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Prostate Cancer Focal Ablative Therapy*

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to describe the current role of focal therapy in management of prostate cancer and the various modalities of partial gland ablation.

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INTRODUCTION

Men who are diagnosed with localized prostate cancer are typically managed with active surveillance, radical prostatectomy or radiation therapy based on risk stratification. In the ProtecT (Prostate Testing for Cancer and Treatment) trial 1643 men with clinically localized prostate cancer were randomized to active surveillance, radical prostatectomy (nerve sparing when possible) or external beam 3-dimensional conformal radiation therapy (74 Gy in 37 fractions).[1] Ten-year prostate cancer specific survival rates were 98.8%, 99.0% and 99.6%, respectively. Given the low rates of disease specific mortality associated with prostate cancer in the current era, discussion and counseling regarding treatment related adverse effects have a significant role in management decisions. Concern over these harms prompted the U.S. Preventive Services Task Force to take a stance against prostate specific antigen screening in 2012, although its position has since been modified.[2] Accurate diagnosis, improved patient selection and strategies to reduce treatment related morbidity remain important clinical requirements in the management of prostate cancer.

In recent years focal therapy and partial gland ablation have emerged as treatment options for prostate cancer**. Focal ablative therapy of localized prostate cancer aims to reduce the treatment related adverse outcomes and health care burden associated with radical therapy modalities such as surgery and radiation.** Focal therapy is an investigational strategy to address localized, clinically significant prostate tumors while minimizing negative effects on quality of life. Focal therapy aims to treat the index lesion, generally defined as the largest tumor within the prostate, which is most likely to represent the highest grade and stage, and is also most likely to influence the biological behavior of the cancer.[3] Focal therapy specifically refers to image guided treatment directed at the tumor, whereas partial gland ablation describes treatment of a region of the prostate gland (eg hemigland) independent of the imaging that identified the cancer. For the purposes of this Update we refer to both types of treatment as focal therapy. The goal of focal therapy is to destruct the index lesion while preserving the surrounding normal prostatic parenchyma and key structures such as the neurovascular bundles, external sphincter, bladder neck and rectum. As such, focal therapy provides an opportunity to achieve acceptable cancer control while minimizing treatment related adverse outcomes compared to conventional radical therapy options.

PATIENT SELECTION

Efforts to identify and establish the clinical parameters of cases that may benefit from focal therapy vs active surveillance or radical treatment have been evolving. Conceptually focal therapy has the potential to be an intermediate treatment between active surveillance and radical therapy. A significant proportion of men initially managed by active surveillance will subsequently undergo radical therapy,[1] while some men will be overtreated with radical surgery or radiation therapy. **Carefully selected men, particularly those with low volume, intermediate risk disease, may derive the most benefit from focal therapy.** Numerous consensus reports have been published that provide guidance in defining the ideal patient population (see figure).[4-14] Although there is no consensus definition of eligibility criteria for focal therapy of prostate cancer, many agree that the ideal candidates should have an index lesion encompassing less than 20% of the prostate gland (assessed by multiparametric magnetic resonance imaging) and favorable intermediate risk disease (grade group 2) or low volume grade group 3 disease as determined by targeted and systematic biopsy of the index lesion. Some researchers have reported the benefits of transperineal mapping biopsy for pretreatment planning as well as posttreatment follow-up. PSA should generally be less than 10 to 15 ng/ml. Grade group 1 disease in a small number of cores in the non-treated region is acceptable according to most consensus statements and represents a treatment paradigm for overcoming the multifocality of prostate cancer.[15] Once ideal candidates are identified, the ablative energy should be delivered with a margin of at least 5 mm around the index lesion to ensure complete destruction of the target lesion. However, based on recent data, treatment that encompasses 1 cm margins within the prostate gland and spares vital structures is suggested to achieve optimal coverage of the index lesion.[16]

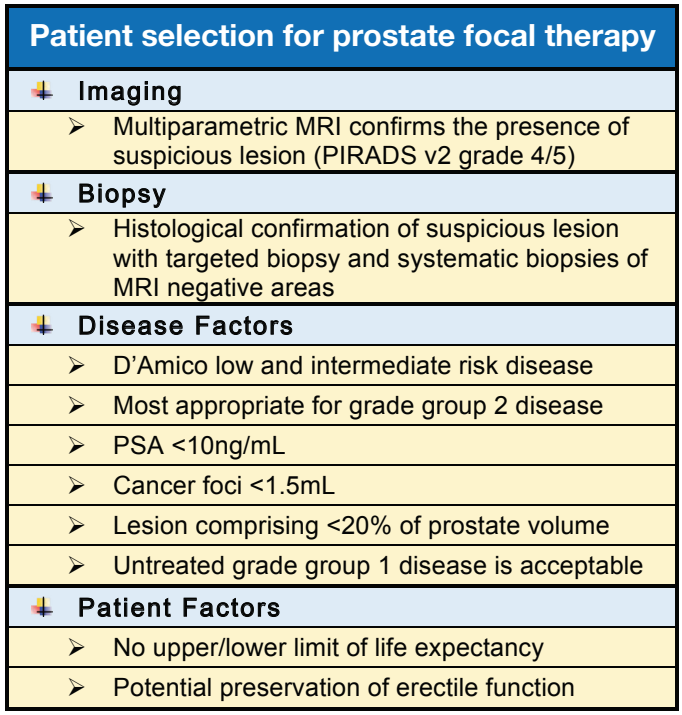

Figure. Selection criteria are derived from expert opinion level of evidence.[13] *PIRADS*, Prostate Imaging-Reporting and Data System.

The majority of published studies have used a wide range of inclusion criteria, complicating the definition of character-

ABBREVIATIONS: ED (erectile dysfunction), HIFU (high intensity focused ultrasound), IRE (irreversible electroporation), MRI (magnetic resonance imaging), PSA (prostate specific antigen), RFA (radio frequency ablation), VTP (vascular targeted photodynamic therapy)

istics of ideal candidates. Additionally the number of ablation technologies currently available and restrictions in insurance coverage due to the paucity of long-term oncologic outcomes are barriers to wide acceptance and use of focal therapy. **Multi-institutional collaborative efforts and provision of focal therapy under trial settings are essential to incorporating focal therapy as a routine management option for patients with localized prostate cancer.**

FOCAL THERAPY MODALITIES

Focal therapy modalities can be categorized based on whether tissue destruction occurs by a thermal or non-thermal reaction. Thermal ablative modalities include high intensity focused ultrasound, cryoablation, focal laser ablation and radio frequency ablation. Non-thermal ablative modalities include vascular targeted photodynamic therapy and irreversible electroporation. Presently thermal ablative modalities such as HIFU and cryotherapy are described more extensively than non-thermal modalities in published studies. HIFU has been used in Europe and Canada for more than a decade. In 2015 the U.S. Food and Drug Administration approved HIFU for general ablation of prostate tissue, although this approval is not specific to prostate cancer treatment. While non-thermal modalities have been studied less extensively than thermal modalities, they have demonstrated similarly promising outcomes. Currently there is no established comparative evidence for the various modalities of prostate focal therapy.

THERMAL ABLATIVE MODALITIES

High intensity focused ultrasound. **HIFU uses ultrasonic waves to deliver thermal energy to the target tissue. HIFU causes tissue destruction by coagulative necrosis from temperatures of 60C or higher and internal cavitation from negative pressure of the ultrasonic waves.[17, 18]**

The largest prospective study of focal HIFU included 625 consecutive patients with non-metastatic prostate cancer who were treated between 2006 and 2015.[19] The majority of patients (84%) had intermediate or high risk disease. The primary end point was failure-free survival, defined as freedom from radical or systemic therapy, metastases and cancer specific mortality. At 5-year follow-up (median 56 months) failure-free, metastasis-free, cancer specific and overall survival rates were 88%, 98%, 100% and 99%, respectively (95% CI 85–91). Additionally pad-free continence rates were 97% at 1 year and 98% at 3 years of follow-up. A strength of this study is the high percentage of intermediate/high risk cases. Limitations include non-standardized use of biopsy after treatment and the lack of robust quality of life outcomes.

In a prospective multi-institutional study Rischmann et al reported on 111 patients (68% with low risk and 32% with intermediate risk disease) who underwent HIFU hemiablation for unilateral localized prostate cancer.[20] Clinically significant cancer was absent in 95% of treated lobes and 93% of contralateral lobes. Radical treatment-free survival at 2 years was 89%. A total of 11 patients underwent salvage therapy (radical prostatectomy in 6, external beam radiation therapy in 3, HIFU in 2), which did not significantly increase morbidities in these patients. At 12-month follow-up continence and erectile function were preserved in 97% and 78% of patients, respectively. The primary limitation of the study is its inclusion of low risk cases (68%), which are now typically managed by active surveillance. Nonetheless, the study highlights an alternative for patients with low risk disease who are opposed to active surveillance and for whom the morbidities of radical treatment greatly outweigh the benefits.

Mistry et al reported their single center experience using image guided focal HIFU in 164 patients with localized prostate cancer.[21] Of the patients 20% had low risk, 71% had intermediate risk and 9% had high risk disease. After a median follow-up of 50 months the metastasis-free survival rate was 99.4% and cancer specific survival was 100%. Seven patients underwent additional rounds of HIFU, 5 underwent radical prostatectomy and 1 received radiation therapy. One patient underwent cryotherapy and HIFU for contralateral disease, and 1 patient required systemic hormonal therapy for metastatic progression. Pad-free continence rate was 100% at 3 months, and 82% of patients who had satisfactory preoperative erections maintained potency.

Cryotherapy. **Cryotherapy uses alternating cycles of tissue freezing and thawing to induce direct cytolysis through intracellular and extracellular ice crystal formation. Generally the use of double freeze-thaw cycles and rapid freezing up to –40C with a slow, passive thaw is recommended. A continuous urethral warmer is used to protect the urethra from tissue destruction.**

Bianco et al reported a prospective study of 348 patients who underwent MRI/ultrasound targeted cryoablation of localized prostate cancer between 2013 and 2017.[22] The pretreatment Gleason grade groups ranged from 1 to 4, with 37% of patients having Gleason grade group 1, 36% Gleason grade group 2, 18% Gleason grade group 3 and 9% Gleason grade group 4 or higher disease. At a mean follow-up of 2 years, of 166 patients at risk 50 (14%) required repeat focal cryoablation and 15 (4%) underwent conversion to surgery or radiation therapy. Median time to recover baseline erectile function was 33 days and ejaculation was preserved in 85% of eligible patients. The strength of this study is the inclusion of patients with grade group 2 or higher disease (63% of the cohort), while the lack of posttreatment biopsy data at the time of analysis is a major limitation.

In 2019 Shah et al reported a prospective, registry based case series of 122 consecutive patients undergoing focal cryotherapy at 5 centers in the United Kingdom.[23] Based on the National Comprehensive Cancer Network® criteria, 71% of patients had intermediate risk and 29% had high risk disease. Overall failure-free survival at 3 years was 90.5% (95% CI 84.2–97.3). When stratified by risk group, the failure-free survival rates were 93.3% (95% CI 86.8–100) for intermediate risk cases and 84.7% (95% CI 71.4–100) for high risk cases. For cause biopsies, which were performed in 29 patients with rising PSA and suspicious MRI, revealed evidence of clinically significant cancer in 20 (16%) and insignificant cancer in 1 (4%). Of these 21 patients 9 had in field disease only, 9 had out of field disease only and 3 had both. Of patients in whom the treatment failed 5 underwent radical prostatectomy, 4 received radiation therapy and 4 underwent systemic therapy. During follow-up 4 patients died of a non-prostate cancer related cause. Pad-free continence rate was 100% and ED was observed in 16.1% of patients.

Barret et al published a single center series of 107 patients (76.6% with grade group 1 and 23.4% with grade group 2 disease) who underwent focal cryoablation of unilateral localized prostate cancer diagnosed by transperineal mapping biop-

sy.[24] After a mean follow-up of 64 months cancer was detected in 34.6% and 28% of cases within and outside the treatment region, respectively. On multivariable analysis preoperative Gleason 7 disease was associated with a higher rate of treatment failure (HR 2.62, 95% CI 1.05–6.55, p=0.04). The large proportion of patients with grade group 1 disease (76.6%) and relatively high treatment failure rate are limitations of the study. Also, the grade of cancer detected following posttreatment biopsy was not reported.

Focal laser ablation. **Focal laser ablation uses laser fibers to deliver heat to the target region, thereby causing tissue destruction. Although many phase I studies have demonstrated the safety of focal laser ablation, high quality evidence regarding the efficacy and functional outcomes on long-term follow-up is limited.**

Feller et al evaluated the oncologic and functional outcomes of 98 patients with 138 cancer foci treated with focal laser ablation using 1.5 T MRI for image acquisition and real-time thermometry.[25] At 6 months 23% of treatment site biopsies showed evidence of residual or recurrent cancer. No serious adverse events were observed, and no statistically significant changes in International Prostate Symptom Score or Sexual Health Inventory for Men score were identified. However, pretreatment disease characteristics or grade of cancer found in the treatment site were not reported, making critical appraisal of the data challenging.

Elkhoury et al summarized the findings of 2 trials investigating focal laser ablation of prostate cancer in a MRI gantry (in bore) and in a clinic setting (out of bore).[26] A total of 18 men with grade group 2 or lower prostate cancer diagnosed by MRI/ultrasound fusion biopsy underwent focal laser ablation in clinic (in bore in 8 and out of bore in 10). At follow-up biopsy, which was performed at a median of 12 months after the procedure, 5 patients had no evidence of disease, 4 had improved disease (lower Gleason score or tumor volume) and 9 showed evidence of treatment failure (unchanged or higher Gleason score). Eight patients (44%) received secondary treatment after focal laser ablation, of whom 4 underwent radical prostatectomy, 3 received radiation therapy and 1 underwent cryotherapy.

Lindner et al reported a phase I study of 38 men with organ confined prostate cancer undergoing in bore, MRI guided focal laser ablation.[27] Of the patients 64% had Gleason 6 and 36% had Gleason 3+4 disease. At 4 months 26% of patients had prostate cancer in the contralateral lobe, and at a median follow-up of 538 days 26% had evidence of residual or recurrent cancer in the ablated region. Transient stress urinary incontinence developed in 1 patient, which resolved within 8 weeks, and 96% of patients maintained potency following the procedure.

Radio frequency ablation. **RFA uses radio frequency waves to deliver thermal energy to the target tissue. This causes ionic agitation and molecular friction, resulting in protein denaturation and cell membrane disintegration.**

Orczyk et al reported a prospective experience in which 20 patients were treated with RFA.[28] Patients had lesions that were visible on MRI and concordant with transperineal biopsy pathology and no clinically significant disease elsewhere. Six months after RFA no significant residual or new cancer was found in 80% of patients by MRI targeted transperineal biopsy of the ablation zone and any new suspicious areas. Urinary, erectile and bowel function remained stable at 12-month follow-up, although 1 patient who required urethral dilation for stricture reported urinary incontinence.

Taneja et al reported the results of a prospective development study investigating focal RFA in 21 patients with up to 2 MRI visible lesions that were pathologically confirmed on systematic and MRI/ultrasound fusion targeted biopsy.[29] Residual prostate cancer was found in the ablation region in 43% of patients. Interestingly MRI findings were not a significant predictor of residual cancer, highlighting the importance of follow-up biopsy rather than relying solely on imaging. Urinary and sexual function and health related quality of life were maintained following the procedure.

NON-THERMAL ABLATIVE MODALITIES

Vascular targeted photodynamic therapy. **VTP uses a photosensitizing agent that produces reactive oxygen species on activation by light of a specific wavelength, which subsequently damage the target tissue.**

VTP is the first focal therapy modality to show efficacy in a randomized phase III trial in patients with low risk prostate cancer.[30] The PCM301 trial, which randomized 207 men to hemigland ablation with VTP and 206 men to active surveillance, revealed a lower rate of conversion to radical treatment after VTP compared to active surveillance at 2 years (7% vs 32%), 3 years (15% vs 44%) and 4 years (24% vs 53%, HR 0.31, 95% CI 0.21–0.46, p <0.001). When comparing patients with objective evidence of disease progression only, the rate of conversion to radical treatment was lower in those undergoing VTP, indicating that VTP is effective in controlling cancer and not merely reducing anxiety with ongoing surveillance. Two-year biopsies were negative in 50% of the VTP cohort and 14% of the active surveillance cohort (risk difference 36%, 95% CI 28–44, p <0.001). Metastasis-free (99% vs 99%), cancer specific (100% vs 100%) and overall survival rates (98% vs 99%) at 4 years were similar between the 2 cohorts and were consistent with contemporary data from other studies. The trial did not use any additional staging techniques such as confirmatory, saturation or targeted biopsy or multiparametric MRI. However, by performing hemiablation rather than ablation of the index lesion, the treatment zone was widened. Although the study included patients with low risk prostate cancer with grade group 1 disease, there appeared to be a benefit from reducing the rate of conversion to radical therapy, thereby minimizing treatment related morbidities in patients with prostate cancer.

Irreversible electroporation. **IRE uses short pulses of electric current that travel between probes placed around the target lesion, causing irreversible pores in the cell membrane and resulting in cell death.**

van den Bos et al reported on 63 patients who underwent focal IRE for high volume grade group 1 disease or any grade group 2 or 3 disease.[31] A total of 45 patients underwent a follow-up biopsy (transperineal template guided mapping, saturation transrectal ultrasound or targeted biopsy) at 6 to 12 months. Of the patients 34 had no evidence of significant cancer, 7 had significant in field disease and 4 had significant out of field disease, demonstrating in field and whole gland oncologic control of 84% and 76%, respectively. There was no high grade adverse event, and quality of life questionnaires indicated no significant change in physical, mental, bowel or urinary domains. A mild decrease in the sexual domain was identified at 6 months.

Murray et al reported on 25 patients with localized prostate cancer (72% with low risk and 28% with intermediate

risk disease) who underwent focal IRE and observed a 72% cancer-free rate at 6 months.[32] In a follow-up prospective phase II trial from the same institution Lee et al reported on 19 patients (89% with grade group 2 and 11% with grade group 3 disease) who underwent focal IRE.[33] At 12 months 74% of patients had no evidence of significant cancer in the prostate and 89% had no evidence of significant cancer in the ablated zone. Four patients eventually required radical prostatectomy due to disease progression, representing a 79% radical treatment-free survival at 12 months. No high grade adverse events were reported, and urinary, erectile and bowel function was well maintained, although there was a decline in ejaculatory function at 12 months.

PATIENT FOLLOW-UP

While there is no accepted follow-up recommendation after prostate focal therapy, various consensus statements by expert panels suggest that patients be followed for a minimum of 5 years.[13] Parameters that should be evaluated are histology (prostate biopsies), PSA, prostate imaging and functional outcome measures, including erectile function, urinary function and quality of life.

Prostate biopsy of the treated region at 1 year after therapy is generally recommended, although some experts advocate additional biopsy at 3 or 6 months to assess for incomplete tissue destruction due to inaccurate targeting or inadequate tissue response. The untreated region of the prostate should also be biopsied for ongoing surveillance.

PSA should be measured every 3 months in the first year after treatment and then every 6 months. While PSA doubling time appears to be an appropriate parameter to suggest treatment failure, there is no accepted definition of biochemical failure.

Multiparametric MRI of prostate can be obtained at 6 months following treatment and repeated every 6 to 12 months or if there is suspicion of disease recurrence or progression. Any suspicious lesion found on follow-up imaging should be investigated with targeted biopsy of the area.

Currently there is no accepted definition of disease recurrence following focal therapy for prostate cancer. However,

Table. Oncologic and functional outcomes after focal ablative therapy for localized prostate cancer

References	Treatment Modality	No. Pts	% Clinically Significant Disease	% Neg Follow-up Biopsy*	% Radical Treatment-Free Survival*	Erectile Function*	Urinary Function*
Guillaumier et al[19]	HIFU	625	84	75	88	15% New ED	2% New incontinence
Rischmann et al[20]	HIFU	111	32	93	89	22% New ED	3% New incontinence
Mistry et al[21]	HIFU	164	80	Not available	96	18% New ED	0% New incontinence
Bianco et al[22]	Cryotherapy	301	63	Not available	96	0% New ED	Improved flow rates
Shah et al[23]	Cryotherapy	122	100	Not available	91	16% New ED	0% New incontinence
Barret et al[24]	Cryotherapy	107	23	37	Not available	Not available	Not available
Feller et al[25]	Focal laser ablation	98	Not available	69	Not available	0% New ED	No change
Elkhoury et al[26]	Focal laser ablation	18	56	28	61	0% New ED	11% Nocturia
Lindner et al[27]	Focal laser ablation	38	36	47	Not available	4% New ED	0% New incontinence
Orczyk et al[28]	RFA	20	Not available	80	90	0% New ED	5% New incontinence
Taneja et al[29]	RFA	21	Not available	57	Not available	0% New ED	No change
Gill et al[30]	VTP	207	0	50	76	1% New ED	Not available
van den Bos et al[31]	IRE	63	86	76	89	Mild decrease in scores†	No change
Murray et al[32]	IRE	25	28	72	84	0% New ED	No change
Lee et al[33]	IRE	19	100	74	79	Mild decrease in ejaculatory function‡	No change

*Outcomes after varying lengths of follow-up.
†Per EPIC (Expanded Prostate Cancer Index Composite).
‡Per MSHQ (Male Sexual Health Questionnaire).

definitions advocated by various experts in the field include 1) any cancer, including grade group 1, found in the treated region on follow-up biopsy and 2) any grade group 2 or higher cancer found in the treated region on follow-up biopsy. Defining cancer recurrence is challenging as patient selection criteria for focal therapy differ from center to center. For example some experts have advocated targeting lesions with any cancer, while others prefer to target only lesions that contain clinically significant prostate cancer. In the current state of clinical heterogeneity we believe that recurrence is defined based on individual goals of treatment (ie ablation of all prostate cancer vs ablation of clinically significant prostate cancer).

CONCLUSION

Focal ablative therapy for prostate cancer offers promising outcomes data with acceptable oncologic control and reduced treatment related morbidities in carefully selected patients (see table). **Identification of ideal candidates for focal therapy remains a complex clinical challenge that incorporates numerous diagnostic and staging considerations.** These include selecting imaging (eg multiparametric MRI) and biopsy modalities (eg systematic, targeted, saturation, transrectal, transperineal), and defining objective patient and disease related criteria for ideal candidacy. In addition, there is no consensus on optimal follow-up of patients undergoing focal therapy (eg imaging, biopsy, PSA). Considering the low cancer specific mortality of men who may be considered for focal therapy, radical treatment-free survival may be a meaningful outcome for trials investigating focal ablative modalities. **In summary, patients should be counseled that there is a paucity of long-term comparative data on oncologic and functional outcomes. The possibility of repeat focal therapy or requirement for subsequent radical treatment should be discussed, along with associated morbidities. Currently focal therapy for prostate cancer is a novel treatment modality that is emerging as a viable option for carefully selected men with favorable intermediate risk prostate cancer.** Clinical trials investigating the safety and efficacy of various focal ablative modalities are ongoing (see Appendix).

DID YOU KNOW?

- Focal ablative therapy of localized prostate cancer aims to reduce treatment related adverse outcomes and health care burden associated with radical treatment modalities such as surgery or radiation.
- Focal ablative therapy modalities can be categorized based on whether tissue destruction occurs by a thermal or non-thermal reaction. Thermal ablative modalities include high intensity focused ultrasound, cryoablation, focal laser ablation and radio frequency ablation. Non-thermal ablative modalities include vascular targeted photodynamic therapy and irreversible electroporation.
- The identification of ideal candidates for prostate focal therapy is a complex clinical challenge that incorporates numerous diagnostic and staging considerations.
- Patients should be counseled that there is a paucity of long-term data on oncologic and functional outcomes. The possibility of repeat focal therapy or subsequent radical treatment should be discussed, along with associated morbidities.
- Currently focal therapy for prostate cancer is a novel treatment modality emerging as a viable treatment option for carefully selected men with favorable intermediate risk prostate cancer.

Appendix. Clinical trials investigating the efficacy and role of prostate cancer focal therapy

Title	Status	Interventions	Locations
Continued Access of Focal MR-Guided Focused Ultrasound for Localized Intermediate Risk Prostate Lesions (NCT03998657) PI: Behfar Ehdaie	Recruiting	MR-guided HIFU Exablate Prostate Treatment	Memorial Sloan-Kettering Cancer Center, New York, New York Stanford University School of Medicine, Stanford, California Prostate Center, Delray Beach, Florida Brigham and Women's Hospital, Boston, Massachusetts Mayo Clinic, Rochester, Minnesota
MRI Guided Focal Laser Ablation of Prostate Cancer (NCT03650595) PI: Sangeet Ghai	Recruiting	The TRANBERGCLS Thermal Therapy	Toronto, Ontario, Canada
HIFU for Focal Ablation of Prostate Tissue: An Observational Study (NCT03620786) PI: Leonard Marks	Enrolling by invitation	Sonablate HIFU device	University of California, Los Angeles, Los Angeles, California

***Appendix**, continued*

***Appendix**, continued*

Outcomes of Focal Therapies for Prostate Cancer (NCT03492424) PI: Jim Hu	Recruiting	Cryotherapy	Weill Cornell Medicine, New York, New York
Study of the Efficacy, Safety, and Quality of Life after Tookad Soluble (VTP) for Intermediate Risk Prostate Cancer (NCT03315754) PI: Jonathan Coleman	Accrued	Tookad Soluble (VTP)	Memorial Sloan-Kettering Cancer Center, New York, New York
Fusion Guided Focal Laser Ablation of Prostate Cancer (NCT02759744) PI: Bradford Wood	Enrolling by invitation	Ultrasound image-guided ablation	National Institutes of Health Clinical Center, Bethesda, Maryland
Focal Laser Ablation of Prostate Cancer Tumors (NCT02600156) PI: David Woodrum	Recruiting	Focal laser ablation of the prostate	Mayo Clinic, Rochester, Minnesota
Phase II Laser Focal Therapy of Prostate Cancer (NCT02243033) PI: John Feller	Recruiting	MR-guided laser focal therapy	Desert Medical Imaging, Indian Wells, California
Focal MR-Guided Focused Ultrasound Treatment of Localized Intermediate Risk Prostate Lesions (NCT01657942) PI: Behfar Ehdaie	Accrued	MR-guided HIFU Exablate Prostate Treatment	Memorial Sloan-Kettering Cancer Center, New York, New York Stanford University School of Medicine, Stanford, California Prostate Center, Delray Beach, Florida Brigham and Women's Hospital, Boston, Massachusetts Mayo Clinic, Rochester, Minnesota

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Study Questions Volume 39 Lesson 16

1. The primary role of focal ablative therapy in the treatment of patients with prostate cancer is to
   a. reduce treatment related adverse outcomes and health care burden associated with radical treatment modalities such as surgery or radiation
   b. treat patients with low risk prostate cancer in place of active surveillance for men who are not amenable to surveillance
   c. treat prostate cancer in place of radical treatment for men who have significant medical comorbidities
   d. be offered as a standard of care treatment option for select men with prostate cancer

2. High intensity focused ultrasound uses
   a. alternating cycles of tissue freezing and thawing to induce cellular lysis
   b. radio frequency waves to deliver thermal energy causing cellular membrane disintegration
   c. ultrasonic waves to deliver thermal energy to the target tissue, leading to tissue destruction
   d. short pulses of electric current that travel between probes placed around the target lesion, causing irreversible pores in the cell membrane

3. A 70-year-old man with favorable intermediate risk prostate cancer elects cryotherapy. MRI reveals a 1.2 cm lesion on the posteromedial aspect of the right hemigland. Post-cryotherapy, he develops a urethral fistula. This complication could have been prevented intraoperatively by the use of
   a. a larger treatment zone
   b. continuous urethral warmer
   c. 3, rather than 2, freeze-thaw cycles
   d. high intensity focused ultrasound instead of cryotherapy

4. A non-thermal focal therapy modality is
   a. cryotherapy
   b. radio frequency ablation
   c. high intensity focused ultrasound
   d. vascular targeted photodynamic therapy

5. In PCM301, the trial that compared the efficacy of vascular targeted photodynamic therapy to active surveillance, patients treated with VTP, compared to those treated with active surveillance, had
   a. improved metastasis-free survival
   b. improved cancer specific survival
   c. improved overall survival
   d. a lower rate of conversion to radical treatment

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