

MR Imaging for Prostate Cancer Screening and Active Surveillance

Sasha C. Druskin, MD^a, Katarzyna J. Macura, MD, PhD^{a,b,*}

KEYWORDS

• Prostate cancer • MR imaging • Biopsy • Active surveillance • Cancer screening

KEY POINTS

- The risk that an MR imaging–detected prostate lesion represents cancer is highly dependent on the setting (diagnostic, confirmatory, active surveillance) in which the MR imaging is conducted. In the active surveillance setting, even high Prostate Imaging Reporting and Data System score lesions are rarely aggressive cancer.
- In the prostate cancer screening setting, the use of MR imaging for men with elevated prostate-specific antigen may reduce overdiagnosis.
- Men considering active surveillance likely benefit from MR imaging at the time of enrollment, because at least half may be made ineligible based on the MR imaging results.

INTRODUCTION

Prostate Cancer Screening

The screen-diagnose-treat paradigm of prostate cancer (PCa) management has been criticized in recent years for contributing to the overdiagnosis and overtreatment of the disease,¹ leading the US Preventative Services Task Force to recommend against prostate-specific antigen (PSA) screening for PCa.² Despite this criticism, screening for PCa has been shown in multiple large trials, namely the Göteborg³ and European Randomized Study of Screening for Prostate Cancer⁴ trials, to contribute to decreased rates of PCa-specific mortality (PCSM). Nonetheless, with numbers needed to screen (NNS) and diagnose in order to prevent one PCa death ranging from 293 to 781 and 12 to 27, respectively, in those 2 studies, clearly, an improved strategy to diagnose and treat PCa is warranted. The high NNS is in part due to the low

specificity and sensitivity of PSA for PCa,^{5,6} whereby it can be abnormally elevated in men who do not have PCa or in the normal range for men with PCa. It is also due to the fact that most PCa detected by screening is low-risk disease,⁷ which is unlikely to be clinically significant during a man's lifetime.⁸ In order to address deficits in screening, multiple urine and serum markers, including percentage of free-to-total PSA,⁵ PSA density,⁵ prostate health index (PHI)⁹ and PHI density,¹⁰ 4K score (OPKO Lab, Nashville, TN),¹¹ and PCA3,¹¹ have become available and may help more precisely select patients for prostate biopsy. Another approach to screening is the use of multi-parametric prostate MR imaging (mpMRI). mpMRI has been shown to have good performance for the detection of clinically significant PCa^{12–14} and has been used to decide on whether or not to biopsy and to help target lesions during initial biopsy.^{13,15–18}

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^a James Buchanan Brady Urological Institute, Johns Hopkins University School of Medicine, 600 North Wolfe Street, Marburg 134, Baltimore, MD 21287, USA; ^b Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, 600 North Wolfe Street, Sheikh Zayed Tower, Baltimore, MD 21287, USA

* Corresponding author.

E-mail address: kmacura@jhmi.edu

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Active Surveillance for Prostate Cancer

In order to address overtreatment of PCa, which is the case when disease that is unlikely to affect a man's well-being during his lifetime is nonetheless treated, active surveillance (AS) has taken an increasing role in the management of PCa.¹⁹ AS is generally chosen as a management strategy for men with favorable-risk disease.¹⁹ The premise of AS is that instead of treating PCa at the time of diagnosis, a patient is monitored at frequent intervals for signs of disease progression, at which point the plan is to treat the cancer with definitive curative therapy.¹⁹ Cancer progression is usually monitored with a combination of PSA, digital rectal examination (DRE), and systematic transrectal ultrasound-guided (TRUS) biopsy (SB).¹⁹ Progression on AS is generally regarded as upgrading (so-called grade-reclassification), or an increase in PCa volume (usually seen as an increase in the number of positive biopsy cores or percentage of a core that is positive for cancer, so-called volume-reclassification).¹⁹ In general, progression of disease out of AS eligibility is the trigger for urologists to recommend definitive treatment (generally radical prostatectomy [RP] or radiation therapy for localized disease).¹⁹ There are multiple institutions throughout the world that have been leaders in studying AS, and each has its own specific eligibility criteria¹⁹; however, most require National Comprehensive Cancer Network (NCCN) very-low-risk (T1c, Gleason ≤ 6 , PSA < 10 ng/mL, < 3 positive biopsy cores, $\leq 50\%$ of each core with cancer, PSA density < 0.15 ng/mL/g) or low-risk (T1-2a, Gleason ≤ 6 , PSA < 10 ng/mL) disease,²⁰ and a few allow for NCCN low-intermediate-risk disease (low-volume Gleason score 3 + 4) for men with limited life expectancy.¹⁹

The 2016 NCCN guidelines²⁰ on PCa provide AS as a management option for men with low- or very-low-risk disease and ≥ 10 years of life expectancy. Under the 2016 European Association of Urology guidelines,²¹ qualifying for AS requires that a man have greater than 10 years of life expectancy and a cancer profile that is similar to NCCN very-low-risk criteria, except that T2 disease also qualifies, and there is no PSA density cutoff.

In general, oncologic outcomes have been excellent, with rates of metastatic disease ranging from 0.1% to 2.8%, overall PCSM ranging from 0% to 1.5%, 15-year PCSM ranging from 0.1% to 5.7%, and rates of secondary definitive treatment ranging from 24% to 40% at 5 years and 36% to 55% at 10 years.¹⁹ Despite these successes, AS is not without its difficulties, which include a laborious monitoring program (with frequent PSA checks and prostate biopsies every

1–2 years^{19–21}) and the occasional inaccurate risk-classification of a patient that results in cancer-related morbidity and mortality. As with screening, biomarkers and MR imaging are being investigated in the AS realm²² in order to improve patient risk classification.

In AS, MR imaging has had multiple roles. The first is in identifying potential disease that was missed on SB, in order to evaluate a patient's eligibility for AS.^{23–30} SB generally samples only the posterior prostate, with limited sampling of the apex of the prostate³¹; indeed, in patients going on to RP, Gleason score is upgraded from SB to RP in 36.3%, according to one large study.³² MR imaging can potentially identify an apical (Fig. 1) or anterior cancer (Fig. 2) missed on SB that could be sampled with targeted biopsy (TB).³³ Using this approach, a patient eligible for AS based on the pathology on their SB could be reassured that they likely do not have more extensive disease (given a negative MR imaging),¹⁸ or made ineligible for AS (with a lesion on MR imaging that is found to be higher-grade cancer on TB) (see Fig. 1). The second role for MR imaging in AS is in monitoring during AS (Fig. 3).^{12,34–36} In this article, the authors review the current literature on MR imaging in the screening and AS realms.

LITERATURE REVIEW

MR Imaging Diagnostic Performance

The ability of MR imaging to detect clinically significant prostate cancer

The ability of MR imaging to detect clinically significant PCa is dependent on the clinical setting. Ma and colleagues¹² showed in a study of MR imaging–TRUS fusion biopsy that the pathologies of lesions seen on MR imaging are very different for patients in the diagnostic setting versus the AS setting, with more aggressive cancer being detected and a higher incidence of cancer detection in the former. Those rates in the confirmatory biopsy setting, which is a surveillance biopsy within 1 year of AS enrollment, were in between those of the diagnostic and AS settings.

In the diagnostic setting, there are multiple ways that lesions on MR imaging can be compared with biopsy pathology. Looking at RP specimens³⁷ would be the definitive reference standard, but that limits the cohort to patients with a diagnosis of cancer and a diagnosis of aggressive enough cancer that treatment is warranted. Another strategy is to use MR imaging–TRUS fusion TB,¹² which can include patients with and without cancer (ie, the diagnostic setting). With that strategy, there is the risk for inaccurate targeting³⁷ and

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