

8.01.61 Focal Treatments for Prostate Cancer

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Section:	8.0 Therapy	Page:	Page 1 of 16

Policy Statement

- I. Use of any focal therapy modality to treat individuals with localized prostate cancer is considered **investigational**.

NOTE: Refer to [Appendix A](#) to see the policy statement changes (if any) from the previous version.

Policy Guidelines**Coding**

See the [Codes table](#) for details.

The two procedures that have codes are high intensity–focused ultrasound (HIFU) and focal laser ablation of malignant prostate tissue. There are no specific CPT codes for focal therapy using cryoablation, focal therapy using radiofrequency ablation, or focal therapy using photodynamic therapy. It is likely they are reported with CPT code 55899 unlisted procedure, male genital system.

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 (e.g., focal laser ablation, high-intensity focused ultrasound [HIFU], cryoablation, radiofrequency ablation [RFA], photodynamic therapy, irreversible electroporation).

Related Policies

- Brachytherapy for Clinically Localized Prostate Cancer Using Permanently Implanted Seeds
- Magnetic Resonance-Guided Focused Ultrasound
- Saturation Biopsy for Diagnosis, Staging, and Management of Prostate Cancer
- Whole Gland Cryoablation of Prostate Cancer

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these

instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

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. In 2020, the FDA cleared the Avenda Health focal laser ablation system and in 2021, the FDA granted a breakthrough device designation for the Avenda artificial intelligence (AI)-enabled focal therapy system for the treatment of localized prostate cancer. In 2023, FDA cleared the Elesta Laser Thermal Therapy Kit to direct laser energy to soft tissue, to necrotize or coagulate soft tissue through interstitial irradiation in medicine and surgery including urology, at a wavelength of 1064nm. 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 U.S. In November 2015, Ablatherm® HIFU (EDAP TMS) was cleared for marketing by the FDA through the 510(k) process. In June 2018, EDAP received 510(k) clearance for its Focal-One® HIFU device designed for prostate tissue ablation procedures. This device fuses magnetic resonance and 3D biopsy data with real-time ultrasound imaging, allowing urologists to view detailed images of the prostate on a large monitor and direct high-intensity ultrasound waves to ablate the targeted area.

Cryoablation

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

Photodynamic Therapy

The 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 the FDA through the 510(k) process. FDA product code: FTC.

In 2020, an FDA advisory committee voted against recommending approval of padeliporfin di-potassium (Tookad®; Steba Biotech), a minimally invasive photodynamic therapy for localized prostate cancer, citing concerns that men with very low-risk disease would potentially choose this therapy instead of active surveillance, despite the unproven long-term benefits and harms of treatment.

Magnetic Nanoparticles

MagForce® USA, Inc. is conducting a clinical study evaluating NanoTherm® under an FDA Investigational Device Exemption (IDE) (NCT05010759). NanoTherm uses magnetic nanoparticles

and an alternating magnetic field to create heat and local ablation in the ablation of prostate cancer.

Irreversible electroporation

The NanoKnife System was cleared through the 510(k) process (K102329) in 2011 for the surgical ablation of soft tissue. NanoKnife has not received clearance for the treatment of any specific disease.

Rationale

Background

Prostate Cancer

Prostate cancer is the second most common cancer diagnosed among men in the U.S. According to the National Cancer Institute, nearly 268,490 new cases are estimated to be diagnosed in the U.S. in 2022, associated with around 34,500 deaths.¹ Prostate cancer is more likely to develop in older men and in non-Hispanic Black men. About 6 in 10 cases are diagnosed in men who are ≥ 65 years of age, and it is rare in men < 40 years of age. 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.² However, the National Cancer Institute Surveillance Epidemiology and End Results Program data have shown that age-adjusted cancer-specific mortality rates for men with prostate cancer declined from 40 per 100,000 in 1992 to 19 per 100,000 in 2018. This decline has been attributed to a combination of earlier detection via PSA screening and improved therapies.

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.^{3,4,5,6,7}

Modalities Used to Ablate Lesions

The following ablative methods for which clinical evidence is available are considered herein: focal laser ablation; high-intensity focused ultrasound (HIFU); cryoablation; radiofrequency ablation (RFA); photodynamic therapy and irreversible electroporation.^{3,4,6,7,8,9,10,11,12,13,14} 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 Blue Shield of California Medical Policy: Brachytherapy for Clinically Localized Prostate Cancer Using Permanently Implanted Seeds).

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QoL), and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

This review only assesses evidence on focal therapy for primary localized prostate cancer; it does not consider the recurrent or salvage setting.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations."

Focal Therapy Overview

Clinical Context and Therapy Purpose

The purpose of focal therapy using either laser ablation, high-intensity focused ultrasound (HIFU), cryoablation, radiofrequency ablation (RFA), or photodynamic therapy in men who have primary localized prostate cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is men with primary localized prostate cancer.

Diagnosis

From a clinical standpoint, different types of localized prostate cancers may appear similar during initial diagnosis.¹⁵ However, prostate cancer often exhibits varying degrees of risk progression that may not be captured by accepted clinical risk categories (e.g., D'Amico criteria) or prognostic tools based on clinical findings (e.g., PSA titers, Gleason grade, or tumor stage).^{16,17,18,19,20} 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%^{21,22} to 20%²³ to perhaps 27% at 20-year follow-up.²⁴ Among elderly men (≥ 70 years) with this type of low-risk disease, comorbidities typically supervene as a cause of death; these men will die from the comorbidities of prostate cancer rather than from cancer itself. Other very similar-appearing low-risk tumors may progress unexpectedly and rapidly, quickly disseminating and becoming incurable.

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.²⁵ 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.²⁶

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 presumed multifocal disease actually have a unilaterally confined discrete lesion, which, when removed, would “cure” the patient.^{27,28,29} 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.⁸ 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.⁹ 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.^{30,31} This concept is supported by molecular genetics evidence that suggests that a single index tumor focus is usually responsible for disease progression and metastasis.^{10,32} The index lesion approach leaves in place small foci less than 0.5 cm³ in volume, with a Gleason score less than 7, that are considered unlikely to progress over a 10- to 20-year period.^{11,33,34} 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).^{26,9} Systematic transrectal ultrasound-guided biopsy alone has been investigated; however, it has been considered insufficient for patient selection or disease localization for focal therapy.^{12,35,36,37,38} see Blue Shield of California Medical Policy: Saturation Biopsy for Diagnosis, Staging, and Management of Prostate Cancer 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.^{25,9,12} Evidence has shown mpMRI can detect high-grade, large prostate cancer foci with performance similar to transperineal prostate mapping using a brachytherapy template.³⁹ For example, for the primary endpoint definition (lesion, ≥ 4 mm; Gleason score, $\geq 3+4$), 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 (e.g., mpMRI requires highly specialized MRI-compatible equipment; biopsy within the magnetic resonance imaging (MRI) scanner is challenging; interpretation of prostate MRI images requires experienced urologists) and it is still necessary to histologically confirm suspicious lesions using transperineal prostate mapping.⁴⁰

Interventions

The therapy being considered is focal therapy using either laser ablation, HIFU, cryoablation, RFA, photodynamic therapy or irreversible electroporation.

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 transperineally or transrectally 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.⁴¹

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 3x3x10 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 prostate mapping 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 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. 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.

Irreversible electroporation

Electroporation generates high-frequent electric pulses between two or more electrodes which produces an electric current that damages the cell membrane and allows molecules to pass into the cell passively. Electroporation can be temporary (reversible electroporation) or permanent (irreversible electroporation or IRE). In IRE the cell membrane is permanently damaged causing cell death due to the inability to maintain homeostasis. IRE achieves its action with no thermal effect. IRE appears to preserve vessels, nerves and the extracellular matrix.⁴²

Comparators

The following therapies and practices are currently being used to make decisions about managing men with primary localized prostate cancer: surgery (radical prostatectomy), external-beam radiotherapy, and active surveillance.

Treatments

The divergent behavior of localized prostate cancers creates uncertainty about whether to treat immediately.^{43,44} A patient may choose definitive treatment up front.⁴⁵ Surgery (radical prostatectomy) or external-beam radiotherapy are frequently used to treat patients with localized prostate cancer.^{44,46} Complications most commonly reported with radical prostatectomy or external-beam radiotherapy and with the greatest variability are incontinence (0% to 73%) and other genitourinary toxicities (irritative and obstructive symptoms); hematuria (typically $\leq 5\%$);

gastrointestinal and bowel toxicity, including nausea and loose stools (25% to 50%); proctopathy, including rectal pain and bleeding (10% to 39%); and erectile dysfunction, including impotence (50% to 90%).⁴⁶

American Urological Association guidelines state that for patients with low-risk prostate cancer, clinicians should recommend active surveillance.⁴⁷ With this approach, patients forego immediate therapy but continue regular monitoring until signs or symptoms of disease progression are evident, at which point curative treatment is instituted.^{48,49}

Outcomes

The general outcomes of interest are overall survival (OS), tumor progression and recurrence, incontinence, and sexual dysfunction.

As a therapy situated between active surveillance and definitive therapy, focal therapy is a tissue-sparing procedure intended to maximize QoL (e.g., incontinence, sexual dysfunction) by treating the index lesion. An international multidisciplinary panel of urologists, radiologists and biomedical engineers recommended that follow-up after focal therapy should be a minimum of 5 years and should include multiparametric MRI, biopsies, assessment of erectile function, QoL, urinary symptoms and incontinence.⁵⁰

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

No prospective, comparative studies were identified for the majority of the ablative technologies; however, RCTs comparing focal therapy to radical therapy are underway for focal prostate ablation (NCT03668652, NCT06223295), irreversible electroporation (NCT01835977), and HIFU (NCT03531099); see Table 1. The current evidence primarily comprises systematic reviews of noncomparative studies, case series, and other observational studies. The pivotal trial for the irreversible electroporation system (NanoKnife) in the US is a single arm study and has only preliminary results available.⁵¹ Prospective, comparative studies compared to standard therapy are needed therefore, noncomparative studies and case series will not be discussed further.

Of note, an RCT of padeliporfin (a photodynamic therapy) versus active surveillance in men with low-risk prostate cancer was published by Azzouzi et al (2017)⁵²; however, an FDA Advisory Committee voted against the approval of this agent in 2020 (see the Regulatory Status section).

Systematic Reviews

Bates et al (2021) undertook a PRISMA-adhering systematic review that evaluated the evidence base (from January 2000 to June 2020) for focal therapy as a treatment strategy for men with histologically proven, clinically localized prostate cancer as compared to standard management options.⁵³ Focal therapy interventions included HIFU, vascular targeted photodynamic therapy, laser ablation, thermal ablation, focal brachytherapy, radiofrequency waves, microwave ablation, focal external-beam radiotherapy, and irreversible electroporation. The comparator intervention included any standard management option such as radical prostatectomy, external beam radiotherapy, whole gland brachytherapy, and active surveillance/monitoring. Overall, 5 articles reporting on 4 primary comparative studies (1 RCT and 3 retrospective nonrandomized comparative studies;

N=3961) and 10 eligible systematic reviews were identified. The RCT compared a vascular targeted photodynamic therapy (padeliporfin) versus active surveillance among patients with low-risk prostate cancer and concluded that patients who underwent photodynamic therapy had less progression (28% vs. 58%; adjusted hazard ratio [HR], 0.34; 95% confidence interval [CI], 0.24 to 0.46; $p<.0001$) and needed less radical therapy (6% vs. 29%; $p<.0001$) at 24 months.⁵² Despite these "positive" results, an FDA staff analysis cited issues with the trial design, endpoints, missing data, and adverse events of padeliporfin therapy, resulting in the decline to recommend for approval by the FDA advisory committee. One retrospective study comparing focal HIFU with robotic radical prostatectomy found no significant difference in treatment failure at 3 years, with better continence and erectile function recovery with HIFU. The other 2 retrospective cohort studies compared focal laser ablation with radical prostatectomy and external beam radiotherapy and reported significantly worse oncologic outcomes with the focal treatment. Regarding the included systematic reviews, virtually all concluded that there was insufficient high certainty evidence to make definitive conclusions regarding the clinical effectiveness of focal therapy. Additionally, the certainty of the evidence regarding the comparative effectiveness of focal therapy as a primary treatment for localized prostate cancer was low, with significant uncertainties and until higher certainty evidence emerges..."focal therapy should ideally be performed within clinical trials or well-designed prospective cohort studies."

Hopstaken et al (2022) reported on an updated systematic review on focal therapy in localized prostate cancer in terms of functional and oncological outcomes that included 72 studies published between October 2015 and December 31, 2020.⁵⁴ Of the included studies, 27 reported on HIFU, 9 on irreversible electroporation, 11 on cryoablation, 8 each on focal laser ablation and focal brachytherapy, 7 on photodynamic therapy, 2 on RFA, and 1 on prostatic artery embolization. Results revealed photodynamic therapy and HIFU to have potentially promising results. HIFU studies reported a median of 95% pad-free (regarding continence) patients and a median of 85% of patients with no clinically significant cancer in the treated area. No changes in continence were noted and a median of 90% of patients were without clinically significant cancer in the treated area among those receiving photodynamic therapy. Both treatments were well-tolerated. Despite these positive results, the authors noted that the majority of studies concerning focal therapy are still in an early research stage and that definitive proof of oncological effectiveness of focal therapy against standard of care is still pending.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Urological Association et al

The American Urological Association, in collaboration with the American Society for Radiation Oncology (ASTRO) with additional representation from the American Society of Clinical Oncology (ASCO), and Society of Urologic Oncology (SUO) published updated guidelines on the management of clinically localized prostate cancer in 2022.⁴⁷ The guidelines included the following recommendation on focal treatments:

- "Clinicians should inform patients with intermediate-risk prostate cancer considering whole gland or focal ablation that there are a lack of high-quality data comparing ablation outcomes to radiation therapy, surgery, and active surveillance. (Expert Opinion)"

- "Clinicians should not recommend whole gland or focal ablation for patients with high-risk prostate cancer outside of a clinical trial. (Expert Opinion)"

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN) guidelines for prostate cancer (v4.2024) recommend only cryosurgery and high-intensity focused ultrasound (HIFU) as local therapy options for radiotherapy *recurrence* in the absence of metastatic disease (category 2B). Cryotherapy or other local therapies are not recommended as routine *primary* therapy for localized prostate cancer due to lack of long-term data comparing these treatments to radiation or radical prostatectomy.⁵⁵

National Cancer Institute

The National Cancer Institute (NCI; 2023) updated its information on prostate cancer treatments.⁵⁶ The NCI indicated that cryoablation, photodynamic therapy, and HIFU were new treatment options currently being studied in national trials. The NCI offered no recommendation for or against these treatments.

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (2019; updated in 2021) issued guidance on management for localized prostate cancer.¹³ Cryoablation and high-intensity ultrasound are not recommended for the treatment of localized prostate cancer because there is a lack of evidence on quality of life benefits and long-term survival.

U.S. Preventive Services Task Force Recommendations

The U.S. Preventive Services Task Force published recommendations for prostate cancer screening.⁵⁷

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT05454488	An Evidence-Based Focal Cryotherapy Protocol for Focal Ablation of Intermediate Risk Prostate Cancer	30	Jan 2024
NCT04972097	Pivotal Study of the NanoKnife System for the Ablation of Prostate Tissue (PRESERVE)	121	Jul 2024
NCT04045756	Short-term Efficacy of Transperineal Laser Ablation (TPLA) with Image Fusion and Multi-parametric (mpMRI) Follow-up in Focal Low-intermediate Risk Prostate Cancer: Interventional Pilot Study	50	Aug 2024
NCT03668652	A Randomized Control Trial of Focal Prostate Ablation Versus Radical Prostatectomy	200	Sep 2024
NCT01835977	Multi-Center Randomized Clinical Trial Irreversible Electroporation for the Ablation of Localized Prostate Cancer	106	Jan 2025
NCT03568188	Phase 2, Multicenter, Prospective Cohort Study, Estimating the Efficacy of Focused HIFU Therapy in Patients with Localized Intermediate Risk Prostate Cancer	170	Sep 2025
NCT03531099	Phase 3, Multicenter, Randomized Study, Evaluating the Efficacy and Tolerability of Focused HIFU Therapy Compared to Active Surveillance in Patients With Significant Low Risk Prostate Cancer	108	Oct 2026
NCT04049747	Imperial Prostate 4: Comparative Health Research Outcomes of NOvel Surgery in Prostate Cancer	2450	May 2027

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT05610852	Prospective Single-Center Randomized Study Of Single-Port Transvesical Partial Prostatectomy Versus High Intensity Focused Ultrasound (HIFU)	276	Jul 2028
NCT04549688	Active Surveillance Plus (AS+): Local Tumor Control with High-intensity Focused Ultrasound (HIFU) in Patients with Localized Prostate Cancer	250	Sep 2030
NCT06223295	Effectiveness of Focal Therapy in Men With Prostate Cancer (ENFORCE)	356	Feb 2031
NCT06451445	A Pan-Canadian, Investigator Initiated Clinical Trial With Focal IRE Directed to Intermediate-Risk Prostate Cancer (WIRED)	100	May 2032
NCT05027477	Customized Ablation of the Prostate With the TULSA Procedure Against Radical Prostatectomy Treatment: a Randomized Controlled Trial for Localized Prostate Cancer (CAPTAIN)	201	Dec 2032
<i>Unpublished</i>		276	Jul 2028
NCT04307056	Evaluation of high intensity focused ultrasound (hifu) in curative treatment of localized prostate cancer at low or intermediate risk and in treatment of recurrence after radiotherapy	3862	Aug 2022 (completed)

NCT: national clinical trial.

ª Denotes industry-sponsored or cosponsored trial.

References

1. American Cancer Society. Key statistics for prostate cancer. January 12, 2022. <https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html>. Accessed July 11, 2023.
2. Dall'Era MA, Cooperberg MR, Chan JM, et al. Active surveillance for early-stage prostate cancer: review of the current literature. *Cancer*. Apr 15 2008; 112(8): 1650-9. PMID 18306379
3. Jácome-Pita F, Sánchez-Salas R, Barret E, et al. Focal therapy in prostate cancer: the current situation. *Ecancermedicalscience*. 2014; 8: 435. PMID 24944577
4. Nguyen CT, Jones JS. Focal therapy in the management of localized prostate cancer. *BJU Int*. May 2011; 107(9): 1362-8. PMID 21223478
5. Lindner U, Lawrentschuk N, Schatloff O, et al. Evolution from active surveillance to focal therapy in the management of prostate cancer. *Future Oncol*. Jun 2011; 7(6): 775-87. PMID 21675840
6. Iberti CT, Mohamed N, Palese MA. A review of focal therapy techniques in prostate cancer: clinical results for high-intensity focused ultrasound and focal cryoablation. *Rev Urol*. 2011; 13(4): e196-202. PMID 22232569
7. Lecornet E, Ahmed HU, Moore CM, et al. Conceptual basis for focal therapy in prostate cancer. *J Endourol*. May 2010; 24(5): 811-8. PMID 20443699
8. Muto S, Yoshii T, Saito K, et al. Focal therapy with high-intensity-focused ultrasound in the treatment of localized prostate cancer. *Jpn J Clin Oncol*. Mar 2008; 38(3): 192-9. PMID 18281309
9. Kasivisvanathan V, Emberton M, Ahmed HU. Focal therapy for prostate cancer: rationale and treatment opportunities. *Clin Oncol (R Coll Radiol)*. Aug 2013; 25(8): 461-73. PMID 23759249
10. Liu W, Laitinen S, Khan S, et al. Copy number analysis indicates monoclonal origin of lethal metastatic prostate cancer. *Nat Med*. May 2009; 15(5): 559-65. PMID 19363497
11. Ahmed HU, Emberton M. Active surveillance and radical therapy in prostate cancer: can focal therapy offer the middle way?. *World J Urol*. Oct 2008; 26(5): 457-67. PMID 18704441
12. van den Bos W, Muller BG, Ahmed H, et al. Focal therapy in prostate cancer: international multidisciplinary consensus on trial design. *Eur Urol*. Jun 2014; 65(6): 1078-83. PMID 24444476
13. National Institute for Health and Care Excellence (NICE). Prostate cancer: diagnosis and management. [NG131]. 2019; <https://www.nice.org.uk/guidance/ng131/chapter/Recommendations>. Accessed July 11, 2023.

14. National Institute for Health and Care Excellence (NICE). Focal Therapy Using High-Intensity Focused Ultrasound for Localized Prostate Cancer [IPG424]. 2012; <https://www.nice.org.uk/guidance/ipg424>. Accessed July 11, 2023.
15. Bangma CH, Roemeling S, Schröder FH. Overdiagnosis and overtreatment of early detected prostate cancer. *World J Urol*. Mar 2007; 25(1): 3-9. PMID 17364211
16. Johansson JE, Andrén O, Andersson SO, et al. Natural history of early, localized prostate cancer. *JAMA*. Jun 09 2004; 291(22): 2713-9. PMID 15187052
17. Ploussard G, Epstein JI, Montironi R, et al. The contemporary concept of significant versus insignificant prostate cancer. *Eur Urol*. Aug 2011; 60(2): 291-303. PMID 21601982
18. Harnden P, Naylor B, Shelley MD, et al. The clinical management of patients with a small volume of prostatic cancer on biopsy: what are the risks of progression? A systematic review and meta-analysis. *Cancer*. Mar 01 2008; 112(5): 971-81. PMID 18186496
19. Brimo F, Montironi R, Egevad L, et al. Contemporary grading for prostate cancer: implications for patient care. *Eur Urol*. May 2013; 63(5): 892-901. PMID 23092544
20. Eylert MF, Persad R. Management of prostate cancer. *Br J Hosp Med (Lond)*. Feb 2012; 73(2): 95-9. PMID 22504752
21. Eastham JA, Kattan MW, Fearn P, et al. Local progression among men with conservatively treated localized prostate cancer: results from the Transatlantic Prostate Group. *Eur Urol*. Feb 2008; 53(2): 347-54. PMID 17544572
22. Bill-Axelson A, Holmberg L, Ruutu M, et al. Radical prostatectomy versus watchful waiting in early prostate cancer. *N Engl J Med*. May 12 2005; 352(19): 1977-84. PMID 15888698
23. Thompson IM, Goodman PJ, Tangen CM, et al. Long-term survival of participants in the prostate cancer prevention trial. *N Engl J Med*. Aug 15 2013; 369(7): 603-10. PMID 23944298
24. Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. *JAMA*. May 04 2005; 293(17): 2095-101. PMID 15870412
25. Tay KJ, Mendez M, Moul JW, et al. Active surveillance for prostate cancer: can we modernize contemporary protocols to improve patient selection and outcomes in the focal therapy era?. *Curr Opin Urol*. May 2015; 25(3): 185-90. PMID 25768694
26. Passoni NM, Polascik TJ. How to select the right patients for focal therapy of prostate cancer?. *Curr Opin Urol*. May 2014; 24(3): 203-8. PMID 24625428
27. Scales CD, Presti JC, Kane CJ, et al. Predicting unilateral prostate cancer based on biopsy features: implications for focal ablative therapy--results from the SEARCH database. *J Urol*. Oct 2007; 178(4 Pt 1): 1249-52. PMID 17698131
28. Mouraviev V, Mayes JM, Sun L, et al. Prostate cancer laterality as a rationale of focal ablative therapy for the treatment of clinically localized prostate cancer. *Cancer*. Aug 15 2007; 110(4): 906-10. PMID 17587207
29. Mouraviev V, Mayes JM, Madden JF, et al. Analysis of laterality and percentage of tumor involvement in 1386 prostatectomized specimens for selection of unilateral focal cryotherapy. *Technol Cancer Res Treat*. Apr 2007; 6(2): 91-5. PMID 17375971
30. Mouraviev V, Villers A, Bostwick DG, et al. Understanding the pathological features of focality, grade and tumour volume of early-stage prostate cancer as a foundation for parenchyma-sparing prostate cancer therapies: active surveillance and focal targeted therapy. *BJU Int*. Oct 2011; 108(7): 1074-85. PMID 21489116
31. Mouraviev V, Mayes JM, Polascik TJ. Pathologic basis of focal therapy for early-stage prostate cancer. *Nat Rev Urol*. Apr 2009; 6(4): 205-15. PMID 19352395
32. Guo CC, Wang Y, Xiao L, et al. The relationship of TMPRSS2-ERG gene fusion between primary and metastatic prostate cancers. *Hum Pathol*. May 2012; 43(5): 644-9. PMID 21937078
33. Stamey TA, Freiha FS, McNeal JE, et al. Localized prostate cancer. Relationship of tumor volume to clinical significance for treatment of prostate cancer. *Cancer*. Feb 01 1993; 71(3 Suppl): 933-8. PMID 7679045
34. Nelson BA, Shappell SB, Chang SS, et al. Tumour volume is an independent predictor of prostate-specific antigen recurrence in patients undergoing radical prostatectomy for clinically localized prostate cancer. *BJU Int*. Jun 2006; 97(6): 1169-72. PMID 16686706

35. Mayes JM, Mouraviev V, Sun L, et al. Can the conventional sextant prostate biopsy accurately predict unilateral prostate cancer in low-risk, localized, prostate cancer?. *Urol Oncol*. 2011; 29(2): 166-70. PMID 19451000
36. Sinnott M, Falzarano SM, Hernandez AV, et al. Discrepancy in prostate cancer localization between biopsy and prostatectomy specimens in patients with unilateral positive biopsy: implications for focal therapy. *Prostate*. Aug 01 2012; 72(11): 1179-86. PMID 22161896
37. Gallina A, Maccagnano C, Suardi N, et al. Unilateral positive biopsies in low risk prostate cancer patients diagnosed with extended transrectal ultrasound-guided biopsy schemes do not predict unilateral prostate cancer at radical prostatectomy. *BJU Int*. Jul 2012; 110(2 Pt 2): E64-8. PMID 22093108
38. Briganti A, Tutolo M, Suardi N, et al. There is no way to identify patients who will harbor small volume, unilateral prostate cancer at final pathology. implications for focal therapies. *Prostate*. Jun 01 2012; 72(8): 925-30. PMID 21965006
39. Arumainayagam N, Ahmed HU, Moore CM, et al. Multiparametric MR imaging for detection of clinically significant prostate cancer: a validation cohort study with transperineal template prostate mapping as the reference standard. *Radiology*. Sep 2013; 268(3): 761-9. PMID 23564713
40. Dickinson L, Ahmed HU, Allen C, et al. Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European consensus meeting. *Eur Urol*. Apr 2011; 59(4): 477-94. PMID 21195536
41. Lee T, Mendhiratta N, Sperling D, et al. Focal laser ablation for localized prostate cancer: principles, clinical trials, and our initial experience. *Rev Urol*. 2014; 16(2): 55-66. PMID 25009445
42. Scheltema MJ, van den Bos W, de Bruin DM, et al. Focal vs extended ablation in localized prostate cancer with irreversible electroporation; a multi-center randomized controlled trial. *BMC Cancer*. May 05 2016; 16: 299. PMID 27150293
43. Borley N, Feneley MR. Prostate cancer: diagnosis and staging. *Asian J Androl*. Jan 2009; 11(1): 74-80. PMID 19050692
44. Freedland SJ. Screening, risk assessment, and the approach to therapy in patients with prostate cancer. *Cancer*. Mar 15 2011; 117(6): 1123-35. PMID 20960523
45. Ip S, Dahabreh IJ, Chung M, et al. An evidence review of active surveillance in men with localized prostate cancer. Evidence Report/Technology Assessment no. 204 (AHRQ Publication No. 12-E003-EF). Rockville, MD: Agency for Research and Quality; 2011.
46. American Urological Association. Guideline for management of clinically localized prostate cancer: 2007 update. Linthicum, MD: American Urological Association Education and Research; 2007.
47. Eastham JA, Aufferberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO Guideline. 2022; <https://www.auanet.org/guidelines/guidelines/clinically-localized-prostate-cancer-ava/astro-guideline-2022>. Accessed July 11, 2023.
48. Whitson JM, Carroll PR. Active surveillance for early-stage prostate cancer: defining the triggers for intervention. *J Clin Oncol*. Jun 10 2010; 28(17): 2807-9. PMID 20439633
49. Albertsen PC. Treatment of localized prostate cancer: when is active surveillance appropriate?. *Nat Rev Clin Oncol*. Jul 2010; 7(7): 394-400. PMID 20440282
50. Muller BG, van den Bos W, Brausi M, et al. Follow-up modalities in focal therapy for prostate cancer: results from a Delphi consensus project. *World J Urol*. Oct 2015; 33(10): 1503-9. PMID 25559111
51. George AK, Miocinovic R, Patel AR, et al. A Description and Safety Overview of Irreversible Electroporation for Prostate Tissue Ablation in Intermediate-Risk Prostate Cancer Patients: Preliminary Results from the PRESERVE Trial. *Cancers (Basel)*. Jun 08 2024; 16(12). PMID 38927884
52. Azzouzi AR, Vincendeau S, Barret E, et al. Padeliporfin vascular-targeted photodynamic therapy versus active surveillance in men with low-risk prostate cancer (CLIN1001 PCM301): an open-label, phase 3, randomised controlled trial. *Lancet Oncol*. Feb 2017; 18(2): 181-191. PMID 28007457

53. Bates AS, Ayers J, Kostakopoulos N, et al. A Systematic Review of Focal Ablative Therapy for Clinically Localised Prostate Cancer in Comparison with Standard Management Options: Limitations of the Available Evidence and Recommendations for Clinical Practice and Further Research. *Eur Urol Oncol*. Jun 2021; 4(3): 405–423. PMID 33423943
54. Hopstaken JS, Bomers JGR, Sedelaar MJP, et al. An Updated Systematic Review on Focal Therapy in Localized Prostate Cancer: What Has Changed over the Past 5 Years?. *Eur Urol*. Jan 2022; 81(1): 5–33. PMID 34489140
55. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: prostate cancer. Version 4.2022. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed July 11, 2023.
56. National Cancer Institute. Prostate Cancer Treatment (PDQ) Patient Version: Treatment Option Overview. 2021. https://www.cancer.gov/types/prostate/patient/prostate-treatment-pdq#link/_142. Accessed July 11, 2023.
57. U.S. Preventive Services Task Force. Final Recommendation Statement: Prostate Cancer: Screening. 2018; <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prostate-cancer-screening>. Accessed July 11, 2023.

Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	0582T	Transurethral ablation of malignant prostate tissue by high-energy water vapor thermotherapy, including intraoperative imaging and needle guidance
	0655T	Transperineal focal laser ablation of malignant prostate tissue, including transrectal imaging guidance, with MR-fused images or other enhanced ultrasound imaging
	0738T	Treatment planning for magnetic field induction ablation of malignant prostate tissue, using data from previously performed magnetic resonance imaging (MRI) examination
	0739T	Ablation of malignant prostate tissue by magnetic field induction, including all intraprocedural, transperineal needle/catheter placement for nanoparticle installation and intraprocedural temperature monitoring, thermal dosimetry, bladder irrigation, and magnetic field nanoparticle activation
	51721	Insertion of transurethral ablation transducer for delivery of thermal ultrasound for prostate tissue ablation, including suprapubic tube placement during the same session and placement of an endorectal cooling device, when performed (Code effective 01/01/2025)

Type	Code	Description
	53854	Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy
	55880	Ablation of malignant prostate tissue, transrectal, with high intensity-focused ultrasound (HIFU), including ultrasound guidance
	55881	Ablation of prostate tissue, transurethral, using thermal ultrasound, including magnetic resonance imaging guidance for, and monitoring of, tissue ablation <i>(Code effective 01/01/2025)</i>
	55882	Ablation of prostate tissue, transurethral, using thermal ultrasound, including magnetic resonance imaging guidance for, and monitoring of, tissue ablation; with insertion of transurethral ultrasound transducer for delivery of thermal ultrasound, including suprapubic tube placement and placement of an endorectal cooling device, when performed <i>(Code effective 01/01/2025)</i>
	55899	Unlisted procedure, male genital system
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
07/31/2015	BCBSA Medical Policy adoption
11/01/2016	Policy revision without position change
07/01/2017	Coding update
11/01/2017	Policy revision without position change
11/01/2018	Policy revision without position change
02/01/2019	Coding update
12/01/2019	Policy revision without position change
03/01/2020	Coding update
11/01/2020	Annual review. No change to policy statement. Literature review updated.
01/01/2021	Coding Update
02/01/2021	Coding Update
08/01/2021	Coding Update
11/01/2021	Annual review. Policy statement and literature review updated.
11/01/2022	Annual review. Policy statement and literature review updated.
03/01/2023	Coding Update
11/01/2023	Annual review. Policy statement and literature review updated.
11/01/2024	Annual review. No change to policy statement. Policy guidelines and literature review updated.
02/01/2025	Coding update.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not

more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	AFTER
<p>Focal Treatments for Prostate Cancer 8.01.61</p> <p>Policy Statement:</p> <p>I. Use of any focal therapy modality to treat individuals with localized prostate cancer is considered investigational.</p>	<p>Focal Treatments for Prostate Cancer 8.01.61</p> <p>Policy Statement:</p> <p>I. Use of any focal therapy modality to treat individuals with localized prostate cancer is considered investigational.</p>