Saturation biopsy for Diagnosis and Staging of Prostate Cancer

Medical Policy

Section: Surgery
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Description

Saturation biopsy, generally considered obtaining more than 20 biopsy tissue cores from the prostate in a systematic manner has been proposed in the diagnosis (for initial or repeat biopsy), staging, and management of patients with prostate cancer. Prostate cancer is a common cancer and is the second leading cause of cancer-related deaths in men in the U.S. 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 (PSA) screening programs that identify cancer in prostates that are normal to palpation and to transrectal ultrasound. For patients with an elevated PSA level but with a normal biopsy, questions exist about subsequent evaluation, since 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 the diagnosis of 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 10–14 cores. Additional concerns have been raised about drawing conclusions about the stage (grade) of prostate cancer based on limited biopsy material. 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 may increase the cancer detection rate by approximately 25%. (1)

Another approach to increase the number of biopsy tissue cores is use of the “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 undersampled in standard peripheral zone biopsy strategies and may lead to 17% of cancers being
missed, according to one study. (2) Saturation biopsy may be performed transrectally or with a transperineal approach; the transperineal approach is generally performed as a stereotactic template-guided procedure with general anesthesia.

Policy
Saturation biopsy, taking 20 or more core tissue samples at one time, is considered investigational in the diagnosis, staging, and management of prostate cancer.

Policy Guidelines
A CPT code for this procedure became effective in 2009:
55706: Biopsies, prostate, needle, transperineal, stereotactic template guided saturation sampling, including imaging guidance.

Some Plans have found that this procedure may be reported with code 55700 (biopsy, prostate; needle or punch, single or multiple, any approach) when it is performed without stereotactic template guidance. This method may involve ultrasound guidance which is reported with code 76942 (ultrasonic guidance for needle placement (eg, biopsy, aspiration, injection, localization device), imaging supervision and interpretation).

There are specific HCPCS “G” codes for the pathology services associated with this service:
G0416: Surgical pathology, gross and microscopic examination for prostate needle saturation biopsy sampling, 1-20 specimens
G0417: Surgical pathology, gross and microscopic examination for prostate needle saturation biopsy sampling, 21-40 specimens
G0418: Surgical pathology, gross and microscopic examination for prostate needle saturation biopsy sampling, 41-60 specimens
G0419: Surgical pathology, gross and microscopic examination for prostate needle saturation biopsy sampling, greater than 60 specimens

A single G code would be reported depending on the total number of specimens on which the laboratory performed pathology examinations (e.g., for 50 specimens only G0418 is reported).

Rationale
This policy was created in 2009 and has been updated with a literature review conducted through September 2012. In reviewing the studies, it is important to note that most studies reflect diagnostic yields (finding cancer) or changes in tumor stage/grade. Studies that link the use of saturation biopsy to clinical outcomes are lacking. In addition, the majority of studies were case series of patients who underwent saturation biopsy, rather than a comparative study of various biopsy techniques.

Initial Biopsy
A number of studies have compared the yield (finding prostate cancer) and have not found that use of saturation biopsy improves cancer detection rates compared with extended biopsy strategies. Authors suggest that large, easy-to-identify tumors in the general population are usually identified without a need for saturation biopsy. For example, Ashley et al. performed a study of 469 consecutive prostate biopsies to determine whether saturation biopsy (at least 24 cores) that was performed in 168 patients detected more prostate cancer than a standard 12–18 core office biopsy technique. (3) After adjustments for covariates, saturation biopsy did not
detect more prostate cancer (odds ratio [OR]: 1.2; p=0.339). The authors concluded that saturation biopsy did not appear to detect more abnormal prostate pathology than the control.

**Repeat Biopsy**

Mabjeesh and colleagues reported on a high-risk group of men with at least 2 previous negative transrectal biopsies who then underwent transperineal template-guided saturation biopsy. (4) Prostate cancer was detected in 26% of the 92 patients, predominantly in the anterior zones. A median of 30 cores was taken in the saturation biopsies. Gleason score of equal to or greater than 7 was detected in 46% of the diagnosed men. Most of the tumors (83.3%) were found in the anterior zones of the gland, with a significantly higher number of positive cores versus the posterior zones (mean 4.9 vs. 1.5, p= 0.015).

Lee and colleagues evaluated the role of transrectal saturation biopsy for cancer detection in men with high-grade prostatic intra-epithelial neoplasia (HGPIN) diagnosed by extended biopsy. (5) From 1999 to 2009, 314 men had at least 1 or more repeat biopsies due to the presence of exclusive HGPIN (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 up using a second standard extended biopsy scheme, and 136 were followed up using the saturation biopsy scheme. In the standard repeat biopsy group, 35 of 178 (19.7%) men had cancer on initial repeat biopsy. In the saturation biopsy group, 42 of 136 (30.9%) 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 (OR: 1.85, (95% confidence interval [CI]: 1.03, 3.29), exclusive of age, prostate-specific antigen (PSA) level, days from initial biopsy, digital rectal exam (DRE) status, and multifocal prostatic epithelial neoplasia (PIN). Pathologic findings on repeat biopsies demonstrated similar Gleason grades, regardless of biopsy technique: Gleason 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.

Giulianelli and colleagues evaluated whether or not the saturation biopsy technique increased the cancer detection rate in patients with PSA less than 10 ng/mL, after a first negative biopsy. (6) From January 2004 to January 2006, 780 patients underwent prostate ultrasound-guided transrectal core biopsies: 186 (23.8%) were diagnosed with prostate cancer, while 594 (76.2%) had negative biopsies. For 1 year, all of the patients with no evidence of cancer were observed according to a follow-up schedule including PSA every 3 months and DRE every 6 months. During this period, 140 patients showed an increase of PSA (<10 ng/mL) or a low PSA free/total. This group underwent a second ultrasound-guided transrectal core biopsy with saturation technique under general anesthesia. Of the 140 patients, 50 (35.7%) had prostate cancer showing a Gleason score of 4 or 5 in 26%, 6 or 7 in 75%, and 8 to 10 in 9%, respectively. Apical biopsies carried out in the anterior horn of peripheral zone tissue showed cancer in 35 patients (70% of those rebiopsied), versus 24% in lateral zones, and 5% for parasagittal. Cancer in the patients who underwent the saturation biopsy was considered clinically significant (defined as Gleason score of ≥7 and tumor volume >0.5 cc) in 47 patients (94%). Forty-eight of 50 underwent a radical prostatectomy and 2 underwent external beam radiation therapy. The authors concluded that the saturation biopsy technique increased the cancer detection rate by 36% in patients with PSA less than 10 ng/mL, after a first negative biopsy, and showed a higher positivity (70% prostate cancer detection rate) if the saturation biopsy included the anterior horn of peripheral zone tissue. No significant pain or side effects were observed.
Zaytoun and colleagues reported the results of a prospective, non-randomized comparative study of extended biopsy versus office-based transrectal saturation biopsy in a repeat biopsy population. (7) After an initially negative biopsy, 1,056 men underwent either 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 examination (DRE), persistently increased prostate-specific antigen (PSA), and PSA increasing greater 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=0.0075). Of the 315 positive biopsies, 119 (37.8%) revealed clinically insignificant cancer (defined as Gleason sum <7, a total of 3 or fewer positive cores, and a maximum of 50% or less of cancer in any positive core). There was a trend toward increased detection of clinically insignificant cancer detection in the saturation versus the extended biopsy cases, 40.1% versus 32.6%, respectively (p=0.02).

Simon and colleagues reported on the results of using an extensive saturation biopsy in 40 men with a clinical suspicion of prostate cancer after previous negative prostate biopsies. (8) The median number of cores taken was 64 (range: 39–139) and was adjusted to the size of the prostate. Of the 40 men, 18 (45%) had cancer in at least 1 core. Sixteen men had marked hematuria after the biopsy procedure. The investigators concluded there was no significant increase in the cancer detection rate with this extensive saturation biopsy regimen compared to published series with fewer cores, but there was increased morbidity.

Eichler and colleagues conducted a systematic review of cancer detection rates and complications of various prostate biopsy schemes. (9) They pooled data that compared various extended biopsy schemes in studies involving 20,698 patients. The authors 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.

**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 (see MPRM policy 7.01.79). 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 investigational.

**Active Surveillance**

While some have suggested that saturation biopsy could be a part of active surveillance (a treatment approach for men with prostate cancer that involves surveillance with PSA, DRE, and routine prostate biopsies, in men whose cancers are small and expected to behave indolently)) in terms of being able to possibly and more accurately assess tumor volume and/or tumor grade, there are no studies that link this potential use to improved outcomes.

Ayres and colleagues evaluated the role of transperineal template prostate biopsies in 101 men on active surveillance for prostate cancer. (10) The men underwent restaging transperineal template prostate biopsies at a single center. The criteria for active surveillance were: age 75 years or younger, Gleason ≤3+3, PSA equal to or less than ng/mL, clinical stage T1-2a, and equal to or less than 50% ultrasound-guided transrectal biopsy cores positive for cancer, with equal to or less than 10 mm of disease in a single core. The number of men with an increase in
disease volume or Gleason grade on transperineal template biopsy and the number of men who later underwent radical treatment were assessed. The role of PSA and PSA kinetics were studied. In all, 34% of men had more significant prostate cancer on restaging transperineal template biopsies compared with their transrectal biopsies. Of these men, 44% had disease predominantly in the anterior part of the gland, an area often under-sampled by transrectal biopsies. In the group of men who had their restaging transperineal template biopsies within 6 months of commencing active surveillance, 38% had more significant disease. There was no correlation with PSA velocity or PSA doubling time. In total, 33% of men stopped active surveillance and had radical treatment. The study concluded that around one-third of men have more significant prostate cancer on transperineal template biopsies and that this probably reflects under-sampling by initial transrectal biopsies rather than disease progression.

Improving Correlation between Biopsy and Operative Stage

Similarly, data are lacking on a potential use of saturation biopsy to assist in more accurately assessing tumor grade/stage when the treatment regimen is determined through biopsy rather than through surgical removal of the prostate. Evaluation of such an approach would require either a randomized trial or determining treatment plans for a group of patients based on use of varying numbers of their biopsy specimens.

Review articles

A 2009 review of studies of saturation biopsy by Patel and Jones, (11) makes the following comments/conclusions: the new standard of initial prostate biopsy involves obtaining 10–14 cores; further studies are needed to evaluate use of saturation biopsy over extended biopsy schemes for repeat biopsy and active surveillance; and while current biopsy strategies may not accurately predict final Gleason score, additional studies are needed using both extended biopsy or saturation biopsy protocols.

A 2011 review by Chun and colleagues of the current evidence regarding the performance and interpretation of initial, repeat, and saturation prostatic biopsy recommends a minimum of 10 but not greater than 18 systematic cores at initial biopsy and that further biopsy sets, either as an extended repeat or as a saturation biopsy, are warranted in young and fit men with a persistent suspicion of cancer. (12)

Summary

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. However, evidence is lacking as to whether this leads to improved health outcomes, including the possibility of detecting clinically insignificant cancers, which could lead to unnecessary treatment. Few studies show improvement in clinical outcomes with the use of saturation biopsy as part of active surveillance. Thus, the technique of saturation biopsy, taking 20 or more core tissue samples, is considered investigational.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network (NCCN) Guidelines
NCCN guidelines (v2.2012) on prostate cancer early detection state that in patients with 2 negative extended biopsies, yet persistently rising PSA values, a saturation biopsy may be considered. (category 2A) (13)

Medicare National Coverage

No national coverage decision identified.

References:


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