Visibility of MRI prostate lesions on B-mode transrectal ultrasound

Fabian Steinkohl¹, Anna Katharina Luger¹, Renate Pichler², Jasmin Bektic², Peter Rehder², Andrei Lebovici³, Friedrich Aigner¹

¹Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria, ²Department of Urology, Medical University of Innsbruck, Innsbruck, Austria, ³Department of Radiology, County Emergency Hospital Cluj-Napoca, Romania

Abstract

Aim: Prostate biopsies are usually done with transrectal ultrasound (TRUS) in B-mode (B TRUS) but multiparametric MRI (mpMRI) is the gold imaging standard for the visualization of clinically significant prostate cancer (PCa), since a low PCa detection rate is reported for B TRUS. The aim of this study was to assess the visibility of MRI lesions on B TRUS and to determine which factors may influence the visibility on B TRUS. **Material and methods:** 142 men with 148 lesions reported on mpMRI underwent a B TRUS/mpMRI fusion targeted biopsy of the prostate and were included in this retrospective study. During the biopsy, images were obtained and stored in the institution's PACS. These images were reviewed by two radiologists to determine, whether an mpMRI lesion was or was not visible on B TRUS. **Results:** Overall 92 from 148 mpMRI lesions (62.2%) were visible on B TRUS. The location of the lesion in the prostate, the PIRADS classification of the lesions and the size of the lesion had no significant influence on the visibility on B TRUS. Only the prostate volume had a significant influence on visibility: in smaller prostates significantly more lesions were visible on B TRUS than in large glands ($p=0.041$; 45.1 ml vs 54 ml). **Conclusion:** The use of newer high-end ultrasound units as well as experience gained from fusion biopsies enables us to see 62.2 % of all suspicious mpMRI lesions on B TRUS. B TRUS images merit a thorough examination during a conventional biopsy setting.

Keywords: prostate cancer; multiparametric MRI; transrectal ultrasound; TRUS; fusion biopsy

Introduction

Since B-mode transrectal ultrasound (B TRUS) guided prostate biopsy was introduced by Holm et al in 1981 [1] it has become the primary detection method of prostate cancer (PCa). B TRUS guided biopsies only sample predefined anatomical zones of the prostate, since the sensitivity of B-mode ultrasound for PCa detection is very low [2]. Therefore, Trabulsi et al stated that "*Gray scale characteristics alone are insufficient to identify a target for prostate biopsy*" [3]. This also means that the classical systematic biopsy is a randomized and not a tar-

geted approach and thus significant PCa may be missed in up to 35% [4]. To overcome this limitation, imaging techniques for visualisation of PCa have been further developed in such a way that they can detect significant PCa with high reliability [5]. Currently multiparametric magnetic resonance imaging of the prostate (mpMRI) is seen as the gold standard in prostate imaging [6]. Since the introduction of mpMRI and MRI/TRUS fusion targeted biopsies (FTB) it has been noticed that more lesions are visible on B TRUS as is reported in the literature. Recently a Dutch study assessing 34 patients evidenced a visibility on B TRUS of 42.9% for all MRI lesions and of 62% for all PI-RADS (Prostate Imaging Reporting and Data System) 5 lesions [7] and an American study demonstrated a visibility on B TRUS of 40.3% [8].

Thus, the aim of this study was to further assess the visibility of mpMRI lesions on B TRUS in a larger cohort and to identify factors influencing visibility of mpMRI lesions on B TRUS.

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Corresponding author: Dr. Fabian Steinkohl

Medical University of Innsbruck

35 Anichstr. 6020 Innsbruck, Austria

E-mail: Fabian.Steinkohl@i-med.ac.at

Materials and methods

Patients

Between April 2013 and August 2016, 180 consecutive patients were included in this retrospective single-centre study. Patients' characteristics are shown in Table I. This study was approved by the Ethics Committee of Innsbruck (study number: AN2016-0170 365/4.3). Inclusion criteria were the indications for a prostate biopsy (elevated PSA level of >4.0 ng/ml; or free PSA $<18\%$ and PSA values of 1.75 ng/ml for patients aged 45-49 years, 2.25 ng/ml for patients aged 50-59 years, 2.75 ng/ml for patients aged 60-69 years, 4.0 ng/ml for patients aged 70-79 years; or PSA velocity of ≥ 0.4 ng/ml per year; and/or a suspicious digital rectal examination) and a recent mpMRI of the prostate. All patients underwent a FTB of the prostate and the generated images were stored while performing FTB. One hundred and eighty-six MRI lesions were described but 38 patients had to be excluded due to poor documentation of images. Thus 148 lesions in 142 patients were eligible for analysis.

Image acquisition

All included patients underwent MRI/TRUS fusion targeted biopsy of the prostate performed by an urologist with 12 years' experience of imaging targeted biopsy of the prostate (F.A.). MpMRI was performed according to the current guidelines of the European Society of Urogenital Radiology [9].

The mpMRI dataset was uploaded on the day of biopsy onto the ultrasound unit equipped with fusion software (LOGIQ E9, GE Healthcare, Chalfont St Giles, UK or HI VISION Ascendus, Hitachi medical systems, Tokyo, Japan). After in plane co-registration of the live B-mode ultrasound with the mpMRI dataset the FTB was performed using a high resolution transrectal ultrasound probe with a frequency up to 10.0 MHz. Fusion images and cine loops were routinely stored and saved in our institution's PACS (Agfa IMPAX EE, Agfa HealthCare, Mortsel, Belgium) (fig 1).

Image interpretation

The stored images of the study patients were analysed in the PACS. The described PI-RADS lesions were

Fig 1. Plane registration of the B TRUS image (left) and the angled MR image (right). Note the landmarks.

Fig 2. Visible lesion within the TZ (red circle) on B TRUS (left) and MR image (right). Dotted lines on the left are the biopsy target device. It was a low grade prostate cancer (Gleason score 6, 3+3).

viewed by two radiologists (F.S.; F.A.) and the visibility of mpMRI lesions on B TRUS images was assessed. If the FTB was poorly documented, images were excluded from this study ($n=38$) (fig 2).

Statistical analysis

Quantitative variables were normally distributed, as demonstrated by the Kolmogorov-Smirnov test. Thus, t-test was used for between-group comparisons. Categorical variables were compared using the chi-square test. Odds ratios (OR) were calculated with logistic regression analysis and are given with 95% confidence intervals (95% CI). The significance level was set at $p<0.05$. SPSS 22.0 was used for all statistical analyses.

Table I. Patients' characteristics

N = 142	Mean $\pm$ SD	Median (25 th -75 th Percentile)
Age at biopsy (years)	64.8 $\pm$ 7.9	65.95 (60.47-70.89)
PSA at biopsy (ng/ml)	8.5 $\pm$ 6.9	6.59 (4.58-9.52)
Prostate volume (ml)	48.4 $\pm$ 23.1	43.00 (30-61.25)
Number of previous biopsies	1.41 $\pm$ 1.13	1 (1-2)

N – number of patients; SD – standard deviation; PSA – prostatic specific antigen

Results

Overall 148 of 186 (79.6%) lesions were eligible for analysis with a median size on mpMRI of 12.45 ± 6.3 mm and a median PI-RADS score of 4.14 ± 0.0522 . Eighty-eight of 148 (59.5%) of all mpMRI lesions were located in the peripheral zone (PZ) and 60/148 (40.5%) in the transition zone (TZ). Overall 73/148 (49.3%) mpMRI lesions were histologically proven to be cancer. Of all analysed 148 lesions 92 MRI lesions (62.2%) were visible on B TRUS.

Visibility rates in dependence of location

In the PZ 58 of a total of 88 (65.9%) MRI lesions were visible on B TRUS and in the TZ 34 of a total of 60 (56.7%), respectively ($p=0.301$). In the posterior parts of the prostate 33 of a total of 49 (67.3%) MRI lesions were seen on B TRUS and in the anterior parts 59 of a total of 99 (59.6%; $p=0.375$). The visibility of mpMRI lesions located at the apex ($n=68$), at the mid ($n=59$) and at the base ($n=21$) of the prostate was 47 (69.1%), 33 (55.9%) and 12 (57.1%) on B TRUS, respectively ($p=0.273$). No statistically significant differences for visibility rates on dependence of location were found. These results are summarised in Table II.

Visibility rates in dependence of PI-RADS score, lesion and prostate size

The size of prostates with visible lesion on B TRUS was 45.1 ± 20.2 ml while prostates with invisible lesions on B TRUS were significantly larger and had a size of 54 ± 26.7 ml ($p=0.039$). The lesion's size on mpMRI did not differ significantly between visible lesions (13.05 ± 7.39 mm) and invisible lesions (12.09 ± 5.56 mm) ($p=0.40$) (fig 3).

Two-thirds (66.7%) of mpMRI lesions scored as PI-RADS 2 were seen on B TRUS, 2/2 (100%) scored as PI-RADS 3, 64/114 (56.1%) scored as PI-RADS 4 and

Fig 3. Due to the high resolution of B TRUS even small lesions (red circle) are visible on B TRUS images (left) and MR images (right). This was not a carcinoma.

Table II. Visibility of suspicious mpMRI lesions on TRUS depending on the location within the prostate

	Visible on TRUS	Invisible on TRUS	p-value
Overall visibility n (%)	92 (62.2)	56 (37.8)	
Location of mpMRI lesion n (%)			
Peripheral zone	58 (65.9)	30 (34.1)	0.301
Transitional zone	34 (56.7)	26 (43.3)	
Apex	47 (69.1)	21 (30.9)	0.273
Mid	33 (55.9)	26 (44.1)	
Base	12 (57.1)	9 (42.9)	0.375
Anterior	59 (59.6)	40 (40.4)	
Posterior	33 (67.3)	16 (32.7)	

mpMRI – multiparametric magnetic resonance imaging; TRUS – transrectal ultrasound

Table III. Visibility of suspicious mpMRI lesions on TRUS depending on the size of the prostate, the size of the lesion in mpMRI and the PI-RADS scores

	Visible on TRUS	Invisible on TRUS	p-value
Prostate size (ml)	45.1 ± 20.2	54.0 ± 26.7	0.039
Lesion size in mpMRI (mm)	13.05 ± 7.39	12.09 ± 5.56	0.401
PI-RADS scores			
2	2/3	1/3	0.116
3	2/2	0	
4	64/114	50/114	
5	24/29	5/29	

mpMRI – multiparametric magnetic resonance imaging; TRUS – transrectal ultrasound; PI-RADS – Prostate Imaging Reporting and Data System

Table IV. Visibility of prostate cancer lesions on TRUS depending on Gleason Scores

Gleason Scores	Visible on TRUS	p value
6	8/15 (50.7%)	0.021
7 = (3 + 4)	28/36 (77.8%)	
7 = (4 + 3)	2/3 (66.7%)	
8	10/13 (76.9%)	
9	6/6 (100%)	

24/29 (82.8%) scored as PI-RADS 5. The PIRADS score of the mpMRI lesion did not significantly influence visibility on B TRUS ($p=0.116$) (Table III).

Visibility rates in dependence of histology

Seventy-three lesions (49.3%) contained histologically proven PCa. Of these 73 PCa lesions 74% were visible on B TRUS ($p=0.004$). There was a significant connection between the aggressiveness of the PCa and the visibility of the lesion on B TRUS. While only 53.3% of all PCa with Gleason Score (GS) 6 = (3 + 3) were visible on B TRUS, 100% of PCa with GS 9 were visible on B TRUS (Table IV).

Discussions

We found that 62.2% of all mpMRI lesions were visible on B TRUS. The value of B TRUS should be reconsidered for PCa detection. So far, B TRUS was mainly used for volumetry and was hardly used for PCa detection because of its low sensitivity of 15% [10]. A paradigm shift could be initiated in this regard because of the technical improvement of high-end ultrasound machines and because of improved perceptibility of changes on B TRUS image when the MR images appear simultaneously on the ultrasound monitor during the technical fusion. For example, Helck et al achieved a clearly better identifiability of renal lesions during a technical fusion in comparison to B mode ultrasound alone (2.7 ± 1.2 vs 2.0 ± 1.3) [11].

Park et al used technical fusion for breast imaging. They also reported a higher detection rate on ultrasound during the simultaneous ultrasound/MRI navigation (64 of 67; 95.5%) than on ultrasound alone (41 of 67; 61.2%; $p<0.01$) [12].

Similar to Van de Ven et al we did not find a significant difference of visibility rates in dependence of the PI-RADS scoring ($p=0.116$) [7]. But in contrast to their results we were able to visualize also PI-RADS 3 lesions on B TRUS. This may be an interesting issue as Rosenkrantz et al stated that also PI-RADS 3 lesions should be an indication for targeted prostate biopsy even in the absence of PI-RADS 4 or 5 lesions [13]. As the PI-RADS

score did not have a significant influence on visibility on B TRUS we reckon that visibility on B TRUS is determined by other parameters than visibility on mpMRI. The lesion's size did not influence visibility on B TRUS ($p=0.401$). Furthermore, if lesions are also visible on B TRUS and not only on MRI the quality of an imaging targeted biopsy rises, resulting in a higher detection rate of significant cancer [14]. This finding is confirmed by Garcia-Reyes et al who stated that a lesion which is visible on B TRUS and mpMRI has a greater probability of harboring clinically significant PCa [8].

A study from 1998 reported that up to 60% of all hypoechoic lesions in the posterior prostate are benign [15]. Our data showed that mpMRI lesions harbouring PCa are visible on B TRUS in 74% of our cases. We could also show that cancerous lesions with higher GS are more often visible than those with low grade PCa. Therefore, we share Noh et al opinion that all visible abnormalities should be biopsied, especially the hypoechoic lesions that can be seen as a marker for clinically significant PCa [16]. It is assumed that there is an association between PCa alterations in tissue composition and changes in MR images [17]. Although our study does not offer sufficient data to confirm this assumption, we speculate that this might be true for B TRUS images as well.

In our patient cohort 40.5% of all mpMRI lesions were localised in the TZ. We were able to detect 56.7% of them on B TRUS. This is noteworthy for two reasons. Firstly, the TZ is regarded as a challenge for all imaging modalities especially for B TRUS [18]. Therefore, we did not expect to find so many lesions of the TZ on B TRUS. Secondly, a previously published histological study showed that 68% of all PCa are located in the peripheral zone and only 24% are located in the TZ [19]. As a consequence, current EAU Guidelines on Prostate Cancer do not recommend to biopsy the TZ during a B TRUS guided biopsy in the primary setting [20]. Of course, not all mpMRI lesions which are visible on B TRUS turn out to be PCa on biopsy.

It has been reported that anteriorly located tumours are often underdiagnosed on B TRUS [21,22]. Although there was no statistically difference for visualisation of anterior and posterior located mpMRI lesions on B TRUS ($p=0.375$) we could visualize fewer anterior lesions. With regard to factors which influence visibility of mpMRI lesions on B TRUS we found a statistically significance of prostate size: the size of prostates with a visible lesion on B TRUS was 45.1 ± 20.2 ml while prostates with invisible lesions on B TRUS were significantly larger and had a size of 54 ± 26.7 ml ($p=0.039$). This confirms findings from a former study and can be explained by the fact that the quality of ultrasound conduction is reduced in

the presence of calcifications (sound cancellation) or in larger sized prostates (depth penetration) [23].

This study has several limitations. The most important is its retrospective design. As we included only patients with well documented FTB, patients with invisible mpMRI lesions might have been unwillingly excluded. Furthermore, there was only one operator, so we could not calculate an inter-observer variability. The single operator was experienced in the field of prostate ultrasound and used a high end ultrasound machine. Therefore, these results might not be reached by an averagely trained operator. In some cases, only images not movies were stored in the institution's PACS. Therefore, we could not assess the overall quality of the FTB.

In **conclusion** B TRUS seems to be an underestimated tool for the visualization of suspicious prostate lesions as over 62% of mpMRI lesions can be seen. It highlights the importance of a thorough analysis of TRUS images while performing a prostate biopsy.

Conflict of interest: none

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