

## Prostate MRI Model Policy

**Subject:** prostate MRI for the detection, localization, and characterization of primary cancer within the prostate

**Scope:** Prostate MRI, also referred to as multi-parametric or bi-parametric MRI depending on the examination protocol, is a diagnostic test intended to detect, localize, and characterize primary cancer within the prostate. It entails obtaining high-resolution MR images of the prostate using multiple tissue contrast mechanisms and in multiple planes. Abnormalities in the prostate that are detected on MRI may, in turn, serve as targets for a subsequent MRI-targeted prostate biopsy, often using advanced technologies to direct the biopsy to the area of the abnormality on MRI. This document addresses prostate MRI in a range of pre-treatment settings, including biopsy-naïve patients, patients with a prior negative prostate biopsy, and patients with a prior prostate biopsy who are undergoing active surveillance or pre-operative staging.

Please note that this model coverage policy will only be addressing the use of prostate MRI in the work-up of suspected or known malignancies of the prostate. Prostate MRI is not currently indicated in men with no risk factors such as an abnormal PSA, abnormal serum or urinary biomarker, family history, or abnormal digital rectal exam. Potential uses of prostate MRI in the work-up of advanced (metastatic) and other prostate disorders will not be addressed in this document.

### Coverage:

#### -Biopsy-naïve:

In biopsy-naïve patients, prostate MRI is considered **medically necessary** as an alternative to standard prostate biopsy alone for increasing the detection of clinically significant cancer on prostate biopsy in patients with one or more of the following:

- PSA > 4.0
- PSA density > 0.15
- Other abnormal serum or urinary biomarker
- Abnormal digital rectal examination
- Family history of prostate cancer

#### -Prior negative biopsy:

In patients with a prior negative prostate biopsy, prostate MRI is considered **medically necessary** as an alternative to a repeat standard biopsy alone for increasing the detection of clinically significant cancer on prostate biopsy in patients with a persistent clinical suspicion prostate cancer based on a persistent elevation of PSA or a persistent abnormality of another serum or urinary biomarker.

#### -Prior positive biopsy (local staging and active surveillance):

In patients with a prior positive prostate biopsy, MRI is considered **medically necessary** in either of the following two circumstances:

- For assessment of the appropriateness of active surveillance
- For pre-surgical planning

## Description

Prostate cancer is the most common non-cutaneous cancer in adult men in the U.S. However, it is a heterogeneous disease process, ranging from indolent tumors that will never affect survival to highly lethal cancers that can advance rapidly. Historically, prostate cancer has been diagnosed through a non-targeted transrectal ultrasound systematic (TRUS) biopsy. However, the inherent limitations of this procedure have led to a range of challenges in prostate cancer management. A standard biopsy is prone to missing clinically significant cancers as well as to commonly detecting indolent tumors. Because of these issues, patients and treating physicians often lack confidence in the results of the biopsy, leading to anxiety, uncertainty, and potentially serial repeat biopsies in attempting to establish a diagnosis and overall level of risk.

Prostate MRI addresses these challenges by identifying areas in the prostate suspicious for clinically significant cancer while tending not to detect many clinically insignificant ones. Prostate MRI entails obtaining high-resolution images of the prostate using multiple tissue contrast mechanisms and in multiple planes. Following prostate MRI, a targeted biopsy can be performed, potentially using advanced technologies to direct the biopsy to the suspicious areas on MRI. Peer-reviewed literature supports added clinical value of prostate MRI in a range of clinical scenarios, and prostate MRI is being increasingly recognized by medical practitioners and key stakeholder organizations.

## Rationale

-Biopsy-naïve:

Three prospective multicenter randomized trials support the value of prostate MRI in biopsy-naïve patients, providing compelling level 1 evidence in support of the service. In the PRECISION trial, among 500 men, randomized to either TRUS biopsy or MRI-targeted biopsy, clinically significant cancer was detected in 38% of those undergoing MRI-targeted biopsy vs. 26% of those undergoing a standard biopsy; MRI-targeted biopsy also diagnosed fewer insignificant tumors.<sup>1</sup> In the 4M trial of 626 men, targeted and systematic biopsies detected identical numbers of clinically significant cancers, though targeted biopsy detected significantly fewer insignificant cancers.<sup>2</sup> Furthermore, both biopsies were obtained at the same time, potentially increasing the yield of systematic biopsies. In the MRI-FIRST trial of 275 men including 94 found to have clinically

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<sup>1</sup> Kasivisvanathan V, Rannikko, M. Borghi, V. Panebianco et al., MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. *N Engl J Med.* 2018 May 10;378(19):1767-1777. doi: 10.1056/NEJMoa1801993.

<sup>2</sup> van der Leest M, Cornel E, Israël B et al., Head-to-head Comparison of Transrectal Ultrasound-guided Prostate Biopsy Versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonance-guided Biopsy in Biopsy-naïve Men with Elevated Prostate-specific Antigen: A Large Prospective Multicenter Clinical Study. *Eur Urol.* 2019 Apr;75(4):570-578. doi: 10.1016/j.eururo.2018.11.023.

significant cancer, 20% were diagnosed by targeted biopsy alone.<sup>3</sup> In the PROMIS trial of 576 biopsy-naïve men from eleven NHS hospitals in England, prostate MRI was more sensitive than TRUS biopsy for clinically significant cancer (93% vs. 48% respectively), and as a triage test could have allowed 27% of men to avoid an initial biopsy and for 5% fewer insignificant cancers to be diagnosed.<sup>4</sup> In the paired prospective cohort BIDOC study of 1,020 biopsy-naïve men, MRI-targeted biopsies resulted in detection of 11% more significant cancers and 40% fewer insignificant cancers vs. TRUS biopsies, and could have avoided biopsy in 30% of patients.<sup>5</sup> In a single-center prospective randomized study by Panebianco et al of 1,140 patients, MRI-targeted biopsy also achieved greater detection, than did a systematic biopsy, of clinically significant cancer.<sup>6</sup>

The international PI-RADS Steering Committee, in its PI-RADS Multiparametric MRI and MRI-Directed Biopsy Pathway based on high-quality evidence, recommends prostate MRI in biopsy-naïve men and men with a prior negative biopsy with clinical suspicion for prostate cancer.<sup>7</sup>

**-Prior negative biopsy:**

Persistent clinical suspicion for prostate cancer following a negative prostate biopsy represents one of the most widely accepted and clinically adopted reasons for performing prostate MRI. This scenario also represents the context of much of the early peer-reviewed literature regarding multiparametric prostate MRI. In a study by Mendhiratta et al of 210 patients, among Gleason score  $\geq 7$  cancers, targeted biopsy detected 90%, while standard biopsy detected 52%.<sup>8</sup> In a study by Abdi et al of 86 patients, clinically significant cancer was detected in 35% of patients undergoing both systematic and targeted biopsy, compared with 16% of matched controls undergoing only

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<sup>3</sup> Rouvière O, Puech P, Renard-Penna R et al., Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naive patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. *Lancet Oncol.* 2019 Jan;20(1):100-109. doi: 10.1016/S1470-2045(18)30569-2.

<sup>4</sup> Ahmed HU, El-Shater Bosaily A, Brown LC et al., Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet.* 2017 Feb 25;389(10071):815-822. doi: 10.1016/S0140-6736(16)32401-1.

<sup>5</sup> Boesen L, Nørgaard N, Løgager V, et al., Assessment of the Diagnostic Accuracy of Biparametric Magnetic Resonance Imaging for Prostate Cancer in Biopsy-Naive Men: The Biparametric MRI for Detection of Prostate Cancer (BIDOC) Study. *JAMA Netw Open.* 2018 Jun 1;1(2):e180219. doi: 10.1001/jamanetworkopen.2018.0219.

<sup>6</sup> Panebianco V, Valerio MC, Giuliani A et al., Clinical Utility of Multiparametric Magnetic Resonance Imaging as the First-line Tool for Men with High Clinical Suspicion of Prostate Cancer. *Eur Urol Oncol.* 2018 Aug;1(3):208-214. doi: 10.1016/j.euo.2018.03.008.

<sup>7</sup> Padhani AR, Barentsz J, Villeirs G, et al., PI-RADS Steering Committee: The PI-RADS Multiparametric MRI and MRI-directed Biopsy Pathway. *Radiology.* 2019 Jun 11:182946. doi: 10.1148/radiol.2019182946. [Epub ahead of print]

<sup>8</sup> Mendhiratta N, Meng X, Rosenkrantz AB et al., Prebiopsy MRI and MRI-ultrasound Fusion-targeted Prostate Biopsy in Men With Previous Negative Biopsies: Impact on Repeat Biopsy Strategies. *Urology.* 2015 Dec;86(6):1192-8. doi: 10.1016/j.urology.2015.07.038.

SB.<sup>9</sup> In a study by Salami et al. of 140 patients, clinically significant cancer was detected in 31% of patients undergoing standard biopsy vs. 48% of those undergoing targeted biopsy.<sup>10</sup> In 2016, the American Urological Association and Society of Abdominal Radiology released a joint consensus statement recommending that prostate MRI be strongly considered in any patient with a prior negative biopsy who has persistent clinical suspicion for prostate cancer and who are undergoing a repeat biopsy.<sup>11</sup>

-Prior positive biopsy (active surveillance and local staging):

In patients with a prior prostate biopsy positive for cancer, prostate MRI can help in risk stratification in terms of determining eligibility and appropriateness of active surveillance. In a study by Abdi et al of 111 patients on active surveillance for localized prostate cancer, MRI led to surveillance being terminated in 24%, and MRI suspicion score was the only independently significant predictor of surveillance termination in multivariable analysis.<sup>12</sup> In a study by Da Rosa et al of 72 men on active surveillance, MRI-targeted biopsy was 6.3 times more likely to yield a core with clinically significant cancer than a systematic biopsy.<sup>13</sup> In a study by Pessoa et al. of 105 patients being considered for active surveillance, only MRI and PSA density were significant independent predictors of disease reclassification at multivariable analysis.<sup>14</sup> Based on a meta-analysis conducted by Schoots et al, MRI is useful to detect clinically significant cancer at the time of initial assessment of men being considered for active surveillance.<sup>15</sup> Based on a meta-analysis by Guo et al. of 7 studies totaling 1028 active surveillance candidates, MRI revealed an unrecognized significant lesion in 33% of patients, and when MRI was not suspicious, the likelihood of reclassification on repeat biopsy was very low at 6%.<sup>16</sup> A meta-analysis by van den

<sup>9</sup> [Abdi H](#), [Zargar H](#), [Goldenberg SL](#) et al., Multiparametric magnetic resonance imaging-targeted biopsy for the detection of prostate cancer in patients with prior negative biopsy results *Urol Oncol*. 2015 Apr;33(4):165.e1-7. doi: 10.1016/j.urolonc.2015.01.004. Epub 2015 Feb 7.

<sup>10</sup> [Salami SS](#), [Ben-Levi E](#), [Yaskiv O](#), et al., In patients with a previous negative prostate biopsy and a suspicious lesion on magnetic resonance imaging, is a 12-core biopsy still necessary in addition to a targeted biopsy? *BJU Int*. 2015 Apr;115(4):562-70. doi: 10.1111/bju.12938.

<sup>11</sup> Rosenkrantz AB, Verma S, Choyke P, et al. Prostate Magnetic Resonance Imaging and Magnetic Resonance Imaging Targeted Biopsy in Patients with a Prior Negative Biopsy: A Consensus Statement by AUA and SAR. *J Urol*. 2016;196(6):1613–1618. doi:10.1016/j.juro.2016.06.079

<sup>12</sup> [Abdi H](#), [Pourmalek F](#), [Zargar H](#) et al., Multiparametric magnetic resonance imaging enhances detection of significant tumor in patients on active surveillance for prostate cancer. *Urology*. 2015 Feb;85(2):423-8. doi: 10.1016/j.urology.2014.09.060.

<sup>13</sup> [Da Rosa MR](#), [Milot L](#), [Sugar L](#), et al., A prospective comparison of MRI-US fused targeted biopsy versus systematic ultrasound-guided biopsy for detecting clinically significant prostate cancer in patients on active surveillance. *J Magn Reson Imaging*. 2015 Jan;41(1):220-5. doi: 10.1002/jmri.24710.

<sup>14</sup> [Pessoa RR](#), [Viana PC](#), [Mattedi RL](#) et al., Value of 3-Tesla multiparametric magnetic resonance imaging and targeted biopsy for improved risk stratification in patients considered for active surveillance. *BJU Int*. 2017 Apr;119(4):535-542. doi: 10.1111/bju.13624.

<sup>15</sup> [Schoots IG](#), [Petrides N](#), [Giganti F](#) et al., Magnetic resonance imaging in active surveillance of prostate cancer: a systematic review. *Eur Urol*. 2015 Apr;67(4):627-36. doi: 10.1016/j.eururo.2014.10.050.

<sup>16</sup> [Guo R](#), [Cai L](#), [Fan Y](#), Magnetic resonance imaging on disease reclassification among active surveillance candidates with low-risk prostate cancer: a diagnostic meta-analysis. *Prostate Cancer Prostatic Dis*. 2015 Sep;18(3):221-8. doi: 10.1038/pcan.2015.20.

Bergh et al also concluded, based on 14 studies, that MRI may improve patient selection for active surveillance.<sup>17</sup>

The 2019 NCCN guidelines on prostate cancer recommend the role of prostate MRI in men on active surveillance.<sup>18</sup>

In patients with a prior positive biopsy who are undergoing local staging prior to surgery, MRI can localize dominant tumors in the gland to help guide decision-making regarding nerve-sparing surgical approaches, preserve the neurovascular bundles, and achieve negative surgical margins. In a study by McClure et al. of 104 patients, MRI changed the surgical plan in 27%, all of whom had a negative surgical margin ipsilateral to the change in treatment plan.<sup>19</sup> In a study by Jäderling et al of 557 patients, undergoing pre-operative MRI was also associated with the degree of nerve-sparing surgery and reduced likelihood of positive surgical margins.<sup>20</sup>

-Additional supporting evidence:

Additional meta-analyses by Fütterer et al (12 studies; biopsy-naïve and prior negative biopsy)<sup>21</sup> and Valerio et al (14 studies; biopsy-naïve, prior negative biopsy, active surveillance) also support the role of prostate MRI in improving the detection of clinically significant cancer relative to standard biopsy.<sup>22</sup>

A comprehensive Cochrane review in 2019 encompassing 18 studies across all three clinical scenarios also concluded that MRI-targeted biopsy increases detection of clinically significant cancer with lesser detection of insignificant cancer compared with systematic biopsy.<sup>23</sup>

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<sup>17</sup> [van den Bergh RC](#), [Ahmed HU](#), [Bangma CH](#) et al., Novel tools to improve patient selection and monitoring on active surveillance for low-risk prostate cancer: a systematic review. [Eur Urol](#). 2014 Jun;65(6):1023-31. doi: 10.1016/j.eururo.2014.01.027.

<sup>18</sup> [Mohler JL](#), [Antonarakis ES](#), [Armstrong AJ](#) et al., Prostate Cancer, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology. [J Natl Compr Canc Netw](#). 2019 May 1;17(5):479-505. doi: 10.6004/jnccn.2019.0023.

<sup>19</sup> [McClure TD](#), [Margolis DJ](#), [Reiter RE](#), et al., Use of MR imaging to determine preservation of the neurovascular bundles at robotic-assisted laparoscopic prostatectomy. [Radiology](#). 2012 Mar;262(3):874-83. doi: 10.1148/radiol.11103504

<sup>20</sup> [Jäderling F](#), [Akre O](#), [Aly M](#) et al., Preoperative staging using magnetic resonance imaging and risk of positive surgical margins after prostate-cancer surgery. [Prostate Cancer Prostatic Dis](#). 2018 Nov 30. doi: 10.1038/s41391-018-0116-z

<sup>21</sup> [Fütterer JJ](#), [Briganti A](#), [De Visschere P](#) et al., Can Clinically Significant Prostate Cancer Be Detected with Multiparametric Magnetic Resonance Imaging? A Systematic Review of the Literature. [Eur Urol](#). 2015 Dec;68(6):1045-53. doi: 10.1016/j.eururo.2015.01.013.

<sup>22</sup> [Valerio M](#), [Donaldson I](#), [Emberton M](#) et al., Detection of Clinically Significant Prostate Cancer Using Magnetic Resonance Imaging-Ultrasound Fusion Targeted Biopsy: A Systematic Review. [Eur Urol](#). 2015 Jul;68(1):8-19. doi: 10.1016/j.eururo.2014.10.026.

<sup>23</sup> [Drost FH](#), [Osses DF](#), [Nieboer D](#) et al., Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. [Cochrane Database Syst Rev](#). 2019 Apr 25;4:CD012663. doi: 10.1002/14651858.CD012663.pub2.

Studies also support a particular role of prostate MRI in detecting anterior cancers that may be more challenging to diagnose by standard biopsies that use a posterior approach.<sup>24,25</sup>

**-Additional considerations**

A range of factors will affect the impact of prostate MRI in clinical practice. In order for prostate MRI to achieve maximal efficacy, it is imperative that the images and interpretation be of high quality. Radiologists must have familiarity and experience in the area, adhering to practice standards and performing routine and rigorous quality assurance efforts to ensure achieving sufficient performance. While the available literature provides a range of actual values in terms of the benefit of prostate MRI, such studies are heterogeneous due to variable patient selection, MRI acquisition protocols, radiologist experience, urologist experience, targeted biopsy methods and approaches for histologic correlation. Nonetheless, the weight of the available literature supports a positive impact on patient care of prostate MRI across the outlined scenarios.

**Not medically indicated**

Multi-parametric prostate MRI is not medically indicated when not meeting any of the above specified clinical scenarios (e.g., for lymphoma or other biopsy-proven secondary malignancies of the prostate)

**Summary of covered CPT/ICD-10 code combinations**

**CPT**

72195	MRI pelvis without intravenous contrast
72196	MRI pelvis with intravenous contrast
72197	MRI pelvis with and without intravenous contrast

**ICD-10 Diagnosis**

N40.2	Nodular prostate without lower urinary tract symptoms
N40.3	Nodular prostate with lower urinary tract symptoms
N42.30	Unspecified dysplasia of prostate
N42.31	Prostatic intraepithelial neoplasia
N42.32	Atypical small acinar proliferation of prostate
N42.39	Other dysplasia of prostate
N42.83	Cyst of prostate

<sup>24</sup> [Lawrentschuk N, Haider MA, Daljeet N](#) et al., 'Prostatic evasive anterior tumours': the role of magnetic resonance imaging. [BJU Int.](#) 2010 May;105(9):1231-6. doi: 10.1111/j.1464-410X.2009.08938.x.

<sup>25</sup> [Radtke JP, Boxler S, Kuru TH](#) et al., Improved detection of anterior fibromuscular stroma and transition zone prostate cancer using biparametric and multiparametric MRI with MRI-targeted biopsy and MRI-US fusion guidance. [Prostate Cancer Prostatic Dis.](#) 2015 Sep;18(3):288-96. doi: 10.1038/pcan.2015.29.

N42.89	Other specified disorders of prostate
N42.9	Disorder of prostate, unspecified
C61	Malignant neoplasm of prostate
C79.82	Secondary malignant neoplasm of genital organs
D07.5	Carcinoma in situ of prostate
D29.1	Benign neoplasm of prostate
D40.0	Neoplasm of uncertain behavior of prostate
D49.89	Neoplasm of unspecified behavior of other specified sites
Z12.5	Encounter for screening for malignant neoplasm of prostate
Z85.46	Personal history of malignant neoplasm of prostate
Z80.42	Family history of malignant neoplasm of prostate
R97.20	Elevated prostate specific antigen [PSA]
R97.21	Rising PSA following treatment for malignant neoplasm of prostate
R97.8	Other abnormal tumor markers

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