MRI-TRUS Fusion Guided Prostate Biopsy
Initial Experience and a Review of the Literature

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Abstract

Introduction and Objectives. The screening based on PSA has led to an important rate of overdiagnosis and overtreatment of clinically insignificant prostate cancer. On the other hand, the systematic ultrasound guided prostate biopsy has a rate of false negative results up to 40%. New methods of assisting prostate biopsy have emerged as a result of the development of the MRI evaluation of patients with prostate cancer. The objective of our study was to assess the initial results of MRI-TRUS fusion guided prostate biopsy in our department and to perform a short review of the recent literature on the subject.

Materials and methods. We included in the present study a number of 43 patients under 70 years, with suspicion for prostate cancer either because of PSA, or an abnormal digital rectal examination. All patients underwent multiparametric MRI and if the radiologist identified a lesion with PIRADS score higher than 3, they underwent MRI-transrectal ultrasound guided prostate biopsy.

Results. Multiparametric MRI identified a lesion with a PIRADS score of at least 3 in 44.18% of cases. The mean age was similar between the patients with or without suspicious lesions (59.5 vs 56.9 years, p=0.27), but the mean PSA was significantly higher for patients with suspicious lesions (8.22 vs 4.44 ng/ml, p=0.04). At MRI-TRUS fusion guided biopsy, prostate cancer was identified in 6 patients (all with PIRADS score 4 or 5). The mean percentages of positive biopsy cores out of total/systematic/MRI-guided number of cores were 30.16%, 22.18% and 75%, respectively. Four out of six patients were diagnosed with clinically significant disease.

Conclusions. MRI visible lesions with PIRADS 4 and 5 correlate with the presence of significant disease. The MRI-TRUS guided fusion biopsy can better detect patients with aggressive PCa or disease progression during active surveillance, thus improving the risk stratification and treatment planning. On the other hand, by identifying low-risk patients MRI-TRUS fusion biopsy can be a factor to overcome the high rate of overdiagnosis and overtreatment of indolent PCa.

Keywords: Multiparametric MRI, MRI-TRUS fusion prostate biopsy, prostate cancer

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Introduction

The current standard approach for performing prostate biopsy as recommended by the European Association of Urology Guidelines is ultrasound-guided prostate biopsy, either transrectal or transperineal, with 10-12 systematic cores that randomly sample the peripheral gland as far posterior and lateral as possible [1]. No differences in terms of cancer detection between transrectal and transperineal biopsies have been observed [2], although transperineal approach diagnoses more anterior located cancers [3]. It is well known that transrectal ultrasound (TRUS) has low sensitivity and specificity for identifying prostate cancer (PCa) [4], as 30% of PCa appear as isoechoic [5] and even when a hypoechoic lesion is present, the risk for the presence of PCa is under 10% [6]. So, TRUS is far from the ideal imaging modality for targeting prostate biopsy and an important number of patients will undergo repeat biopsy for a persistent elevated PSA or abnormal digital rectal examination (DRE), up to 50% of them being subsequently diagnosed with PCa [7].

Multiparametric magnetic resonance imaging (MRI) has emerged as a more accurate imaging modality for the diagnosis and staging of clinically significant (CS) PCa [8], thus enabling the possibility to assist the biopsy, treatment planning and focal therapy in PCa. It has been shown that a normal multiparametric MRI has a negative predictive value of almost 98% for the presence of significant PCa in biopsy [9].

Multiparametric MRI consists in one anatomical sequence, T2-weighted imaging (T2-WI), and at least two functional sequences: dynamic contrast enhancement MRI (DCE-MRI) and diffusion-weighted MRI (DWI-MRI) [10].

In order to standardize the reporting of the MRI results and to increase the inter-reader reliability, Prostate Imaging-Reporting and Data System (PIRADS) classification was introduced in 2012 and recently updated [10,11]. PIRADS score predicts the risk of harboring clinically significant disease and implies the assignment of scores for the lesions identified on every sequence. The final PIRADS score is a five-point scale as follows: 1 = CS PCa highly unlikely to be present, 2 = CS PCa unlikely to be present, 3 = CS PCa is equivocal, 4 = CS PCa is likely to be present and 5 = CS PCa is highly likely to be present [10]. PIRADS v2 simplifies and standardizes the terminology used by radiologists and renames the risk categories from 1 = very low to 5 = very high risk of CS disease [11].

Considering the advances made in the MRI evaluation of patients with PCa, various strategies for the integration of this imaging modality in the diagnostic pathway of PCa have been proposed [12]. Currently, there are three types of possible MRI guided prostate biopsies:

MRI-targeted (cognitive) prostate biopsy: the lesion is identified on pre-operative MRI, and the biopsy is performed in a cognitive manner using TRUS guidance [13].

MRI-TRUS fusion guided prostate biopsy: the lesion is identified on the MRI images and transposed in real-time onto the TRUS image using a special software [14].

In-bore MRI-guided biopsy: the biopsy is performed inside the MRI gantry with magnetic-compatible devices, using serial scans and real-time MRI-guidance [15].

Irrespective of the employed technique, MRI-guided prostate biopsy has been shown to detect more clinically significant PCa in comparison with systematic biopsy and less indolent PCa. By omitting TRUS-guided prostate biopsies approximately 50% of indolent tumors would not be diagnosed, thus decreasing the rate of overdiagnosis [12].

In-bore MRI-guided prostate biopsy has shown a superior performance for overall PCa detection in comparison with cognitive TRUS-guided biopsy and a similar performance with MRI-TRUS fusion guided prostate biopsy for clinically significant PCa detection [12]. Studies to compare the three MRI-guided prostate biopsy modalities published so far are heterogenous, but a randomized controlled trial is currently ongoing [16].

The objective of our study was to assess the initial results of MRI-TRUS fusion guided prostate biopsy in our department and to perform a short review of the recent literature on the subject.

Materials and methods

We included in the present study a number of 43 patients under 70 years, with suspicion for prostate cancer (either because of PSA, or an abnormal digital rectal examination). For PSA we used the following cut-off values: ≥1.5 ng/ml in patients younger than 50 years, ≥2.5 ng/ml between 50-60 years and ≥4 ng/ml for patients older than 60 years. All patients signed the informed consent and the study was approved by the local ethical committee.

All the patients included in the study underwent multiparametric MRI, including T2-WI, DWI and DCE-MRI, without endorectal coil. When the mpMRI identified a lesion with a PIRADS score equal or above 3, we performed MRI-TRUS fusion guided prostate biopsy with 12 systematic cores and 2 additional cores for
every lesion identified on MRI. We categorized the patients into group 1 if they had any suspicious lesion on prostate MRI and group 2 if the MRI was normal.

The multiparametric MRI was performed using Siemens MAGNETOM Aera 1.5 T. For every lesion identified on MRI, the radiologist mainly assessed two types of information: 1) the location of the tumor (right/left lobe, base/middle/apex, anterior/transitional zone/posterior) and 2) the appearance of the lesion in terms of PIRADS score.

For the MRI-TRUS fusion guided prostate biopsy we used Arietta 70a system from Hitachi, Japan with endfire endocavity probe C41V1 2-10mHz, with 200 degrees field of vision and RVS (real time virtual sonography) fusion software.

**The technique of MRI-TRUS fusion guided prostate biopsy** can be divided into the following steps:

1. Import the MRI images into the ultrasound system. Only T2WI in axial and sagittal planes will be used for fusion-guided biopsy; when available, isotropic MRI can offer a higher resolution

2. Manually align and synchronize the two planes of the MRI images (axial and sagittal) by identifying a common landmark between the two sections (either pubic bone, or a calcification in the prostate)

3. Using the plane in which prostate biopsy is performed (sagittal plane, in our case), identify and mark the lesion suspicious for prostate cancer; also in the same plane, mark the edges of the prostate which will be deformed during the biopsy by the endorectal probe (Fig. 1)

4. Mark the urethral axis, which is the most visible structure for the initial synchronization with the ultrasound (Fig. 2)

5. Perform transrectal ultrasound; the purpose is to find a similar plane to the one you can see on MRI – the easiest being the urethral axis (Fig. 2)

6. Correct the angulation between the ultrasound and the MRI images and when both show the same position synchronize them; now, when the endorectal probe moves, the MRI image should also move in real time

7. If the synchronization between MRI and ultrasound is not perfect, refine the tuning by identifying structures visible on both examinations and repeat the synchronization

8. Scan the prostate and find the suspicious lesion; the mark should appear now both on MRI and ultrasound images (Fig. 3)

9. Check to see if the line marks are correct and are in contact with the deformable edges of the prostate, this meaning that the deformation caused by the transrectal ultrasound is minimal (Fig. 3)

10. Perform the biopsy from the suspicious lesion in the plane where the cross is visible – this represents the largest diameter of the lesion (Fig. 3)

In order to save time, the first four steps can be performed and saved onto the hard drive before the patient enters the examination room.

The statistical analysis was performed using Medcalc, version 12.4. Statistical significance was considered to be reached when \( p < 0.05 \).
Results

The mean age of the patients in the study group was 58.3 years (± 7.6 years) and the median PSA was 4.38 ng/ml (95% CI: 3.47-5.44 ng/ml). Multiparametric MRI identified a lesion with a PIRADS score of at least 3 in 19 cases (44.18%).

The mean age was similar between the patients with or without suspicious lesions (59.5 years ± 6.5 years in group 1 vs 56.9 years ± 8.3 in group 2, p=0.27). The mean PSA was significantly higher for patients in group 1 (8.22 ng/ml, 95% CI: 4.91-11.5 ng/ml) in comparison with group 2 (4.44 ng/ml, 95% CI: 2.48-6.4 ng/ml), p=0.04.

MRI identified two suspicious lesions in two patients, and a single lesion in each of the other 17. Of the 19 patients that underwent prostate biopsy, 12 had a PIRADS score 3 lesion, 3 patients harbored a PIRADS 4 lesion and 4 patients had a PIRADS 5 lesion.

Prostate cancer was identified in 6 patients (31.5%) and atypical small acinar proliferation (ASAP) in 2 patients. For the other 11 patients, the biopsy was negative for malignancy.

The PIRADS score in patients with negative biopsy was 3 in 10 cases. A single patient with negative biopsy had a PIRADS score of 4. The two patients with ASAP had a PIRADS score of 3.

All patients diagnosed with prostate cancer had a PIRADS score of 4 or 5 and almost all had a single lesion identified on MRI. The mean percentages of positive biopsy cores out of total/systematic/MRI-guided number of cores were 30.16%, 22.18% and 75%, respectively. Four out of six patients were diagnosed with clinically significant disease – Gleason grade group 2. A single patient presented perineural invasion.

The characteristics of the 6 patients diagnosed with prostate cancer by MRI-TRUS fusion guided biopsy are summarized in Table 1.

Table 1. The characteristics of the patients diagnosed with prostate cancer by MRI-TRUS fusion guided prostate biopsy

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>PSA (ng/ml)</th>
<th>DRE</th>
<th>PIRADS</th>
<th>No of MRI suspicious lesions</th>
<th>PBC/total (%)</th>
<th>PBC/systematic (%)</th>
<th>PBC/MRI-TRUS fusion guided (%)</th>
<th>Gleason group WHO 2016</th>
<th>Perineural invasion</th>
<th>Lympho-vascular invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>3.16</td>
<td>abnormal</td>
<td>5</td>
<td>1</td>
<td>42.8</td>
<td>33.3</td>
<td>100</td>
<td>2</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
<td>5.1</td>
<td>abnormal</td>
<td>5</td>
<td>1</td>
<td>21.4</td>
<td>8.3</td>
<td>100</td>
<td>1</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>9</td>
<td>abnormal</td>
<td>5</td>
<td>1</td>
<td>21.4</td>
<td>16.6</td>
<td>100</td>
<td>2</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>4</td>
<td>66</td>
<td>20</td>
<td>abnormal</td>
<td>4</td>
<td>1</td>
<td>50</td>
<td>41.6</td>
<td>100</td>
<td>2</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>13</td>
<td>normal</td>
<td>4</td>
<td>1</td>
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<td>8.3</td>
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</tr>
<tr>
<td>6</td>
<td>70</td>
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<td>5</td>
<td>2</td>
<td>31.2</td>
<td>25</td>
<td>50</td>
<td>1</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>

DRE= digital rectal examination, PBC= positive biopsy cores

Discussions

Drawbacks of the current diagnosis pathway in PCa

The current standard pathway for the assessment of PCa implies PSA, DRE and TRUS-guided systematic prostate biopsy, but this approach yields an almost 40% rate of false negative results [17]. On the other hand, the screening based on PSA has led to an important rate of overdiagnosis and overtreatment of clinically insignificant disease [18]. So, there is a need for a better characterization of PCa in order to perform a more accurate selection of patients that undergo prostate biopsy and subsequent invasive treatment.

Possible incorporation of MRI in the screening for PCa

During the last years, MRI has become the most sensitive and specific imaging technique for the evaluation of PCa [19] and its implementation into a screening program seems to have the potential of decreasing the risk of overdetection of indolent PCa and improve the early detection of CS PCa [20]. A visible lesion on multiparametric MRI (PIRADS score 4 or 5) has been shown to be a strong predictor of CS disease in patients otherwise suitable for active surveillance [21]. So, multiparametric MRI might be used to select the patients that undergo prostate biopsy or in whom the biopsy can be deferred [22]. Pre-biopsy multiparametric MRI has shown at least similar detection rates of CS PCa in comparison with TRUS-guided biopsy, but with a lower detection rate of indolent PCa [23,24].
The current indications of MRI-TRUS fusion guided prostate biopsy: previous negative biopsy

MRI-TRUS fusion guided prostate biopsy is primarily indicated in patients with persistently elevated PSA despite a previous negative biopsy and during the follow-up of patients on active surveillance [25].

Roehl et al [26] has shown that the probability of identifying PCA at first, second, third and fourth repeat TRUS guided biopsy is 17%, 14%, 11%, and 9%, respectively. In comparison, MRI-TRUS fusion guided prostate biopsy achieves a rate of PCA detection at repeat biopsy of 34%. When including only patients with PIRADS 4 and 5 the PCA yield reaches 50%[27].

In this context, the question that raises is whether a systematic biopsy is still necessary in addition to MRI-TRUS fusion in patients with visible lesions on MRI. Salami et al [28] analyzed 140 men with at least one previous negative biopsy and observed that although MRI-TRUS fusion biopsy detected more CS PCa than systematic biopsy, it still missed almost 4% of CS PCa when performed exclusively.

However, the first randomized controlled trial that compared MRI-TRUS fusion biopsy with standard systematic biopsy concluded that, in biopsy naïve men, two-core MRI-TRUS fusion prostate biopsy is comparable with 12-core systematic biopsy in terms of CS PCa detection rate [29].

The current indications of MRI-TRUS fusion guided prostate biopsy: active surveillance

For patients on active surveillance, MRI-TRUS guided prostate biopsy has been proved to increase the Gleason score upgrading otherwise not detected by systematic biopsy by 14% [30]. The lack of progression of lesions on multiparametric MRI was able to predict a low rate of pathologic progression of patients on active surveillance (negative predictive value of MRI progression of 81%) [31], so the incorporation of MRI-TRUS guided biopsy into the active surveillance protocol might improve PCA risk stratification.

Conclusions

In conclusion, MRI visible lesions with PIRADS 4 and 5 correlate with the presence of significant disease. The MRI-TRUS guided fusion biopsy can better detect patients with aggressive PCa or disease progression during active surveillance, thus improving the risk stratification and treatment planning. On the other hand, by identifying low-risk patients MRI-TRUS fusion biopsy can be a factor to overcome the high rate of overdiagnosis and overtreatment of indolent PCa.

References

Clinical studies


20. Thompson J, Lawrencechuk N, Frydenberg M, Thompson L, Stricker P; USANZ. The role of magnetic resonance imaging in the diagnosis and management of prostate cancer. BJU Int 2013;112 Suppl 2:6–20


28. Salami SS, Ben-Levi E, Yaskiv O et al.: In patients with a previous negative prostate biopsy and a suspicious lesion on magnetic resonance imaging, is a 12-core biopsy still necessary in addition to a targeted biopsy? BJU Int 2015;115(4):562–70

