Protocol

Magnetic Resonance Imaging–Targeted Biopsy of the Prostate

(701152)

Medical Benefit		**Effective Date**: 01/01/18	**Next Review Date**: 09/20
Preauthorization	No	**Review Dates**: 09/17, 09/18, 09/19	

Preauthorization is not required.

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

Populations	Interventions	Comparators	Outcomes
Individuals: • With suspicion of prostate cancer	Interventions of interest are: • Magnetic resonance imaging–targeted biopsy	Comparators of interest are: • Standard transrectal ultrasound-guided biopsy	Relevant outcomes include: • Overall survival • Disease-specific survival • Test accuracy • Morbid events • Quality of life
Individuals: • With prostate cancer and in active surveillance	Interventions of interest are: • Magnetic resonance imaging–targeted biopsy	Comparators of interest are: • Standard transrectal ultrasound-guided biopsy	Relevant outcomes include: • Overall survival • Disease-specific survival • Test accuracy • Morbid events • Quality of life

DESCRIPTION

Before a transrectal ultrasound-guided biopsy, a magnetic resonance imaging (MRI) scan can be used to pinpoint the location of suspicious lesions in the prostate. MRI permits a targeted biopsy (as opposed to a blind biopsy, which is the current standard of care). The use of an MRI-guided prostate biopsy serves two functions: (1) to identify areas in the prostate that could harbor a high-grade tumor; and (2) to divert attention from any clinically insignificant cancers not needing treatment. In accomplishing the secondary function, patients are placed into one of two categories: those only needing active surveillance; and those needing definitive intervention.

SUMMARY OF EVIDENCE

For individuals who have a suspicion of prostate cancer who receive an MRI-targeted biopsy, the evidence includes numerous prospective and retrospective studies of paired cohorts, two randomized controlled trials and systematic reviews and meta-analyses of these studies comparing MRI-targeted biopsy with transrectal ultrasound (TRUS)-guided biopsy in detecting overall, clinically significant and insignificant prostate cancers. Relevant outcomes are overall survival, disease-specific survival, test accuracy, morbid events, and quality of life. Studies on the use of MRI-targeted prostate biopsy have shown that the technology may diagnose more clinically significant cancers than TRUS biopsy and fewer clinically insignificant cancers, which might stratify patients for treat-

ment and active surveillance. Considering the prognostic value of risk stratification based on prostate biopsy, better diagnostic accuracy is likely to identify patients more accurately with clinically significant prostate cancer leading to changes in management that would be expected to result in clinically meaningful outcomes in terms of survival or quality of life. The evidence is sufficient to determine that the technology results in a meaningful improvement in net health outcome.

For individuals who have prostate cancer and in active surveillance who receive an MRI-targeted biopsy, the evidence includes a systematic review and observational studies of paired cohorts comparing MRI-targeted biopsy with TRUS biopsy in detecting pathologic progression of prostate cancer in terms of Gleason score and detection of higher grade (Gleason score greater than seven) cancer. Relevant outcomes are overall survival, disease-specific survival, test accuracy, morbid events, and quality of life. Current evidence has suggested that, compared with TRUS biopsy, an MRI-targeted biopsy is better at detecting those patients in active surveillance who have progressed and need definitive intervention. With the greater ability to detect prostate cancer with a Gleason score seven or higher, which is a critical parameter for definitive therapy in prostate cancer, use of this biopsy guidance technique is likely to translate into positive clinically meaningful outcomes (e.g., survival, quality of life) in this population. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

POLICY

Magnetic resonance imaging–targeted biopsy of the prostate may be considered **medically necessary** for diagnosis and active surveillance of prostate cancer.

BACKGROUND

PROSTATE CANCER

Prostate cancer is the most commonly diagnosed cancer and the third leading cause of cancer deaths among men in the United States, with an estimated 161,360 new cases and 26,730 deaths in 2017.[1] {Siegel, 2017 #82}

Diagnosis

The diagnosis and grading of prostate cancer are performed by taking a biopsy of the prostate gland. A prostate biopsy typically is performed in men who have an elevated prostate-specific antigen level or who present with symptoms. The purpose of the biopsy is to determine whether cancer is present and to determine tumor grade. Tumor grade (as measured by the Gleason score) is a major determinate in whether a patient is eligible for active surveillance (lower grade tumors) or a factor for determining definitive intervention (higher grade tumors). Patients on active surveillance undergo periodic follow-up prostate biopsies to assess cancer progression (upgrading of Gleason score).

Prostate biopsies are currently performed using transrectal ultrasound (TRUS) guidance with a 12-core sampling strategy. TRUS was introduced in the late 1980s; with this technique, tissue cores are obtained systematically under ultrasound guidance throughout the whole prostate, although this approach still represents blind biopsy of the prostate as to the location of possible cancer. Before 12-core sampling, 6-core (sextant) sampling was thought to miss too many cases of cancer. However, the 12-core sampling method may over diagnose clinically insignificant disease and underdiagnose clinically significant disease. Compared with subsequent prostatectomy, TRUS underestimates tumor grade up to 40% of the time and too often detects clinically insignificant disease.

Therefore, the ideal biopsy strategy would only identify men with prostate cancer of clinical significance to direct interventional therapy, and to minimize the detection of clinically insignificant prostate cancer and the risk of consequent overtreatment.

For men undergoing an initial biopsy for an elevated prostate-specific antigen, the systematic 12-core TRUS biopsy detection rate for prostate cancer is approximately 40% to 45%. If an initial 12-core biopsy is negative, and there is still a clinical suspicion of cancer, subsequent serial 12-core biopsies may detect cancer, or, other biopsy techniques such as transperineal template-guided saturation biopsy (in which 30-80 cores are typically obtained) may be used. Saturation biopsy allows for anterior and apical sampling and may detect significant cancer, but also oversamples insignificant types of cancer. In addition, transperineal biopsy requires general anesthesia and is associated with increased morbidity.

Multiparametric Magnetic Resonance Imaging

Multiparametric magnetic resonance imaging (MRI) includes anatomic T2-weighted imaging for localization of the normal gland and cancer foci and two functional imaging techniques: diffusion-weighted and perfusion imaging. Multiparametric MRI evaluation permits identifying tumor location and extent, oversampling areas of interest, undersampling (or not sampling nontarget areas), and sampling of clinically significant disease (higher grade tumor). T2-weighted images reflect water content of tissues and can define the zonal anatomy of the prostate and the presence of prostate cancer as focal areas of low-signal intensities. The degree of intensity decrease differs with Gleason score; higher Gleason score prostate cancer shows lower signal intensities.[2] False-positive findings can occur with benign abnormalities including prostatitis, atrophy, fibrosis, gland hyperplasia, or irradiation or hormonal treatment effects. Diffusion-weighted images measure the random motion of water molecules. Low diffusion coefficients are associated with prostate cancer, and there is an inverse correlation between these values and Gleason score; however, confidence intervals overlap. Perfusion imaging permits assessment of contrast kinetics in focal lesions; prostate tumors typically enhances faster and to a greater extent than the surrounding prostate; however, the nonspecificity of patterns limits the usefulness of this technique in isolation.

Several methods of MRI guidance are available for prostate biopsy: cognitive (or visual), direct (“in-bore”), and MRI-ultrasound fusion (visual targeted or software-based targeted). Image fusion is the process of combining information from more than one image into a single image, which may be more informative than any of the images separately. Based on MRI, suspicious areas are identified (i.e., regions of interest) and subjected to targeted biopsy.

With the visual method, the ultrasound operator simply aims the biopsy needle at the area of the prostate where prior MRI indicated the lesion. This method requires the MRI unit, a conventional TRUS facility, and an ultrasound operator with no additional training beyond TRUS biopsy. The disadvantage is the potential for human error in the extrapolation from MRI to TRUS without an overlay of the images.

Direct (in-bore) MRI-targeted biopsy requires the MRI tube, fusion of a prior MRI demonstrating a lesion with a contemporaneous MRI to confirm biopsy needle location, and needles introduced into the regions of interest. Serial MRI scans are performed to confirm biopsy needle placement. Studies have demonstrated that in-bore MRI-targeted biopsies have a median cancer detection rate significantly higher than random biopsies; however, this technique is time-consuming and costly, including the in-bore time and the two MRI sessions necessary. In addition, only suspicious lesions are sampled, because tissues with a “normal” appearance on MRI are not obtained.

MRI-TRUS fusion biopsy, done visually or using software, superimposes preprocedure (stored) MRI over an intraprocedural (real-time) ultrasound to direct the biopsy needle to an ultrasound region of interest defined by multiparametric MRI.

Table 1 summarizes the MRI requirements for the three different MRI-guided prostate biopsy techniques described.

Table 1. Techniques for MRI-Guided Prostate Biopsy

Method	MRI Requirement(s)	Description
Visual	• Prior MRI of prostate lesion	US operator targets the biopsy needle at the area of the prostate where prior MRI indicated a lesion during TRUS
Direct	• Prior MRI of prostate lesion • Contemporaneous MR images of biopsy needle in prostate lesion location	Fusion of a prior MRI demonstrating a lesion with a contemporaneous MRI to confirm biopsy needle location, and needles introduced into the regions of interest
MRI-US fusion (visual targeted or software-based targeted)	• Prior MRI of prostate lesion • Overlay of prior MR image over real-time US	Prior MR image superimposed over an intraprocedure (real-time) US to direct the biopsy needle during TRUS

MR: magnetic resonance; MRI: magnetic resonance imaging; TRUS: transrectal ultrasound; US: ultrasound.

Currently, there is evidence comparing these three techniques in terms of their ability to detect overall or clinically significant prostate cancer.

Proposed clinical indications for use of MRI-targeted prostate biopsy include: (1) as initial biopsy, (2) rebiopsy after a first negative standard biopsy in men with persistent suspicion of disease, including those with persistently increased prostate-specific antigen levels, suspicious digital rectal exam, previous biopsy with an atypical focus on histology, or extensive high-grade prostatic intraepithelial neoplasia, (3) follow-up for active surveillance to determine initial eligibility for active surveillance and assessing progression disease over time, and (4) for local recurrence after radical prostatectomy, after external-beam radiotherapy, or after high-intensity focused ultrasound.

REGULATORY STATUS

MRI-targeted or MRI-TRUS fusion biopsy is a medical procedure that uses MRI and ultrasound devices previously approved by the U.S. Food and Drug Administration (FDA). Prostate biopsy is a surgical procedure and, as such, is not subject to regulation by FDA.

FDA product code, ultrasound devices: IYN, ITX, IYO. FDA product code, MRI devices: LNH, LNI, MOS.

Several MRI-US fusion software-based targeted prostate biopsy platform specifications have been cleared for marketing by FDA through the 510(k) process. Fusion software includes Artemis™ (Eigen), BioJet™ (D&K Technologies), BiopSee® (MedCom), Real-time Visual Sonography (Hitachi, Tokyo, Japan), UroNav™ (Invivo/Philips), Urostation® (Koelis), and Virtual Navigator (Esaote).

RELATED PROTOCOL

Saturation Biopsy for Diagnosis, Staging and Management of Prostate Cancer

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

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced

procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

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

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