Prostate Imaging

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Highlights

- Background of prostate cancer in the setting of rising PSA and negative biopsy
- Techniques for detection of cancer by MRI
- Techniques for repeat biopsy
- Future directions

Rising PSA and Prior Negative Biopsy in Prostate Cancer

Target audience: physicians and scientists involved with prostate cancer patients

Outcome/Objective: Understand the problem of, and solutions for, men with rising PSA and negative prostate biopsies

Purpose: Present MRI as a solution to the above problem

Methods: Literature review

Abstract

Current screening for prostate cancer in American men consists of physical examination and serum prostate specific antigen (PSA). If either are abnormal, the standard of care is systematic (non-targeted) transrectal ultrasound (TRUS) with biopsy. Over a million men in North America have an elevated PSA but negative TRUS biopsies. The false-negative rate has been reported as high as 47%. Magnetic resonance imaging (MRI) of the prostate has evolved from a technique aimed primarily for staging based on T2-weighted imaging (T2WI) to current multiparametric MRI (mpMRI) protocols including diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) perfusion imaging for lesion detection. The rate of lesion detection on MRI (non-negative MRI) ranges from 73-96% in published studies, depending on the protocol and criteria used. Detection of any cancer in targets ranges from 22-55%. Techniques include repeat TRUS with the location based on the description from the MRI, to image-fusion targeted biopsy where computer software fuses the location of the target on the MRI with the segmentation of the prostate by ultrasound to provide real-time targeting or retrospective confirmation of biopsy location choice, to in-bore direct MRI-guided targeting of suspicious areas with direct imaging confirmation of needle placement. In over two dozen investigations (some with overlapping populations) yield of any cancer, and especially significant cancer, is improved with use of mpMRI. However, all series report that some significant cancer can be missed by targeted biopsy. Whether a “negative” mpMRI with no targets is sufficient to defer repeat biopsy remains a matter of debate, made all the more complex by the continual improvement in mpMRI protocols and interpretation criteria.

Background: Prostate Cancer in the Setting of Rising PSA and Negative Biopsy

Approximately 16% of American men will be diagnosed with prostate cancer in their lifetime, but only 2.6% die of it.[1] This is complicated by the fact that the PIVOT trial found no benefit from prostatectomy with PSA<10 ng/mL, and that the USPSTF gives PSA screening a “D” score, meaning that the morbidity associated with screening outweighs the decreased mortality.[2] Although surveillance costs much less than radiation therapy or surgery (approximately $4,152 vs $17,795 or $15,467), it has its own inherent risks – not only infection or drug reactions to anesthesia associated with transrectal or

transperineal biopsy approaches respectively, but a significant risk of underdiagnosis. There is also the risk of "overdiagnosis," or treatment of otherwise indolent cancer for fear of missing significant cancer on systematic biopsies.

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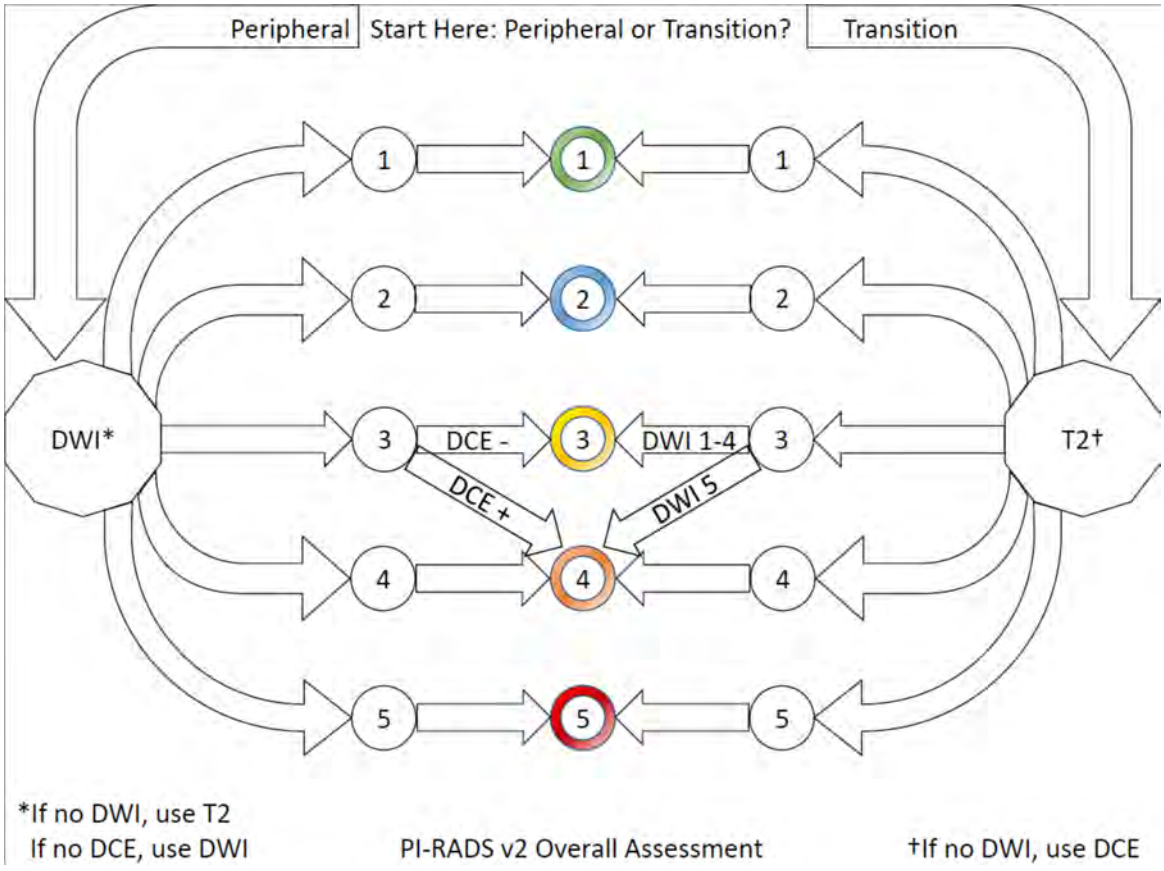
Methods for Detection of Cancer by MRI in the Setting of Rising PSA and Negative Biopsy

The evolution of prostate MRI has in no small part been evident by the continued technical presentations at ISMRM past. The protocol has evolved from one based primarily on T2WI and spectroscopic imaging for staging to one for lesion detection. It took nearly 2 decades from the first publication in 1983 describing the anatomy of the male pelvis to a pilot study in 1999 to evaluate men with prior negative biopsy.[4, 5] The first reported MRI-guided in-bore prostate biopsy followed a year later, but it was nearly another decade before the performance of image fusion software for real-time localization of mpMRI-detected targets using TRUS was published. [6, 7] In the intervening years, over a dozen articles have been published looking at targeted biopsies in the face of negative systematic biopsies and elevated PSA.[8-22] The rate of lesion detection on MRI (non-negative MRI) ranges from 73-96% in published studies, depending on the protocol and criteria used. Detection of any cancer in targets ranges from 22-55%.



The current recommendations for Prostate Imaging Reporting and Data Systems, including the performance and interpretation of mpMRI, is a joint collaboration of the American College of Radiology (ACR) and European Society of Uroradiology (ESUR), and released as PI-RADS v2. This document was largely formulated with the goal of a standardized way to scan for, identify, and report on *in situ* prostate cancer using mpMRI. A simply flow-chart is now used to determine suspicion levels, presented above.

Methods for Repeat Biopsy

Techniques include repeat TRUS with the location based on the description from the MRI, to image-fusion targeted biopsy where computer software fuses the location of the target on the MRI with the segmentation of the prostate by ultrasound to provide real-time targeting or retrospective confirmation of biopsy location choice, to in-bore direct MRI-guided targeting of suspicious areas with direct imaging confirmation of needle placement. "Cognitive" or "mental fusion" for repeat TRUS without software assistance is the simplest and most straightforward method to implement, especially if attention is paid to ultrasound features as they reflect those seen on MRI. However, a phantom study found that nearly a quarter of all targets invisible on ultrasound were missed by more than 3 mm even using image fusion. [23]

There are 3 main systems for image fusion TRUS targeted biopsy. An excellent review was published in 2013.[24] External magnetic field tracking allows "Wii" style freehand manipulation but could experience interference. Mechanical arm is initially cumbersome but stablizes probe. Image registration requires no additional hardware, but provides only retrospective targeting

Mechanical Articulated Arm	**Electromagnetic Tracking**	**Software Image Registration**
New hardware: mechanical arm	New hardware: EM tracker	Software only (may need new computer)
Real-time target tracking	Real-time target tracking	"Step-and-shoot" updating
Patient motion requires reregistration	Patient motion requires reregistration	Automatically comp-ensates for motion
Arm partially restricts motion	Susceptible to electro-magnetic interference	Steep angles limit registration
Setup requires attaching arm	Setup requires electro-magnetic registration	Only software registration
May require manual contouring of prostate	May require manual contouring of prostate	Must confirm software registration

There are some differences between in-bore and image fusion targeted biopsies, as well:

In-bore MRI Targeting	**Image Fusion TRUS Targeting**
Imaging confirmation of targeting	Image fusion accurate to within 3 mm
Can target all locations	Apex, far anterior hard
½ hr + 15 min/target	<30 min 12core+targets
Just targets	Can add systematic
Sedation	Local anesthesia
Requires dedicated hardware and software	Requires dedicated hardware and software

Discussion: Future Directions

As promising as mpMRI seems, all series described above report that some significant cancer can be missed by targeted biopsy. Whether a "negative" mpMRI with no targets is sufficient to defer repeat biopsy remains a matter of debate, made all the more complex by the continual improvement in mpMRI protocols and interpretation criteria. Depending on how one interprets the current literature, the risk of missing significant cancer is low, around 10%-25%. It can be argued that many of these men may be

safely captured on a repeat annual MRI and targeted biopsy, and that the risk of missing a small amount of what may yet be indolent is justified by the decreased morbidity of multiple biopsies. It may also be that one of these techniques will be shown superior for a specific population of men. Complicating this are new techniques which may improve prostate cancer detection, and therefore targeted biopsy, as well as innovations in both in-bore robotic-assisted biopsy and image fusion registration.[25-27]

Conclusion: mpMRI has been shown to be an effective way to identify cancer, and especially significant cancer, in men with rising PSA and prior negative biopsies.

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