Regence

Medical Policy Manual Surgery, Policy No. 222

Focal Laser Ablation of Prostate Cancer

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

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. Other terms for focal laser ablation include photothermal therapy, laser interstitial therapy, and laser interstitial photocoagulation.

MEDICAL POLICY CRITERIA

Use of focal laser therapy to treat patients with localized prostate cancer is considered **investigational**.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Magnetic Resonance (MR) Guided Focused Ultrasound (MRgFUS) and High Intensity Focused Ultrasound (HIFU) Ablation, Surgery, Policy No. 139
2. Cryosurgical Ablation of Miscellaneous Solid Tumors Outside of the Liver, Surgery, Policy No. 132

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 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).[3-7] 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 (≥70 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% to 73%) and other genitourinary toxicities (irritative and obstructive symptoms); hematuria (typically ≤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%).[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. 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.[16-18]

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–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.[19-23] 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.[26-28] 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 cm3 in volume, with a Gleason score less than 7, that are considered unlikely to progress over a 10- to 20-year period.[35-37] 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 three 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.[38-42]

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 (e.g., 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]

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.[45]

Regulatory Status

In 2020, the Avenda Health Treatment System was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for use in surgical applications requiring ablation, vaporization, excision, incision, and coagulation of soft tissue in multiple areas of surgery including urology at a wavelength of 980nm. 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.

EVIDENCE SUMMARY

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

SYSTEMATIC REVIEWS

Hopstaken (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.[46] 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.

Bates (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.[47] Focal therapy interventions included high-intensity focused ultrasound (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, five articles reporting on four primary comparative studies (one RCT and three retrospective nonrandomized comparative studies; n=3,961) 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<0.0001) and needed less radical therapy (6% vs. 29%; p<0.0001) at 24 months.[48] 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 three years, with better continence and erectile function recovery with HIFU. The other two 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. The authors concluded that 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 that "until higher certainty evidence emerges...focal therapy should ideally be performed within clinical trials or well-designed prospective cohort studies."

A high-quality systematic review published by Valerio (2014) compiled the bulk of the evidence available in the literature on focal ablation technologies through 2012.[49] This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[50] Only studies that reported actual focal therapy procedures were included. Specific categories of data to be collected were prespecified. Study selection criteria were prespecified, with dual review and data extraction, and senior author arbitration as needed. The quality of included studies was assessed using the Oxford Centre for Evidence-based Medicine level of evidence for therapy. This review and its summarized statistics serve as the initial evidence source for this evidence review. Additional prospective studies of a comparative nature are reviewed in subsequent sections below.

Twenty-five series were included that evaluated a number of focal therapy methods used in the primary setting. The quality of evidence was low to medium, with no study yielding a level of evidence greater than 2b (individual cohort study). Twelve series used high-intensity focused ultrasound (n=226); six series (n=1,400) used cryoablation (one study included 1,160 treated in the primary setting, 1,400 total treated with cryoablation); three used focal laser ablation (n=16); one used RFA (n=14); and one used photodynamic therapy (n=6). In two series, focal treatments were mixed or included brachytherapy.

Of the studies of focal laser ablation, patients included had disease defined as low-risk in two, while risk categories were not available in third. The median prostate-specific antigen (PSA) level of patients ranged from 3.76 to 5.7 ng/mL. The median follow-up for the laser ablation series ranged from one week to six months.

Overall for all the ablation methods, the median age of patients ranged from 56 to 73 years. Individual Gleason scores were available in 20 series, with 1,503 men having Gleason scores less than 6; 521 with Gleason scores of 7; and 82 had Gleason scores higher than 8. The disease was localized as follows: transrectal ultrasound biopsy in two series; transrectal ultrasound biopsy with Doppler ultrasound in two series; transrectal ultrasound biopsy plus magnetic resonance imaging in six series; transperineal template-guided mapping biopsy and multiparametric magnetic resonance imaging in four series; the preoperative assessment was not reported in 11 studies.

In all studies reporting such data in the Valerio (2014) systematic review, all known areas of cancer were treated; in no study was it explicitly stated the index lesion was ablated and that other lesions were left untreated. Biochemical control based on PSA levels was reported in five series using the Radiation Therapy Oncology Group-ASTRO Phoenix Consensus Conference criteria.[51] Other definitions used to define biochemical control were American Society for Radiation Oncology (ASTRO; five series), Stuttgart (one series), and Phoenix plus PSA velocity greater than 0.75 ng/mL annually (one series). Biochemical control rates ranged from 86% at eight-year follow-up (n=318) to 60% at five-year follow-up (n=56). Because follow-up was too short, progression to metastatic disease was not reported for most studies in the Valerio (2014) review; in those reporting follow-up data, metastatic progression rates were very low (0% to 0.3%). Although a cancer-specific survival rate of 100% was reported in all series, such rates must be considered in the context of the small numbers of patients in individual studies and the short follow-up (only three studies had follow-up greater than five years).

Across all studies, the median hospital length of stay was one day; other perioperative outcomes were poorly reported. Across studies, the most frequent complications associated with the treatment of prostate cancer–urinary retention, urinary stricture, and urinary tract

infection–occurred in 0% to 17%, 0% to 5%, and 0% to 17%, respectively, of patients. Only five studies reported all three complications. Validated questionnaires were used in nine series to report urinary functional outcomes; physician-reported rates were used in five studies. According to the questionnaires, the pad-free continence rate varied between 95% and 100%, whereas the range of leak-free rates was 80% to 100%. Validated questionnaire data showed erectile functional rates in 54% to 100%, while physician-reported data showed erectile functional rates of 58% to 85%. Other adverse outcomes were poorly reported, particularly the QOL data, with only three studies reporting.

NONRANDOMIZED STUDIES

Li (2022) compared the efficacy of focal laser ablation (FLA) to active surveillance/watchful waiting (AS/WW) in people with low-risk prostate cancer using Surveillance Epidemiology and End Results (SEER) data.[52] Outcome measures were cancer-specific survival (CSS) and overall survival (OS). The study cohort consisted of 18,841 patients who had been diagnosed between 2010 and 2016 with low-risk prostate cancer, defined as clinical tumor stage between T1 and T2, Gleason score <7, and prostate specific antigen (PSA) <10 ng/ml^{-1}. 18,611 of patients had AS/WW and 230 had FLA treatment. Significant differences at baseline between the two groups included the FLA group was older than the AS/WW group ($p<0.001$). With a median follow-up time of 36 months, there was no significant difference in CSS between the two groups ($p=0.32$), but OS was increased in the AS/WW group ($p=0.009$). The difference persisted after adjustment for age, insurance status, year of diagnosis, race, tumor stage, and PSA level (HR: 1.69, 95% CI: 1.02-2.81, $p=0.043$). The authors concluded that both AS/WW and FLA have fewer side effects than standard treatment and AS/WW may offer a survival benefit for patients with low-risk prostate cancer.

Zhou (2020) conducted analyses on data from the SEER database comparing survival outcomes between radiotherapy and focal laser ablation for the treatment of prostate cancer.[53] Of the 93,469 patients, 428 were treated with laser ablation and the remainder received radiation therapy. Radiation-treated patients had better overall survival (OS) in the adjusted multivariate regression, in the propensity score-matched analysis, and in the instrumental variate (IV)-adjusted analysis. In the subgroup analyses of patients with PSA < 4 ng/mL, those treated with focal laser ablation had significantly worse OS and cancer-specific mortality (CSM) outcomes (OS HR = 1.89; 95% CI 1.01 to 3.53; $p=0.0466$ and CSM HR = 4.25; 95% CI 1.04 to 17.43; $p=0.044$).

In a matched cohort study, Zheng (2019) compared focal laser ablation with radical prostatectomy for localized prostate cancer. A total of 12,875 patients were identified for inclusion from the Surveillance, Epidemiology, and End Results database. Of these, 12,433 were treated with radical prostatectomy and 442 with focal laser therapy. The propensity score matched cancer-specific mortality was not significantly different between groups (HR, 0.82; 95% CI 0.18 to 3.67; $p=0.7936$), while any-cause mortality was higher in the focal laser ablation group (HR, 2.35; 95% CI 1.38 to 3.98; $p=0.0016$).

Additional case series and nonrandomized studies have assessed focal laser ablation[54-58] since the Valerio (2014) review. Studies were mostly small (range, 8 to 120), single-arm, lacked long-term follow-up (range, three to 36 months) and did not report clinical outcomes (e.g., progression-free survival, OS).

SUMMARY OF EVIDENCE

For individuals who have primary localized prostate cancer who receive focal laser ablation, the evidence includes a high-quality systematic review and 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 laser ablation 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. The available comparative studies have reported mixed outcomes in terms of OS and mortality, and the evidence is limited in its quality, reporting, and scope. The evidence is insufficient to determine the effects of the technology on health outcomes.

PRACTICE GUIDELINE SUMMARY

NATIONAL COMPREHENSIVE CANCER NETWORK

Focal laser ablation is not included in the National Comprehensive Cancer Network (NCCN) guidelines for prostate cancer (v.1.2023) recommended options for localized prostate cancer.[59]

AMERICAN UROLOGICAL ASSOCIATION

The American Urological Association, along with the American Society for Radiation Oncology (ASTRO) (endorsed by the Society for Urologic Oncology) updated their joint guidelines on the management of clinically localized prostate cancer in 2022. The guidelines included the following recommendation on focal treatments:[18]

“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)”

SUMMARY

There is not enough research to show that focal laser ablation improves health outcomes for people with localized prostate cancer. No clinical guidelines based on evidence recommend focal laser ablation for the treatment of localized prostate cancer. Therefore, focal laser ablation is considered investigational for the treatment of localized prostate cancer.

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CODES

Codes	Number	Description
CPT	0655T	Transperineal focal laser ablation of malignant prostate tissue, including transrectal imaging guidance, with MR-fused images or other enhanced ultrasound imaging
HCPCS	None	

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