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Original article

An initial negative round of targeted biopsies in men with highly suspicious multiparametric magnetic resonance findings does not exclude clinically significant prostate cancer—Preliminary experience

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Abstract

Background: Targeted prostate biopsies are changing the landscape of prostate cancer (PCa) diagnosis with the degree of suspicion on multiparametric magnetic resonance imaging (mpMRI) being a strong predictor of targeted biopsy outcome. Data regarding the rate and potential causes of false-negative magnetic resonance imaging-transrectal ultrasound (MRI-TRUS) fusion–targeted biopsy in patients with highly suspicious mpMRI findings are lacking.

Objectives: To determine the rate of clinically significant PCa detection in repeat targeted biopsy or surgery in patients with highly suspicious mpMRI findings and in an initial negative MRI-TRUS fusion–targeted biopsy.

Materials and methods: In this single-center, retrospective study of prospectively generated data, men with highly suspicious lesions (Likert 5 score) on mpMRI and an initial negative MRI-TRUS fusion–targeted biopsy were reviewed. The rate of PCa detection in a subsequent MRI-TRUS fusion–targeted biopsy or radical prostatectomy was determined. Tumors in the intermediate- and high-risk groups according to the National Comprehensive Cancer Network criteria were considered clinically significant.

Results: A total of 32 men with 38 Likert 5 lesions were identified. Repeat targeted biopsy or surgery detected cancer in 42% (16/38) of the Likert 5 lesions with initial negative targeted biopsy. Most of these cancers were intermediate- (69%; 11/16) or high-risk (25%; 4/16) tumors.

Conclusion: A negative round of targeted biopsies does not exclude clinically significant PCa in men with highly suspicious mpMRI findings. Patients with imaging-pathology disagreement should be carefully reviewed and considered for repeat biopsy or for strict surveillance.

Keywords: Prostate cancer; Diagnosis; Early detection; Biopsy; Magnetic resonance imaging

1. Introduction

Targeted prostate biopsies are changing the landscape of prostate cancer (PCa) diagnosis and have shown to improve the detection of clinically significant PCa [1]. Software-based magnetic resonance imaging-transrectal ultrasound (MRI-TRUS) fusion systems that overlay MRI findings on the TRUS screen distinguish themselves by combining efficiency and lower cost compared to direct, in-bore MRI guidance, and by improved accuracy compared to cognitive MRI-TRUS image fusion [2].

The performance of software-based MRI-TRUS fusion is dependent on the acquisition of high-quality multiparametric magnetic resonance (MR) images, adequate MR interpretation,

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MR image segmentation (i.e., prostate contouring and target delineation), ultrasound (US) image segmentation of prostate boundaries, fusion of MR and US images, precise target sampling based on navigation of fused images, adequate tissue samples, and sound histological interpretation [3]. Deficiencies in one or more of these multiple steps may compromise the accuracy of targeted biopsies using this approach.

The degree of suspicion on multiparametric MRI (mpMRI) is the strongest predictor of a positive targeted biopsy with positive rates of 70% to 90% when the MRI findings are highly suspicious for PCa (i.e., PI-RADS or Likert score of 5) [4–11]. Thus, a negative targeted biopsy of a highly suspicious lesion on mpMRI must be interpreted with caution and additional actions (e.g., repeat biopsy and imaging follow-up) may be required depending on the clinical context. However, data regarding the rate and potential causes of false-negative MRI-TRUS fusion–targeted biopsy in patients with highly suspicious mpMRI findings are lacking.

Hence, the goal of this study was to determine the rate of clinically significant PCa detection in repeat targeted biopsy or surgery in patients with highly suspicious mpMRI findings and an initial negative targeted biopsy. Secondarily, we aimed to determine potential reasons for failures and features associated with an increased risk of a falsely negative targeted biopsy.

2. Materials and methods

This Institutional Review Board–approved and Health Insurance Portability and Accountability Act–compliant study is a retrospective collection and analysis of prospectively generated clinical, imaging, and histopathological data.

2.1. Patient eligibility

All patients without previous diagnosis of PCa who underwent prostate mpMRI for cancer detection in our institution between February 2013 and December 2015 were reviewed. Men with highly suspicious mpMRI findings (i.e., at least one Likert scale score 5 lesion) followed by a targeted MRI-TRUS biopsy were eligible for this study. Indications for mpMRI included elevated prostate-specific antigen (PSA), abnormal rise in PSA or abnormal findings on digital rectal examination.

2.2. Multiparametric MRI

All MRI studies were performed in a 3-T MRI scanner (Achieva or Ingenia, Philips; Best, The Netherlands) with an endorectal and a phased-array surface coil. Each MRI examination was prospectively and independently interpreted by 1 of 7 radiologists with advanced training in body MRI and not blinded to the clinical context. Our routine, clinical interpretation includes the assignment of a per-lesion score using a 1 to 5 Likert scale score as a subjective assessment of the likelihood of the presence of a clinically significant cancer (score 1, highly unlikely; score 2, unlikely; score 3, equivocal; score 4, likely; and score 5, highly likely), based on its appearance on T2-weighted, diffusion-weighted, and dynamic contrast-enhanced images [7,12,13].

2.3. Targeted MRI-TRUS fusion biopsy

A commercially available workstation (VersaVue, iCAD) was used by a radiologist to generate volumetric reconstructions of the prostate using an automated segmentation tool and to delineate the biopsy targets, the latter using a freehand region of interest tool. These data were uploaded to the MRI-TRUS fusion system (UroStation, Koelis). Each biopsy was performed by 1 of 4 urologists with 3 years of experience with targeted biopsies using an ultrasound machine (HD9, Philips Medical Systems; Best, The Netherlands) with an endocavitary 4 to 9 MHz broadband curved array end-fire transducer (Philips Medical Systems) and an 18-gauge needle mounted on a reusable core biopsy system (Pro-Mag, Angiotech). The targeted biopsy generally consisted of 2 or 3 cores from each target and was performed immediately after the standard 12-core systematic TRUS biopsies. Cores from each lesion were numbered and labeled according to the target location (e.g., lesion 1, left anterior mid gland) enabling the radiology-pathology correlation in patients with multiple targets.

2.4. Standard of reference

In men who underwent surgery for cancer detected by nontargeted, systematic biopsies (performed concomitantly with the targeted session), step-sectioned radical prostatectomy specimen served as the standard of reference. In patients who did not undergo surgery, repeat targeted biopsy was used as the standard of reference. The decision to re-biopsy patients was at the discretion of the provider. All specimens were prospectively analyzed by 1 of 4 dedicated genitourinary pathologists using the report template recommended by the College of American Pathologists [14].

PSA, PSA density, prostate volume as measured by MRI, lesion size (greatest diameter) and location, biopsy operator experience, and number of targeted cores were recorded for each patient as potential predictors of diagnostic performance of targeted MRI/TRUS biopsies. For lesion location, lesions in the anterior half of the prostate were considered anterior lesions. Conversely, lesions in the posterior half of the gland were considered posterior lesions. If the lesion crossed this boundary, the predominant component prevailed. At our institution, we performed 638 mpMRIs of the prostate, more than 400 MRI-TRUS fusion–targeted biopsies, and 333 radical prostatectomies in 2015. In all, 2 of the 4 operators who had performed more than 50 MRI-TRUS fusion–targeted biopsies per year were considered more experienced.