Prostate Biopsies

Policy Number: AHS – G2007 – Prostate Biopsies	Prior Policy Name and Number, as applicable:
Effective Date: 01/01/2023	

I. Policy Description

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, 2020).

II. Related Policies

Policy Number	Policy Title
AHS-G2008	Prostate Specific Antigen (PSA) Testing
AHS-G2013	Testosterone Testing
AHS-G2124	Serum Tumor Markers For Malignancies

III. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Medical Policy Statements do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination. Specifications pertaining to Medicare and Medicaid can be found in Section VII of this policy document.

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. If there is a conflict between this Policy and any relevant, applicable government policy [e.g. National Coverage Determinations (NCDs) for Medicare] for a particular member, then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit their search website https://www.cms.gov/medicare-coverage-database/search.aspx or the manual website.

1) Prostate biopsy involving 12 core extended sampling* (see Note 1 below) **MEETS COVERAGE CRITERIA** 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.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of a patient's illness.

2) Prostate saturation biopsy **DOES NOT MEET COVERAGE CRITERIA** for the diagnosis, staging and management of prostate cancer.

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

IV. Scientific Background

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 191,930 new cases and 33,330 deaths in the US in 2020 (Siegel, Miller, & Jemal, 2020). About 11% of men will be diagnosed with prostate cancer during his lifetime (Kantoff, Taplin, & Smith, 2018; Kantoff et al., 2020).

Many cases of prostate cancer do not become clinically evident, as indicated in autopsy series, where prostate cancer is detected in approximately 30% of men age 55 and approximately 60% 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. 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%, compared with 31% among those diagnosed with distant metastases (Hoffman, 2020).

Findings on digital rectal examination (DRE) 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 (Hoffman, 2020).

Multiple sampling schemes have been developed 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). During transrectal ultrasound (TRUS)-guided biopsy, a six-core, or sextant biopsy technique, takes one sample each from the apex, base, and mid-prostate on each side (Hodge, McNeal, Terris, & Stamey, 1989). However, this method may miss approximately 30% of clinically significant cancers 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 (B. Benway, Andriole, Gerald, 2021). A meta-analysis by Eichler et al found that schemes with 12 core samples that took additional laterally directed cores detected 31% more cancers compared with a six-core approach, with increasing number of cores significantly associated with increased detection of prostate cancer (Eichler et al., 2006). This biopsy method has been used to obtain up to 18 cores for evaluation (B. Benway & Andriole, 2021).

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 can be considered after one or more negative TRUS-biopsies. Saturation biopsy detects prostate cancer in approximately 22% to 33% of patients undergoing repeat biopsy, but it is associated with a higher incidence of complications (B. Benway & Andriole, 2021).

Several complications may occur with biopsy. Firstly, the samples from a biopsy may be inadequate to make a diagnosis; the cores obtained may not be of high enough quality or more cores may be needed.

Other findings such as an abnormal but nonmalignant histology may warrant a repeat biopsy. Clinical complications such as inflammation, bleeding, infection, and urinary obstruction are also possible (B. Benway, Andriole, Gerald, 2021). Pepe et al. estimated the rate of clinical complication after a transperineal biopsy to be as high as 40% (Pepe & Aragona, 2007).

Clinical Validity and Utility

Thompson et al. (2015) studied whether saturation or transperineal biopsy altered oncological outcomes as compared with standard transrectal biopsy. 650 men were analyzed, and saturation biopsy was associated with "increased objective biopsy progression requiring treatment" on both the Kaplan-Meier analysis and multivariate Cox analysis. A logistic regression analysis of 179 men undergoing a radical prostatectomy (RP) found that transperineal biopsy was associated with lower likelihood of "unfavourable" RP pathology. 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." 1056 men were included, with 393 men undergoing a 12-14 core biopsy ("extended") and 663 men undergoing a 20-24 core biopsy ("saturated"). Overall, prostate cancer was detected in 315 patients, but saturated biopsy detected a third more cancers and identified more cancers in a benign initial biopsy. 119 biopsies identified clinically "insignificant" cancer. The authors concluded, "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" (Zaytoun et al., 2011).

The PROstate Magnetic Resonance Imaging Study (PROMIS) study (Brown et al., 2018) "assessed the ability of multi-parametric MRI (mpMRI) to identify men who can safely avoid unnecessary biopsy" and compared mpMRI to TRUS-guided biopsy. A TPM-biopsy was included for comparison, and 576 men underwent all three tests. Clinically significant (CS) cancer was defined as "a Gleason score of $\geq 4 + 3$ and/or cancer core length of ≥ 6 mm". For CS cancer, TRUS-guided biopsy showed a sensitivity of 48%, specificity of 96%, PPV of 90%, and NPV of 74%. The sensitivity of mpMRI was 93%, specificity was 41%, PPV was 51%, and NPV was 89%. A negative mpMRI scan was recorded for 158 men (27%). Of these, 17 were found to have CS cancer on TPM-biopsy. The authors also found that 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" (Brown et al., 2018).

Sidana et al. (2018) compared the yield of MRI fusion biopsy (FBx) to 12-core TRUS biopsy (SBx) in patients with prior negative biopsies. 779 patients were included, and a total of 346 cancers were detected with 239 of 346 considered clinically significant. FBx diagnosed a total of 205 patients with SBx diagnosing an additional 34 patients. FBx identified high proportions of clinically significant cancers over all amounts of prior negative biopsies. The authors stated that "SBx added a relatively small diagnostic value to FBx for detecting CS disease" and concluded that "repeat SBx alone in patients with multiple prior negative biopsies will be hindered by lower yield and FBx should be utilized concurrently in these patients" (Sidana et al., 2018).

Pepe et al. (2018) investigated the diagnostic accuracies for clinically significant prostate cancer, multiparametric magnetic resonance imaging (MRI) and transperineal saturation prostate biopsy. Lesions with PI-RADS (Prostate Imaging Reporting and Data System) scores of 3 or higher were subjected to additional targeted fusion prostate biopsy. 1032 patients were included, with 372 deemed

to have T1c prostate cancer. Further, 272 of these cases were considered "clinically significant". Saturation biopsy missed 12 of 272 clinically significant cancers, and targeted fusion prostate biopsy with the score cutoff of 3 missed 44 cases. However, the authors noted that using multiparametric MRI in combination with a score cutoff of 3 in PI-RADS would've prevented 49.3% of biopsies, and a score cut-off of 4 would've prevented 73.6% of biopsies, although the score cutoff of 4 missed 108 of 272 clinically significant cases. The authors concluded that multiparametric MRI could "significantly reduce the number of unnecessary repeat prostate biopsies in about 50% of cases in which a PI-RADS score of 3 or greater is used" (Pepe et al., 2018).

Pepe et al. (2020) investigated the amount of cores (combined with multiparametric MRI [mpMRI]) needed to diagnose "all clinically significant cases of prostate cancer (csPCa) in men subject to transperineal saturation biopsy (SPBx; 30 cores)". 875 patients were included. Stage 1 prostate cancer was found in 306 of these patients, with 222 of these classified as "clinically significant". The initial 20 needle cores obtained from SPBx identified all 222 cases of clinically significant prostate cancer, although it missed 84 of 129 indolent cases. Overall, the "diagnostic accuracy, sensitivity, and specificity [were] equal to 83.1%, 100%, and 65.1%, respectively." The authors concluded that "in men subject to mpMRI and/or TPBx, a maximum of 20 systematic transperineal needle cores detected all cases of csPCa and minimized the diagnosis of indolent cancers" (Pepe, Pennisi, & Fraggetta, 2020).

Klotz et al. (2021) investigated magnetic resonance imaging (MRI) with targeted biopsy against TRUS-guided biopsy to determine whether MRI with a targeted biopsy was as effective in detecting a grade 2 or greater prostate cancer. 453 patients underwent tests and were randomized to receive TRUS biopsy or MRI-TB. Cancers of grade 2 or greater (GG2) were identified in "67 of 225 men (30%) who underwent TRUS biopsy vs 79 of 227 (35%) allocated to MRI-TB." The authors concluded that "magnetic resonance imaging followed by selected targeted biopsy is noninferior to initial systemic biopsy in men at risk for prostate cancer in detecting GG2 or greater cancers"(Klotz et al., 2021).

V. Guidelines and Recommendations

The American Urological Association (AUA) (Samir S. Taneja, 2015)

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".

The AUA / American Society for Radiation Oncology (ASTRO) / Society of Urologic Oncology (SUO) published guidelines (Sanda et al., 2017) which state:

- "Localized prostate cancer patients who elect active surveillance should have accurate disease staging including systematic biopsy with ultrasound or MRI-guided imaging."
- "Localized prostate cancer patients undergoing active surveillance should be encouraged to have a confirmatory biopsy within the initial two years and surveillance biopsies thereafter."

In 2018, the American Society of Clinical Oncology (ASCO) endorsed the above 2017 AUA/ASTRO/SUO joint guideline, with only a minor disagreement on two cryosurgery recommendations (Bekelman et al., 2018).

In 2020, The American Urological Association and the Society of Abdominal Radiology Prostate Disease Focus Panel published a guideline (Bjurlin et al., 2020) on standard operating procedures for multiparametric magnetic resonance imaging in the diagnosis, staging, and management of prostate cancer. The guideline states:

- "mpMRI of the prostate allows for risk stratification of men at risk for prostate cancer including its ability to predict cancer aggressiveness prior to biopsy."
- "The performance of prostate mpMRI in men with no prior biopsy is now supported by randomized clinical trials, while its use in men with a prior negative biopsy continues to be endorsed by consensus statements and national guidelines" (Bjurlin et al., 2020).

National Comprehensive Cancer Network (NCCN, 2021a, 2021b)

NCCN Guidelines on Early Detection for Prostate Cancer (NCCN, 2021b) state that "systematic prostate biopsy under TRUS guidance with or without targeted of lesions seen on pre-biopsy MRI 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. Moreover, the NCCN states,

- "Anteriorly 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".
- "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 results."
- "Despite this emerging evidence, the panel does not recommend a saturation biopsy strategy for all men with previous negative biopsies at this time given the benefits seen for MRI and MRI-targeted biopsy in this patient population."
- "After 1 or more negative TRUS biopsies, men who are considered high-risk (e.g. those with persistently elevated or rising PSA) can be considered for MRI followed by targeted biopsy". The NCCN notes that targeted biopsy techniques include "cognitive or visual targeting, TRUS-MRI fusion platforms, and direct in-bore magnetic resonance biopsy-guided biopsy.
- "Overall, the panel believes that the data for the use of MRI and MRI-targeted biopsies in the initial biopsy setting are increasingly compelling. However, studies using both targeted and systematic sampling routinely demonstrate higher yield of clinically significant cancer with the combined approach and improved sensitivity. Therefore, a combination of systematic and targeted procedures is preferred when MRI-targeting capabilities are available."
- "The panel believes that MRI-guided targeted biopsies can be considered in place of standard 12-core TRUS biopsies in initial biopsy setting…however…more information is needed about the generalizability of the findings of the trials mentioned above".

The NCCN also addressed prostate biopsy in their Prostate Cancer guideline. The NCCN remarks that biopsy (and/or multiparametric MRI) can be considered for active surveillance for patients with over 10 years life expectancy. The NCCN also states that a prostate biopsy should not be repeated "no more often than 12 months" unless clinically indicated (such as PSA increase). Finally, the NCCN states that a repeat biopsy can be indicated within 6 months "if the initial biopsy was less than 10 cores, or if assessment results show discordance"(NCCN, 2021a).

American College of Radiology (ACR) (Coakley et al., 2017)

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" (Coakley et al., 2017).

American Cancer Society (ACS) (Wolf et al., 2010)

The ACS published guidelines (Wolf et al., 2010) which state:

"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."

According to the ACS, an update to the guidelines for prostate cancer was initiated in 2019 (Smith et al., 2018; Smith et al., 2019).

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" (USPSTF, 2018).

European Society for Medical Oncology (ESMO) (Parker et al., 2020)

ESMO includes some recommendations for prostate biopsies:

- "Transperineal biopsies are recommended, rather than transrectal ultrasound (TRUS)-guided biopsies". ESMO further noted that "Targeted transperineal biopsies, in comparison with systematic transrectal biopsies, result in an increased detection rate of clinically significant prostate cancer, a decreased detection rate of clinically insignificant prostate cancer, and fewer adverse events".
- When multiparametric MRI is positive (defined as [PI-RADS] ≥3), ESMO recommends performing a targeted (systematic or non-systematic) biopsy. However, when multiparametric MRI is negative (PI-RADS ≤2) and clinical suspicion of cancer is low, the biopsy can be omitted (Parker et al., 2020).

European Association of Urology (EAU, 2021)

The EAU's recommendations on prostate biopsy include the following:

- The need for biopsy is based on PSA level or suspicious DRE/imaging, although limited PSA elevation alone should not prompt biopsy.
- "Ultrasound (US)-guided biopsy is now the standard of care…transurethral resection of the prostate should not be used as a tool for cancer detection".
- "Systematic biopsy is an acceptable approach in case mpMRI [multiparametric MRI] is unavailable".
- "Sextant biopsy is no longer considered adequate. At least eight systematic [core] biopsies are recommended in prostates with a size of about 30 cc. Ten to twelve core biopsies are recommended in larger prostates, with > twelve cores not being significantly more conclusive" (EAU, 2021).

VI. State and Federal Regulations, as applicable

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

The FDA has cleared numerous devices including needles, reagents, instrumentation, and imaging systems for use in prostate biopsy as of June 30, 2021. Additionally, many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

VII. Applicable CPT/HCPCS Procedure Codes

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all inclusive and is subject to updates. In addition, codes listed are not a guarantee of payment.

Code Number	Code Description
88305	Level IV – Surgical pathology, gross and microscopic examination
G0416	Surgical pathology, gross and microscopic examinations, for prostate needle biopsy, any method

VIII. Evidence-based Scientific References

Balducci, L., Pow-Sang, J., Friedland, J., & Diaz, J. I. (1997). Prostate cancer. *Clin Geriatr Med, 13*(2), 283-306. Retrieved from http://dx.doi.org/

Bekelman, J. E., Rumble, R. B., Chen, R. C., Pisansky, T. M., Finelli, A., Feifer, A., . . . Freedland, S. J. (2018). Clinically Localized Prostate Cancer: ASCO Clinical Practice Guideline Endorsement of

an American Urological Association/American Society for Radiation Oncology/Society of Urologic Oncology Guideline. *Journal of Clinical Oncology, 36*(32), 3251-3258. doi:10.1200/JCO.18.00606
Bell, K. J., Del Mar, C., Wright, G., Dickinson, J., & Glasziou, P. (2015). Prevalence of incidental prostate cancer: A systematic review of autopsy studies. *Int J Cancer, 137*(7), 1749-1757. doi:10.1002/ijc.29538
Benway, B., & Andriole, G. (2021). Prostate biopsy. Retrieved from https://www.uptodate.com/contents/prostate-biopsy?search=prostate%20biopsy&source=search_result&selectedTitle=1~60&usage_type=default&display_rank=1#H31
Benway, B., Andriole, Gerald. (2021). Prostate biopsy. Retrieved from https://www.uptodate.com/contents/prostate-biopsy?search=prostate%20biopsy&source=search_result&selectedTitle=1~60&usage_type=default&display_rank=1#H3138437049
Bjurlin, M. A., Carroll, P. R., Eggener, S., Fulgham, P. F., Margolis, D. J., Pinto, P. A., . . . Turkbey, B. (2020). Update of the Standard Operating Procedure on the Use of Multiparametric Magnetic Resonance Imaging for the Diagnosis, Staging and Management of Prostate Cancer. *J Urol, 203*(4), 706-712. doi:10.1097/ju.0000000000000617
Brown, L. C., Ahmed, H. U., Faria, R., El-Shater Bosaily, A., Gabe, R., Kaplan, R. S., . . . Emberton, M. (2018). Multiparametric MRI to improve detection of prostate cancer compared with transrectal ultrasound-guided prostate biopsy alone: the PROMIS study. *Health Technol Assess, 22*(39), 1-176. doi:10.3310/hta22390
Coakley, F. V., Oto, A., Alexander, L. F., Allen, B. C., Davis, B. J., Froemming, A. T., . . . Eberhardt, S. C. (2017). ACR Appropriateness Criteria((R)) Prostate Cancer-Pretreatment Detection, Surveillance, and Staging. *J Am Coll Radiol, 14*(5s), S245-s257. doi:10.1016/j.jacr.2017.02.026
EAU. (2021). Prostate Cancer. Retrieved from https://uroweb.org/guideline/prostate-cancer/#5
Eichler, K., Hempel, S., Wilby, J., Myers, L., Bachmann, L. M., & Kleijnen, J. (2006). Diagnostic value of systematic biopsy methods in the investigation of prostate cancer: a systematic review. *J Urol, 175*(5), 1605-1612. doi:10.1016/s0022-5347(05)00957-2
Gosselaar, C., Roobol, M. J., Roemeling, S., Wolters, T., van Leenders, G. J., & Schroder, F. H. (2008). The value of an additional hypoechoic lesion-directed biopsy core for detecting prostate cancer. *BJU Int, 101*(6), 685-690. doi:10.1111/j.1464-410X.2007.07309.x
Hodge, K. K., McNeal, J. E., Terris, M. K., & Stamey, T. A. (1989). Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol, 142*(1), 71-74; discussion 74-75. Retrieved from http://dx.doi.org/
Hoffman, R. (2020). Screening for prostate cancer - UpToDate. *UptoDate.* Retrieved from https://www.uptodate.com/contents/screening-for-prostate-cancer?source=see_link#H30
Kantoff, P., Taplin, M.-E., & Smith, J. (2018). Clinical presentation and diagnosis of prostate cancer - UpToDate. In M. Ross (Ed.), *UptoDate*. Retrieved from https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-prostate-cancer?source=search_result&search=prostate%20cancer&selectedTitle=2~150#H74636058
Kantoff, P., Taplin, M.-E., & Smith, J. (2020). Clinical presentation and diagnosis of prostate cancer - UpToDate. *UptoDate.* Retrieved from https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-prostate-cancer?source=search_result&search=prostate%20cancer&selectedTitle=2~150#H74636058
Klotz, L., Chin, J., Black, P. C., Finelli, A., Anidjar, M., Bladou, F., . . . Haider, M. A. (2021). Comparison of Multiparametric Magnetic Resonance Imaging-Targeted Biopsy With Systematic Transrectal Ultrasonography Biopsy for Biopsy-Naive Men at Risk for Prostate Cancer: A Phase 3 Randomized Clinical Trial. *JAMA Oncol, 7*(4), 534-542. doi:10.1001/jamaoncol.2020.7589

NCCN. (2021a). NCCN Clinical Practice Guidelines in Oncology; Prostate Cancer. *v2*. Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf
NCCN. (2021b). NCCN Clinical Practice Guidelines in Oncology; Prostate Cancer Early Detection. *v2*. Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf
Parker, C., Castro, E., Fizazi, K., Heidenreich, A., Ost, P., Procopio, G., . . . Gillessen, S. (2020). Prostate Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. doi:10.1016/j.annonc.2020.06.011
Pepe, P., & Aragona, F. (2007). Saturation prostate needle biopsy and prostate cancer detection at initial and repeat evaluation. *Urology, 70*(6), 1131-1135. doi:10.1016/j.urology.2007.07.068
Pepe, P., Garufi, A., Priolo, G. D., Galia, A., Fraggetta, F., & Pennisi, M. (2018). Is it Time to Perform Only Magnetic Resonance Imaging Targeted Cores? Our Experience with 1,032 Men Who Underwent Prostate Biopsy. *J Urol, 200*(4), 774-778. doi:10.1016/j.juro.2018.04.061
Pepe, P., Pennisi, M., & Fraggetta, F. (2020). How Many Cores Should be Obtained During Saturation Biopsy in the Era of Multiparametric Magnetic Resonance? Experience in 875 Patients Submitted to Repeat Prostate Biopsy. *Urology, 137*, 133-137. doi:10.1016/j.urology.2019.11.016
Samir S. Taneja, M. C., Marc A. Bjurlin, DO, H. Ballentine Carter, MD, Michael S. Cookson, MD, MMHC, Leonard G. Gomella, MD, FACS, David F. Penson, MD, MPH, Paul Schellhammer, MD, Steven Schlossberg MD, MBA, Dean Troyer, MD,. (2015). American Urological Association - Optimal Techniques of Prostate Biopsy and Specimen Handling. Retrieved from http://www.auanet.org/guidelines/prostate-biopsy-and-specimen-handling. http://www.auanet.org/guidelines/prostate-biopsy-and-specimen-handling
Sanda, M. G., Cadeddu, J. A., Kirkby, E., Chen, R. C., Crispino, T., Fontanarosa, J., . . . Treadwell, J. R. (2017). Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline. Part I: Risk Stratification, Shared Decision Making, and Care Options. *J Urol*. doi:10.1016/j.juro.2017.11.095
Sidana, A., Watson, M. J., George, A. K., Rastinehad, A. R., Vourganti, S., Rais-Bahrami, S., . . . Pinto, P. A. (2018). Fusion prostate biopsy outperforms 12-core systematic prostate biopsy in patients with prior negative systematic biopsy: A multi-institutional analysis. *Urol Oncol, 36*(7), 341.e341-341.e347. doi:10.1016/j.urolonc.2018.04.002
Siegel, R. L., Miller, K. D., & Jemal, A. (2020). Cancer statistics, 2020. *CA: A Cancer Journal for Clinicians, 70*(1). doi:10.3322/caac.21551
Smith, R. A., Andrews, K. S., Brooks, D., Fedewa, S. A., Manassaram-Baptiste, D., Saslow, D., . . . Wender, R. C. (2018). Cancer screening in the United States, 2018: A review of current American Cancer Society guidelines and current issues in cancer screening. *CA: A Cancer Journal for Clinicians, 68*(4), 297-316. doi:10.3322/caac.21446
Smith, R. A., Andrews, K. S., Brooks, D., Fedewa, S. A., Manassaram-Baptiste, D., Saslow, D., & Wender, R. C. (2019). Cancer screening in the United States, 2019: A review of current American Cancer Society guidelines and current issues in cancer screening. *CA: A Cancer Journal for Clinicians, 69*(3), 184-210. doi:10.3322/caac.21557
Tabayoyong, W., & Abouassaly, R. (2015). Prostate Cancer Screening and the Associated Controversy. *Surg Clin North Am, 95*(5), 1023-1039. doi:10.1016/j.suc.2015.05.001
Thompson, J. E., Hayen, A., Landau, A., Haynes, A. M., Kalapara, A., Ischia, J., . . . Stricker, P. D. (2015). Medium-term oncological outcomes for extended vs saturation biopsy and transrectal vs transperineal biopsy in active surveillance for prostate cancer. *BJU Int, 115*(6), 884-891. doi:10.1111/bju.12858
USPSTF. (2018). Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *JAMA, 319*(18), 1901-1913. doi:10.1001/jama.2018.3710
Wolf, A. M., Wender, R. C., Etzioni, R. B., Thompson, I. M., D'Amico, A. V., Volk, R. J., . . . Smith, R. A. (2010). American Cancer Society guideline for the early detection of prostate cancer: update 2010. *CA Cancer J Clin, 60*(2), 70-98. doi:10.3322/caac.20066

Zaytoun, O. M., Moussa, A. S., Gao, T., Fareed, K., & Jones, J. S. (2011). Office based transrectal saturation biopsy improves prostate cancer detection compared to extended biopsy in the repeat biopsy population. *J Urol*, *186*(3), 850-854. doi:10.1016/j.juro.2011.04.069

IX. Revision History

Revision Date	Summary of Changes
01/01/2023	Initial Effective Date