Multiparametric Magnetic Resonance Imaging Guided Diagnostic Biopsy Detects Significant Prostate Cancer and could Reduce Unnecessary Biopsies and Over Detection: A Prospective Study

James E. Thompson,* Daniel Moses, Ron Shnier, Phillip Brenner, Warick Delprado, Lee Ponsky,† Marley Pulbrook, Maret Böhm, Anne-Maree Haynes, Andrew Hayen and Phillip D. Stricker

From the St. Vincent's Prostate Cancer Centre (JET, PB, LP, PDS), Garvan Institute of Medical Research (JET, PB, LP, MP, MB, AMH, PDS), Kinghorn Cancer Centre (JET, PB, LP, MP, MB, AMH, PDS) and University of Notre Dame (WD), Darlinghurst and Schools of Medicine (JET, DM, RS, PB, PDS) and Public Health and Community Medicine (AH), University of New South Wales, Kensington, New South Wales, Australia, and University Hospitals Case Medical Center, Case Western Reserve University School of Medicine (LP), Cleveland, Ohio

Purpose: Multiparametric magnetic resonance imaging appears to improve prostate cancer detection but prospective studies are lacking. We determined the accuracy of multiparametric magnetic resonance imaging for detecting significant prostate cancer before diagnostic biopsy in men with abnormal prostate specific antigen/digital rectal examination.

Materials and Methods: In this single center, prospective study men older than 40 years with abnormal prostate specific antigen/digital rectal examination and no previous multiparametric magnetic resonance imaging underwent T2-weighted, diffusion-weighted and dynamic contrast enhanced imaging without an endorectal coil. Imaging was allocated alternately to 1.5/3.0 Tesla. Imaging was double reported independently using PI-RADS (Prostate Imaging Reporting and Data System) by specialist radiologists. Transperineal grid directed 30-core biopsy was performed with additional magnetic resonance imaging directed cores for regions of interest outside template locations. Four significant cancer definitions were tested. Chi-square and logistic regression analysis was done. Men undergoing prostatectomy were analyzed.

Results: Of the 165 men who enrolled in the study 150 were analyzed. Median age was 62.4 years, median prostate specific antigen was 5.6 ng/ml, 29% of patients had an abnormal digital rectal examination and 88% underwent initial biopsy. Multiparametric magnetic resonance imaging was positive (PI-RADS 3 to 5) in 66% of patients, 61% had prostate cancer and 30% to 41% had significant prostate cancer (definitions 1 to 4). For significant cancer sensitivity was 93% to 96%, specificity was 47% to 53%, and negative and positive predictive values were 92% to 96% and 43% to 57%, respectively (definitions 1 to 4). Radical prostatectomy results in 48 men were similar. Aggregate PI-RADS (4 to 20)

Abbreviations and Acronyms

DCEI = dynamic contrast enhanced imaging
DRE = digital rectal examination
DWI = diffusion-weighted imaging
ESUR = European Society of Urogenital Radiology
mpMRI = multiparametric magnetic resonance imaging
NPV = negative predictive value
PCa = prostate cancer
PI-RADS = Prostate Imaging Reporting and Data System
PPV = positive predictive value
PSA = prostate specific antigen
ROI = region of interest
RP = radical prostatectomy
T2WI = T2-weighted imaging
TRUS = transrectal ultrasound

Accepted for publication January 6, 2014.
Study received institutional review board approval.
Supported by St. Vincent's Clinic Foundation Sydney Research Grant 2013, Royal Australasian College of Radiologists Research Grant 2013, St. Vincent's Prostate Cancer Research Centre MRI Research Fund, Tony Perich and Rotary Club Narellan, New South Wales.
* Correspondence: Prostate Clinical Research Group, Kinghorn Cancer Centre/Garvan Institute of Medical Research, Level 6, 370 Victoria St., Darlinghurst, New South Wales 2010, Australia.
† Financial interest and/or other relationship with Tengion.

For another article on a related topic see page 252.

0022-5347/14/1921-0067/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2014.01.014
Vol. 192, 67-74, July 2014
Printed in U.S.A.

performed similarly to overall PI-RADS (1 to 5). Negative and positive predictive values (100% and 71%, respectively) were similar in men at higher risk, defined as prostate specific antigen greater than 10 ng/ml with abnormal digital rectal examination. On multivariate analysis PI-RADS score was associated with significant prostate cancer ($p < 0.001$) but magnet strength was not. Adding PI-RADS to the multivariate model improved the AUC from 0.810 to 0.913 (95% CI 0.038−0.166, $p = 0.002$). Radiologist agreement was substantial (weighted $\kappa = 0.626$).

Conclusions: Multiparametric magnetic resonance imaging reported by expert radiologists achieved an excellent negative predictive value and a moderate positive predictive value for significant prostate cancer at 1.5 and 3.0 Tesla.

Key Words: prostate, prostatic neoplasms, magnetic resonance imaging, prostate-specific antigen, mass screening

A major limitation of PCa screening with PSA and DRE is poor specificity at acceptable sensitivity thresholds.[1] A 12-core transrectal biopsy is recommended as the initial prostate biopsy despite limited sensitivity and concordance with prostatectomy[2] as well as over detection of insignificant cancer in a third of cases.[3] Saturation templates may improve detection but increase over detection and complication rates.[4]

mpMRI provides anatomical and functional information by combining T2WI with DWI, DCEI and/or spectroscopy. Sensitivity for PCa was 80% to 98% in recent studies[5,6] and reviews.[7,8] mpMRI may improve PCa screening by 1) ruling out significant PCa, and decreasing unnecessary biopsies and over detection, 2) directing biopsy, and increasing sensitivity and grade/volume assessment, and 3) decreasing the number of cores, complications and over detection.

Despite promising results most MRI studies have had methodological limitations. Studies using prostatectomy as the reference standard may be confounded (if MRI is performed after biopsy) by radiologist awareness of PCa in participants (reporting bias), by biopsy artifact and by exclusion of men with negative biopsy/alternative treatments (selection bias). Studies using 12-core biopsy as the reference standard may have high false-negative and cancer underestimation rates. Other common methodological limitations include retrospective design, small sample size, heterogeneous scan protocols, inadequate functional parameters and single reporting. A mpMRI scoring system was recently validated and higher scores correlated strongly with more significant cancer.[9] In 2012 the PI-RADS system was proposed by the ESUR[10] but it requires external validation, as discussed in a recent review of standardized mpMRI reporting.[11]

We determined the accuracy of mpMRI for significant cancer detection before diagnostic biopsy in a prospective cohort with abnormal PSA/DRE.

MATERIALS AND METHODS

This prospective study was done at St. Vincent's Clinic, Sydney, Australia. Institutional review board approval was granted and informed consent was obtained. Two urologists (PDS and PB) invited all men who met selection criteria to participate in the study. Selection criteria were age greater than 40 years, planned biopsy for abnormal PSA/DRE, life expectancy greater than 10 years, as assessed by age, family longevity and comorbidity, and no previous prostate MRI. No PSA/DRE criteria were set to maximize finding generalizability.

MRI Protocol

All mpMRIs were performed at 2 centers using a standardized protocol (Appendix 1). A 1.5 Tesla magnet was used at 1 center and a 3 Tesla magnet was used at the other. Participants were allocated alternately to center 1 or 2 in order of enrollment.

Reporting Protocol

Two radiologists (DM at center 1 and RS at center 2) double reported in independent fashion while blinded to each other. Each radiologist had reported more than 1,000 prior prostate mpMRIs. A total of 20 pretrial mpMRIs were reviewed together using the PI-RADS system[10] to establish consensus. Radiologists received clinical data (PSA, DRE and family history) according to routine practice. Standardized PI-RADS reporting comprised a 5-point scale on which the presence of clinically significant cancer is 1—extremely unlikely, 2—unlikely, 3—equivocal, 4—likely or 5—extremely likely.

Using objective criteria ROIs were assigned a score of 1 to 5 for each parameter (T2WI, DCEI and DWI) and then an overall ROI score (mean of parameter scores). The highest overall ROI score was termed the overall study score. The aggregate of the 4 scores was calculated for each ROI and the highest aggregate score was considered the overall aggregate score. The mean of the 2 overall study scores (1 per radiologist) was calculated and a binary variable was defined, including 1 to 2—negative and 2.5 to 5—positive. ROIs were indicated on a topographic map with 18 regions corresponding to biopsy template locations (fig. 1). Anterior and transition zones were subdivided into apex/mid/base to create 26 ROI locations. Color mpMRI images