Focal Treatments for Prostate Cancer

Description

Prostate cancer is the second most common cancer diagnosis men receive in the United States, and the behavior of localized prostate cancer can prove difficult to predict on a case-by-case basis. Most men with the cancer undergo whole-gland treatments, which can often lead to substantial adverse events. To reduce tumor burden and minimize morbidity associated with radical treatment, investigators have developed a therapy known as focal treatment. Focal treatment seeks to ablate either an “index” lesion (defined as the largest cancerous lesion with the highest grade tumor), or alternatively, to ablate non-index lesions and other areas where cancer has been known to occur. Addressed in this review are several ablative methods used to remove cancerous lesions in localized prostate cancer (e.g., focal laser ablation, high-intensity focused ultrasound, cryoablation, radiofrequency ablation, photodynamic therapy). All methods, except focal laser ablation, use ultrasound guidance to focus on the tumor (focal laser ablation uses magnetic resonance imaging to guide the probe).

Five ablative methods for which clinical evidence is available are considered herein: focal laser ablation; high-intensity focused ultrasound; cryoablation; radiofrequency ablation; and photodynamic therapy. Each method requires placement of a needle probe into a tumor volume followed by delivery of some type of energy that destroys the tissue in a controlled manner. All methods except focal laser ablation currently rely on ultrasound guidance to the tumor focus of interest; focal laser ablation uses MRI to guide the probe. This evidence review does not cover focal brachytherapy (see evidence review 8.01.14).

Focal Laser Ablation

Focal laser ablation refers to the destruction of tissue using a focused beam of electromagnetic radiation emitted from a laser fiber introduced transperineal or transrectal into the cancer focus. The tissue is destroyed through thermal conversion of the focused electromagnetic energy into heat, causing coagulative necrosis. Other terms for focal laser ablation include photothermal therapy, laser interstitial therapy, and laser interstitial photocoagulation.
**High-Intensity Focused Ultrasound**

High-intensity focused ultrasound focuses high-energy ultrasound waves on a single location, which increases the local tissue temperature to over 80°C. This causes a discrete locus of coagulative necrosis of approximately 3×3×10 mm. The surgeon uses a transrectal probe to plan, perform, and monitor treatment in a real-time sequence to ablate the entire gland or small discrete lesions.

**Cryoablation**

Cryoablation induces cell death through direct cellular toxicity from disruption of the cell membrane caused by ice-ball crystals and vascular compromise from thrombosis and ischemia secondary to freezing below -30°C. Using a TPM template, cryoablation is performed by transperineal insertion under transrectal ultrasound guidance of a varying number of cryoprobe needles into the tumor.

**Radiofrequency Ablation**

Radiofrequency ablation uses energy produced by a 50-watt generator at a frequency of 460 kHz. Energy is transmitted to the tumor focus through 15 needle electrodes inserted transperineally under ultrasound guidance. Radiofrequency ablation produces an increase in tissue temperature causing coagulative necrosis.

**Photodynamic Therapy**

Photodynamic therapy uses an intravenous photosensitizing agent, which distributes through prostate tissue, followed by light delivered transperineally by inserted needles. The light induces a photochemical reaction that produces reactive oxygen species that are highly toxic and causes functional and structural tissue damage (i.e., cell death). A major concern with photodynamic therapy is that real-time monitoring of tissue effects is not possible, and the variable optical properties of prostate tissue complicate the assessment of necrosis and treatment progress.

**OBJECTIVE**

The objective of this evidence review is to determine whether the use of focal therapy administered with different ablative techniques improves the net health outcome in individuals with primary localized prostate cancer.

**POLICY STATEMENT**

Use of any focal therapy modality to treat patients with localized prostate cancer is investigational.

**BENEFIT APPLICATION**

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

**FDA REGULATORY STATUS**

**Focal Laser Ablation**

In 2010, the Visualase® Thermal Therapy System (Medtronic) and, in 2015, the TRANBERG CLS|Laser fiber (Clinical Laserthermia Systems) were cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process to necrotize or coagulate soft tissue through interstitial irradiation or thermal therapy under MRI guidance for multiple indications including urology, at wavelengths from 800 to 1064 nm. FDA product code: LLZ, GEX, FRN.

**High-Intensity Focused Ultrasound**

In October 2015, the Sonablate® 450 (SonaCare Medical) was cleared for marketing through the 510(k) process after approval of a de novo request and classification as class II under the generic name "high intensity ultrasound system for prostate tissue ablation". This device was the first of its kind to be
approved in the United States. In November 2015, Ablatherm®-HIFU (EDAP TMS) was cleared for marketing by FDA through the 510(k) process.

**Cryoablation**
Some cryoablation devices cleared for marketing by FDA through the 510(k) process for cryoablation of the prostate include: Visual-ICE® (Galil Medical), Ice Rod CX, CryoCare® (Galil Medical), IceSphere (Galil Medical), and Cryocare® Systems (Endocare®; HealthTronics). FDA product code: GEH.

**Radiofrequency Ablation**
Radiofrequency ablation devices have been cleared for marketing by FDA through the 510(k) process for general use for soft tissue cutting and coagulation and ablation by thermal coagulation. Under this general indication, radiofrequency ablation may be used to ablate tumors. FDA product code: GEI.

**Photodynamic Therapy**
FDA has granted approval to several photosensitizing drugs and light applicators. porfimer sodium (Photofrin®; Axcan Pharma) and psoralen are photosensitizer ultraviolet lamps used to treat cancer; they were cleared for marketing by FDA through the 510(k) process. FDA product code: FTC.

**RATIONALE**

**Summary of Evidence**
For individuals who have primary localized prostate cancer who receive focal therapy using laser ablation, high-intensity focused ultrasound, cryoablation, radiofrequency ablation, or photodynamic therapy, the evidence includes a high-quality systematic review, studies from a registry cohort, and numerous observational studies. Relevant outcomes are overall survival, disease-specific survival, symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. The evidence is highly heterogeneous and inconsistently reports clinical outcomes. No prospective, comparative evidence was found for focal ablation techniques vs current standard treatment of localized prostate cancer, including radical prostatectomy, external-beam radiotherapy, or active surveillance. Methods have not been standardized to determine which and how many identified cancerous lesions should be treated for best outcomes. No evidence supports which, if any, of the focal techniques, leads to better functional outcomes. Although high disease-specific survival rates have been reported, the short follow-up periods and small sample sizes preclude conclusions on the effect of any of these techniques on overall survival rates. The adverse event rates associated with focal therapies appear to be superior to those associated with radical treatments (e.g., radical prostatectomy, external-beam radiotherapy); however, the evidence is limited in its quality, reporting, and scope. The evidence is insufficient to determine the effects of the technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

**Practice Guidelines and Position Statements**

**National Comprehensive Cancer Network**
The National Comprehensive Cancer Network guidelines for prostate cancer (v.3.2018) recommend cryosurgery or high-intensity focused ultrasound (HIFU) as options for radiotherapy recurrence for nonmetastatic disease; cryosurgery is not recommended for the initial treatment of localized prostate cancer.58

**National Institute for Health and Care Excellence**
The National Institute for Health and Care Excellence (NICE; 2012) issued guidance on the use of cryoablation for localized prostate cancer.55 NICE concluded that current evidence on focal therapy using...
cryoablation for localized prostate cancer raised no major safety concerns. However, evidence on efficacy was limited in quantity, with concern that prostate cancer is commonly multifocal.

NICE (2014) issued guidance on the diagnosis and management of prostate cancer. The recommendations stated that neither cryotherapy or HIFU should be offered to men with localized prostate cancer or locally advanced prostate cancer outside of controlled trials comparing their use with established interventions.39

American Urological Association et al
The American Urological Association, along with the American Society for Radiation Oncology and the Society for Urologic Oncology (2017) updated their joint guidelines on the management of clinically localized prostate cancer.58 The guidelines included the following recommendation on focal treatments:

“Clinicians should inform low-risk prostate cancer patients who are considering focal therapy or high intensity focused ultrasound (HIFU) that these interventions are not standard care options because comparative outcome evidence is lacking. (Expert Opinion)”

“Clinicians should inform intermediate-risk prostate cancer patients who are considering focal therapy or HIFU that these interventions are not standard care options because comparative outcome evidence is lacking. (Expert Opinion)”

“Cryosurgery, focal therapy and HIFU treatments are not recommended for men with high-risk localized prostate cancer outside of a clinical trial. (Expert Opinion)”

National Cancer Institute
The National Cancer Institute (NCI) updated its information on prostate cancer treatments in 2018.60 NCI indicated that cryoablation and HIFU were new treatment options currently being studied in national trials. NCI offered no recommendation for or against these treatments.

U.S. Preventive Services Task Force Recommendations
The U.S. Preventive Services Task Force published recommendations for prostate cancer screening.61 However, there are no recommendations for focal treatment of prostate cancer.

Medicare National Coverage
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


25. Passoni NM, Polascik TJ. How to select the right patients for focal therapy of prostate cancer? *Curr Opin Urol.* May 2014;24(3):203-208. PMID 24625428


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FEP X8.01.61 Focal Treatments for Prostate Cancer


**POLICY HISTORY**

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<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tr>
<td>December 2016</td>
<td>Update Policy</td>
<td>Policy updated with literature review through July 26, 2016; references 55-57, and 59-64 were added. Policy statement unchanged.</td>
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<tr>
<td>December 2018</td>
<td>Update Policy</td>
<td>Policy updated with literature review through July 9, 2018; reference 57 added; reference 61 updated; several references removed. Policy statement unchanged.</td>
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