

Protocol

Saturation Biopsy for Diagnosis, Staging, and Management of Prostate Cancer

(701121)

Medical Benefit		Effective Date: 01/01/15	Next Review Date: 11/19
Preauthorization	No	Review Dates: 09/09, 03/10, 01/11, 01/12, 01/13, 01/14, 11/14, 11/15, 11/16, 11/17, 11/18	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none">• With suspected prostate cancer	Interventions of interest are: <ul style="list-style-type: none">• Initial saturation biopsy	Comparators of interest are: <ul style="list-style-type: none">• Standard biopsy	Relevant outcomes include: <ul style="list-style-type: none">• Overall survival• Disease-specific survival• Test accuracy• Treatment-related morbidity
Individuals: <ul style="list-style-type: none">• With suspected prostate cancer	Interventions of interest are: <ul style="list-style-type: none">• Repeat saturation biopsy	Comparators of interest are: <ul style="list-style-type: none">• Standard biopsy	Relevant outcomes include: <ul style="list-style-type: none">• Overall survival• Disease-specific survival• Test accuracy• Treatment-related morbidity
Individuals: <ul style="list-style-type: none">• With prostate cancer who are candidates for active surveillance	Interventions of interest are: <ul style="list-style-type: none">• Saturation biopsy	Comparators of interest are: <ul style="list-style-type: none">• Standard biopsy	Relevant outcomes include: <ul style="list-style-type: none">• Overall survival• Disease-specific survival• Test accuracy• Treatment-related morbidity

DESCRIPTION

Saturation biopsy of the prostate, in which more cores are obtained than by standard biopsy protocol, has been proposed in the diagnosis (for initial or repeat biopsy), staging, and management of patients with prostate cancer.

SUMMARY OF EVIDENCE

For individuals who have suspected prostate cancer who receive initial saturation biopsy, the evidence includes randomized controlled trials, observational studies, and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, test accuracy, and treatment-related morbidity. A 2013 systematic review found higher rates of cancer detection with saturation biopsy than with extended biopsy overall, but, in the subgroup of men with prostate-specific antigen levels less than 10 ng/mL, the degree of difference was small and possibly not clinically significant. Health outcomes (e.g., survival rate) were not reported. Although several studies were published after the systematic review, none showed that initial saturation biopsy improved the

detection of clinically significant cancers and none reported progression or survival outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have suspected prostate cancer who receive repeat saturation biopsy, the evidence includes observational studies and a systematic review. Relevant outcomes are overall survival, disease specific survival, test accuracy, and treatment-related morbidity. Several studies have compared saturation with standard prostate biopsies in the repeat biopsy setting and have found significantly higher detection rates with saturation biopsy. However, at least one study found that about one-third of the positive findings with saturation biopsy were clinically insignificant cancers. Moreover, studies of saturation biopsy as the repeat prostate biopsy strategy focused on cancer detection rates and did not report health outcomes (e.g., progression or survival). Evidence is lacking as to whether saturation biopsy leads to improved health outcomes, including the possibility of detecting clinically insignificant cancers, which could lead to unnecessary treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have prostate cancer and are candidates for active surveillance who receive saturation biopsy, the evidence includes two nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy, and treatment-related morbidity. Both studies retrospectively compared standard biopsy with saturation biopsy for selecting patients for active surveillance; neither found that saturation biopsy improved the ability to select patients. In one study, biopsy method was not a significant predictor of upstaging and, in the other study, biopsy method was not significantly associated with selecting patients with a high Gleason score. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

Saturation biopsy is considered **investigational** in the diagnosis, staging, and management of prostate cancer.

POLICY GUIDELINES

Saturation biopsy is generally considered to be obtaining more than 20 biopsy tissue cores from the prostate in a systematic manner; it is occasionally defined as obtaining more than 18 biopsy tissue cores.

BACKGROUND

PROSTATE CANCER

Prostate cancer is common and is the second leading cause of cancer-related deaths in men in the United States.

Diagnosis

The diagnosis of prostate cancer is made by biopsy of the prostate gland. The approach to biopsy has changed over time, especially with the advent of prostate-specific antigen screening programs that identify cancer in prostates that are normal to palpation and to transrectal ultrasound. For patients with an elevated prostate-specific antigen level but with a normal biopsy, questions exist about subsequent evaluation, because repeat biopsy specimens may be positive for cancer in a substantial percentage of patients.

In the early 1990s, use of sextant biopsies involving six random, evenly distributed biopsies became the standard approach to diagnose prostate cancer. In the late 1990s, as studies showed high false-negative rates for this strategy (missed cancers), approaches were developed to increase the total number of biopsies and to change the location of the biopsies. While there is disagreement about the optimal strategy, most would agree that initial prostate biopsy strategies should include at least 10 to 14 cores. Additional concerns have been raised about

drawing conclusions about the stage (grade) of prostate cancer based on limited biopsy specimens. Use of multiple biopsies has also been discussed as an approach to identify tumors that may be eligible for subtotal cryoablation therapy.

At present, many practitioners use a 12- to 14-core “extended” biopsy strategy for patients undergoing initial biopsy. This extended biopsy is done in an office setting and allows for more extensive sampling of the lateral peripheral zone; a sampling of the lateral horn might increase the cancer detection rate by approximately 25%.¹

Another approach to increasing the number of biopsy tissue cores is “saturation” biopsy. In general, saturation biopsy is considered as more than 20 cores taken from the prostate, with an improved sampling of the anterior zones of the gland, which may be undersampled in standard peripheral zone biopsy strategies and might lead to missed cancers. Saturation biopsy might be performed transrectally or transperineally; the transperineal approach is generally performed as a stereotactic template-guided procedure with general anesthesia.

Surveillance

In addition to the diagnosis of prostate cancer, some have suggested that saturation biopsy could be a part of active surveillance (a treatment approach that involves surveillance with prostate-specific antigen, digital rectal exam, and routine prostate biopsies in men whose cancers are small and expected to behave indolently). Saturation biopsy has the potential to identify tumor grade more accurately than standard biopsy.

REGULATORY STATUS

Saturation biopsy is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration.

RELATED PROTOCOL

Whole Gland Cryoablation of Prostate Cancer

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Zaytoun OM, Jones JS. Prostate cancer detection after a negative prostate biopsy: lessons learnt in the Cleveland Clinic experience. *Int J Urol.* Aug 2011;18(8):557-568. PMID 21692866

2. Jiang X, Zhu S, Feng G, et al. Is an initial saturation prostate biopsy scheme better than an extended scheme for detection of prostate cancer? A systematic review and meta-analysis. *Eur Urol*. Jun 2013;63(6):1031-1039. PMID 23414775
3. Xue J, Qin Z, Cai H, et al. Comparison between transrectal and transperineal prostate biopsy for detection of prostate cancer: a meta-analysis and trial sequential analysis. *Oncotarget*. Apr 04 2017;8(14):23322-23336. PMID 28177897
4. Li YH, Elshafei A, Li J, et al. Transrectal saturation technique may improve cancer detection as an initial prostate biopsy strategy in men with prostate-specific antigen <10 ng/ml. *Eur Urol*. Jun 2014;65(6):1178-1183. PMID 23768632
5. Li YH, Elshafei A, Li J, et al. Potential benefit of transrectal saturation prostate biopsy as an initial biopsy strategy: decreased likelihood of finding significant cancer on future biopsy. *Urology*. Apr 2014;83(4):714-718. PMID 24680442
6. Eichler K, Hempel S, Wilby J, et al. Diagnostic value of systematic biopsy methods in the investigation of prostate cancer: a systematic review. *J Urol*. May 2006;175(5):1605-1612. PMID 16600713
7. Mabweesh NJ, Lidawi G, Chen J, et al. High detection rate of significant prostate tumours in anterior zones using transperineal ultrasound-guided template saturation biopsy. *BJU Int*. Oct 2012;110(7):993-997. PMID 22394668
8. Lee MC, Moussa AS, Zaytoun O, et al. Using a saturation biopsy scheme increases cancer detection during repeat biopsy in men with high-grade prostatic intra-epithelial neoplasia. *Urology*. Nov 2011;78(5):1115-1119. PMID 22054382
9. Zaytoun OM, Moussa AS, Gao T, et al. Office based transrectal saturation biopsy improves prostate cancer detection compared to extended biopsy in the repeat biopsy population. *J Urol*. Sep 2011;186(3):850-854. PMID 21788047
10. Linder BJ, Frank I, Umbreit EC, et al. Standard and saturation transrectal prostate biopsy techniques are equally accurate among prostate cancer active surveillance candidates. *Int J Urol*. Sep 2013;20(9):860-864. PMID 23278942
11. Quintana L, Ward A, Gerrin SJ, et al. Gleason misclassification rate is independent of number of biopsy cores in systematic biopsy. *Urology*. May 2016;91:143-149. PMID 26944351
12. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer Early Detection. Version 2.2018. https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf. Accessed June 7 2018.
13. U.S. Preventive Services Task Force (USPSTF). Archived: Prostate Cancer: Screening. 2012 May; <https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/prostate-cancer-screening>. Accessed June 7, 2018.
14. U.S. Preventive Services Task Force (USPSTF). Final Recommendation Statement: Prostate Cancer: Screening. 2018 May; <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prostate-cancer-screening1>. Accessed June 8, 2018.