Prostate Biopsies AHS – G2007

Description of Procedure or Service

Prostate cancer is characterized by a malignancy of the small walnut shaped gland that produces seminal fluid in males which ranges clinically from a microscopic, well-differentiated tumor that may never be clinically significant to an aggressive, high-grade cancer (Kantoff, Taplin, & Smith, 2017).

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for prostate biopsy when it is determined the medical criteria or reimbursement guidelines below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When prostate biopsy is covered

Reimbursement for prostate biopsy involving 12 core extended sampling* (see Note 1 below) is allowed in the initial diagnosis of prostate cancer as a follow up to abnormal PSA results, presence of a palpable nodule on digital rectal examination, or suspicious radiologic findings.

*Note 1: One vial per sextant, with no more than two core samples per vial.

When prostate biopsy is not covered

Prostate saturation biopsy is considered investigational in the diagnosis, staging and management of prostate cancer.

Policy Guidelines

Prostate cancer is the most common cancer in American men and the second leading cause of death in men aged 65 years or older (Balducci, Pow-Sang, Friedland, & Diaz, 1997; Tabayoyong & Abouassaly, 2015) with an estimated 161,000 cases and 26,700 deaths in the US in 2017.
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(Siegel, Miller, & Jemal, 2017). About 1 man in 6 will be diagnosed with prostate cancer during his lifetime (Kantoff et al., 2017).

Many cases of prostate cancer do not become clinically evident, as indicated in autopsy series, where prostate cancer is detected in approximately 30 percent of men age 55 and approximately 60 percent of men by age 80 (Bell, Del Mar, Wright, Dickinson, & Glasziou, 2015). These data suggest that prostate cancer often grows so slowly that most men die of other causes before the disease becomes clinically advanced (Hoffman, 2017).

Prostate cancer survival is related to many factors, especially the extent of tumor at the time of diagnosis. The five-year relative survival among men with cancer confined to the prostate (localized) or with just regional spread is 100 percent, compared with 29.3 percent among those diagnosed with distant metastases (Hoffman, 2017).

Findings on digital rectal examination including the presence of nodules, induration, or asymmetry or elevated prostate specific antigen (PSA) levels indicate the need for prostate biopsy. Although generally considered safe, prostate biopsy is an invasive procedure and recommendations for its use are limited to a subset of patients. Screening the general population for prostate cancer remains a controversial issue, since improved patient outcomes have not been demonstrated (Andriole et al., 2009; Hoffman, 2017; NCCN, 2017; Schroder et al., 2009).

Multiple sampling schemes have been developed in an effort to improve the accuracy of prostate biopsy in the detection of cancer. Systematic prostate sampling is performed and augmented by additional sampling of any abnormal areas found on ultrasound or rectal examination (Gosselaar et al., 2008). Originally during transrectal ultrasound (TRUS)-guided biopsy, a six-core, or sextant biopsy technique, was commonly employed taking one sample each from the apex, base, and mid-prostate on each side (Hodge, McNeal, Terris, & Stamey, 1989). However, this method misses approximately 30 percent of clinically significant cancers (Babaian et al., 2000; Epstein, Walsh, Sauvageot, & Carter, 1997; Norberg et al., 1997; Roehl, Antenor, & Catalona, 2002), and has been replaced by extended core biopsy which obtains five to seven evenly-distributed specimens from each side, sampling more extensively from the lateral aspects of the prostate (Babaian et al., 2000; Eskicorapci et al., 2004; Ukimura et al., 2013; Uno, Nakano, Ehara, & Deguchi, 2008). Systematic reviews have found that and schemes with 12 core samples that took additional laterally directed cores detected 31 percent more cancers compared with a six-core approach increasing number of cores were significantly associated with increased detection of prostate cancer (Eichler et al., 2006; Hoffman, 2017).

Saturation biopsy involves extensive sampling of the prostate, obtaining up to 24 core samples. Saturation biopsy is not appropriate for initial screening as it does not provide increased cancer detection when used for first-time biopsy but may provide increased sensitivity when repeat biopsies are performed and should be considered after two negative TRUS-biopsies (Li et al., 2014; Sajadi, Kim, Terris, Brown, & Lewis, 2007; Zaytoun, Moussa, Gao, Fareed, & Jones, 2011). Saturation biopsy detects prostate cancer in 22 to 33 percent of patients undergoing repeat biopsy (Pepe & Aragona, 2007; Stewart, Leibovich, Weaver, & Lieber, 2001), but is associated with a higher incidence of complications (Hoffman, 2017).

Clinical Validity and Utility

Benway and Andriole (2017) stated that “saturation biopsy detects prostate cancer in 22 to 33 percent of patients undergoing repeat biopsy but is associated with a higher incidence of complications. Magnetic Resonance (MR) imaging, which provides superior resolution to ultrasound (Ward et al., 2012), can also be used to guide biopsy (Hoeks et al., 2011; Pinto et al., 2011). Kasivisvanathan et al (2018) found that in a randomized study of 500 men, the use of risk assessment with MRI before biopsy and MRI-targeted biopsy was superior to standard transrectal ultrasonography-guided biopsy in men at clinical risk for prostate cancer who had not undergone biopsy previously.

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complications.” The authors further stated that saturation biopsy does not provide increased
cancer detection when used for first-time biopsy and is not appropriate for initial screening.
However, it provides increased sensitivity when repeat biopsies are performed and should be
performed after a second negative TRUS-biopsy in the patient for whom clinical suspicion for
prostate cancer remains high.

Thompson et al (2015) studied whether saturation or transperineal biopsy altered oncological
outcomes, compared with standard transrectal biopsy. They conducted a retrospective analysis of
prospectively collected data from two cohorts with localised prostate cancer (1998-2012)
undergoing active surveillance for low-risk prostate cancer. Outcomes were compared for
standard vs saturation biopsy as well as transrectal vs transperineal biopsy. The authors
concluded that “saturation biopsy increased progression to treatment on AS; longer follow-up is
needed to determine if this represents beneficial earlier detection of significant disease or over-
treatment. Transperineal biopsy reduced the likelihood of unfavourable disease at RP, possibly
due to earlier detection of anterior tumours (Thompson et al., 2015).”

Zaytoun et al (2011) “compared saturation and extended repeat biopsy protocols after initially
negative biopsy.” They found that “Saturation biopsy detected almost a third more cancers
(32.7% vs 24.9%, p=0.0075). In patients with a benign initial biopsy saturation biopsy achieved
significantly greater prostate cancer detection (33.3% vs 25.6%, p=0.027). For previous atypical
small acinar proliferation and/or high grade prostatic intraepithelial neoplasia there was a trend
toward higher prostate cancer detection rate in the saturation group but it did not attain statistical
significance (31.2% vs 23.3%, p=0.13). Of 315 positive biopsies 119 (37.8%) revealed clinically
insignificant cancer (40.1% vs 32.6%, p=0.2).” The authors concluded that: “Compared to
extended biopsy, office based saturation biopsy significantly increases cancer detection on repeat
biopsy. The potential for increased detection of clinically insignificant cancer should be weighed
against missing significant cases.”

The PROMIS study (Brown et al., 2018) assessed the ability of multi-parametric MRI (mpMRI)
to identify men who can safely avoid unnecessary biopsy, the ability of the mpMRI-based
pathway to improve the rate of detection of clinically significant (CS) cancer compared with
TRUS-guided biopsy and estimated the cost-effectiveness of a mpMRI-based diagnostic pathway
in 740 men. They found that “For CS cancer, TRUS-guided biopsy showed a sensitivity of 48%
(95% CI 42% to 55%), specificity of 96% (95% CI 94% to 98%), PPV of 90% (95% CI 83% to
94%) and NPV of 74% (95% CI 69% to 78%). The sensitivity of mpMRI was 93% (95% CI 88%
to 96%), specificity was 41% (95% CI 36% to 46%), PPV was 51% (95% CI 46% to 56%) and
NPV was 89% (95% CI 83% to 94%). A negative mpMRI scan was recorded for 158 men (27%).
Of these, 17 were found to have CS cancer on TPM-biopsy. Economic evaluation - the most cost-
effective strategy involved testing all men with mpMRI, followed by MRI-guided TRUS-guided
biopsy in those patients with suspected CS cancer, followed by rebiopsy if CS cancer was not
detected.”

State and Federal Regulations, as applicable
The FDA has cleared devices including needles, reagents, instrumentation, and imaging systems
for use in prostate biopsy.

Guidelines and Recommendations

The American Urological Association (AUA)
The AUA published a paper (2015) on Optimal Techniques of Prostate Biopsy and Specimen
Handling which recommended: “12-core systematic sampling methodology that incorporates
apical and far-lateral cores in the template distribution. The results of our literature review
suggest that collecting more than 12 cores or sampling the transition zone offer no benefit for
initial diagnostic biopsies. However, such approaches might be useful for resampling following a
negative biopsy”
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The AUA/ASTRO/SUO published guidelines (Sanda et al., 2017) which state

“28. Localized prostate cancer patients who elect active surveillance should have accurate disease staging including systematic biopsy with ultrasound or MRI-guided imaging. (Clinical Principle)”

**National Comprehensive Cancer Network (NCCN)**

NCCN Guidelines (NCCN, 2018) stated that “systemic prostate biopsy under TRUS guidance is the recommended technique for prostate biopsy.” It recommends the use of an extended pattern at least 12 core biopsies as it has been validated and results in enhances cancer detection compared to sextant biopsy schemes.

Anterior directed biopsy is not supported in routine biopsy. However, this can be added to an extended biopsy protocol in a repeat biopsy if PSA is persistently elevated”.

“At present the panel does not recommend the use of advanced biopsy techniques or specific imaging other than TRUS for initial biopsy, although they can be considered in the repeat biopsy setting.”

“Overall the panel believes that the data for the use of MRI and MRI targeted biopsies in the initial biopsy setting are insufficient, as yet, to recommend them over standard, US-guided biopsies in this setting at this time. However, data showing that the use of MRI may reduce unnecessary biopsies, lower detection of clinically insignificant disease, and better identify high risk cancer are accumulating. MRI and MRI targeted biopsy can be considered in the setting of repeat biopsy”

“A negative biopsy does not preclude a diagnosis of prostate cancer on subsequent biopsy. If clinical suspicion of cancer persists after a negative biopsy, consideration can be given to saturation biopsy strategies and/or the use of multiparametric MRI followed by an appropriate targeted biopsy technique based on the result.”

“Based on emerging evidence, the panel believes that a saturation biopsy strategy can be considered for very high-risk men with previous negative biopsies”

**American College of Radiology**

The ACR (Coakley et al., 2017) rated TRUS guided biopsy a 9, and MRI targeted prostate biopsy a 7 in the most recent ACR Appropriateness Criteria for Prostate cancer Pretreatment detection, surveillance and staging for clinically suspected prostate cancer with no prior biopsy. A rating of 7, 8 or 9 are usually appropriate. MRI targeted biopsy was rated an 8 and repeat TRUS biopsy rated a 7 in clinically suspected prostate cancer, prior negative TRUS biopsy as well as Clinically established low risk prostate cancer for active surveillance.

They note that “Overall, the clinical paradigm for prostate cancer diagnosis is rapidly moving towards MRI-targeted transrectal biopsy, based on substantial evidence from several centers (notably the National Institutes of Health; New York University [NYU]; University of California, Los Angeles [UCLA]; and Nijmegen) that this approach can transform baseline cancer evaluation when compared with traditional systematic biopsy, with fewer false negatives, better tumor characterization, improved tumor localization, and better treatment stratification, especially stratification to lower-risk cohorts that may be appropriate for active surveillance or focal therapy”

**American Cancer Society**

The American Cancer Society published guidelines (Wolf et al., 2010) which state:
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- A PSA level of 4.0 ng/mL or greater historically has been used to recommend referral for further evaluation or biopsy, which remains a reasonable approach for men at average risk for prostate cancer.

- For PSA levels between 2.5 ng/mL and 4.0 ng/mL, health care providers should consider an individualized risk assessment that incorporates other risk factors for prostate cancer, particularly for high-grade cancer, that may be used to recommend a biopsy. Factors that increase the risk of prostate cancer include African American race, family history of prostate cancer, increasing age, and abnormal DRE. A previous negative biopsy lowers the risk. Methods are available that merge this information to achieve an estimate of a man's overall risk of prostate cancer and, more specifically, of his risk of high-grade prostate cancer

**US Preventive Services Task Force (USPSTF, 2018)**

Within the 2018 USPSTF recommendation statement regarding prostate screening, they state, “Men with a positive PSA test result may undergo a transrectal ultrasound-guided core-needle biopsy of the prostate to diagnose prostate cancer... Although protocols vary, active surveillance usually includes regular, repeated PSA testing and often repeated digital rectal examination and prostate biopsy, with potential for exposure to repeated harms from biopsies.”

**Billing/Coding/Physician Documentation Information**

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: 88305, G0416,55706*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

**Scientific Background and Reference Sources**


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Policy Implementation/Update Information

1/1/19 New policy developed. BCBSNC will provide coverage for prostate biopsy when it is determined to be medically necessary because the medical criteria and guidelines are met. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (sk)

10/29/19 Wording in the Policy, When Covered, and/or Not Covered section(s) changed from Medical Necessity to Reimbursement language, where needed. (gm)

12/10/19 Specialty Matched Consultant Advisory Panel review 11/20/2019. Reviewed by Avalon 3rd Quarter CAB. No change in overall intent of policy. (sk)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.