Improving Detection of Clinically Significant Prostate Cancer: Magnetic Resonance Imaging/Transrectal Ultrasound Fusion Guided Prostate Biopsy

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Purpose: Given the limitations of prostate specific antigen and standard biopsies for detecting prostate cancer, we evaluated the cancer detection rate and external validity of a magnetic resonance imaging/transrectal ultrasound fusion guided prostate biopsy system used at the National Institutes of Health.

Materials and Methods: We performed a phase III trial of a magnetic resonance imaging/transrectal ultrasound fusion guided prostate biopsy system with participants enrolled between 2012 and 2013. A total of 153 men consented to the study and underwent 3 Tesla multiparametric magnetic resonance imaging with an endorectal coil for clinical suspicion of prostate cancer. Lesions were classified as low or moderate/high risk for prostate cancer. Magnetic resonance imaging/transrectal ultrasound fusion guided biopsy and standard 12-core prostate biopsy were performed and 105 men were eligible for analysis.

Results: Mean patient age was 65.8 years and mean prostate specific antigen was 9.5 ng/ml. The overall cancer detection rate was 62.9% (66 of 105 patients). The cancer detection rate in those with moderate/high risk on imaging was 72.3% (47 of 65) vs 47.5% (19 of 40) in those classified as low risk for prostate cancer ($p < 0.05$). Mean tumor core length was 4.6 and 3.7 mm for fusion biopsy and standard 12-core biopsy, respectively ($p < 0.05$). Magnetic resonance imaging/transrectal ultrasound fusion guided biopsy detected prostate cancer that was missed by standard 12-core biopsy in 14.3% of cases (15 of 105), of which 86.7% (13 of 15) were clinically significant. This biopsy upgraded 23.5% of cancers (4 of 17) deemed clinically insignificant on 12-core biopsy to clinically significant prostate cancer necessitating treatment.

Conclusions: Magnetic resonance imaging/transrectal ultrasound fusion guided biopsy can improve prostate cancer detection. The results of this trial support the external validity of this platform and may be the next step in the evolution of prostate cancer management.

Key Words: prostate, prostatic neoplasms, biopsy, magnetic resonance imaging, ultrasonography

Abbreviations and Acronyms

ADC = apparent diffusion coefficient
CaP = prostate cancer
CDR = cancer detection rate
DRE = digital rectal examination
ERC = endorectal coil
MP = multiparametric
MR = magnetic resonance
MRI = MR imaging
NIH = National Institutes of Health
PSA = prostate specific antigen
TRUS = transrectal ultrasound
USPSTF = United States Preventive Services Task Force

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SINCE the 1980s, screening methods for CaP have been static, including serum PSA measurement and DRE on a periodic basis. If either is abnormal or suspicious for cancer, TRUS guided systematic prostate

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biopsy is performed. Although this biopsy uses ultrasound guidance and selects defined zones in the prostate, there is no certainty that the actual tumor is being biopsied. CaP is the only solid organ tumor still diagnosed by a nontargeted sampling method. Using this approach for the last 30 years has yielded limited and varied results.[1,2] The USPSTF recently categorized PSA based CaP screening as a grade D recommendation in a goal to prevent over diagnosis, overtreatment, and physical and emotional suffering.[3] The USPSTF recommendation regarding PSA based screening was based on the inability to effectively select patients whose benefit from treatment would outweigh the harms associated with screening, diagnosis and treatment.

Improvements in MRI quality, technique and technology have led to increased use in patients with or suspected of having CaP. Although prostate MRI is limited in its ability to detect low grade cancer and lesions less than 5 mm, it is ideal to select patients with intermediate and high risk CaP with greater than 90% negative and positive predictive values.[4,5]

A new methodology of screening men for CaP was reported by NIH investigators in which patients with increased PSA underwent MP prostate MRI and areas suspicious for CaP were identified.[6] In the office/outpatient setting prostate MR images of suspicious lesions/targets are fused with real-time TRUS biopsy techniques to guide needles to suspicious areas in the prostate using electromagnetic tracking. To our knowledge we report the first application of this newly Food and Drug Administration cleared UroNav MR/TRUS fusion guided prostate biopsy system (Invivo, Gainesville, Florida) outside a research hospital setting (NIH).

MATERIALS AND METHODS

We performed a phase III trial, MRI/TRUS Fusion Guided Prostate Biopsy—An Improved Way to Detect and Quantify Prostate Cancer, which was approved by our institutional review board (ClinicalTrials.gov NCT 01566045). Enrollment began May 2012 and the results of this trial have not been published previously. Subjects with increased PSA/abnormal DRE and MP-MRI with suspicious lesion(s) were included in study.

All study participants underwent MP prostate specific 3 Tesla MRI using a Magnetom® Verio device. MRI was obtained with a 16-channel Sense cardiac coil (Invivo) placed on the anterior pelvis and a BPX-30 ERC (Medrad, Warrenton, Pennsylvania) filled with PFC-770 (3M™). An ERC was used to detect CaP because of a reported 36% increase in sensitivity compared to that in patients without ERC use.[7] Prostate specific pulse sequences included a minimum of triplanar T2-weighted, axial diffusion weighted with ADC mapping (B values 0, 500, 1,000, 1,500 and 2,000) and dynamic contrast enhanced MRI sequences according to European Society of Urogenital Radiology guidelines.[8] Three radiologists (ARR, EB-L and RV) identified and graded all lesions suspicious for cancer according to the NIH risk stratification systems, NIH prostate zones and nonvisual reporting (fig. 1).[8,9]

The NIH MP-MRI scoring system was based on the number of positive sequences. A lesion was considered low risk if positive on 1 or 2 of the 3 sequences. If all 3 parameters were positive, the lesion was considered moderate/high risk.[9] At the NIH a lesion is considered high risk if all 4 parameters are positive, including MR spectroscopy. MR spectroscopy was not performed in this trial due to cost, time and little impact on overall CDR, as previously reported by Turkbey et al.[4] All lesions locations were recorded by T2 axial slice number and zone number. Each axial slice of the T2 sequence of the prostate was divided into 9 zones (fig. 1). All lesions are described as the respective zones of involvement for each MRI slice (3 mm).

Subjects with a positive MP-MRI entered the phase III trial. Demographics and common data elements, including prior prostate biopsy history, family history of CaP, PSA and prior imaging, were collected before protocol prostate biopsy. All data were collected prospectively.

The MR/TRUS fusion guided biopsy system is based on ultrasound guided rigid registration with visual correction using UroNav 3.0. All images were processed on a DynaCAD work station (Invivo) before biopsy. According to the protocol subjects underwent electromagnetically tracked MR/TRUS fusion guided biopsy of MRI suspicious lesions before standard 12-core TRUS guided biopsy (endfire iU22 Philips ultrasound). MR/TRUS fusion guided biopsy was completed first due to the significant edema that develops after 12-core biopsy, limiting fusion system performance. The principal investigator (ARR) was then blinded to target location by turning off the MR/TRUS fusion biopsy system. Standard 12-core biopsy was then performed under ultrasound guidance. All specimens were placed in separate pathology containers for each location. Our institutional pathologist (OY) reviewed all pathology slides.

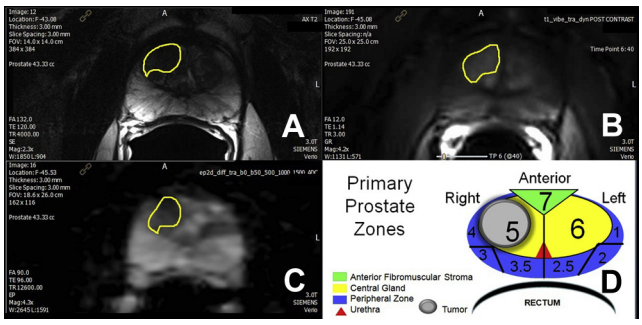

Figure 1. Prostate MP-MRI in 66-year-old male with PSA 5.6 ng/ml. *A*, T2-weighted axial image shows anterior right central lesion with charcoal sign (yellow outline). *B*, dynamic contrast enhanced with type 3 focal enhancement curve. *C*, ADC map with ADC value 487 $\times$ 10^{-6} $\times$ mm^2 per second. *D*, primary prostate zones with MR tumor volume (1.5 $\times$ 1.4 $\times$ 1.3 cm) = 1.4 cm^3 and target core calculated volume (11 mm cancer) = 0.7 cm^3.