Multiparametric Magnetic Resonance Imaging and Ultrasound Fusion Biopsy Detect Prostate Cancer in Patients with Prior Negative Transrectal Ultrasound Biopsies

Srinivas Vourganti,*,† Ardeshir Rastinehad,†,‡ Nitin K. Yerram,* Jeffrey Nix,* Dmitry Volkin,* An Hoang,* Baris Turkbey,* Gopal N. Gupta,* Jochen Kruecker,‡ W. Marston Linehan,* Peter L. Choyke,* Bradford J. Wood§ and Peter A. Pinto*,‖

From the Urologic Oncology Branch (SV, AR, NKY, JN, DV, AH, GNG, WML, PAP) and Molecular Imaging Program (BT, PLC), National Cancer Institute, and Center for Interventional Oncology, Department of Radiology and Imaging Sciences (BJW, PAP), National Institutes of Health, Bethesda, Maryland, and Philips Research North America, Briarcliff Manor, New York (JK)

Abbreviations and Acronyms

DRE = digital rectal examination
GS = Gleason score
mpMRI = multiparametric magnetic resonance imaging
MRI = magnetic resonance imaging
PSA = prostate specific antigen
PSAD = prostate specific antigen density
TRUS = transrectal ultrasound
US = ultrasound

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† Equal study contribution.

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§ Financial interest and/or other relationship with the National Institutes of Health and Philips Healthcare.

‖ Correspondence: Urologic Oncology Branch, National Cancer Institute, 10 Center Drive MSC 1210, Building 10, CRC, Room 2W-5940, Bethesda, Maryland 20892-1210 (telephone: 301-496-6353; FAX: 301-402-0922; e-mail: pintop@mail.nih.gov).

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Editor's Note: This article is the third of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 2446 and 2447.

Purpose: Patients with negative transrectal ultrasound biopsies and a persistent clinical suspicion are at risk for occult but significant prostate cancer. The ability of multiparametric magnetic resonance imaging/ultrasound fusion biopsy to detect these occult prostate lesions may make it an effective tool in this challenging scenario.

Materials and Methods: Between March 2007 and November 2011 all men underwent prostate 3 T endorectal coil magnetic resonance imaging. All concerning lesions were targeted with magnetic resonance imaging/ultrasound fusion biopsy. In addition, all patients underwent standard 12-core transrectal ultrasound biopsy. Men with 1 or more negative systematic prostate biopsies were included in our cohort.

Results: Of the 195 men with previous negative biopsies, 73 (37%) were found to have cancer using the magnetic resonance imaging/ultrasound fusion biopsy combined with 12-core transrectal ultrasound biopsy. High grade cancer (Gleason score 8+) was discovered in 21 men (11%), all of whom had disease detected with magnetic resonance imaging/ultrasound fusion biopsy. However, standard transrectal ultrasound biopsy missed 12 of these high grade cancers (55%). Pathological upgrading occurred in 28 men (38.9%) as a result of magnetic resonance imaging/ultrasound fusion targeting vs standard transrectal ultrasound biopsy. The diagnostic yield of combined magnetic resonance imaging/ultrasound fusion platform was unrelated to the number of previous negative biopsies and persisted despite increasing the number of previous biopsy sessions. On multivariate analysis only prostate specific antigen density and magnetic resonance imaging suspicion level remained significant predictors of cancer.

Conclusions: Multiparametric magnetic resonance imaging with a magnetic resonance imaging/ultrasound fusion biopsy platform is a novel diagnostic tool for detecting prostate cancer and may be ideally suited for patients with negative transrectal ultrasound biopsies in the face of a persistent clinical suspicion for cancer.

Key Words: prostatic neoplasms, biopsy

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SINCE the advent of PSA screening, the pathological diagnosis of prostate cancer has been based on the use of systematic transrectal ultrasound guided biopsies. It is now well understood that systematic 12-core TRUS biopsies can under sample apical and anterior areas of the prostate, particularly in large glands.[1] As a result, prostate cancer biopsy diagnosis has traditionally been fraught with poor sensitivity (as low as 53% in autopsy studies),[2] raising diagnostic concerns of missed prostate cancers.

A particular challenge is presented by the patient with continued clinical suspicion of prostate cancer (whether based on PSA, PSA velocity, PSAD or DRE) after repeated negative biopsies. Different strategies have been used in this setting to minimize false-negative biopsy results including repeat biopsy,[3–5] the addition of anterior directed biopsy cores,[6] saturation biopsy templates[7,8] and transperineal template guided biopsy.[9] While all of these strategies add some diagnostic usefulness, they ultimately remain dependent on random sampling.

Recent advances in mpMRI have allowed high quality visualization of the prostate and are aiding in identification of prostate cancer lesions.[10] We previously reported on the use of a novel MRI/US fusion biopsy system for the targeted detection of lesions detected on MRI.[10] In this series we present our experience in patients with no prior prostate cancer diagnosis with at least 1 previous negative TRUS biopsy and a continued clinical suspicion of cancer. We show the diagnostic usefulness of mpMRI and this novel MRI/US fusion biopsy platform in this challenging clinical scenario.

METHODS AND MATERIALS

This study was approved by the institutional review board of the National Cancer Institute of the National Institutes of Health. Patients eligible for this study were consented and informed appropriately of the potential harms and benefits. Study enrollment began in March 2007 and continued through November 2011.

All patients initially underwent mpMRI using a 3.0 T MRI scanner (Achieva, Philips Healthcare, Best, The Netherlands) in addition to a 16-channel cardiac surface coil (SENSE, Philips Healthcare) placed over the pelvis with an endorectal coil (BPX-30, Medrad, Pittsburgh, Pennsylvania) as previously described.[10] MRI sequences were also routinely obtained, including tri-planar T2-weighted imaging, axial diffusion weighted imaging with apparent diffusion coefficient mapping, 3-dimensional point resolved spatially localized spectroscopy and axial dynamic contrast enhanced MRI. Details of these imaging sequences have been described previously.[11,12] All imaging underwent blinded centralized radiological evaluation.[10] MRI lesions were graded by suspicion based on the number of positive imaging sequences (low—fewer than 2, moderate—3 and high suspicion—4).

Patients with lesions suspicious for cancer on MRI were enrolled in a prostate biopsy protocol. All patients undergoing prostate biopsy were given antibiotic prophylaxis and a cleansing Fleet® enema. Biopsies were performed with the patient under local anesthesia with lidocaine jelly and injectable lidocaine for analgesia. All patients first underwent a standard 12-core transrectal ultrasound biopsy. For this biopsy the operator was blinded to the location of suspicious lesions detected on the MRI. Following TRUS biopsy the patients subsequently underwent MRI/US fusion guided biopsy of suspicious lesions found on MRI. An electromagnetic field generator was placed above the pelvis to track the rectal probe in real time during the biopsy and sensors were placed on the transrectal ultrasound probe. After a 2-dimensional sweep of the ultrasound probe through the prostate, the real-time US image was manually registered to the magnetic resonance image, allowing the operator to guide the ultrasound probe to biopsy previously identified suspicious lesions. A full description of this procedure was published recently.[10] A minimum of 2 biopsy cores were obtained from each lesion (1 in the axial plane, 1 in the sagittal plane). All biopsies underwent blinded centralized pathological evaluation by a genitourinary pathologist. For this retrospective study all consecutive patients were included in the analysis if they had undergone at least 1 prior biopsy which did not reveal cancer. All patients with a previous biopsy confirmed diagnosis of prostate cancer were excluded from analysis. Patients with a prior diagnosis of prostatic intraepithelial neoplasia or atypia were included in the analysis.

Descriptive statistics were used to describe patient demographics. Univariate analysis was performed using a t test for continuous variables, and chi-square and Fisher's exact tests for nominal variables. For patients with multiple lesions, MRI suspicion was assigned by the lesion with the highest MRI suspicion level and Gleason score was assigned based on the cancer with the highest Gleason score. Multivariate analysis was performed using regression models and tests were considered significant if $p < 0.05$. All tests were 2-tailed.

RESULTS

Demographics

A total of 195 patients were eligible for this case series. The median number of prior biopsies was 2 (range 1 to 9). A median of 2 lesions per patient (range 1 to 7) were identified on MRI. A median of 5 (range 2 to 14) MRI guided cores was taken during MRI/US fusion guided biopsy (table 1).

Diagnostic Yield of MRI Fusion Platform

Cancer was detected on biopsy (combined standard 12-core TRUS guided and MRI targeted) in 73 of the 195 men (37.4%). High grade cancer (GS 8 or greater) was found in 21 men (10.8%). MRI targeting detected cancer in 56 of the 73 men and found all 21 cases of high grade cancer. Furthermore, MRI targeted biopsies upgraded tumors detected on stan-