

Imaging of Clinically Localized Prostate Cancer



Arman S. Walia, MD, William Huang, MD*

KEYWORDS

• Prostate cancer • MRI • PSMA • Micro-ultrasound • Focal therapy

KEY POINTS

- Although MRI is considered the standard for imaging of localized prostate cancer, alternative modalities such as micro-ultrasound and prostate-specific membrane antigen PET are increasing in utility.
- Incorporating imaging into active surveillance improves appropriate patient selection and may reduce the need for biopsy.
- Imaging should be obtained before and after treatment as it provides valuable information for more precise management, regardless of approach.
- Relying on frameworks for imaging assessment is essential in standardizing the growing complexity.

BACKGROUND

MRI

MRI has significantly transformed prostate cancer screening over the past 2 decades. The multiplanar views and high soft tissue contrast make MRI an ideal method for imaging of the prostate and surrounding pelvic structures. To standardize image acquisition and interpretation, the European Society of Urogenital Radiology developed the Prostate Imaging Reporting and Data System (PI-RADS) in 2012, an adaptation of the framework established in breast imaging.¹ This scoring system comprises 3 main sequences: T2-weighted imaging (T2W), dynamic contrast enhancement (DCE), and diffusion-weighted imaging (DWI).

On the T2W sequence, malignant lesions appear as discrete areas of low signal intensity in the peripheral zone (PZ). This is confounded by benign entities that may appear similar, such as prostatitis or post-treatment changes. Extraprostatic extension can be visualized as an irregular bulge along the rim of the prostate. Seminal vesicle invasion can be identified by low signal intensity or obscured visualization of the ejaculatory

duct. Transition zone (TZ) lesions similarly appear hypointense, but the presence of benign adenomas limits interpretation. Morphology is helpful as lenticular shape and ill-defined borders are suggestive of malignancy compared with well-circumscribed, homogeneous adenomas.

DWI utilizes the motion of water molecules to differentiate between malignant and benign tissue.² In DWI, multiple gradient pulses are applied at differing strengths known as *b*-values. More densely packed water molecules (diffusion-restricted) appear brighter, which raises suspicion of malignancy. The apparent diffusion coefficient (ADC) is a calculation of differing *b*-values that isolates the images of diffusion restriction from confounding noise, with higher restriction appearing darker on ADC maps.³

DCE is valuable in adjudicating suspicious lesions on T2W imaging. Malignant angiogenesis often leads to both increased vessel presence and permeability.⁴ Therefore, DCE focuses on both the intensity of uptake and the rapidity of uptake and washout. T1-weighted fast gradient images are obtained before, during, and after gadolinium-based contrast administration, over a

Department of Urology, NYU Langone Health, 222 E 41st street, 12th Floor, New York, NY 10016, USA

* Corresponding author.

E-mail address: William.huang@nyulangone.org

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Abbreviations	
ADC	apparent diffusion coefficient
AS	active surveillance
bpMRI	biparametric MRI
CDR	cancer detection rate
csPCA	clinically significant prostate cancer
DCE	dynamic contrast enhancement
DWI	diffusion-weighted imaging
FLAME	Focal Lesion Ablative Microboost
GG	grade group
mpMRI	multiparametric MRI
mUS	micro-ultrasound
P-GAP	PSMA-Guided Ablation of the Prostate
PI-FAB	Prostate Imaging after Focal Ablation
PI-RADS	Prostate Imaging Reporting and Data System
PI-RR	Prostate Imaging for Recurrence Reporting
PRECISE	Prostate Cancer Radiological Estimation of Change in Sequential Evaluation
PR-IMUS	Prostate Risk Identification using Micro-Ultrasound
PROMISE	Prostate Cancer Molecular Imaging Standardized Evaluation
PSMA	prostate-specific membrane antigen
PZ	peripheral zone
SUV	standardized uptake value
TARGET	Transatlantic Recommendations for Prostate Gland Evaluation with MRI After Focal Therapy
TRUS	transrectal ultrasound
T2W	T2-weighted imaging
TZ	transition zone

period of 2 to 5 minutes. Contrast-enhancing lesions alone are not as reliable for cancer detection, so DCE is used to supplement T2W-detected lesions.

Biparametric MRI (bpMRI) has had growing momentum as a quicker and less invasive alternative given the lack of DCE. There was limited high-level evidence of bpMRI until the results of the PRIME study were recently released at the European Association of Urology 2024 meeting.⁵ This was a prospective investigation to determine the noninferiority of bpMRI versus multiparametric MRI (mpMRI) for the detection of clinically significant prostate cancer (csPCA). Radiologists were initially blinded to the DCE phase to report the bpMRI, and then unblinded for mpMRI assessment. Any patients with PIRADS 3 to 5 lesions underwent targeted and systematic biopsy. The PI-RADS ≥ 3 detection rate was 56% and 57% for bpMRI and mpMRI, respectively. New areas of suspicion detected by DCE were found in 6.3% (4.3% were lesions not seen on bpMRI and 2.0% were

larger than previously appreciated). Both mpMRI and bpMRI identified 29% of csPCA (difference of 0.4%, noninferiority threshold met). Sensitivity and specificity thresholds were also reached, suggesting bpMRI serves as a reliable alternative.

Transrectal Ultrasound

Transrectal ultrasound (TRUS) for prostate biopsy was introduced in the mid-twentieth century as a means of improved prostatic visualization. Ultrasound probes emit sound waves that reflect at varying degrees depending on target tissue density, resulting in differing tissue echogenicity. The transrectal probe is typically 6 to 12 MHz. At initial probe insertion, the distal striated external sphincter muscles are seen with the urethra appearing as a hypoechoic midline tubular structure leading into the prostatic apex. The rim of the prostate is highlighted by the surrounding hyperechoic adipose tissue, which can be used to assess for extra-prostatic extension. The ejaculatory ducts appear as hyperechoic lines in the sagittal plane leading directly to the seminal vesicles. Just posterior to the seminal vesicles are the neurovascular bundles, which are readily identified with color Doppler. These lie above a hyperechoic horizontal line representing the rectal serosa, defining a target space for injection of local anesthetic at the time of biopsy. The zonal anatomy of the prostate is readily apparent, with the posterior PZ, central zone, anterior TZ, and fibromuscular stroma clearly distinguishable.

Micro-ultrasound

Micro-ultrasound (mUS) refers to the utilization of a higher frequency (29 MHz) device for higher resolution. Spatial resolution of 70 microns enables a more accurate evaluation of the prostate's ductal architecture.⁶ Although MRI is today's preferred imaging modality, it requires an additional patient visit, intravenous contrast, and the accuracy is both technology and radiologist-dependent. A lack of contrast enhancement limits mUS but can provide real-time architectural visualization at the time of biopsy. The primary scoring criteria for lesions detected on mUS are the Prostate Risk Identification using Micro-Ultrasound (PR-IMUS) scale, based on an initial pilot investigation comparing images with whole-mount prostatectomy specimens.^{7,8} The PR-IMUS score is summarized in **Table 1**.

Prostate-specific Membrane Antigen PET

Prostate-specific membrane antigen (PSMA) is the clinical term for a transmembrane protein expressed in secretory cells of the prostate luminal

Table 1
Summary of prostate risk identification using micro-ultrasound (PR-IMUS) scoring

PR-IMUS	
Score (Risk)	Criteria
1 (Very low)	Small, regular ducts ("swiss cheese") without heterogeneity
2 (Low)	Hyperechoic with or without ductal patches
3 (Equivocal)	Mild heterogeneity or bright echoes in hyperechoic tissue
4 (High)	Heterogeneous ("cauliflower"), smudgy or mottled, or bright echoes ("starry sky")
5 (Very high)	Irregular shadowing, mixed-echo lesions, irregular prostate border

epithelium (also known as glutamate carboxypeptidase II or folate hydrolase 1).⁹ The discovery of PSMA overexpression in prostate cancer led to US Food & Drug Administration (FDA) approval of Gallium-68 (⁶⁸Ga)-Ga-PSMA-11) in 2020 as a marker for PET imaging for staging and recurrence. Gallium-68 is the most used tracer, beneficial for its lower radiation exposure and more immediate availability via on-site generator. In 2021, the FDA approved [¹⁸F] DCFPyL for similar indications due to the potential higher image resolution of Fluorine-18. Another Fluorine-18 derivative ([¹⁸F] rhPSMA-7) was approved in 2023 due to decreased urinary excretion that could theoretically improve radiologic interpretation. Fluorine-18 remains limited by the need for a cyclotron, but its longer half-life may make it a more preferred radiolabel for high volume production. A 2023 meta-analysis compared the 2 ligands though with limited available data.¹⁰ Fluorine-18 derivatives demonstrated a higher local lesion detection rate, but with higher detection of benign bone lesions as well. Gallium-68 efficacy appeared to improve when combined with diuretic use, suggesting that overall cancer detection had not yet reliably demonstrated a clinical difference.¹⁰ Other diagnostic radioligands being investigated with potential therapeutic promise include Technetium-99m and Copper-64; standardized uptake value (SUV) is the unit of measurement applied to suspicious lesions, accounting for body weight and dosage to reliably compare between scans. Current investigations support an increasing SUV max as indicative of increasing aggressiveness of the disease. However, reliability wanes at lower values, and false positives occur in

various other tissues including the duodenum, liver, and parotid glands, among others. Therefore, differential rather than absolute PSMA expression has been adopted as the primary modality for assessing PSMA PET imaging. The Prostate Cancer Molecular Imaging Standardized Evaluation (PROMISE) classification is a 4-point scale utilized for differential expression scoring, relating the lesion SUV max to uptake in the blood, liver, and parotid glands.¹¹ This expression score is also applied to intraprostatic lesions via the PRIMARY score (PROMISE and PRIMARY scores are provided in [Table 2](#)).

HOW WELL DOES IMAGING IDENTIFY LOCALIZED DISEASE?

Transrectal Ultrasound

Lee and colleagues used various ultrasound characteristics to establish a TRUS scoring system for malignant lesions including location, echotexture, outline, shape, vascularity, and capsular bulging.¹² On multivariate analysis lesion shape, irregular margin, and increased vascularity were significantly associated with prostate cancer detection ($P < .001$). For patients with a PSA less than 10.0 ng/mL, a 5-point Likert scale (0–4) was created with an area under the curve (AUC) of 0.81. The value of TRUS as an independent screening test is limited by a sensitivity of 37.5% when read by urologists.¹³

MRI

The detailed soft-tissue assessment provided by MRI makes it ideal for prostate evaluation. Oerther and colleagues published a thorough meta-analysis of studies evaluating the reliability of PI-RADS for cancer detection.¹⁴ The cancer detection rate (CDR) by PI-RADS category for grade group (GG) ≥ 2 disease was as follows: 1% to 6%, 2% to 6%, 3% to 16%, 4% to 49%, and 5% to 74%. The pooled sensitivity and specificity were 94% and 44% for PI-RADS ≥ 3 , respectively. These results are similar to others reported in the literature. No difference was found when stratifying lesions by PZ or TZ. The CDR for GG 1 disease by PI-RADS score was 1% to 14%, 2% to 10%, 3% to 18%, 4% to 18%, and 5% to 15%.

Some studies suggest a correlation between PI-RADS and tumor aggressiveness. Morote and colleagues retrospectively evaluated men who underwent targeted biopsies, finding higher PI-RADS scores favored worse GG distribution.¹⁵ They found PI-RADS 3, 4, and 5 lesions harbored GG ≥ 4 disease in 7.8%, 16.8%, and 51.7%, respectively. Unfavorable pathology (GG ≥ 3 or pathologic T stage ≥ 3) was found in 44%, 64%, and

Table 2
PROMISE V2 criteria for PSMA PET assessment: PSMA-expression score and PRIMARY score for local lesions

PSMA Expression Score		Description	
0—None		Below blood pool	
1—Low		≥ Blood pool and < liver	
2—Intermediate		≥ Liver and < parotid gland	
3—High		≥ Parotid gland	
PRIMARY Score	Description	PSMA Expression Score	Tumor Staging
PRIMARY Score:			
1	Low grade activity, no discrete lesion	0, 1	T0
2	Contained diffuse TZ or symmetric CZ activity	1, 2	T0
3	Focal TZ activity at least double background	2, 3	T2, T3, or T4
4	Focal PZ activity	1, 2, or 3	T2, T3, or T4
5	Intense uptake (>12 SUV max)	3	T2, T3, or T4
T0 = No tumor			
T2 = Organ-confined tumor			
T3 = Non-organ-confined tumor (seminal vesicle, extraprostatic extension)			
T4 = Locally invasive (sphincter, bladder, rectum, levator, sidewall)			
TZ: Transition zone			
CZ: Central zone			
PZ: Peripheral zone			

For liver-dominant PSMA expression (ie, [18F] F-PSMA), spleen in place of liver as reference.

90% of PI-RADS 3, 4, and 5 lesions, respectively. The results suggest a direct correlation between MRI suspicion and pathologic aggressiveness, but there are some limitations. The prevalence of GG 1 disease was significantly lower in the PI-RADS 4 and 5 cohorts than reported in the literature suggesting potential confounders selecting for more aggressive disease. Additionally, extracapsular extension on MRI is part of the inclusion criteria for PI-RADS 5 which inherently selects for unfavorable pathology in that group. While it is clear csPCa is more prevalent in higher PI-RADS lesions, it is not yet clear if this translates to more aggressive disease.

Multiple studies have evaluated the efficacy of MRI-targeted versus systematic biopsy for prostate cancer screening.^{16–18} Ahmed and colleagues compared MRI and standard TRUS biopsy to template mapping biopsies in over 500 men.¹⁶ Prostate MRI was more sensitive (93% vs 48%, $P < .001$) than standard TRUS biopsy, highlighting MRI as a strong screening tool. Eklund and colleagues compared rates of csPCa in an MRI-based screening versus standard biopsy pathway in a cohort of men with PSA ≥ 3 ng/mL.¹⁷ Participants with PI-RADS ≥ 3 underwent both MRI targeted and systematic biopsy. The overall csPCa detection rate was 21% in the MRI-group versus

18% in the standard biopsy cohort, establishing MRI-based screening as noninferior. Systematic biopsy contributed to 15% of identified malignancies in the MRI-cohort supporting the continued value of systematic sampling. Kasivisvanathan and colleagues adeptly evaluated the value of targeted versus systematic biopsy by randomizing screened men to receive one or the other.¹⁸ Targeted biopsy had a 12% improvement (nearly 50% relative improvement) in detection of GG ≥ 2 disease. This value is highlighted by the EAU 2025 Prostate Cancer Guidelines “strongly” recommending an MRI before biopsy in patients suspected to have prostate cancer.

The differential aggressiveness of MRI visible versus invisible disease has also been investigated. Prostatectomy specimens demonstrate up to 35% of GG ≥ 2 disease is missed by MRI.¹⁹ Lehto and colleagues evaluated a series of prostatectomy specimens (GG 2–3) and compared histologic composition and transcriptomic profiling between MRI visible and invisible lesions.²⁰ Multiple differentially expressed genes were present in MRI visible tumors, with a subset associated with worsened metastasis and cancer-specific survival. Data suggest that MRI-invisible GG 2 to 3 disease is potentially less concerning than MRI-visible disease, and MRI may

therefore identify the more clinically relevant malignancy.

Overall, the data demonstrate that MRI can reliably identify csPCa. Visible lesions suggest more aggressive biology, but further investigation is necessary. Systematic biopsy remains essential, given the persistence of false positives and negatives. An example of prostate MRI is provided in **Fig. 1**.

Micro-ultrasound

Ghai and colleagues compared MRI-targeted, mUS-targeted, and combined MRI/mUS prostate biopsy, detecting csPCa in 39%, 35%, and 40%, respectively.²¹ No significant difference was found between modalities with most MRI-detected lesions visible on mUS. Socarras and colleagues compared mUS to mpMRI specifically for transperineal biopsy at a single institution and found 11% of PCa was uniquely detected by mUS.²² The recently published optimization of prostate biopsy - microultrasound vs MRI (OPTIMUM) trial provides the highest level of evidence to date evaluating mUS.²³ This was a noninferiority randomized trial to compare mUS-targeted to MRI fusion biopsy in detecting csPCa, with a secondary endpoint comparing standard MRI fusion to MRI/mUS together. The mUS and MRI-targeted cohorts identified csPCa in 46% and 43%, respectively (noninferiority met, $P < .001$). Combined mUS/MRI-targeted biopsy identified csPCa in 47%, which similarly met the noninferiority threshold compared with standard MRI fusion. csPCa was detected in 9% of patient without an identified mUS or MRI target. Six percent of mUS-detected malignancies were not seen on MRI compared with 6% of MRI-detected malignancies not seen on mUS. Altogether, the trial highlighted mUS-guided prostate biopsy as a viable alternative to MRI-guided in biopsy-naïve men. The presence of malignancy independently

identified on each imaging modality suggests value in a combined approach for detection.

Prostate-specific Membrane Antigen

The degree of PSMA uptake has been studied for tumor aggressiveness. In a retrospective review of prostatectomy patients with preoperative PSMA scans, median SUV max by GG was GG 1 to 6.45, GG 2 to 11.3, GG 3 to 18.1, GG 4 to 25.5, GG 5 to 24.3 ($P < .001$).²⁴ Of the 19 patients who were upgraded to \geq GG4 at the time of prostatectomy, median SUV max was significantly higher than those not upgraded (22.3 vs 11.3, $P < .001$).

Emmett and colleagues prospectively enrolled men undergoing prostate biopsy, obtaining an mpMRI and PSMA PET in each.²⁵ The addition of PSMA to MRI improved sensitivity (83% vs 97%, $P < .001$), but positive predictive value did not significantly change (64% vs 67%, $P = .4$). Among patients with csPCa, 10% were PSMA negative. In patients with PI-RADS 2/3 lesions and csPCa, PSMA was positive in 90%. In patients with PI-RADS 4/5 lesions and csPCa, PSMA was also positive in 90%. The same authors performed a post hoc analysis to determine the value of the PRIMARY score (1–5) in diagnostic accuracy for csPCa (**Table 2**).²⁶ csPCa detected per PRIMARY score was: 1% to 8.5%, 2% to 27%, 3% to 38%, 4% to 76%, 5% to 100%. Increasing SUV max was associated with higher malignancy detection for focal lesions. Additionally, increasing PRIMARY score was associated with higher GG \geq 3 distribution. An example of localized disease on PSMA PET is shown in **Fig. 2**.

HOW WELL DOES IMAGING STAGE DISEASE?

Current National Comprehensive Cancer Network (NCCN) and European Association of Urology (EAU) guidelines recommend consideration of

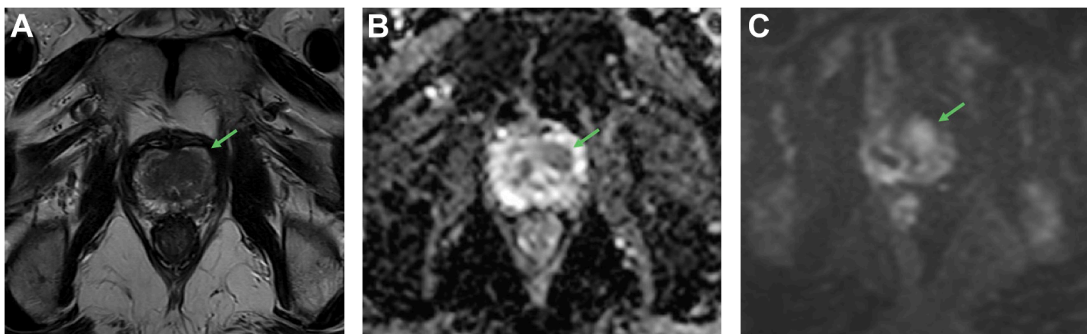


Fig. 1. A 76 year-old male with a left anterior apex 1.3 cm TZ lesion. PI-RADS 4 based on (A) T2W noncircumscscribed homogeneous moderate decreased signal, (B) DWI focal increased high b -value signal, and (C) focal marked decreased. Biopsy confirmed Gleason 3 + 4.

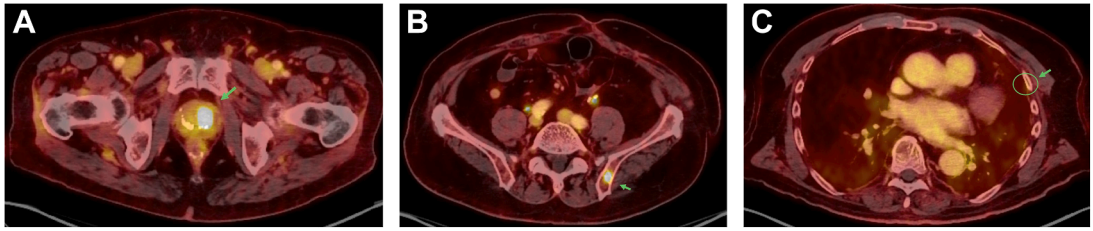


Fig. 2. Corresponding F-18 PSMA PET for patient from **Fig. 1**. Blood pool SUV max 3, liver SUV max 6.8, parotid gland SUV max 21. (A) Left anterior apex TZ PSMA avid lesion, SUV max 37, corresponding to PROMISE score of 3 and PRIMARY score of 5. (B) Left ilium PSMA-avid lesion concerning for metastasis, SUV max 7, PROMISE score of 2, presumed benign given stability over several years. (C) Left fourth rib lesion SUV 4, bone biopsy benign.

bone and soft tissue imaging in unfavorable intermediate or high-risk disease while American Urological Association (AUA) guidelines similarly caution against routine metastatic staging imaging in the asymptomatic low or intermediate risk patient. Given MRI is increasingly utilized in the screening process, it has become the preferred soft tissue imaging option. Similarly, at institutions with PSMA PET available, it has become the preferred option over traditional bone scan. For the purposes of this article, we will focus on MRI and PSMA PET scan.

MRI

Clinical tumor, nodal, metastasis staging can be done regionally via MRI. Reliable assessment of volume and laterality has resulted in the increased application of MRI for cT2a/b/c tumor categorization as opposed to digital examination. Signs of locally advanced disease can also be seen including extraprostatic extension, seminal vesical invasion, or involvement of the bladder neck, pelvic sidewall, and rectum. Nodal involvement is best seen on contrast-enhanced T1-weighted imaging with a broader field of view to the aortic bifurcation. While regional osseous involvement can be seen, additional imaging is typically needed for confirmation. Proper musculoskeletal assessment requires evaluation of the lesion on each dedicated sequence including alternatives such as fat suppression.

Prostate-specific Membrane Antigen

Computed tomography is the most widely used modality for metastatic assessment, due to its relatively lower cost and high accessibility. Common sites of evaluation include the axial skeleton, pelvis, and visceral organs. When available, PSMA PET has become the preferred modality due to its improved sensitivity and specificity. Hope and colleagues evaluated men with intermediate or high-risk prostate cancer who underwent PSMA PET followed by prostatectomy.²⁷ Overall,

27% (75/277) of men had positive pelvic nodes on final pathology. Sensitivity and specificity for PSMA PET were 41% and 95%, respectively. Positive predictive value and negative predictive value were 72% and 81%, respectively. Results were limited by the exclusion of patients with higher PSMA PET disease burden (cN1 rates of 54% in patients excluded from the study vs 14% for those who underwent prostatectomy). Incesu and colleagues evaluated the accuracy of PSMA PET in ruling out nodal disease in an intermediate risk cohort before prostatectomy.²⁸ Negative predictive value was 90%. The difference in negative predictive value from the prior study may be attributed to a lower prevalence in the intermediate risk group compared with the intermediate and high risk groups together. Taken together, PSMA PET demonstrates accuracy for both positive and negative regional nodal assessments, but its effectiveness is likely dependent on the individual's pretest probability.

Distant metastasis has also proved to be more accurate on PSMA PET than conventional imaging. Compared with bone scans, one study found that PSMA PET had higher sensitivity (98% vs 73%) and specificity (96% vs 79%) for detecting bone lesions.²⁹ However, reliability is limited by the presence of false positives. Chen and colleagues investigated the relatively common clinical scenario of localized disease with rib lesions.³⁰ In 62 men, only one false negative was identified. This was a low SUV max solitary lesion that ultimately grew before metastasis after local therapy. Four false positives were identified, of which 3 were biopsied and no malignancy was detected. The authors determined that most solitary rib lesions are benign and biopsy can typically be avoided (**Fig. 2C**).

HOW DOES IMAGING IMPACT ACTIVE SURVEILLANCE?

MRI

The value of MRI in active surveillance (AS) is evident in the higher rates of disease upgrading

in higher PI-RADS lesions. Sundaresan and colleagues retrospectively reviewed patients with PI-RADS 5 lesions diagnosed with GG 1 disease for upgrading to GG ≥ 2 on repeat biopsy.³¹ Of the patients on AS, 71% were upgraded on subsequent biopsies (74% at the second, 21% at the third). Gleason score was upgraded to GG 2, GG 3, and GG ≥ 4 in 70%, 21%, and 9% of men, respectively.

The Active Surveillance MR-Imaging Study (ASIST) trial was a prospective, randomized study comparing the progression rates of men with GG1 disease on AS.³² At the 2-year time point, 27% of men in the systematic biopsy cohort and 10% of men in the MRI cohort were upgraded to GG ≥ 2 disease ($P=.021$). The initial hypothesis was that adding MRI to confirmatory biopsy would show higher rates of disease progression. Though no difference was observed at the time of confirmatory biopsy, the 2-year results demonstrated a significantly lower upgrading rate in the MRI group. This was attributed to the earlier detection of clinically significant cancer in the MRI group, thereby reducing detection at the longer-term 2-year time point.

The widespread adoption of MRI into AS has led to the development of the Prostate Cancer Radiological Estimation of Change in Sequential Evaluation (PRECISE) guideline, which standardizes the assessment of change between MRIs. The summary is provided in **Table 3**, with the aim of providing a structure for reporting on the evolution of an individual's MRI on AS.³³

Micro-ultrasound

mUS is less studied. Albers and colleagues compared upgrading to GG ≥ 2 of patients on AS

using mUS and MRI.³⁴ Men with GG 1 disease underwent MRI/mUS fusion biopsy. The sensitivity and specificity for detection of GG ≥ 2 was 97% and 32% for PR-IMUS ≥ 3 and 85% and 53% for PI-RADS ≥ 3 , respectively. These results were limited by the knowledge of MRI findings at the time of ultrasound.

Prostate-specific Membrane Antigen

AS using PSMA may have potential, given its value in assessing localized disease. Liu and colleagues reviewed 4 relevant studies on PSMA and AS.³⁵ One included study found that higher SUV and evidence of extraprostatic extension on imaging were seen in patients with adverse features at prostatectomy. Another identified higher SUV was associated with an increasing pattern 4 disease. Currently, however, the benefit of PSMA over MRI is not yet evident in the AS space.

HOW DOES IMAGING IMPACT TREATMENT PLANNING?

Robotic-Assisted Laparoscopic Prostatectomy (RALP)

There are multiple features on MRI to guide a personalized prostatectomy. Suspicious lymph nodes can be seen on T1-weighted imaging and targeted for removal. Prostate size and morphology inform the approach to the bladder neck. Lesion location and capsular abutment are essential to recognize for reducing positive surgical margins. The highest risk is at the apex, where aggressive resection is balanced with preservation of continence.³⁶ Objective measurements such as apical prostate depth (distance of the apex from the proximal pubic symphysis) have been correlated to positive margin risk.³⁶ A tumor along the posterolateral surface impacts decision-making regarding nerve preservation. Panebianco and colleagues determined that MRI changed their approach from bilateral nerve-sparing to either unilateral or non-nerve sparing in 30% of cases.³⁷ Anterior tumors on MRI are important as they may not be detected on biopsy, particularly when considering candidacy for "hood-preservation." Membranous urethral length has also been studied as a predictor of postoperative continence, supported by a recent meta-analysis.³⁸

The use of PSMA in prostatectomy planning has also been reviewed. Similar to MRI, lesion location and the presence of extraprostatic extension can account for the risk of positive margins. More recently, PSMA has been leveraged for intraoperative targeting. Nguyen and colleagues studied IS-002 (a PSMA-binding peptide combined with infrared cyanine dye) for its ability to detect

Table 3
PRECISE version 2 scoring criteria for MRI in active surveillance

PRECISE Score	Description
1	Resolution of suspicious lesions from prior MRI
2	Decrease in size or conspicuity of suspicious lesion
3 (visible)	Stable MRI with a focal lesion
3 (invisible)	Stable MRI without a focal lesion
4	Increase in size or conspicuity of suspicious lesion, appearance of a new focal lesion
5	Evidence of stage progression

locoregional disease at the time of prostatectomy.³⁹ Patients were injected with the dye, and fluorescence imaging was used to detect areas bound by the PSMA fluorophore. Seven patients (29%) were found to have IS-002 detectable disease that was not seen in conventional white-light imaging.

Focal Therapy

For the index lesion(s), MRI is used to define size, location, and focal extent. This is important not only for effective targeting but also for device selection. Large or adjacent multifocal lesions can be managed with more confluent ablations such as cryoablation, whereas a more focal lesion in proximity to critical structures may require a more controlled energy (ie, laser or irreversible electroporation). Anterior tumors may benefit from transperineal approaches (ie, cryoablation) while posterior tumors are more accessible transrectally (ie, high-intensity focused ultrasound [HIFU]). Basing the margin of treatment on MRI appearance has also been studied. Le Nobin and colleagues demonstrated that MRI underestimated lesion size on histology by approximately 2 mm, and calculated that a 9 mm margin would yield complete treatment in all specimens included.⁴⁰

The role of PSMA in treatment planning is relatively new. Shin and colleagues identified a patient with MRI-negative but PSMA-positive GG 2 disease that was successfully treated with irreversible electroporation.⁴¹ Albers and colleagues are currently enrolling patients into the PSMA-Guided Ablation of the Prostate (P-GAP) randomized controlled trial to study MRI-based ablation versus the addition of preoperative PSMA on postoperative oncologic outcomes.⁴² The addition of PSMA PET may help identify concerning areas earlier and include them in treatment planning. It is feasible that PSMA PET/MRI will ultimately become the imaging modality of choice for focal therapy candidates.

Radiation

The widespread use of MRI in prostate cancer has made it one of the leading fields of MRI-based radiation treatment planning. The soft tissue definition provides improved contouring, resulting in a reduction of up to 40% in the clinical target volume (tumor plus microscopic disease) and subsequent reduced toxicity.⁴³ The value of MRI was furthered by the Focal Lesion Ablative Microboost (FLAME) trial.⁴⁴ Intermediate and high-risk prostate cancer patients were randomized to standard treatment versus the addition of focal boost up to 95 Gy to the dominant intraprostatic lesion on MRI. The intervention arm resulted in a higher 5-year biochemical disease-free survival with limited toxicity.

Integrating PSMA into radiation planning is also of interest. In a multicenter series of men with intermediate or high-risk prostate cancer, clinicians filled a treatment questionnaire before and after reviewing the results of a pre-treatment PSMA.⁴⁵ The imaging resulted in the identification of further localized disease in 27%, nodal disease in 39%, and metastatic disease in 10%. Multiple studies have demonstrated that PSMA may be more accurate in measuring gross tumor volume, which is often underestimated by MRI alone.⁴⁶ Ensuring accurate tumor volume is particularly meaningful given the current trend toward focal boost to index lesions.

HOW WELL DOES IMAGING ASSESS FOR LOCAL RECURRENCE?

Focal

Localized recurrence can occur after focal or radiation therapy. Post-treatment tissue effects make PI-RADS assessments and comparison to preoperative MRI difficult to rely upon. As a result, multiple proposed frameworks for reporting post-treatment MRI have been developed.

Early and late post-focal MRIs provide differential clinical value. Early imaging (weeks after

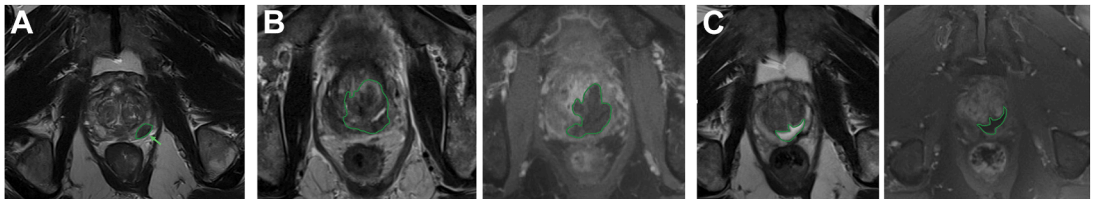


Fig. 3. A 67-year-old male with favorable intermediate risk disease. (A) A PI-RADS 4 9 mm left posterolateral PZ lesion was identified—biopsy demonstrated Gleason 3 + 4. (B) One-week post-focal treatment MRI shows heterogeneity on T2W imaging from inflammation, and an ablation cavity on perfusion imaging. (C) Six-month imaging shows a smaller ablation cavity on T2W imaging and perfusion imaging shows lack of enhancement consistent with successful treatment.

Table 4
Prostate Imaging after Focal Ablation scoring criteria for post-focal MRI recurrence

DCE	DWI	ADC	T2W	PI-FAB Score
-	-	+	+	1
+	-	+	+	2 ^a
+	+	+	+	3

DCE (+): focal early enhancement
 DWI (+): focal hyperintensity
 ADC (+): focal hypointensity
 T2W (+): focal hypointensity

^a If PI-FAB 2: a linear lesion away from the treated tumor is downgraded to PI-FAB 1. If within the ablated zone (site of initial tumor) or increased in size, then upgrade to PI-FAB 3.

treatment) enables assessment of the ablation size and confluence. Still, evaluation for recurrence is limited due to the heterogeneity of the treated tissue resulting from hemorrhage and necrosis.⁴⁷ Intermediate follow-up over 6 to 12 months will show decreased T2W intensity due to fibrosis and scarring, and is the optimal timing to identify persistent disease from incomplete treatment. **Fig. 3** demonstrates MRI findings at early and intermediate follow-up. Delayed imaging (ie, >12 months) provides information on recurrence over the longer term. The difficulty in interpreting PI-RADS lesions post-focal is due to the presence of a hypointense scar at the treatment site on T2W and DWI. More reliance is placed on enhancement within and adjacent to the treated tissue, making mpMRI imperative for post-treatment evaluation. In-field recurrence is detected by early enhancement at the treatment margins, while out-of-field recurrence can still rely on PI-RADS scoring. Two

scoring criteria have been proposed: PI-FAB (Prostate Imaging after Focal Ablation) and TARGET (Transatlantic Recommendations for Prostate Gland Evaluation with MRI After Focal Therapy). The PI-FAB scoring system uses a 3-point scale of increasing suspicion for biopsy (**Table 4**).⁴⁸ The TARGET system is a 5-point scale for increasing suspicion for biopsy, where each sequence is given a 3-point score (**Table 5**).⁴⁹ Long-term validation studies are required for both.

Post-focal PSMA has also been studied. Berger and colleagues obtained a PSMA PET/MRI in patients undergoing evaluation for post-HIFU recurrence.⁵⁰ In their initial 10-patient series, 6 (60%) were found to have biopsy-concordant lesions on PSMA not identified on conventional mpMRI. Further studies on the role of PSMA post-focal treatment are ongoing, with the goal of improving early detection for repeat treatment.

Radiation

Local recurrence after radiation treatment similarly requires a different approach to imaging evaluation. Radiation causes glandular atrophy, resulting in a smaller volume and diffuse hypointensity on T2W imaging. Zonal differentiation is more challenging due to inflammation and fibrosis, as is the identification of malignant disease. This makes DCE the more reliable sequence when increased vascularity is present in malignant tissue. To streamline reporting, the Prostate Imaging for Recurrence Reporting (PI-RR) framework was proposed.⁵¹ The DWI and DCE sequences dictate the risk of recurrence, whereas T2W is used independently to compare to pretreatment imaging and rule out benign nodules. It should be acknowledged that postbrachytherapy recurrences are

Table 5
Transatlantic recommendations for prostate gland evaluation with MRI after focal therapy (TARGET) scoring criteria for post-focal MRI recurrence

DCE Score	Description	Max T2W or DWI Score ^a	Overall Score
1	No early enhancement OR focal late enhancement OR any finding not seen in 2 or 3	1–2	1 (very low suspicion)
		3	2 (low suspicion)
2	Early enhancement that is focal nodular mild OR thin linear or curvilinear	1–2	3 (equivocal)
		3	4 (high suspicion)
3	Focal nodular strong early enhancement	Any	5 (very high suspicion)

DCE/T2W/DWI Scoring:
 1—Nonsuspicious
 2—Equivocal
 3—Suspicious

^a No specific objective criteria for DWI or T2W sequences proposed.

evaluated similarly but are limited by the presence of seed implants.

Postradiation assessment with PSMA may help overcome some of the limitations of MRI. Focal enhancement suggestive of malignancy is more identifiable due to high tissue contrast. Liu and colleagues obtained a PSMA PET in a series of patients being evaluated for radio-recurrent disease.⁵² There was a clear increase in upstaging for oligometastatic disease in the PSMA group versus standard imaging (27% vs 10%). Recurrence localized to the prostate was identified in 68% and 63% for the PSMA and MRI cohorts, respectively. The results suggest that local recurrence detection by PSMA is comparable to MRI, with the added benefit of more accurate extraprostatic evaluation.

SUMMARY

Technological innovations in imaging for localized prostate cancer have led to significant advancements in our management pathways, and continued investigation will further enhance our ability to detect, characterize, and monitor the disease.

FUTURE DIRECTIONS

While diagnostic imaging has advanced, there is much room for improvement. Further studies supporting real-world bpMRI and mUS accuracy could significantly improve access and cost, particularly in the pre-biopsy space. Low-field, in-office MRI companies are already on the market and have the potential to increase access and biopsy precision. The contemporary utilization of machine learning can be applied to newer, advanced MRI techniques such as hybrid multidimensional imaging and magnetic resonance fingerprinting to improve diagnostic accuracy. Each new FDA approved PSMA radioligand has provided a unique benefit. Continued refinement in diagnostic accuracy may also improve therapeutic precision, potentially allowing for reduced dose and therefore reduced adverse effects with maintained treatment efficacy.

CLINICS CARE POINTS (PEARLS AND PITFALLS)

- Biparametric MRI has a similar cancer detection rate as multiparametric MRI and should be considered as a cost-efficient alternative.
- MRI-visible csPCa appears to harbor more concerning genomic expressions than MRI-invisible disease, and this should be considered for management decision-making.

- Increasing evidence suggests micro-ultrasound may be noninferior to MRI in detection of csPCa.
- Prostate-specific membrane antigen (PSMA) imaging should be increasingly considered for localized disease treatment planning. Specific lesions can be targeted at the time of prostatectomy using a fluorescent, PSMA-bound molecule. Focal therapy candidacy and appropriate treatment can also be improved by the addition of PSMA to preoperative work up.
- Local recurrence after focal treatment or radiation therapy cannot be readily identified by PI-RADS scoring. Clinicians must rely on contrast enhancement for recurrence assessment.

DISCLOSURE

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DECLARATION OF AI-ASSISTED TECHNOLOGY

No AI-assisted technologies were utilized in the creation of this article.

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