MASSACHUSETTS

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Medical Policy

Focal Treatments for Prostate Cancer

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Policy Number: 733

BCBSA Reference Number: 8.01.61
NCD/LCD: Local Coverage Determination (LCD): Salvage High-intensity Focused Ultrasound (HIFU) Treatment in Prostate Cancer (PCa) (L38262)

Related Policies

- Cryosurgical Ablation of Miscellaneous Solid Tumors Other Than Liver, Prostate, or Dermatologic Tumors, #260
- Magnetic Resonance Imaging–Guided Focused Ultrasound #243
- Saturation Biopsy for Diagnosis, Staging, and Management of Prostate Cancer, #307
- Brachytherapy for Clinically Localized Prostate Cancer Using Permanently Implanted Seeds, #175

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

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

Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Medical necessity criteria and coding guidance for **Medicare Advantage members living in Massachusetts** can be found through the link(s) below.

Local Coverage Determinations (LCDs) for National Government Services, Inc.

Local Coverage Determination (LCD): Salvage High-intensity Focused Ultrasound (HIFU) Treatment in Prostate Cancer (PCa) (L38262)

Note: To review the specific LCD, please remember to click “accept” on the CMS licensing agreement at the bottom of the CMS webpage.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is **not** a covered service.
Commercial PPO and Indemnity	This is **not** a covered service.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The following HCPCS code is considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

HCPCS Codes

HCPCS codes:	Code Description
C9747	Ablation of prostate, transrectal, high intensity focused ultrasound (HIFU), including imaging guidance

Description

Prostate Cancer

Prostate cancer is the second most common cancer diagnosed among men in the U. S. According to the National Cancer Institute, nearly 240000 new cases were diagnosed in the U. S. in 2013 and would be associated with around 30000 deaths. Autopsy studies in the pre-prostate-specific antigen (PSA) screening era identified incidental cancerous foci in 30% of men 50 years of age, with incidence reaching 75% at age 80 years.[1,] However, the National Cancer Institute Surveillance Epidemiology and End Results Program data have shown age-adjusted cancer-specific mortality rates for men with prostate cancer declined from 40 per 100000 in 1992 to 22 per 100000 in 2010. This decline has been attributed to a combination of earlier detection via PSA screening and improved therapies.

Diagnosis

From a clinical standpoint, different types of localized prostate cancers may appear similar during initial diagnosis.[2,] However, prostate cancer often exhibits varying degrees of risk progression that may not be captured by accepted clinical risk categories (eg, D'Amico criteria) or prognostic tools based on clinical findings (eg, PSA titers, Gleason grade, or tumor stage).[3,4,5,6,7,] In studies of conservative management, the risk of localized disease progression based on prostate cancer-specific survival rates at 10 years may range from 15%[8,9,] to 20%[10,] to perhaps 27% at 20-year follow-up.[11,] Among elderly men (³70 years) with this type of low-risk disease, comorbidities typically supervene as a cause of death; these men will die from the comorbidities with prostate cancer present rather than from cancer itself. Other very similar-appearing low-risk tumors may progress unexpectedly and rapidly, quickly disseminating and becoming incurable.

Treatments

The divergent behavior of localized prostate cancers creates uncertainty whether to treat immediately.[12,13,] A patient may choose definitive treatment upfront.[14,] Surgery (radical prostatectomy) or external-beam radiotherapy are frequently used to treat patients with localized prostate cancer.[13,15,] Complications most commonly reported with radical prostatectomy or external-beam radiotherapy and with the greatest variability are incontinence (0%-73%) and other genitourinary toxicities (irritative and obstructive symptoms); hematuria (typically ≤5%); gastrointestinal and bowel toxicity, including nausea and loose stools (25%-50%); proctopathy, including rectal pain and bleeding (10%-39%); and erectile dysfunction, including impotence (50%-90%).[15,]

American Urological Association guidelines have suggested patients with low- and intermediate-risk disease have the option of entering an "active surveillance" protocol, which takes into account patient age, patient preferences, and health conditions related to urinary, sexual, and bowel function.[16,] With this approach, patients forgo immediate therapy but continue regular monitoring until signs or symptoms of disease progression are evident-at which point curative treatment is instituted.[17,18,]

Focal Treatments for Localized Prostate Cancer

Given significant uncertainty in predicting the behavior of individual localized prostate cancers, and the substantial adverse events associated with definitive treatments, investigators have sought a therapeutic middle ground. The latter seeks to minimize morbidity associated with radical treatment in those who may not actually require surgery while reducing tumor burden to an extent that reduces the chances for rapid progression to incurability. This approach is termed *focal treatment*, in that it seeks to remove-using any of several ablative methods described next-cancerous lesions at high-risk of progression, leaving behind uninvolved glandular parenchyma. The overall goal of any focal treatment is to minimize the risk of early tumor progression and preserve erectile, urinary, and rectal functions by reducing damage to the neurovascular bundles, external sphincter, bladder neck, and rectum.[19,20,21,22,23,] Although focal treatments are offered as an alternative middle approach to manage localized prostate cancer, several key issues must be considered in choosing it. They include patient selection, lesion selection, therapy monitoring, and modalities used to ablate lesions.

Patient Selection

A proportion of men with localized prostate cancer have been reported to have (or develop) serious misgivings and psychosocial problems in accepting active surveillance, sometimes leading to inappropriately discontinuing it.[24,] Thus, the appropriate patient selection is imperative for physicians who must decide whether to recommend active surveillance or focal treatment for patients who refuse radical therapy or for whom it is not recommended due to the risk/benefit balance.[25,]

Lesion Selection

Proper lesion selection is a second key consideration in choosing a focal treatment for localized prostate cancer. Although prostate cancer is a multifocal disease, clinical evidence has shown that between 10% and 40% of men who undergo radical prostatectomy for a presumed multifocal disease actually have a unilaterally confined discrete lesion, which, when removed, would "cure" the patient.[26,27,28,] This view presumably has driven the use of regionally targeted focal treatment variants, such as hemiablation of half the gland containing the tumor, or subtotal prostate ablation via the "hockey stick" method.[29,] While these approaches can be curative, the more extensive the treatment, the more likely the functional adverse outcomes would approach those of radical treatments.

The concept that clinically indolent lesions comprise most of the tumor burden in organ-confined prostate cancer led to the development of a lesion-targeted strategy, which is referred to as "focal therapy" in this evidence review.[30,] This involves treating only the largest and highest grade cancerous focus (referred to as the "index lesion"), which has been shown in pathologic studies to determine the clinical progression of the disease.[31,32,] This concept is supported by molecular genetics evidence that suggests a single index tumor focus is usually responsible for disease progression and metastasis.[33,34,] The index lesion approach leaves in place small foci less than 0.5 cm^3 in volume, with a Gleason score less than 7, that are

considered unlikely to progress over a 10- to 20-year period.[35,36,37,] This also leaves available subsequent definitive therapies as needed should disease progress.

Identification of prostate cancer lesions (disease localization) particularly the index lesion, is critical to the oncologic success of focal therapy; equally important to success is the ability to guide focal ablation energy to the tumor and assess treatment effectiveness. At present, no single modality reliably meets the requirements for all 3 activities (disease localization, focal ablation energy to the tumor, assessment of treatment effectiveness).[25,30,] Systematic transrectal ultrasound-guided biopsy alone has been investigated; however, it has been considered insufficient for patient selection or disease localization for focal therapy.[38,39,40,41,42,] See policy #307 on saturation biopsy for prostate cancer for additional information.

Multiparametric magnetic resonance imaging (mpMRI), typically including T1-, T2-, diffusion-weighted imaging, and dynamic contrast-enhanced imaging, has been recognized as a promising modality to risk-stratify prostate cancer and select patients and lesions for focal therapy.[24,30,38,] Evidence has shown mpMRI can detect high-grade, large prostate cancer foci with performance similar to transperineal prostate mapping using a brachytherapy template.[43,] For example, for the primary endpoint definition (lesion, ≥4 mm; Gleason score, ≥3+4), with transperineal prostate mapping as the reference standard, sensitivity, negative predictive value, and negative likelihood ratios with mpMRI were 58% to 73%, 84% to 89%, and 0.3 to 0.5, respectively. Specificity, positive predictive value, and positive likelihood ratios were 71% to 84%, 49% to 63%, and 2.0 to 3.44, respectively. The negative predictive value of mpMRI appears sufficient to rule out clinically significant prostate cancer and may have clinical use in this setting. However, although mpMRI technology has the capability to detect and risk-stratify prostate cancer, several issues constrain its widespread use for these purposes (eg, mpMRI requires highly specialized MRI-compatible equipment; biopsy within the MRI scanner is challenging; interpretation of prostate MRI images requires experienced uroradiologists) and it is still necessary to histologically confirm suspicious lesions using transperineal prostate mapping.[44,]

Therapy Monitoring

Controversy exists about the proper endpoints for focal therapy of prostate cancer. The primary endpoint of focal ablation of clinically significant disease with negative biopsies evaluated at 12 months posttreatment is generally accepted according to a European consensus report.[38,] The clinical validity of an MRI to analyze the presence of residual or recurrent cancer compared with histologic findings is offered as a secondary endpoint. However, MRI findings alone are not considered sufficient in a follow-up.[38,] Finally, although investigators have indicated PSA levels should be monitored, PSA levels are not considered valid endpoints because the utility of PSA kinetics in tissue preservation treatments has not been established.[35,]

Modalities Used to Ablate Lesions

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.[19,20,22,23,29,30,33,35,38,45,46,] 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 policy #175).

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 the 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.[47,]

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 transperineal prostatemapping template, cryoablation is performed by transperineal insertion under transrectal ultrasound guidance of a varying number of cryoprobe needles into the tumor.

Radiofrequency Ablation

RFA uses the 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. RFA 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 (ie, 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.

Summary

Description

Prostate cancer is the second most common cancer diagnosis men receive in the U. S., and the behavior of localized prostate cancer can prove difficult to predict on a case-by-case basis. Most men with prostate 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 nonindex 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 (eg, 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).

Description

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 (eg, 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.

Policy History

Date	Action
11/2020	BCBSA National medical policy review. Description, summary, and references updated. Policy statements unchanged.
6/2020	Local Coverage Determination (LCD): Salvage High-intensity Focused Ultrasound (HIFU) Treatment in Prostate Cancer (PCa) (L38262) added. Effective 4/1/2020.
10/2019	BCBSA National medical policy review. Description, summary, and references updated. Policy statements unchanged.
10/2018	BCBSA National medical policy review. Description, summary, and references updated. Policy statement unchanged.
10/2017	New references added from BCBSA National medical policy.
7/2017	Clarified coding information.
10/2016	New references added from BCBSA National medical policy.
11/2015	New references added from BCBSA National medical policy.
9/2015	New medical policy describing investigational indications. Effective 9/1/2015.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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