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Saturation Biopsy for Diagnosis, Staging and Management of Prostate Cancer, Including Comprehensive 3D Mapping with Biopsy

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Related Policies (if applicable)
None

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Coverage

Saturation biopsy or comprehensive 3D (three-dimensional) mapping with biopsy of the prostate **may be considered medically necessary** for men with a prior non-diagnostic transrectal ultrasound guided biopsy (performed within the prior 12 months) and one or more of the following:

- Elevated prostate specific antigen (PSA) that is persistently rising; OR
- Histologic evidence of atypia on prior prostate biopsy; OR
- Histologic findings of high-grade prostatic intraepithelial neoplasia (PIN) on prior biopsy; OR
- Findings of a palpable lesion on digital rectal examination (DRE).

Saturation biopsy or comprehensive 3D mapping with biopsy of the prostate **is considered experimental, investigational and/or unproven** for all other indications.

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. CPT code (effective in 2009) 55706 may be utilized for this service.

The procedure may be also reported with CPT code 55700 when it is performed without stereotactic template guidance. Ultrasound guidance may be the method utilized, which would be reported using CPT code 76942.

Category III code 0443T reflects a biopsy system (ClariCore™) that is not approved by the U.S. Food and Drug Administration and can be used during the saturation biopsy procedure.

As of 1/1/2015, the following HCPCS codes were deleted – G0417, G0418, and G0419. HCPCS code G0416 was revised by removing the number of specimens (10-20) from the description. Although not specific to saturation biopsies, G0416 may be used for surgical pathology associated with this procedure as well as other prostate needle biopsies.

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. Saturation biopsy is meant to describe more than 12 specimens being obtained from the prostate through the rectum under ultrasound guidance. Saturation biopsy is typically done in the operating room under general or spinal anesthesia. The number of specimens obtained, and the location from which they were taken, is subjective in technique. The medical community believes there is a distinct difference between the term saturation biopsy and comprehensive 3D (three-dimensional, 3-dimensional) mapping biopsy.

Background

Prostate cancer is a common cancer and is the second leading cause of cancer-related deaths in men in the U.S.

Diagnosis

The diagnosis of prostate cancer is made by the biopsy of the prostate gland. The approach to biopsy has changed over time, especially with the advent of prostate-specific antigen (PSA) screening programs that identify cancer in prostates that are normal to palpation (digital rectal exam; DRE) and to transrectal ultrasound. For patients with an elevated PSA 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 6 random, evenly distributed biopsies became the standard approach to diagnosis 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; sampling of the lateral horn might increase the cancer detection rate by approximately 25%. (1)

Another approach to increase the number of biopsy tissue cores is the use of "saturation" biopsy. In general, saturation biopsy is considered as more than 20 cores taken from the prostate, with improved sampling of the anterior zones of the gland, which may be under-sampled 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.

Comprehensive 3D mapping prostate biopsy, while also performed under general or spinal anesthesia, is comprehensive and objective. The comprehensive 3D mapping places the prostate in a virtual 3D grid. Under transrectal ultrasound imaging, the prostate is positioned on the perineal template grid using the X and Y coordinates corresponding to the template grid. Biopsies are taken from the prostate according to the template coordinates and systematically recorded for the pathologist to identify the exact location from which they were obtained from the prostate gland. The number of specimens obtained is dependent on the size of the prostate gland. Typically, 1 biopsy sample is taken for every 1.25 gram of prostate volume.

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 (FDA). The ClariCore™ Biopsy System (Precision Biopsy, Aurora, CO) has not been approved by the FDA. The needle in the ClariCore™ Handpiece contains a single optical fiber that transmits light of different wavelengths to illuminate the tissue to

enable rapid spectral analysis. Spectral analysis, in turn, may help determine if the tissue is normal or possibly suspicious. This could reduce the need for tissue samples and related pathology of normal tissue. This system can be used during the saturation biopsy procedure.

Rationale

This policy was created in 2013 and has been updated regularly with searches of the PubMed database, most recently through May 20, 2022. The following is a summary of the key literature.

Medical policies assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Medical policies assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Initial or Repeat Saturation Biopsy

Clinical Context and Test Purpose

The proposed clinical utility of saturation biopsy for the diagnosis of prostate cancer is to improve health outcomes by detecting more clinically significant cancers and intervening appropriately. To evaluate the impact of saturation biopsy on the net health outcome, studies are needed that compare rates of clinically significant prostate cancers detected using saturation biopsy versus other biopsy methods.

The question addressed in this medical policy is: In individuals with suspected prostate cancer, does initial or repeat saturation biopsy improve the diagnosis of patients with clinically significant prostate cancer and lead to improved patient management decisions and health outcomes?

The following PICO was used to select literature to inform this policy. They apply to the first two indications: initial or repeat saturation biopsy.

Populations

The relevant population of interest is patients with suspected prostate cancer.

Interventions

The therapy being considered is an initial or repeat saturation biopsy. Saturation biopsy is generally considered 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. Saturation biopsy can be performed transrectally or transperineally; the transperineal approach is generally performed as a stereotactic template-guided procedure with general anesthesia.

Comparators
The following practice is currently being used: standard biopsy.

Outcomes
The general outcomes of interest are test accuracy, overall survival, disease-specific survival, and treatment-related morbidity.

Specific outcomes are improving the detection of clinically significant prostate cancer; increasing accurate risk stratification; and reducing the overdiagnosis of indolent tumors requiring only active surveillance. These are outcomes of primary interest because they would inform the patient's treatment plan and consequently, impact health outcomes.

Change in detection rate alone is not sufficient to determine the impact of saturation biopsy on health outcomes compared with other biopsy methods. With higher detection rates, there is the possibility of detecting clinically insignificant cancers, which could lead to unnecessary treatment. False-positive test results can lead to overdiagnosis and overtreatment, which exposes patients to potential treatment morbidity without benefit. False-negative test results can lead to failure to diagnose clinically significant cancers that require definitive treatment. In addition, studies would ideally evaluate the impact of saturation biopsy on health outcomes such as disease progression or mortality.

Diagnostic accuracy is a short-term outcome. Survival outcomes would be measured over the long-term (e.g., 5- or 10-year survival).

Table 1. Outcomes of Interest for Individuals with Suspicion of Prostate Cancer

Outcomes	Details
Test accuracy	Overall prostate cancer detection, clinically significant prostate cancer detection, sensitivity, and specificity [Timing: ≥1 week]
Health Outcomes	Overall survival, disease-specific survival, treatment-related morbidity [Timing: 5 to 10 years]

Study Selection Criteria
For the evaluation of clinical validity of the saturation biopsy test, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores).
- Included a suitable reference standard.
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Initial Saturation Biopsy

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Systematic Reviews

The literature of diagnostic accuracy consists of studies reporting prostate cancer detection rates or diagnostic yields as a primary outcome. These data were summarized in a 2013 systematic review by Jiang et al. on the utility of an initial transrectal saturation biopsy compared with an extended biopsy strategy. (2) Eight studies (N=11,997 participants) met eligibility criteria (i.e., compared 2 biopsy strategies on initial biopsy). Two of the studies were randomized controlled trials (RCTs), one used a paired design, and 5 were nonrandomized trials. Overall, prostate cancer was diagnosed in 2328 (42.4%) of 5486 men who underwent saturation biopsy compared with 2562 (39.3%) of 6511 men who had extended biopsy. The detection rate was statistically significantly higher in the saturation biopsy group (risk difference [RD], 0.004; 95% confidence interval [CI], 0.01 to 0.008; p=0.002). When only the higher quality studies were analyzed (i.e., the RCTs and prospective paired design), the detection rate remained statistically significantly higher for saturation biopsy (RD=0.03; 95% CI, 0.01 to 0.05; p=0.01). Subgroup analysis found that the difference in detection rates between saturation and extended biopsy strategies was limited to the subgroup of men with prostate-specific antigen (PSA) levels less than 10 ng/mL. Within this group, prostate cancer was diagnosed in 998 (38%) of 2597 men who had saturation biopsies and in 1135 (34%) of 3322 men with extended biopsies (RD=0.04; 95% CI, 0.01 to 0.07; p=0.002). Although the subgroup analyses included individual risk factors such as PSA level, they did not differentiate between detection of lower and higher risk prostate cancers. In addition, differences in health outcomes (e.g., progression-free survival [PFS], overall survival [OS]) were not reported.

A related meta-analysis was published by Xue et al. (2017). (3) Reviewers evaluated the literature comparing transrectal and transperineal biopsy approaches for the detection of prostate cancer. In an analysis stratified by the number of biopsy cores, there was no significant difference in the prostate cancer detection rate with the transrectal strategy or the transperineal biopsy strategy in studies using extended biopsy (odds ratio, 1.14; 95% CI, 0.89 to 1.45) or studies using saturation biopsy (odds ratio, 1.11; 95% CI, 0.92 to 1.34).

Observational Studies

A 2014 retrospective nonrandomized study by Li et al. reviewed data on 438 men who received an initial saturation biopsy and 3338 men who had an initial extended prostate biopsy. (4) In an analysis stratified by PSA levels, there was a statistically significantly higher rate of prostate cancer detection using a saturation biopsy strategy in men with a PSA level less than 10 ng/mL. Detection rates among men with a PSA level less than 4 ng/mL were 47.1% (40/85) with saturation biopsy and 32.8% (288/878) with extended biopsy (p=0.008). Rates among men with PSA levels between 4 ng/mL and 9.9 ng/mL were 50.9% (144/283) with saturation biopsy and 42.9% (867/2022) with extended biopsy (p=0.011). There was no statistically significant

difference in detection rates between groups when PSA levels were greater than 10 ng/mL. Detection rates at PSA levels greater than 10/ng/mL were 60% (42/70) with saturation biopsy and 61% (267/438) with extended biopsy (p=0.879).

A related 2014 study by Li et al. evaluated the potential benefit of saturation biopsy as the initial prostate biopsy strategy by examining the yield of repeat saturation biopsy in men with initial negative findings by either saturation or extended prostate biopsy. (5) A total of 561 men were included in the study; the initial strategy was saturation biopsy in 81 men and extended biopsy in 480 men. In all cases, saturation biopsy was used for the first repeat biopsy. The overall prostate cancer detection rates were 19.8% in the group with initial saturation biopsy and 34.8% in the group with initial extended biopsy (p=0.008). Low-risk prostate cancer was defined using the Epstein criteria (i.e., Gleason score ≤6, PSA density of ≤0.15 g/mL per gram, <3 positive cores, and >50% cancer involvement in a single core). The number of intermediate- and/or high-risk prostate cancers (i.e., not low-risk) identified at first repeat biopsy was 4 (4.9%) of 81 in the initial saturation biopsy group and 85 (17.3%) of 490 in the initial extended biopsy group (p=0.048). The statistically significantly lower prostate cancer detection rate among men who initially underwent saturation biopsy would suggest that initial saturation biopsy might be less likely to miss prostate cancer than extended biopsy, and, in this study, prostate cancer diagnosed by repeat saturation after negative initial saturation biopsy was more likely to be clinically insignificant. However, the study indirectly evaluated the initial biopsy, and the number of events in men who underwent an initial saturation biopsy was relatively small.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No direct evidence from studies comparing the impact of saturation biopsy with standard biopsy for patient management decisions or health outcomes in patients with suspected prostate cancer was identified.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the evidence is insufficient to demonstrate the detection of clinically significant cancers with saturation biopsy, no inferences can be made about clinical utility.

Subsection Summary: Initial Saturation Biopsy

Studies on saturation biopsy as the initial prostate biopsy strategy were summarized in a 2013 systematic review of 8 studies (2 were RCTs). The prostate cancer detection rate was significantly higher in men with saturation biopsy than in men with standard biopsy. In a subgroup analysis, the systematic review found that the higher detection rate was limited to men with PSA levels less than 10 ng/mL. Health outcomes (e.g., survival rate) were not reported. Although several studies were published after the systematic review, none showed that initial saturation biopsy detected more clinically significant cancers and none reported progression or survival outcomes.

Repeat Saturation Biopsy

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Systematic Review

In 2006, Eichler et al. published a systematic review of cancer detection rates and complications of various prostate biopsy strategies. (6) They pooled data that compared various extended biopsy schemes for studies involving 20,698 patients. Reviewers concluded that prostate biopsy schemes consisting of 12 cores that add laterally directed cores to the standard sextant scheme seem to have the right balance between the cancer detection rate and adverse events, and that taking more than 12 cores added no significant benefit.

Observational Studies

Representative studies of saturation biopsy in repeat prostate biopsies follow. These studies focused on cancer detection rates and did not report health outcomes (e.g., overall survival [OS], progression-free survival [PFS]).

Mabjeesh et al. (2012) reported on a high-risk group of men with at least 2 previous negative transrectal biopsies who then underwent transperineal template-guided saturation biopsy. (7) Prostate cancer was detected in 24 (26%) of the 92 patients, predominantly in the anterior zones. A median of 30 cores was taken in the saturation biopsies. Gleason scores of 7 or higher were detected in 11 (46%) of the diagnosed men. Most tumors (83.3%) were found in the anterior zones of the gland, with a significantly higher number of positive cores than in the posterior zones (mean, 4.9 versus 1.5, p=0.015).

Lee et al. (2011) evaluated the role of transrectal saturation biopsy for cancer detection in men with high-grade prostatic intraepithelial neoplasia diagnosed by extended biopsy. (8) From 1999 to 2009, 314 men had at least 1 or more repeat biopsies due to the presence of exclusive high-grade prostatic intraepithelial neoplasia (without any other pathologic finding) in a previous extended biopsy. They were divided into 2 groups according to the initial follow-up biopsy scheme; 178 men were followed using a second standard extended biopsy scheme, and 136 were followed using the saturation biopsy scheme. In the standard repeat biopsy group, 35 (19.7%) of 178 men had cancer on initial repeat biopsy. In the saturation biopsy group, 42

(30.9%) of 136 had cancer on initial repeat biopsy (overall, p=0.04). Multivariate analysis demonstrated that the biopsy scheme on repeat biopsy was an independent predictor of prostate cancer detection (odds ratio, 1.85; 95% CI, 1.03 to 3.29), exclusive of age, PSA level, days from initial biopsy, digital rectal exam status, and multifocal prostatic epithelial neoplasia. Pathologic findings on repeat biopsies demonstrated similar Gleason scores, regardless of biopsy technique: a Gleason score of 6 was present in 74.3% and 73.1% of specimens in the standard and saturation schemes, respectively. The presence of a Gleason score of 8 or higher was 8.6% and 9.5%, respectively.

Zaytoun et al. (2011) reported the results of a prospective, nonrandomized comparative study of extended biopsy versus office-based transrectal saturation biopsy in a repeat biopsy population. (9) After an initially negative biopsy, 1056 men underwent a repeat 12- to 14-core biopsy (n=393) or a 20- to 24-core repeat biopsy (n=663) at the discretion of the attending urologist's practice pattern. Indications for second biopsy included a previous suspicious pathologic finding and/or clinical indications such as abnormal digital rectal exam, persistently increased PSA level, and PSA level increasing more than 0.75 ng/mL annually. Prostate cancer was detected in 29.8% (n=315) of repeat biopsies. The saturation biopsy group had a detection rate of 32.7% versus 24.9% in the extended biopsy group (p=0.008). Of the 315 positive biopsies, 119 (37.8%) revealed clinically insignificant cancer (defined as Gleason score <7, total of ≤3 positive cores, and maximum of ≤50% of cancer in any positive core). There was a trend toward increased clinically insignificant cancer detection for saturation biopsy (40.1%) versus extended biopsy (32.6%; p=0.02).

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No direct evidence from studies comparing the impact of saturation biopsy with standard biopsy for patient management decisions or health outcomes in patients requiring a repeat biopsy for suspected prostate cancer was identified.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the evidence is insufficient to demonstrate the detection of clinically significant cancers with saturation biopsy, no inferences can be made about clinical utility.

Subsection Summary: Repeat Saturation Biopsy

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. 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).

Localized Disease

There also are discussions of using saturation biopsy as a technique to identify a localized area of prostate cancer that could be treated with subtotal cryoablation. However, given the limited data on the efficacy of this treatment approach, using saturation biopsy to determine if localized disease is present would be considered experimental, investigational and/or unproven without prior negative biopsies or additional key diagnostic features of prostate cancer.

Active Surveillance

Clinical Context and Test Purpose

The proposed clinical utility of saturation biopsy is to improve health outcomes by better identifying patients with prostate cancer who are appropriate candidates for active surveillance through more accurate determination of the Gleason score.

The question addressed in this medical policy is: In individuals with prostate cancer who are candidates for active surveillance, does saturation biopsy improve the identification of tumor grade and improve health outcomes compared with standard biopsy?

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

Populations

The relevant population of interest are patients with prostate cancer who are potential candidates for active surveillance.

Interventions

The test being considered is a saturation biopsy. Saturation biopsy is generally considered 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. Saturation biopsy can be performed transrectally or transperineally; the transperineal approach is generally performed as a stereotactic template-guided procedure with general anesthesia.

Comparators

The following practice is currently being used: standard biopsy.

Outcomes

The general outcomes of interest are test accuracy, overall survival, disease-specific survival,

And treatment-related morbidity.

The Gleason score is a criterion used to select men for active surveillance. More accurate selection of patients for active surveillance could lead to better health outcomes by reducing misclassification of patients as being a sufficiently low-risk that active surveillance is an appropriate approach to patient management.

Diagnostic accuracy is a short-term outcome. Survival outcomes would be measured over the long-term (e.g., 5- or 10-year survival).

Study Selection Criteria

For the evaluation of clinical validity of the saturation biopsy test, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores).
- Included a suitable reference standard.
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Observational Studies

Several studies have evaluated the accuracy of saturation biopsy for identifying patients who might be suitable candidates for active surveillance. Linder et al. (2013) reviewed data on 500 consecutive patients who underwent standard template prostate biopsy (12 cores) or saturation biopsy (at least 18 cores) before radical prostatectomy. (10) They identified 218 patients who would have been candidates for active surveillance. Criteria were a Gleason score no greater than 6, clinical stage T1 or T2a, PSA level less than 10 ng/mL, and involvement of no more than 33% of cores. Among these 218 patients, 124 had undergone standard biopsy and 94 underwent saturation biopsy. In a multivariate analysis, biopsy method was not a significant predictor of upstaging on analysis of pathologic findings (p=0.26). In addition, the 5-year biochemical failure-free survival rates (defined as PSA level of at least 0.4 ng/mL) did not differ significantly between groups: rates were 97% for standard biopsy and 95% for saturation biopsy (p=0.11).

Quintana et al. (2016) compared 12-core biopsy and saturation biopsy (18-33 cores; median, 20 cores) in 375 patients to determine the Gleason score accurately. (11) The authors stated that patients with Gleason scores of 4 or higher were generally not considered candidates for active surveillance. Gleason score was confirmed by pathologic analysis of prostate specimens. For detecting a high Gleason grade (i.e., ≥4), there were no statistically significant differences in the sensitivity, specificity, negative predictive value, or positive predictive value of 12-core versus

saturation biopsies. The areas under the receiver operating characteristic curve were 0.82 for saturation biopsy and 0.84 for 12-core biopsy (p value not reported).

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No direct evidence from studies comparing the impact of saturation biopsy with standard biopsy for patient management decisions or health outcomes in patients with prostate cancer being considered for active surveillance was identified.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the evidence is insufficient to demonstrate that saturation biopsy improves the identification of tumor grade, no inferences can be made about clinical utility.

Review and Other Articles Focused on Comprehensive 3D (Three-Dimensional) Mapping and Biopsy

Several additional studies were reviewed and other articles were evaluated focusing on 3D mapping with biopsy. The following table is an outcome summary of those articles.

Table 2. Published Outcome Summaries of 3D Mapping with Biopsy of Prostate

Author and Study Title	Journal and Publication M/Y	Summary
Moran et al., Re-biopsy of the prostate using a stereotactic transperineal technique (12)	The Journal of Urology (2006 October)	180 consecutive patients with increasing total PSA and one benign transrectal prostate biopsy revealed 68 patients with adenocarcinoma. This was 38% of the patients with a confirmed diagnosis with only the one prior biopsy.
Nafie et al., Transperineal template prostate biopsies in men with	World Journal of Urology (2014 August)	Retrospective review of 122 patients revealed 71 patients confirmed prostate cancer (58%).

raised PSA despite two previous sets of negative TRUS-guided prostate biopsies (13)		
Taira et al., Performance of transperineal template-guided mapping biopsy in detecting prostate cancer in the initial and repeat biopsy setting (14)	Prostate Cancer and Prostate Disease (2010 March)	373 consecutive patients studied. 294 men with ≥ 1 prior negative biopsy and 79 men as the initial biopsy. Cancer detection in initial biopsy was 75.9%. For men with 1, 2, and > or =3 prior negative biopsies detection rates were 55.5%, 41.7%, and 34.4%, respectively. In all, 55.5% of the cancers detected were Gleason score of > or = 7.
Ayres et al., The role of transperineal template prostate biopsies in restaging men with prostate cancer managed by active surveillance (15)	BJU International (2012 April)	101 patients in active surveillance underwent restaging biopsies. 34% had more significant prostate cancer when compared to transrectal biopsies.
Nam et al., Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy (16)	The Journal of Urology (2013 January)	75,190 patients had transrectal biopsy to confirm prostate cancer, of which 33, 508 (44.6%) were diagnosed with prostate cancer. The hospital admission rate for complications within 30 days following the biopsy was 1.9% for those without cancer. The abstract did not cite for those with cancer. The majority of admissions were for infection.
Pepe et al., Prostate biopsy: results and advantages of the transperineal approach—twenty-year experience of a single center (17)	World Journal of Urology (2014 April)	4000 patients had transperineal biopsy of prostate following suspicious digital exam or increasing PSA. Results indicated that a higher number of significant cancer diagnosis was found in the anterior zone biopsies (15% of the cases).

Grummet et al., Sepsis and 'superbugs': should we favor the transperineal over the transrectal approach for prostate biopsy (18)	BJU International (2014 September)	Retrospective review of pooled data for 245 transperineal biopsies. The rate of readmission following procedure was zero. The study cites that literature shows the rate of sepsis however is rising for TRUS biopsy and is as high as 5%. The data reviewed in this study showed zero for sepsis readmissions.
Barqawi et al., The role of 3-dimensional mapping biopsy in decision making for treatment of apparent early stage prostate cancer (19)	The Journal of Urology (2011 July)	180 cases were prospectively reviewed. The authors found that using 3D mapping enabled a number of patients (44) with low-risk disease to elect for surveillance rather than a more active course of treatment.
Numao et al., Characteristics and clinical significance of prostate cancer missed by initial transrectal 12-core biopsy (20)	BJU International (2012 March)	715 patients with high PSA or abnormal digital exam had either a transrectal or transperineal biopsy. The authors concluded transrectal biopsies were probably low-grade and low-volume disease, whereas initial transrectal has a small, but definite risk of missing anterior significant cancers.

Table Key:
3D: three dimensional;
M/Y; month and year;
PSA: prostate-specific antigen;
TRUS: transrectal ultrasound**.**

Subsection Summary: Review and Other Articles Focused on Comprehensive 3D Mapping and Biopsy

These studies confirm the utility and favorable outcomes of comprehensive 3D mapping and biopsy in select patients to accurately sample nonpalpable lesions within the prostate and unexplained rising total PSA results. Complications from this type of prostate sampling have been minimized with nominal post-biopsy pain and reduced urinary retention episodes. Confirmed higher rate of prostate cancer diagnosis, particularly in the anterior zone, was achieved, enabling comprehensive 3D mapping with biopsy as a technique for requiring more aggressive therapy or elect surveillance.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in May 2022 did not identify any ongoing or unpublished trials that would likely influence this policy.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines (v.1.2022) on early detection of prostate cancer state that despite emerging evidence, the panel does not recommend a saturation biopsy strategy for all individuals with previous negative biopsies given the benefits seen for magnetic resonance imaging (MRI) and MRI-targeted biopsy in this patient population. (21) The emerging evidence cited included 1 prospective nonrandomized study (Zaytoun et al. 2011) (9) and uncontrolled observational studies published between 2006 and 2013.

NCCN guidelines on prostate cancer treatment (v.4.2022) do not mention saturation biopsy. (22)

U.S. Preventive Services Task Force Recommendations

The U.S. Preventive Services Task Force (2018) recommendations on prostate cancer screening did not address saturation biopsy. (23)

American Urological Association (AUA) Guidelines

The 2015 AUA guideline on the early detection of prostate cancer does mention saturation biopsy in their Quality Improvement Summit Proceedings Paper, "Optimal Techniques of Prostate Biopsy and Specimen Handling". (24) Their conclusion, "The differences in populations studied makes comparing the results from the studies of protocols involving different numbers of cores challenging. Patient age, serum PSA [prostate-specific antigen], ethnicity, and family history all influence CDR [cancer detection rate] for any biopsy strategy. What can be concluded from the literature is that increasing core number increases CDR and sextant biopsy results in an unacceptably high likelihood of false-negative results, leading to under-detection of clinically significant cancers. Increasing core numbers using saturation techniques might identify cancers missed on extended core sampling but this strategy also increases the risk of over-detection of indolent cancers without significantly improving CDR or pathology concordance.

Summary of Evidence

Studies showing improved initial detection of prostate cancer using saturation biopsy compared to the use of extended biopsies are lacking. The use of saturation biopsy as a repeat biopsy after prior negative biopsies in men with persistent clinical suspicion of prostate cancer appears to increase the detection rate of cancer, particularly in the anterior zones. It is possible that by using this technique, clinically significant cancer could be detected earlier. Comprehensive 3D (three-dimensional) mapping with biopsy has been utilized as well for detecting clinically significant cancer allowing more aggressive therapy or watchful waiting depended on the biopsy results. Therefore, saturation biopsy or comprehensive 3D mapping with biopsy of the prostate may be considered medically necessary for individuals meeting appropriate selection criteria.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	55700, 55706, 0443T
HCPCS Codes	G0416

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References

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) **does not** have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been **developed** since this medical policy document was written. See Medicare's National Coverage at <http://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
01/01/2024	Reviewed. No changes.
01/01/2023	Document updated with literature review. Coverage unchanged. Reference 22 added; some updated and others removed.
01/01/2022	Reviewed. No changes.
08/15/2020	Document updated with literature review. The following change was made to Coverage: "(performed within the prior 12 months)" was added to the following statement: Saturation biopsy or comprehensive 3D (three-dimensional) mapping with biopsy of the prostate may be considered medically necessary for men with a prior non-diagnostic transrectal ultrasound guided biopsy (performed within the prior 12 months) and one or more of the following. Reference 24 was added; other references were removed.
10/15/2018	Reviewed. No changes.
12/15/2017	Document updated with literature review. Coverage unchanged. Title changed from: Saturation Biopsy for Diagnosis and Staging of Prostate Cancer, Including Comprehensive 3D Mapping with Biopsy, with "Management" added to policy title.
11/01/2016	Reviewed. No changes.
12/01/2015	Document updated with literature review. Requirement for two biopsies before considering saturation biopsy as medically necessary was removed from the coverage position. The lead in medically necessary coverage statement was changed to the following, "Saturation biopsy or comprehensive 3D mapping with biopsy of the prostate may be considered medically necessary for men with a prior non-diagnostic transrectal ultrasound guided biopsy and one or more of the following." The following indication was added to the medically necessary criterion, "Findings of a palpable lesion on digital rectal examination (DRE)." The following was added to the experimental, investigational and/or unproven coverage statement, "comprehensive 3D mapping with biopsy." Title changed from Saturation Biopsy for Diagnosis and Staging of Prostate Cancer.

07/01/2014	The following was added to Coverage: NOTE: For DNA Specimen Provenance Assignment (DSPA) Testing (e.g., Know Error® System) of tissue specimens, including but not limited to prostate or breast cancer specimens, see MED208.001 Genetic Tests (Miscellaneous).
11/15/2013	New medical document. Saturation biopsy of the prostate may be considered medically necessary when criteria are met.