Detection of Significant Prostate Cancer with Magnetic Resonance Targeted Biopsies—Should Transrectal Ultrasound-Magnetic Resonance Imaging Fusion Guided Biopsies Alone be a Standard of Care?

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Abbreviations and Acronyms

DCE = dynamic contrast enhanced

ESUR = European Society of Urogenital Radiology

mp = multiparametric

MR = magnetic resonance

MRI = magnetic resonance imaging

PCA = Principal Component Analysis

PI-RADS = Prostate Imaging Reporting and Data System

PSA = prostate specific antigen

PZ = peripheral zone

RP = radical prostatectomy

T2W = T2-weighted

TB = targeted biopsy

TRUS = transrectal ultrasound

TZ = transition zone

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Study received institutional review board approval.

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Purpose: Magnetic resonance imaging-transrectal ultrasound fusion targeted prostate biopsies were suggested to detect significant cancer with more accuracy than systematic biopsies. In this study we evaluate the pathological characteristics of multiparametric magnetic resonance imaging detected and undetected tumor foci on radical prostatectomy specimens.

Materials and Methods: We selected 125 consecutive patients treated with radical prostatectomy for clinically localized prostate cancer diagnosed on magnetic resonance imaging-transrectal ultrasound targeted biopsy and/or systematic biopsy. On multiparametric magnetic resonance imaging each suspicious area was graded according to the PI-RADS score. On radical prostatectomy specimen, tumor foci with a Gleason score greater than 3+3 and/or tumor volume greater than 0.5 ml were considered significant. A correlation analysis between multiparametric magnetic resonance imaging and pathological findings was performed.

Results: Pathological analysis of radical prostatectomy specimens detected 230 tumor foci. Of these, 137 were considered significant (Gleason score greater than 3+3 in 112) and were observed in 111 (89%) glands. A total of 95 individual tumor foci, including 14 significant foci, were missed with multiparametric magnetic resonance imaging. All of them were located in glands where another focus was detected with multiparametric magnetic resonance imaging. An additional 9 individual tumor foci, including 7 significant, were detected on multiparametric magnetic resonance imaging but missed with targeted biopsy, resulting in 5 (4%) significant cancers undetected with magnetic resonance imaging-transrectal ultrasound fusion targeted biopsy. The magnetic resonance imaging target largest diameter was associated with high volume (greater than 0.5 cc) foci detection, while PI-RADS score and cancer involvement on targeted biopsy were associated with significant foci detection.

Conclusions: In these series of men with suspicious prostate multiparametric magnetic resonance imaging findings, magnetic resonance imaging-transrectal ultrasound fusion guided targeted biopsy alone strategy would have resulted in the under detection of only 4% significant cancers.

Key Words: prostatic neoplasms, biopsy, early detection of cancer

THE prostate is the only solid organ in which a standardized approach to biopsy sampling is taken. Despite multiple efforts to improve the accuracy of systematic biopsy schemes, evidence is now established that

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cancer characterization is poor whatever the core number, location or route taken.[1,2] Also, this strategy has led to over diagnosis of clinically insignificant cancers, and as a result to a potential risk of overtreatment. Most urologists now agree that random sampling without localizing a potential lesion may not be clinically pertinent, even with the use of a grid.[3]

Recent advances in prostate multiparametric MRI, combining T2-weighted, diffusion weighted and dynamic contrast enhanced MRI, has shown its value in the detection, localization and characterization of prostatic tumor foci larger than 0.2 cm^3.[4–7] The ESUR recently published a unified scoring system (MR PI-RADS) for the detection of clinically significant tumor foci on mp-MRI.[8] When performed before systematic biopsy, mp-MRI can target suspicious areas to take additional biopsy cores. In this setting, the development of computed MRI-TRUS image registration has enabled clinicians to perform targeted biopsies using these co-registered images.[9–12] Also, MRI-TRUS fusion targeted biopsy strategy alone, without any additional systematic biopsies, has been proposed to decrease the detection rate of insignificant tumors while increasing that of aggressive tumors.[4,13–16] However, the variability in study methodology as well as the absence of a true reference standard to define the significance of prostatic tumors detected by this technique, limit the strength of recommendations that can be made.[4]

Before considering a targeted only biopsy strategy, which would discard systematic biopsies outside the target, the negative predictive value of mp-MRI to rule out significant cancer in areas with no MRI abnormality should be more reliably assessed. Also, the true negative predictive value of TB should be considered separately from that of the precision of mp-MRI targeting. Although such an evaluation may not be theoretically possible without using true prevalence as the reference, a correlation analysis between mp-MRI findings, TB results and prostate whole mounts analysis may demonstrate the rate of significant individual foci that would be missed with an MRI-TRUS fusion TB strategy alone. Therefore, in this study we 1) determine the significance of tumor foci detected by TB, 2) evaluate MRI characteristics associated with their detection, and 3) evaluate the number and characteristics of tumor foci missed with MRI-TRUS fusion TB and mp-MRI.

PATIENTS AND METHODS

Patient Inclusion

Between January 2012 and June 2013, we prospectively included 125 consecutive patients with pre-biopsy suspicious mp-MRI findings, and eventually diagnosed with prostate cancer treated with radical prostatectomy. The study was approved by the institutional review board which issued a waiver of informed consent for review of clinical, biological, histological and MRI data.

MR Imaging

MR images were obtained using a 1.5T scanner with integrated endorectal and pelvic phased-array coils. The endorectal coil was inserted and inflated with air to a volume of approximately 80 to 100 ml. The diffusion weighted and DCE images had the same orientation as the transverse T2W images. DCE images were evaluated qualitatively on a cine loop of subtracted gradient echo images and regions of interest were drawn on foci showing an early and focal enhancement to display the curve type of the kinetics of gadolinium.

A typical suspicious lesion was well circumscribed and of low signal intensity on T2W imaging, showing restricted diffusion on apparent diffusion coefficient maps and early and intense enhancement with rapid washout on DCE imaging. Each suspicious area was further characterized according to the ESUR PI-RADS Likert-like global score,[8] as score 1—clinically significant disease highly unlikely to be present, score 2—clinically significant cancer unlikely to be present, score 3—the presence of clinically significant cancer is equivocal, score 4—clinically significant cancer likely to be present and score 5—clinically significant cancer highly likely to be present. The decision to target a specific location with biopsy was left to the discretion of each investigator.

Prostate Biopsies

All patients underwent 10 to 12-core random systematic biopsies. At least 2 additional TB were performed within the suspicious areas detected on mp-MRI, using an elastic MRI-TRUS image registration (Koelis®) system.

Histological Evaluation

All biopsy cores were individually labelled. The number of cores involved with cancer, the total length of tissue sampled and total length of cancer detected, as well as Gleason score were determined. After radical prostatectomy the glands were cut into 4 mm sections perpendicular to the posterior plane including apex and base, according to a modified Stanford protocol. Paraffin embedded blocks were cut to produce 5 μm whole mount sections, stained with hematoxylin and eosin. All slides were digitized with a high resolution scanner (Hamamatsu, Japan). The total number of tumor foci and their locations were recorded. If the distance between 2 tumor foci was greater than 4.5 mm they were considered separate.[17] Tumor foci were graded according to the modified Gleason grading system and the percentage of grade 4 was recorded.[18] Pathological stage was determined according to the 2002 TNM classification.[19] Tumor volume was calculated by computerized planimetry. Tumor foci were considered clinically insignificant if they were organ confined with a volume less than 0.5 cc and Gleason score 6 or less.