FT could be used for salvage for high-risk PCa patients in the purpose of definitive or palliative treatment. Overall, patient selection success will be defined by not overtreating AS candidates and not undertreating aggressive/multifocal disease.

RELATIONS BETWEEN FT AND AS

In the search for the middle ground between AS and active intervention (AI), there are specific aspects of AS that could be improved with an “adjuvant” approach. As stated, the three constructs of AS are: (1) patient selection, (2) monitoring techniques, and (3) indications for treatment. At the patient selection area, age is not necessarily a criterion, but likely on the most clearly low-grade patients would be offered it, and thresholds for changing to treatment would likely be very low. Therefore, FT may help increase candidacy into higher volumes of disease and possible GS 3 + 4. If FT prevents progression from 3 + 3 to 3 + 4 or more (33% in some studies), that could save an intervention and related quality of life changes.

Next, AS patients need monitoring. In the MD Anderson Cancer Center AS protocol, the initial plan was a transrectal ultrasound (TRUS) biopsy every 1–2 years and PSA every 6 months. FT would then have the opportunity to provide more stability to the picture and less need for such ongoing repeat testing over time.

The cost of FT could then be measured in oncologic success as well as the savings of less intense AS monitoring. The monitoring burden is relevant—frequency and intervals of laboratory tests, imaging, and biopsies. Although AS-related anxiety is much talked about and likely amenable to proper counseling, there are certainly patients who prefer some type of intervention, but less than radical surgery or radical radiation therapy. Early FT efforts mainly selected low-risk patients and established low comorbidity. As selection migrates into intermediate risk, the endpoints can move to the number of avoided radical treatments.

IMAGING: IS IT PRECISION OR ESTIMATION?

Early attempts at focal therapy were TRUS biopsy-based and therefore, larger treatment fields were planned out of uncertainty (i.e., unilateral disease treated with hemiablation). Errors can be both ways: 6% overestimating/24% underestimating in GS or detects lesion volumes smaller than original sizes compared with RP pathology. In addition, clinically, significant prostate cancer may not be detected in 30% of cases. In repeat biopsy scenarios, the yield is 14%–22% for the first repeat and still 4% for the fourth repeat. Furthermore, TRUS biopsy is usually insufficient to detect the dominant lesion when low-grade disease is found. In addition, in cases where the TRUS biopsy lesion is unilaterally detected, there is a possibility of a disease in the contralateral side at 72%, 43–45.

A logical follow-up strategy was to escalate biopsies into the 24 to saturation models, as described by Barzell and Whitmore and Onik and Barzell. These techniques result in increasing cancer yield but less clear impact on clinically significant cancers detection. Are saturation biopsies enough to plan for FT? It has 24% positive predictive value (PPV) in catching unilateral disease and the complication rates are similar to standard TRUS.

Another type of biopsy is “transperineal mapping biopsy (TMB).” A brachytherapy template is used that allows systematic sampling during the process. TMB is much better than the standard TRUS biopsy in detecting the index lesion with a detection rate of 82.9%. Furthermore, it is noted in many studies, TMB is better than standard TRUS biopsy in predicting anterior gland, determining GS, detecting laterality, and performing risk stratification. Besides diagnostic accuracy, TMB avoids most septic complication rates observed in standard TRUS biopsy, but often with the trade-off of higher urinary retention rates.
In the first month, it causes an 18% decrease in erection potential and a 24% decrease in urine function, which rises to normal levels in the third month. However, it has some drawbacks such as the need for general anesthesia, high cost, and takes longer period when we compare with standard biopsy.

The latest evolution of FT is now anchored in multiparametric MRI imaging—an area of improving technique and resolution. Image rendering can be 3D and in different slices (trans/sagittal/coronal). Lesions can be characterized by location, volume, and shape of the cancer site. Baseline images are with anatomic sequencing in T1–T2-weighted sequences, and full multiparametric technique uses functional sequencing in diffusion-weighted imaging (DWI). Multimetric MRI (mpMRI) allows a more focused biopsy besides allowing for better visualization. Based on these, fusion biopsies are developed by recording and processing MRI images or by MRI simultaneously. There are three common types of fusion biopsy technique as follows.

1. **Cognitive fusion biopsy**: It is the simplest fusion biopsy method—a basic operator-dependent needle placement strategy that requires matching the MRI abnormality to the general area of the ultrasound. It does not require any special equipment or incremental cost. However, the operator must be experienced with image interpretation and lesion selection. Therefore, this is potentially error prone in small lesions.

2. **MRI-TRUS fusion biopsy**: It depends on the essential of combining recorded and separated previous MRI images with real-time US images via a dedicated software. The error margin is reduced by software, as long as the operator is experienced in biopsy and utilizing the fusion functionality. Lesions are often segmented by an experienced radiologist. The technology adds cost; however, it can be done in outpatient settings including clinical office or outpatient surgery center.

3. **In-bore biopsy**: It requires application in the MRI device, and therefore requires a magnet compliant environment. The method is more tedious as the needle requires detailed advancement under real-time MRI imaging. Systemic cores are not practical, and rather only the targets. For this reason, cancer detection rate increases and complication rate decreases. Despite these benefits, there are limitations such as the need for general or conscious sedation anesthesia, the long running of the procedure, the discomfort of the surgeon, the need for special equipment, and high costs. Detection of clinically insignificant cancer rate is widely reported, between 19.2% and 78.6%. In a recent study that was published from our clinic, we evaluated 530 prostate biopsy patients. We found that no cancer or low/favorable prostate cancer rates of 48%. Besides this when we compare the costs of biopsies, we found that TMB, IGTP8x, and in-bore biopsies under general anesthesia were 2.2–2.5 times more costly than TRUS-guided biopsy under local anesthesia.

MpMRI is now a requirement for planning FT, as well as follow-up, but it has limitations in diagnosing MRI invisible lesions.

**FOCAL THERAPY METHODS AND DEVICES**

There are several treatment methods in FT as shown in Figure 1. The aim is to destroy the index lesion. If the index lesion is unique or the number of lesions is low, and the index lesion can be easily separated from the others, the lesion(s) should be targeted directly (Figure 1a-1c). However, if the index lesion cannot be distinguished or multifocality is mentioned, a larger ablation should be planned and a hemiablation (Figure 1d) or subtotal (hockey stick) ablation (which was described by Ward et al., Figure 1e) should be performed.

**Cryotherapy**

It causes cell death because of cell membrane disruption by freezing. Depending on ischemia and coagulation necrosis, there is a lesion similar to an ice-ball with central necrotic foci and surrounding edematous tissue. The procedure is performed transperineally and concurrently can be followed up with TRUS, MRI, or thermosensors. It also has a short duration of hospitalization.

One session consists of cooling to –30°C quickly with argon based cryoprobes followed by a 10 min heating cycle. The treatment consists of two consecutive repeat sessions. Hydrogen gas is used in the heating cycle. There are two kinds of heating cycle. The first one is 10 min of the active cycle or the other one is 5 min active and 5 min passive cycle.

The largest series on cryoablation was published by Ward and Jones with 1160 cases in year 2012. At 3 years follow-up, biochemical recurrence-free rate was 75.7%. About 14.1% of the 1160 treated patients were biopsied after the treatment and 26.3% of the biopsies were positive. It was shown that 3.7% (43/1160) of all patients had recurrence after treatment. In addition, according to the same team’s report, the rate of complete continence (0 pad) was found as 98.4%, whereas the rate of spontaneous erection was found as 58%. After the first 30 days, 6 (1.1%) patients had urinary retention and only one patient had rectourethral fistula formation. In a systematic review published by Shah et al., biochemical recurrence-free survival rate were reported as 71%–93% (9–70 months), incontinence rate was 0–3.6%, and ED rate were 0–42%.

It is the most well-known and applied method among the FTs. It also has a short duration of hospitalization. However, it is an expensive method because of requiring special devices.

**High-intensity focused ultrasound**

The procedure is performed with a transrectal probe that visualizes the prostate and delivers a high-focused energy prostate at the same time. When applied with a special probe in the range of 0.8–3.5 MHz, the ultrasonic sound waves exceed the limit of 5 W cm² energy density. When this energy is focused on a single point, the density can rise to 1500 W cm². The energy is absorbed by the target tissue and the temperature of the tissue can rise to 60°C–80°C. As a result of this, coagulation necrosis occurs in the tissue. Another mechanism is cyclic compressions and rarefactions. These cycles are caused to inertial cavitation and cell death occurs.

The other well-known and applied technique, high-intensity focused ultrasound (HIFU), is noninvasive, the duration of hospitalization is short and it is cheaper than cryoablation. However, the effectiveness of technique decreases, especially in prostates with anteroposterior diameter >40 mm and/or have calcifications. Another problem is, it can cause damage to the rectal mucosa. This damage can be minimized by perfect adjustment of the rectal probe position and active cooling of the mucosa. It was used in ablation of extra urogenital tumors since 1940s and it was first used for prostate cancer ablation in 1995 by Madersbacher et al.

In a review by Kasivisvanathan et al., it was reported that continence rates of 90%–100% and potency rates of 89%–95% after HIFU. In another recent review, 14 trials were evaluated, in 303 patients with a follow-up period of 34–127 months, reporting a biochemical recurrence-free survival rate of 54%–91%.

**Other ablative techniques**

Other than cryotherapy and HIFU, there are some newer different techniques with limited and unclear results.
**Focal laser ablation**

This technique is also known as laser-induced interstitial thermotherapy (LITT). In order for the laser to be more effective and less harmful, the energy and heat conduction at the applied tissue must be minimal. Prostate tissue is one of the best matching tissues for laser ablation per this definition. Laser ablation leads to thermal damage to the tissue by the photothermal effect. Tissue absorbs the radiant energy by chemopores and the heat gets higher in the tissue and results in a coagulation necrosis with a sharp demarcation line around it, and chronic inflammation occurs in the form of a hemosiderin reservoir at the out of demarcation line. The procedure is performed transperineally and concurrently can be followed up with TRUS or MRI. However, its application in anterior tumors is difficult and there is not enough data yet.

**Focal photodynamic therapy**

On reaching the target tissue, light active (photosensitized) IV agents release free oxygen radicals and these free radicals cause cellular apoptosis and necrosis. The procedure is performed transperineally and has a short duration of hospitalization. However, there are risks such as the toxicity caused by the photosensitizer given and the high residual risk of residual disease. Furthermore, there is insufficient data about this technique.

**Irreversible electroporation**

It is a nonthermal technique that causes irreversible nanopores on cell membrane with short electric waves. It causes a sudden decrease in the regional microcirculation. Cell death may be caused by nanopores on the cell membrane. This method is already used in the treatment of nonurological cancers. Although the use for prostate cancer is still limited, the results are positive for oncological control, continence and potency preservation. It has short operation and hospitalization period.

**Brachytherapy**

It is a kind of radiotherapy (RT) and also known as Cyberknife®. It was widely used in localized prostate cancer and has recently been started used for FT. Radioisotopes are inserted into the lesions detected in the previous MRI and high-intensity radiation is sent with the help of special transperineal needles to activate them. The half-life of these radioisotopes is 10–60 days. During this time, the multiple ionization induced by the combined effect leads to damage to the DNA. Eventually, the cell cycle arrests and cell death occurs. Depending on the high technology, intense radiation is focused, and the procedure is carried out with a safety margin of 2 mm in the targeted lesion and inversely to the RT, unwanted side effects are avoided.

Although the information on the use of brachytherapy in FT is limited, the oncologic outcome seems to be satisfactory. Biochemical recurrence-free survival rate is 92% and the residual cancer rate is 5%. Clavien Grade 1 and 2 complications of rectal and urinary functions and erectile dysfunction (ED) rates are similar to RT. However, Clavien Grade 3 and 4 complications, rate of ED, and testicular involvement have not yet been reported because of the lack of long-term results. The main handicap of this technique is high-cost rate.

**Radiofrequency ablation**

Radiofrequency ablation performed transperineally by the guidance of TRUS. Through the bipolar radio frequency (RF) probes, thermal damage to the desired target is created with a margin of 0.5 mm. A coagulation necrosis with a secure demarcation line occurs in the ablated region. Although this method has been approved by the FDA for the treatment of prostate cancer, there is not much study has been done yet. Although there is not much study were done, it has been found that HIFU is more affordable compared to cryotherapy and brachytherapy.

There is a table about the results of different FT techniques which was shortened and adapted here from the review of Valerio et al. (Table 1).

Here, we reported several FT techniques. Moreover, there are also studies reported about new one every day. However, comparative randomized controlled studies are scarce, and most of them included low- to intermediate-risk PCa treated with curative intent. The main important point in the treatment of PCa with FT is, completely destruction of tumoral tissue in the prostate by the lesion, hemigland or quadrant targeting, regardless of the technique.

**SUCCESS, FAILURE, AND FOLLOW-UP**

Consensus panel recommendations are available on FT. Oncologic success may be defined as the absence of any tumorous tissue on the treated area for a period of 5 years. Treatment is considered unsuccessful if there is a ≥0.2 cm³ or ≥7 mm in long diameter, and GS ≥3 + 4 tumor detected in the treated area on follow-ups. However, if there is a low-risk lesion in the untreated area, this lesion can be watched in accordance with AS rules.

In the report published by the Delphi consensus in 2016, oncological failure was evaluated in three parts. Ablation failure is the failure of the technique, which is choosing the wrong device/technique to destroy the lesion within the intended treated zone. Posttreatment images should be histopathologically proven if there is any evidence that the remaining malignant tissue is in the treated area (residual tumor). The panel unanimously provided an opinion on mpMRI from the methods of imaging for proving ablation failure. Residual tumor mpMRI is also described as early contrast intensity in dynamic contrast enhanced sequences. Targeting failure, means that applying ablative energy incorrectly or inadequately to a part of the tumor.

The selection failure is caused by the improper patient selection. The evolution of any locally advanced disease or metastases in short term (within 12–18 months) after treatment is often the result of the wrong choice of case.

After FT, if a failure occurs, it is possible to retreat residual tumors with second FT, surgery or RT again. However, the second treatment may be technically limited and challenging, especially if the higher amount of tissue ablated in first treatment.

Functional success is briefly defined as the absence of treatment-related side effects (after healing recovery). These side effects may include reduced quality of life, urinary system problems, erectile and ejaculatory problems, and bowel-related problems. These require long follow-up. Panelists at the Delphi panel in 2015 commented on the follow-up after the FT. They decided that a 5-year follow-up was needed after the disease treatment. Figure 2 highlights their follow-up algorithm. Standardized surveys and tests should be used to assess outcomes. For example, evaluation of urinary functions is performed with the International Prostate Symptom Score (IPSS) or the American Urological Association (AUA) score and uroloumetry. The 24-h pad weight test is a reliable method of assessing incontinence. The erectile function should be evaluated with the short of five questioned International Erectile Function Index (IIEF-5) or Sexual Health Inventory for Men (SHIM) questionnaire, and the ejaculation assessed with questions 9 and 10 of IIEF-5 (Q9: when you had sexual stimulation or intercourse, how often did you ejaculate; and Q10: when you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax).

To assess the quality of life, they have also recommended the use of the
Table 1: The results of different focal therapy techniques

| Kind of focal therapy | Reference | Number of patients | Age (year) | PSA (ng ml⁻¹) | Kind of biopsy | Lesion location | Type of ablation | Length follow-up (month) | Any secondary local treatment (%) | Disease specific survival (%) |
|-----------------------|-----------|--------------------|------------|---------------|----------------|-----------------|-------------------|--------------------------|-------------------------------|--------------------------|
| Cryotherapy           | Truesdale et al.²³ 2010 | 77 | Mean±s.d.: 69.5±6.7 | Mean±s.d.: 6.5±4.9 | Standard TRUS | Unilateral | Hemiablation | Median (range): 24 (0–87) | NR | 100 |
|                       | Ward et al.²⁵ 2012 | 1160 | Mean±s.d.: 67.8±7.9 | NR | NR | Organ-confined | NR | Mean±s.d.: 21.1±19.7 | NR | NR |
|                       | Durand et al.¹⁰¹ 2014 | 48 | Median (IQR): 67 (50–77) | Mean (range): 6.1 (3.1–9.7) | Standard TRUS | Unilateral | Hemiablation | Median (IQR): 13.2 (7.4–26.5) | 14.6 | 100 |
| HIFU                  | Madersbacher et al.²⁶ 1995 | 29 | Mean±s.d.: 64±7.2 | Mean±s.d.: 24.5±18.8 | NR | Unifocal or organ confined | Hemiablation or focal ablation with no intention to treat | 0 | NA | NR |
|                       | Dickinson et al.¹⁰² 2013 | 26 | Mean (range): 61 (40–79) | Mean (range): 7.7 (1.5–14.2) | Template mapping | Unilateral, unifocal, or multifocal | Index lesion ablation or hemi ablation | 0 | NA | NR |
|                       | Ahmed et al.¹⁰³ 2015 | 56 | Mean±s.d.: 63.9±5.8 | Median (IQR): 7.4 (5.6–9.5) | Standard TRUS and/or template mapping | Unifocal or organ confined | Index lesion ablation | Median (range): 12 (NR) | 7.2 | 100 |
|                       | Feijo et al.¹⁰⁴ 2015 | 71 | Mean±s.d.: 70.2±6.8 | Median (IQR): 6.1 (1.6–15.5) | Extended TRUS or template mapping | Unilateral | Hemi-ablation | Median (IQR): 12 (6–50) | NR | NR |
| PDT                   | Moore et al.¹⁰⁵ 2006 | 6 | Mean±s.d.: 63.9±5.3 | Range: 1.9–15 | Standard TRUS | Organ-confined | NR | Median (range): 6 (NR) | NR | 100 |
|                       | Moore et al.¹⁰⁶ 2014 | 42 | Mean±s.d.: 63.9±5.3 | NR | NR | Organ-confined | NR | Median (range): 6 (NR) | NR | 100 |
| LITT                  | Oto et al.¹⁰⁷ 2013 | 9 | Median (range): 61 (52–77) | Median±s.d.: 5.5±2.6 | Standard TRUS | Unifocal | Focal ablation | Median (range): 6 (NR) | 0 | 100 |
|                       | Lepor et al.¹⁰⁸ 2015 | 25 | Median (range): 66 (49–84) | Median (range): 5.3 (2–9.4) | NR | Unifocal or multifocal | Focal ablation | Median (range): 3 (NR) | 0 | 100 |
| Brachytherapy         | Nguyen et al.¹⁰⁹ 2012 | 318 | NR | Median (IQR): 5 (3.8–6.9) | NR | Organ-confined | Peripheral zone ablation | Median (IQR): 61 (33–88) | NR | 99.7 |
|                       | Cosset et al.¹¹⁰ 2013 | 21 | Mean (range): 62.3 (56–75) | Mean (range): 6.9 (3.6–13.9) | Extended TRUS | Unilateral | Focal ablation | NR | 0 | 100 |
|                       | Valerio et al.¹¹¹ 2014 | 34 | Mean±s.d.: 65±6 | Median (IQR): 6.1 (4.3–7.7) | Template mapping and/or targeted | Index lesion ablation | Median (range): 6 (1–23) | 11.8 | 100 |
|                       | Van den et al.¹¹² 2015 | 16 | Median (range): 60 (44–75) | Median (range): 9 (3.6–25) | Standard TRUS | Organ-confined | Focal ablation with no intention to treat | Median (range): 1 (NR) | NR | NR |
| RFA                   | Zlotta et al.¹¹³ 1998 | 15 | NR | NR | NR | Focal ablation with no intention to treat | NR | NR | NR | NR |

This table was shortened and adapted here from the review of Valerio et al.²⁴ HIFU: high-intensity focused ultrasound; IRE: irreversible electroporation; IQR: interquartile range; LITT: laser-induced interstitial thermoablation; NA: not applicable; NR: not reported; PDT: photodynamic therapy; PSA: prostate-specific antigen; RFA: radiofrequency ablation; s.d.: standard deviation; TRUS: transrectal ultrasound

Functional Assessment of Cancer Therapy-Prostate (FACT-P). Although there is no consensus on the evaluation and follow-up of bowel-related symptoms, the bowel symptom scores can be used, and DRE was offered after, especially transrectally applied ablative techniques.²⁴

**CONCLUSION**

FT is an emerging/alternative approach to prostate cancer that needs further refinement in patient selection and oncologic outcomes. Although there is no sufficient randomized controlled study for which one the best technique is, FT are minimally invasive treatment modalities that is somewhere in between AS and radical treatments. Although sufficient data accumulation has not yet been achieved and reported, and treatments are often not covered by health insurance, the experience continues to grow due to the attraction of reduced side effects. It is a potential treatment alternative for low- (avoiding minimal volume disease) and intermediate-risk groups and is a possible...
solution for AS patients having anxiety issues with no therapy. Patients with the low-risk residual disease after FT may also be admitted to the AS pool, thus expanding the AS pool. In the light of available data, urologists should proceed with caution in recommending FT and clinical trial/registry is the better path forward at this time.

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