Medical Coverage Policy | Focal Treatments for Prostate Cancer

EFFECTIVE DATE: 10|01|2015
POLICY LAST UPDATED: 05|02|2017

OVERVIEW

Prostate cancer is the second most common cancer diagnosed among men in the United States. Focal treatment for prostate cancer seeks to ablate either an "index'" lesion (defined as the largest cancerous lesion with the highest grade tumor thought to be the lesion that will drive the natural history of this typically multifocal disease), or, alternatively to ablate additional non-index lesions or all other areas of known cancer. Focal laser ablation (FLA), uses MRI to guide the probe for ablation of the lesion in localized prostate cancer.

MEDICAL CRITERIA

BlueCHiP for Medicare and Commercial Products

Not Applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

BlueCHiP for Medicare and Commercial Products

Use of any focal therapy modality to treat patients with localized prostate cancer is not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

COVERAGE

Benefits may vary between groups/contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for limitations of benefits/coverage when services are not medically necessary.

BACKGROUND

Localized Prostate Cancer and Current Management

Prostate cancer is the second most common cancer diagnosed among men in the United States. According to the National Cancer Institute (NCI), nearly 240,000 new cases are expected to be diagnosed in the United States in 2013 and are associated with around 30,000 deaths. Autopsy studies in the pre-prostate-specific antigen (PSA) screening era have identified incidental cancerous foci in 30% of men 50 years of age, with incidence reaching 75% at age 80 years. However, NCI Surveillance Epidemiology and End Results data show age-adjusted cancer-specific mortality rates for men with prostate cancer have declined from 40 per 100,000 in 1992 to 22 per 100,000 in 2010. This decline has been attributed to a combination of earlier detection via PSA screening and improved therapies.

Localized prostate cancers may appear very similar clinically at diagnosis. However, they often exhibit diverse risk of progression that may not be captured by accepted clinical risk categories (e.g., D'Amico criteria) or prognostic tools that are based on clinical findings, including PSA titers, Gleason grade, or tumor stage.

In studies of conservative management, the risk of localized disease regression based on prostate cancer-specific survival rates at 10 years may range from 15% to 20% to perhaps 27% at 20-year follow-up. Among elderly men (70 years) with this type of low-risk disease, comorbidities typically supervene as a cause of death;

these men will die with prostate cancer present, rather than from the cancer. Other very similar-appearing low-risk tumors may progress unexpectedly rapidly, quickly disseminating and becoming incurable.

The divergent behavior of localized prostate cancers creates uncertainty whether to treat immediately. A patient may choose definitive treatment upfront. Surgery (radical prostatectomy), or EBRT are most commonly used to treat patients with localized prostate cancer. Complications most commonly reported with radical prostatectomy or EBRT 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%).

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

Focal Treatment of Localized Prostate Cancer

Given the uncertainty in predicting behavior of individual localized prostate cancers, and the substantial adverse effects associated with definitive treatments in patients with such disease, investigators have sought a middle ground that seeks to minimize morbidity associated with radical treatment in those who may not actually require it 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 in the Background of this Policy) cancerous lesions at high risk of progression, leaving behind uninvolved glandular parenchyma. The overall goal of focal treatment is to minimize the risk of early tumor progression and preserve erectile, urinary, and rectal functions reducing damage to the neurovascular bundles, external sphincter, bladder neck, and rectum. Although focal treatment is offered as an alternative middle approach to management of localized prostate cancer, several key issues must be considered in choosing it. These include patient selection, lesion selection, therapy monitoring, and the modality used to ablate lesions.

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. Thus, appropriate patient selection is imperative for physicians who must decide whether to recommend active surveillance or focal treatment for individual patients who refuse radical therapy or for whom it is not recommended due to the adverse balance of certain harms with unclear long-term benefit.

Proper lesion selection is a second key consideration in choosing to undertake focal treatment of localized prostate cancer. Although prostate cancer has always been regarded as a multifocal disease, clinical evidence shows 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 patients. This view presumably drove the use of region-targeted focal treatment variants, such as hemi-ablation of the half of the gland containing tumor, or subtotal prostate ablation via the "hockey stick" method. While these approaches could 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 usually comprise most of the tumor burden in a patient with organ-confined prostate cancer led to development of the lesion-targeted strategy, which is referred to as "focal therapy" in this Policy. This involves treating only the largest and highest grade tumor (referred to as the "index lesion"), which has been shown in pathologic studies to determine clinical progression of disease. This concept is supported by molecular genetics evidence that suggests a single index tumor focus is usually responsible for disease progression and metastasis. The index lesion approach leaves in place small foci less

than 0.5 cm in volume, with Gleason score less than 7, that are considered unlikely to progress over a 10 to 20 year period. 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 oncologic success of focal therapy. The ability to guide focal ablation energy to the tumor and assess treatment effectiveness, is additionally important to treatment success. At present, no single modality meets the requirements for all 3 activities. Systematic transrectal ultrasound (TRUS)-guided biopsy alone has been investigated, but is considered insufficient for the purpose of patient selection and disease localization for focal therapy. A 5mm transperineal prostate mapping (TPM) biopsy using a brachytherapy template is the current recommended standard by the European Association of Urology in their 2012 guidelines. TPM can provide 3-dimensional coordinates of cancerous lesions, and has about 87% to 95% accuracy rates in detecting and ruling out clinically significant cancer of all sizes. However, TPM is resource intensive, requires general anesthesia, and has been associated with adverse events including urinary retention (6%), prostatitis (4%), and local events such as perineal hematoma, bruising, or pain (5%). The risk of complications of general anesthesia and the cost of processing multiple biopsy specimens have been considered to limit the practicality and widespread applicability of this approach.

Multiparametric magnetic resonance imaging (mp-MRI), 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. Evidence is available to show mp-MRI can detect high grade, large prostate cancer foci with performance similar to TPM. In this cohort study, for the primary end point definition (lesion, 4 mm; and Gleason score, 3+4), with TPM as the reference standard, sensitivity, negative predictive value, and negative likelihood ratios with mp-MRI 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 mp-MRI appears sufficient to rule out clinically significant prostate cancer and may have clinical use in this setting. However, although mp-MRI technology has capability to detect and risk-stratify prostate cancer, several issues constrain its widespread use for these purposes. Thus, it is still necessary to histologically confirm suspicious lesions using TPM; mp-MRI requires highly specialized MRI-compatible equipment; biopsy within the MRI scanner is challenging; and, interpretation of prostate MRI images requires experienced uroradiologists.

Some controversy exists as to the proper end points for focal therapy of prostate cancer. The primary end point of focal ablation of clinically significant disease with negative biopsies evaluated at 12 months after treatment is generally agreed on according to a European consensus report. The clinical validity of MRI to analyze the presence of residual or recurrent cancer compared with histologic findings is offered as a secondary end point. However, MRI findings alone are not considered sufficient in follow-up. Finally, although investigators indicate PSA levels should be monitored, they are not considered as valid end points because the utility of PSA kinetics in tissue preservation treatments has not been established.

Systematic reviews have reported no published prospective, comparative evidence for focal ablation techniques versus current standard treatment of localized prostate cancer. Evidence consists of case series and non-comparative observational studies. Studies were generally small with short follow-up. Data on clinical outcomes such as progression to metastatic disease were not reported for most studies included in the Valerio review. Perioperative outcomes and other adverse events were also poorly reported.

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 1 high-quality systematic review, studies from 1 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 versus current standard treatment of localized prostate cancer, including radical prostatectomy, external-beam radiotherapy (EBRT), 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 effect rates associated with focal therapies appear to be superior to those associated with radical treatments (eg, radical prostatectomy, EBRT), however, evidence is limited in its quality, reporting, and scope. The evidence is insufficient to determine the effects of the technology on health outcomes.

CODING

BlueCHiP for Medicare and Commercial Products

There is not specific CPT code for these treatment, use the unlisted code below following the unlisted process.

53899 Unlisted procedure, urinary system

The following code is not medically necessary.

C9747 Ablation of prostate, transrectal, high intensity focused ultrasound (HIFU), including imaging guidance. (new code effective 7/1/2017)

RELATED POLICIES

Unlisted Procedures

PUBLISHED

Provider Update, June 2017
Provider Update, November 2016
Provider Update, December 2015

REFERENCES

1.Daii'Era MA, Cooperberg MR, Chan JM, et al. Active surveillance for ear1y-stage prostate cancer: review of the current literature. Cancer. Apr 15 2008;112(8):1650-1659. PMID 18306379

2.Bangma CH, Roemeling S, Schroder FH. Overdiagnosis and overtreatment of ear1y detected prostate cancer.Wor1d J Urol. Mar 2007;25(1):3-9. PMID 17364211

3.Johansson JE, Andren 0, Andersson SO, et al. Natural history of early, localized prostate cancer. JAMA. Jun 9 2004;291(22):2713-2719. PMID 15187052

4.Ploussard G, Epstein Jl, Montironi R, et al. The contemporary concept of significant versus insignificant prostate cancer. Eur Urol. Aug 2011;60(2):291-303. PMID 21601982

5.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 1 2008;112(5):971-981. PMID 18186496

6.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

7.Eylert MF, Persad R. Management of prostate cancer. Br J Hosp Med (Lend). Feb 2012;73(2):95-99. PMID 22504752

8.0Eastham JA, Kattan M'N, 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):347-354. PMID
17544572

9.Biii-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):1977-1984. PMID 15888698

10.Thompson IM, Jr., 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):603-610. PMID 23944298

11.Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. JIWIA. May 4 2005;293(17):2095-2101. PMID 15870412

12.Borley N, Feneley MR. Prostate cancer: diagnosis and staging. Asian J Androl. Jan 2009;11(1):74-80. PMID
19050692

13.Freedland SJ. Screening, risk assessment, and the approach to therapy in patients with prostate cancer. Cancer.
Mar 15 2011;117(6):1123-1135. PMID 20960523

14.lp S, IJ D, Chung M ea. An evidence review of active surveillance in men with localized prostate cancer. Evidence Report/Technology Assessment no. 204 (Prepared by Tufts Evidence-based Practice Center under Contract No. HHSA 290-2007-10055-1). 2011;AHRQ Publication No. 12-E003-EF, Rockville, MD: Agency for Research and Quality.(Available at: www.effectiveheaHhcare.ahrq.gov/reportslfinal.cfm.).

15.Thompson I, Thrasher JB, Aus G ea. American Urological Association guideline for management of clinically
localized prostate cancer: 2007 update. 2007; http://www.auanet.org/common/pdf/education/clinical-guidance/Prostate-Cancer.pdf.

16.Whitson JM, Carroll PR. Active surveillance for early-stage prostate cancer: defining the triggers for intervention. J Clin Oncol. Jun 10 2010;28(17):2807-2809. PMID 20439633

17.Albertsen PC. Treatment of localized prostate cancer: 'When is active surveillance appropriate? Nat Rev Clin Oncol. Jul2010;7(7):394-400. PMID 20440282

18.Jacome-Pita F, Sanchez-Salas R, Barret E, et al. Focal therapy in prostate cancer: the current situation. Ecancerrnedicalscience. 2014;8:435. PMID 24944577

19.Nguyen CT, Jones JS. Focal therapy in the management of localized prostate cancer. BJU Int. May 2011;107(9):1362-1368. PMID 21223478

20.Lindner U, Lawrentschuk N, Schatloff 0, et al. Evolution from active surveillance to focal therapy in the management of prostate cancer. Future Oncol. Jun 2011;7(6):775-787. PMID 21675840

21.lberti 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

22.Lecornet E, Ahmed HU, Moore CM, et al. Conceptual basis for focal therapy in prostate cancer. J Endourol. May 2010;24(5):811-818. PMID 20443699

23.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. Mar 12 2015. PMID 25768694

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

25.Scales CD, Jr., Presti JC, Jr., 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):1249-1252. PMID 17698131

26.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):906-910. PMID 17587207

27.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):91-95. PMID 17375971

28.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. Mar2008;38(3):192-199. PMID 18281309

29.Kasivisvanathan V, Emberton M, Ahmed HU. Focal therapy for prostate cancer: rationale and treatment opportunities. Clin Oncol (R Coli Radiol). Aug 2013;25(8):461-473. PMID 23759249

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):1074-1085. 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):205-215. PMID 19352395

32.Liu W, Laitinen S, KhanS, et al. Copy number analysis indicates monoclonal origin of lethal metastatic prostate cancer. Nat Med. May 2009;15(5):559-565. PMID 19363497

33.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):644-649. PMID 21937078

34.Ahmed HU, Emberton M. Active surveillance and radical therapy in prostate cancer: can focal therapy offer the
middleway?Wor1d J Urol. Oct 2008;26(5):457-467. PMID 18704441

35.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 1 1993;71(3 Suppl):933-938. PMID 7679045

36.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):1169-1172. PMID 16686706

37.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):1078-1083. PMID 24444476

38.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. Mar-Apr 2011;29(2):166-170. PMID
19451000

39.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 1 2012;72(11):1179-1186. PMID 22161896

40.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):E64-68. PMID 22093108

41.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 12012;72(8):925-930. PMID 21965006

42.Heidenreich A, Bastian, PJ, Bellmunt, J, et al. European Association of Urology 2012 guidelines on prostate cancer (available at: http/lwww.uroweb.org/guidelines/online-guidelinesl) Accessed March 30, 2015. Crawford ED, Rove KO, Barqawi AB, et al.

43.Clinical-pathologic correlation between transperineal mapping biopsies of the prostate and three-dimensional reconstruction of prostatectomy specimens. Prostate. May 2013;73(7):778-787. PMID 23169245

44.Hu Y, Ahmed HU, Carter T, et al. A biopsy simulation study to assess the accuracy of several transrectal ultrasonography (TRUS)-biopsy strategies compared with template prostate mapping biopsies in patients who have undergone radical prostatectomy. BJU Int. Sep 2012;110(6):812-820. PMID 22394583

45.Tsivian M, Abem MR, Qi P, et al. Short-term functional outcomes and complications associated with transperineal template prostate mapping biopsy. Urology. Jul2013;82(1):166-170. PMID 23697794

46.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):761-769. PMID 23564713

47.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):477-494. PMID 21195536

48.Nationallnstitue for Health and Care Excellence (NICE). Focal Therapy Using Cryoablation for Localised Prostate Cancer (IPG423). 2012; https:/lwww.nice.org.uk/guidance/ipg423/chapter/1-guidance. Accessed March, 2015.

49.Nationallnstitue for Health and Care Excellence (NICE). Focal Therapy Using High-Intensity Focused Ultrasound for Localized Prostate Cancer (IPG424). 2012; http://www.nice.org.uklguidance/ipg424. Accessed Mach, 2015.

50.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

51.Hand L. FDA Panel Pans HIFU for Prostate Cancer. Jul 31, 2014. Medscape Medical News 2014, WebMD, LLC
http://www.medscape.com/viewarticle/829179. Accessed March, 2015.

52.Valerio M, Ahmed HU, Emberton M, et al. The role of focal therapy in the management of localised prostate cancer: a systematic review. Eur Urol. Oct 2014;66(4):732-751. PMID 23769825

53.Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta- analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol. Oct 2009;62(1O):e1-34. PMID 19631507

54.Roach M, 3rd, Hanks G, Thames H, Jr., et al. Defining biochemical failure following radiotherapy with onvithout hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix Consensus Conference. lnt J Radiat Oncol Bioi Phys. Jul15 2006;65(4):965-974. PMID 16798415

55.American Urological Association (AUA). Guideline for the Management of Clinically Localized Prostate Cancer. 2011; https:/lwww.auanet.org/educationlguidelines/prostate-cancer.cfm. Accessed March, 2015.

56.National Cancer Institute. Prostate Cancer Treatment, Treatment Option Overview. 2014; http:/lwww.cancer.gov/cancertopics/pdqltreatment/prostate/Patient/page4# _172. Accessed March, 2015.

57.National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: prostate cancer. Version 3.2016. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed August 8, 2016.

58. National Institute for Health and Care Excellence (NICE). Prostate cancer: diagnosis and management (CG175). 2014; https://www.nice.org.uk/guidance/cg175/resources/prostate-cancer-diagnosis-and-management-35109753913285. Accessed August 8, 2016.

59. Lepor H, Llukani E, Sperling D, et al. Complications, recovery, and early functional outcomes and oncologic control following in-bore focal laser ablation of prostate cancer. Eur Urol. Dec 2015;68(6):924-926. PMID 25979568

CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS