outcomes must be acceptable and administration may need to be tailored in those patients at greater risk for prostate cancer mortality.

Suggested Reading


Re: Diagnostic Accuracy of Multi-Parametric MRI and TRUS Biopsy in Prostate Cancer (PROMIS): A Paired Validating Confirmatory Study


Division of Surgery and Interventional Science, Faculty of Medical Sciences and MRC Clinical Trials Unit, University College London and Departments of Urology, Histopathology and Radiology, University College London Hospitals NHS Foundation Trust, London, Hull York Medical School and Department of Health Sciences, University of York, York, Department of Urology, Hampshire Hospitals NHS Foundation Trust, Hampshire, Public and Patient Representative, Nottingham and Department of Academic Urology, Royal Marsden Hospital, Sutton, United Kingdom


Editorial Comment: In this study of multiparametric magnetic resonance imaging (MRI) before prostate biopsy men underwent prostatic MRI and 12-core transrectal ultrasound guided (TRUS) biopsy. The results of each test were compared to a transperineal template mapping (TPM) biopsy, also performed in each patient, to assess the predictive accuracy of each parameter for identifying clinically significant cancer, defined as Gleason score 4 + 3 or greater or cancer core length 6 mm or greater. The construct of the study is important as it assumes that TPM biopsy can serve as a referent test to determine the true prevalence of cancer. It is noteworthy that TPM biopsy detected cancer in 71% of men and clinically significant cancer in 40% at a mean age of 63.4 years. This finding is comparable to the results of age stratified autopsy studies, suggesting that the majority of cancers are identified on TPM biopsy. However, a small subset of men had clinically significant cancer on TRUS biopsy that was not found on TPM biopsy, and these results were deemed false-positives, demonstrating the imperfection of the referent test.

The authors found that MRI had greater sensitivity for clinically significant cancer (93%) than TRUS biopsy (48%) when using a cutoff MRI suspicion score of 3 or higher as abnormal. They conclude that if MRI targeting were added to traditional TRUS biopsy, 18% more clinically significant cancers would be identified, although this result relies on the assumption that MRI targeted biopsy would be accurate enough to find these cancers. In the absence of TPM biopsy it is unclear how many cancers identified on MRI would be found on biopsy.

More compelling is the argument that up to 27% of biopsies could be avoided using the negative threshold of MRI, and only 5% of clinically significant cancers would be missed. In practice this outcome relies on skilled and experienced radiologists interpreting the MRI studies but I have generally believed that this is an attainable goal through time. MRI had a much lower specificity than TRUS biopsy but this observation should be viewed with caution. In the context of this study specificity refers to biopsy outcome, not the decision for biopsy. In other words, if clinically significant cancer found on TRUS biopsy is also found on TPM biopsy, this result is a true-positive. As such, false-positives with TRUS biopsy would be rare.

It is generally well known that I am a strong advocate of pre-biopsy MRI as I believe it offers benefit for virtually every man undergoing biopsy. Nonetheless, one should view this study for what it is, a validation of MRI as a predictive tool, not unlike studies that correlate MRI findings with radical prostatectomy. The critical distinction is that prostatectomy studies suffer from selection bias, i.e the prevalence of significant disease in men selected for prostatectomy is much greater than in the current increased prostate specific antigen cohort, making MRI look worse. The findings of the study
do not tell us about the performance of MRI targeted biopsy and whether it would adequately bridge the gap between MRI and TRUS biopsy to justify routine use of pre-biopsy MRI. However, I believe there are already plenty of published data supporting this assertion.

**Suggested Reading**


Rosenkrantz AB, Mendrinos S, Babb JS et al: Prostate cancer foci detected on multiparametric magnetic resonance imaging are histologically distinct from those not detected. J Urol 2012; 187: 2032.


Pinto PA, Chung PH, Rastinehad AR et al: Magnetic resonance imaging/ultrasound fusion guided prostate biopsy improves cancer detection following transrectal ultrasound biopsy and correlates with multiparametric magnetic resonance imaging. J Urol 2011; 186: 1281.


**Uro-Science**

**Re: Rb1 and Trp53 Cooperate to Suppress Prostate Cancer Lineage Plasticity, Metastasis, and Androgen Resistance**


Departments of Pharmacology and Therapeutics, Biostatistics and Bioinformatics, and Pathology, Roswell Park Cancer Institute, Buffalo, and Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York, New York, Center for Functional Cancer Epigenetics and Department of Medical Oncology, Dana-Farber Cancer Institute and Department of Pathology, Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts, Division of Cancer Studies, King’s College London, London, United Kingdom, and Howard Hughes Medical Institute, Chevy Chase, Maryland


**Editorial Comment:** *Rb1* and *Trp53* repress epigenetic reprogramming factors such as Ezh2 and Sox2, which are important in generating induced pluripotent stem cells. The data presented support a hypothesis in which *RB1* and *TP53* loss in prostate cancer de-represses these same factors, creating a stem cell-like epigenetic environment permissive of lineage plasticity. Lineage plasticity is proposed to drive prostate cancer progression by enabling adaptation to selective pressures experienced during metastasis and antiandrogen therapy. Because the mouse models characterized in the study manifest metastatic prostate adenocarcinoma reminiscent of human neuroendocrine prostate cancer variants, they will be useful for testing this hypothesis and identifying molecular mechanisms underlying cancer lineage plasticity. The results also suggest an approach to treating neuroendocrine prostate cancer variants, that is, epigenetic modulation may reverse or delay lineage transformation, extending the durability of clinically beneficial antiandrogen therapy responses. As lineage plasticity is increasingly appreciated in other types of human cancers recurring after molecularly targeted therapy, this approach may be generally applicable.

**Suggested Reading**
