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Prostate Cancer

Magnetic Resonance Imaging–Transectal Ultrasound Image-fusion Biopsies Accurately Characterize the Index Tumor: Correlation with Step-sectioned Radical Prostatectomy Specimens in 135 Patients

Eduard Baco [a,b,†,*], *Osamu Ukimura* [b,†], *Erik Rud* [c], *Ljiljana Vlatkovic* [d], *Aud Svindland* [d], *Manju Aron* [e], *Suzanne Palmer* [f], *Toru Matsugasumi* [b], *Arnaud Marien* [b,g], *Jean-Christophe Bernhard* [b,h], *John C. Rewcastle* [b], *Heidi B. Eggesbø* [i], *Inderbir S. Gill* [b]

[a] *Division for Cancer Medicine, Surgery, and Transplantation, Department of Urology, Oslo University Hospital Aker, Oslo, Norway;* [b] *USC Institute of Urology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA;* [c] *Department of Radiology, Oslo University Hospital Aker, Oslo, Norway;* [d] *Department of Pathology, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway;* [e] *Department of Pathology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA;* [f] *Department of Radiology, Keck School of Medicine, University of Southern California, Los Angeles, USA;* [g] *Department of Urology, Centre Hospitalier Universitaire, Lille, France;* [h] *Chirurgie Urologique et Transplantation rénale – CHU Bordeaux, INSERM U1029 – Université Bordeaux I, France;* [i] *Department of Radiology and Nuclear Medicine, Oslo University Hospital*

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Abstract

Background: Prostate biopsies targeted by elastic fusion of magnetic resonance (MR) and three-dimensional (3D) transrectal ultrasound (TRUS) images may allow accurate identification of the index tumor (IT), defined as the lesion with the highest Gleason score or the largest volume or extraprostatic extension.
Objective: To determine the accuracy of MR-TRUS image-fusion biopsy in characterizing ITs, as confirmed by correlation with step-sectioned radical prostatectomy (RP) specimens.
Design, setting, and participants: Retrospective analysis of 135 consecutive patients who sequentially underwent pre-biopsy MR, MR-TRUS image-fusion biopsy, and robotic RP at two centers between January 2010 and September 2013.
Intervention: Image-guided biopsies of MR-suspected IT lesions were performed with tracking via real-time 3D TRUS. The largest geographically distinct cancer focus (IT lesion) was independently registered on step-sectioned RP specimens.
Outcome measurements and statistical analysis: A validated schema comprising 27 regions of interest was used to identify the IT center location on MR images and in RP specimens, as well as the location of the midpoint of the biopsy trajectory, and variables were correlated.
Results and limitations: The concordance between IT location on biopsy and RP specimens was 95% (128/135). The coefficient for correlation between IT volume on MRI and histology was $r = 0.663$ ($p < 0.001$). The maximum cancer core length on biopsy was weakly correlated with RP tumor volume ($r = 0.466$, $p < 0.001$). The concordance of primary Gleason pattern between targeted biopsy and RP specimens was 90% (115/128; $\kappa = 0.76$). The study limitations include retrospective evaluation of a selected patient population, which limits the generalizability of the results.

† These authors contributed equally.
* Corresponding author. Division for Cancer Medicine, Surgery, and Transplantation, Department of Urology, Oslo University Hospital Aker, P.O. Box 4959, Nydalen, 0424 Oslo, Norway.
Tel. +47 2 3033188; Fax: +47 2 2894240.
E-mail address: eduard.baco@medisin.uio.no (E. Baco).

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Conclusion: Use of MR-TRUS image fusion to guide prostate biopsies reliably identified the location and primary Gleason pattern of the IT lesion in >90% of patients, but showed limited ability to predict cancer volume, as confirmed by step-sectioned RP specimens.
Patient summary: Biopsies targeted using magnetic resonance images combined with real-time three-dimensional transrectal ultrasound allowed us to reliably identify the spatial location of the most important tumor in prostate cancer and characterize its aggressiveness.

1. Introduction

Whole-mount step-section analysis of radical prostatectomy (RP) specimens remains the standard approach for characterizing prostate cancer (PCa). Multifocality and heterogeneity of clinically localized PCa occur in 67–87% of cases [1–3]. In the case of multifocality, the dominant cancer lesion, or index tumor, is defined as the cancer lesion with the highest Gleason score, or the largest volume if Gleason scores are the same for more than one lesion. It has been suggested that the index tumor drives the progression of PCa [4]. Thus, accurate characterization of the index tumor could impact the treatment decision process. The significant sampling error of traditional systematic random prostate biopsies renders them unreliable for accurate characterization of the index tumor location, volume, and Gleason score [5]. Further development of predictive molecular markers from tumor foci may help in determining the lethal potential of the clonal origin [6].

There is growing evidence that multiparametric magnetic resonance imaging (mp-MRI) may detect, localize, and characterize PCa foci that are larger than 0.2 ml and of higher grade [7–9]. Accurate identification of index tumor location on mp-MRI, followed by fusion of the MR image with a transrectal ultrasound (TRUS) image, could potentially guide targeted biopsy (TB) of such index tumors with greater accuracy [10]. However, the precision of such targeting depends on the accuracy of the image fusion technology [11]. The prostate is a mobile organ whose contour can significantly deform at the time of biopsy, so organ deformation tracking and elastic image fusion are necessary to reduce errors during TB [12].

To the best of our knowledge, the accuracy of MR-TRUS image-fusion biopsies in characterizing index tumors has not been confirmed by correlation with step-sectioned RP specimens (standard reference) to date. Therefore, the aim of our study was to evaluate whether the use of MR-TRUS elastic image fusion to guide biopsies can accurately characterize the location, volume, and Gleason score of index tumors, as confirmed by comparison with step-sectioned, whole-mount RP specimens.

2. Patients and methods

This study was approved by the Ethics Committee of Oslo University Hospital (OUH) Aker, Oslo, Norway, and the Institutional Review Board of the University of Southern California (USC), Los Angeles, CA, USA.

2.1. Patient population

This retrospective study included 135 consecutive patients with elevated prostate-specific antigen (PSA) who sequentially underwent (1) prebiopsy mp-MRI, (2) MR-TRUS image-fusion TB, and (3) robotic RP as a primary treatment between January 2010 and September 2013. Prebiopsy clinical data are summarized in Table 1. Table 2 lists prior biopsy status and the outcomes for TB and systematic random biopsies. None of the patients have been included in previously published cohorts. Patients who underwent any treatments for PCa before RP were excluded. A flowchart of the number of men who were included among all patients who underwent MR-TRUS image-fusion TB is shown in Figure 1.

2.2. MRI and registration analysis

A 1.5-T Avanto MR scanner (Siemens, Erlangen, Germany) and a six-channel Body MATRIX coil were used at OUH. Sequences were axial T2-weighted (T2W) and diffusion-weighted images (DWI), using b50 and b1000 to generate an apparent diffusion coefficient (ADC) map and b2000. Nordic ICE software (NordicNeuroLab, Bergen, Norway) was used for post-processing analyses [13]. At USC, a 3-T MR-750 MR scanner (General Electric, Waukesha, WI, USA) and a 16-channel phased-array coil were used. Sequences were axial T2W and DWI, using b600 and b1000 to generate ADC maps, and dynamic contrast-enhanced (DCE) MRI (temporal resolution 7 s) following intravenous injection of 0.2 ml/kg gadobenate dimeglubine (MultiHance, Bracco Diagnostics, Singen, Germany) at 3 ml/s. An iCAD (Nashua, NH, USA) system was used for post-processing analyses [14].

The index tumor was defined as the largest suspect lesion in T2W and/or DWI-ADC sequences by radiologists experienced in prostate MRI (>200 cases; E.R., S.P.). The axial scan of the DWI-ADC slice containing the greatest area of the suspect index lesion was used for location matching analysis, and denoted as the apex, middle, or base of the prostate for analyses of three equal trisections of the prostate. The tumor center of the index lesion on MRI was defined as the lowest ADC value within the lesion identified by the software, and was registered in the

Table 1 – Clinical characteristics of the 135 patients included in the study

Parameter	Value
Age (yr)	64 (45–75)
Prostate-specific antigen (ng/ml)	8.7 (2.5–44.6)
Prostate volume (ml)[a]	38.4 (16–145)
Clinical stage, *n* (%)	
T1c	112 (83)
T2	20 (15)
T3a	3 (2)

Data for continuous variables are presented as median (range).
[a] As measured using transrectal ultrasound.