Value of Endorectal MRI in Romanian Men for High Risk of Prostate Cancer: MRI Findings Compared with Saturation Biopsy

A. Lebovici¹, S. A. Sfrangeu¹, C. Caraiani², C. Lucan³, M. Suciu³, F. Elec³, Gh. Iacob⁴, M. Buruian⁴

¹Department of Radiology, County Emergency Hospital, “Iuliu Hatieganu” University of Medicine and Pharmacy Cluj-Napoca, Romania
²Hiperdia S.A. Medical Center, Cluj-Napoca, Romania
³Department of Urology, Clinical Institute of Urology and Kidney Transplant, Cluj-Napoca, Romania
⁴Department of Pathology, Clinical Institute of Urology and Kidney Transplant, Cluj-Napoca, Romania
⁵Department of Radiology, County Emergency Hospital, University of Medicine and Pharmacy Targu-Mures, Romania

Abstract

Purpose: To evaluate the potentials of T2 weighted (T2W) MRI and diffusion weighted (DW) MRI for prostate cancer (PCA) detection, local staging and treatment planning in high-risk group.

Material and Methods: Endorectal MRI was performed in 17 Romanian men (median age: 66 years; range: 58 – 75 years),...
prostate specific antigen (PSA) serum levels (median: 20 ng/mL; range: 8.6 - 100 ng/mL) with positive findings for PCa (median Gleason score: 8; range: 7 - 9). Imaging findings were compared to standardised 20-core transperineal saturation biopsy. The prostate was divided into 16 standard sectors (10 posterior and 6 anterior).

Results: Overall, prostate cancer was detected in 16 patients (94%) on DW-MRI alone and in all 17 patients (100%) on T2W-MRI alone, and on combined imaging. On T2W-MRI 165 sectors out of 272 were suspicious for PCa and 124 (75%) were cancer positive. On DW-MRI 126 sectors out of 272 were suspicious for PCa and 118 (95%) were cancer positive. On the combined imaging approach 134 sectors out of 272 were suspicious for PCa and 126 (94%) were cancer positive. This resulted in diagnostic accuracies per sector of 76% for T2W-MRI, 86% for DW-MRI and 89% for combined imaging. Multifocal PCa was confirmed both on MR imaging and by biopsy in 8 of the 17 men (47%) Extra capsular extension (ECE) or seminal vesicles invasion (SVI) was highly suspected in 8 (47%) respectively 7 (41%) of the 17 patients. 6 patients (35%) presented both ECE and SVI. MRI findings were taken into account for treatment planning and none of these patients underwent radical prostatectomy and instead was treated with palliative cryotherapy, radiotherapy and hormone therapy.

Conclusions: Endorectal MRI is highly accurate in PCa detection in the high-risk group and seems to have an important role in local staging and treatment planning for Romanian population.

Key words: diffusion, MRI, prostate cancer, saturation biopsy

Introduction

Prostate cancer is a major public health issue through out the world (1). We also noted an increase of PCa cases over the last years in our Romanian population mainly caused by prostate specific antigen (PSA) testing and rising life expectancy (2). The increased use of PSA testing for prostate cancer diagnosis has led to an increased of men scheduled for prostate biopsy in the last decade, which is associated with increased diagnosis of indolent prostate cancer, increasing costs, and biopsy-related complications. Up to 80% of newly diagnosed PCa patients will have localized disease, low PSA serum levels and low risk for tumor recurrence (3). This is true for developed countries with efficient screening programs but in countries with no prompt programme and large percent of the population with poor health education the probability of locally advanced disease in the moment of diagnosis associated with high PSA serum levels and high risk for recurrence, is more likely. The treatment options for PCa are highly variable and consist of watchful waiting, radical prostatectomy, hormone therapy, and radiation therapy and newly introduced focal therapy methods such as cryo-therapy or ablation therapy (4). In generally patient with localised disease will undergo radical prostatectomy while dose with locally advanced cancer will benefit from nonsurgical procedures. Prediction of ECE or SVI will spare the patients from radical prostatectomy and its well-known complications (4) and will guide them to a more suitable treatment option. This is why accurate detection and staging prior to treatment decision is of extreme importance. MRI using endorectal coil combined with phased-array coils is the imaging technique of choice in detection and staging of PCa due to high spatial and contrast resolution and multplanar reconstruction possibilities. This imaging technique is in constant development and it shown in the last decade an important improvement in technology with the introduction of multi-parametric MR and increased reader experience (5). Therefore we evaluated a well-established imaging modality and considering the costs we tested T2W-MRI and DW-MRI for PCa detection, local staging and its influence on treatment decision.

Materials and Methods

Patients

Study data were obtained between January 2011 and October 2012. In this retrospective, single centre study 17 men (median age: 66 years; range: 58 – 75 years) with biopsy proven PCa, belonging to the high risk group having prostate specific antigen (PSA) serum levels (median: 20 ng/mL; range: 8.6 – 100 ng/mL) and assigned Gleason score of (median 8; range 7 - 9) were included. All patients underwent endorectal MRI composed of T2W-imaging and DW imaging at 1.5T 4 to 6 weeks after PCa confirmation by standardized 20-core transperineal saturation biopsy. Patient characteristics are summarized in Table 1. Nobody of the participants has been excluded. Each participant provided written informed consent prior to endorectal MRI and systematic biopsy.

MRI technique and image interpretation

Endorectal MRI was performed with a 1.5T scanner (Symphony, Siemens AG, Erlangen, Germany) using a-8 - channel phased array body coil combined with an endorectal coil (MEDRAD, Inc, Warrendale, PA) After DRE the balloon of the endorectal coil was inflated with 60 mL of air.

T2W-MRI

T2W-MR images were obtained in axial, coronal and sagittal planes using T2W turbo spin echo sequences and the entire prostate was investigated. T2W-MRI parameters are shown in Table 2. Low-signal intensity nodules or ill-defined

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range), years</td>
<td>66 (58 – 75)</td>
</tr>
<tr>
<td>Median prostate specific antigen (range), ng/mL</td>
<td>20(8.6 – 100)</td>
</tr>
<tr>
<td>Median Gleason score (range)</td>
<td>8 (7 – 9)</td>
</tr>
<tr>
<td>Median prostate volume (range), mL</td>
<td>42 (32 – 65)</td>
</tr>
</tbody>
</table>
low-signal intensity areas were considered suspicious for PCa. The criteria for diagnosis of extra-capsular extension included the following: focal bulging of the prostatic contour, disruption of the prostatic capsule, low signal intensity indicative of cancer in periprostatic fat (Fig. 1), asymmetry of the neurovascular bundle and obliteration of the recto-prostatic angle. Seminal vesicle (SV) invasion was suspected by direct invasion of tumor to the Seminal vesicle, low signal intensity within the Seminal vesicle (Fig. 2) and asymmetric seminal vesicles (6).

**DW-MRI**

DW-MR images were obtained in axial planes using EPI sequences at three b-values (b0, b400 and b800) and restriction of diffusion was quantified by the apparent diffusion coefficient (ADC) value. DW-MRI parameters are shown in Table 2. DW-MRI demonstrates PCa as areas with reduced water diffusion due to the high cell density in cancers. To avoid T2-shine-through-effects the ADC value is calculated. On ADC maps PCa is demonstrated as an area with low signal intensity compared to surrounding normal prostatic tissue (7) (Fig. 3, 4 and 5). ADC values < 1.0 x 10⁻³ mm²/sec were considered suspicious for PCa. Low ADC values (<1.0 x 10⁻³ mm²/sec) outside the prostatic capsule or within the seminal vesicles (Fig. 2) were suspicious for extracapsular extension and/or invasion to the seminal vesicles.

**Imaging interpretation**

Image interpretation was performed by two radiologists with 4 years of experience in uro-radiology and prostate imaging (L.A., C.C.) in consensus. The readers were unaware to the results of biopsy and clinical data. Tissue alterations on MRI were assigned to a 16 region standardised prostate reporting scheme including 10 posterior and 6 anterior glandular sectors (Fig. 3) as recommended from a consensus meeting (8). Only areas suspicious for PCa with at least a size of ≥ 5 mm were considered for uro-radiological interpretation and statistical analysis.

**Saturation biopsy**

Saturation biopsy was done in general anaesthesia and in the supine position. The biopsy needle was guided with transrectal ultrasound into the sectors according to the above-mentioned scheme and twenty transperineal cores were obtained.

**Table 2. MRI parameters**

<table>
<thead>
<tr>
<th>Sequence</th>
<th>T2W-MRI</th>
<th>DW-MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE (ms)</td>
<td>104</td>
<td>90</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>5500</td>
<td>3200</td>
</tr>
<tr>
<td>FOV (mm²)</td>
<td>180 x 180</td>
<td>300 x 300</td>
</tr>
<tr>
<td>Matrix</td>
<td>256 x 256</td>
<td>128 x 128</td>
</tr>
<tr>
<td>Voxel size (mm³)</td>
<td>0.7 x 0.7 x 3</td>
<td>2.3 x 2.3 x 4</td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>b-values</td>
<td>-</td>
<td>0/400/800</td>
</tr>
<tr>
<td>NEX</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>TA (min:sec)</td>
<td>4:09</td>
<td>2:40</td>
</tr>
</tbody>
</table>

**Figure 1.** 59 year old patient with PSA level of 26 ng/mL. (A) Axial T2Wi shows multifocal low signal intensity in the right PZ with extension to the inner gland (white arrow) and disruption of the prostate capsule (arrow head) and another low signal intensity foci on the left side (black arrow). (B) ADC map shows the same lesions (black arrows) with low signal intensity values (0.66 x 10⁻³ mm²/sec). Histology revealed Pca with assigned Gleason score of 8(4+4)

**Figure 2.** 76 year old patient with PSA level of 21 ng/mL. (A) Axial T2Wi shows low signal intensity within the seminal vesicles on the right side (white arrow). (B) ADC map shows low signal intensity values (0.6 x 10⁻³ mm²/sec) (black arrows) in the same region. Histology revealed Pca with assigned Gleason score of 7(4+3)
Histopathological analysis

Each biopsy core was numbered, assigned to a sector and reviewed by a pathologist. Results were reported as cancer with an assigned Gleason score or as benign tissue.

Statistical analysis

Patient characteristics were summarized with frequencies and percentages or with median, range, minimum and maximum values. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were calculated on a per patient and on a per sector basis. The chi-square test was used to calculate significant differences between both methods for PCa diagnosis. All statistical calculations were performed using SPSS® 18.0 software and a p < 0.05 was considered statistically significant.

Saturation biopsy findings

On saturation biopsy cancer was detected in 147 of the 340 probes (43%) at a median prostate volume of 42 ml (range: 32 – 65 ml). The median Gleason score was 8 (range: 7 – 9).

Imaging findings

On T2W-MRI cancer was suspected in all 17 men (100%; false positive findings n = 0) and in 165 of the 272 sectors (85%, false positive findings n = 41). On DW-MRI cancer was suspected in 16 men (94%; false positive findings n = 0) and in 126 of the 272 sectors (80%, false positive findings n = 8). On combined imaging cancer was suspected in all 17 men (100%; false positive findings n = 0) and in 134 of the 256 sectors (91%, false positive findings n = 8).

PCa detection rates

By patient

DW-MRI detected cancer in 16 patients (94%). T2W-MRI, and combined imaging detected cancer in all 17 patients (100%). This resulted in 94% sensitivity, 100% PPV and an overall diagnostic accuracy of 94% by patient for DW-MRI and 100% sensitivity, 100% PPV and an overall diagnostic accuracy of 100% by patient for T2W-MRI, and combined imaging.
By sector

T2W-MRI detected cancer in 124 sectors (84%), DW-MRI in 118 sectors (80%) and combined imaging in 126 sectors (86%). Cancer was detected by T2W-MRI alone in 20/147 sectors and by DW-MRI alone in 10/147 (14% vs 7%, chi-square p<0.05).

This resulted in 84% sensitivity, 67% specificity, 75% PPV, 78% NPV and an overall diagnostic accuracy of 86% by sector for T2W-MRI, in 80% sensitivity, 93% specificity, 93% PPV, 80% NPV and an overall diagnostic accuracy of 86% for DW-MRI and in 85% sensitivity, 94% specificity, 94% PPV, 84% NPV and an overall diagnostic accuracy of 89% for combined imaging (Table 3).

Multifocal PCa, ECE and SVI detection rates

Multifocal PCa was suspected in 8 of the 17 men (47%) and was confirmed by biopsy in all 8 (100%). ECE was highly suspected in 8 out of the 17 patients (47%). SVI was detected in 7 out of the 17 patients (41%). 6 patients (35%) presented both ECE and SVI. Sensitivity, specificity, PPV, NPV and diagnosis accuracy couldn't be calculated because of no histopathological confirmation.

Discussion

T2W-MRI demonstrates PCa as low-signal intensity areas and reveals only structural tissue information (Fig. 4, 5 and 6A,B). High NPVs and high sensitivities are reported for this technique, which may exclude patients with elevated PSA serum levels from systematic biopsy in case of negative imaging findings (9). Nevertheless, benign tissue changes like prostatitis; benign prostatic hyperplasia or adenomyomatosis can also cause low signal intensity on T2W-MRI, which makes this modality more unspecific (10).

Nowadays, it is recommended to add functional MRI techniques to raise specificity of T2W-MRI (11).

Our data suggest that using endorectal MRI in our Romanian population provide excellent diagnostic accuracy for prostate cancer diagnosis, but we have to state that a considerable number of cancers were large. Transrectal ultrasound normally is used in the B-mode to assess prostate anatomy and to guide the biopsy to standardized areas of the prostate. Unfortunately, B-mode ultrasound has low diagnostic accuracy for prostate cancer detection and staging therefore other imaging modalities should be chosen for a targeted approach (12). We have to keep in mind that enhanced transrectal ultrasound techniques, i.e. elastography or contrast media ultrasound lack of availability with its possibility of targeted biopsy under real-time conditions. MRI targeted biopsy of the prostate show cancer detection rates nearly of 60%, but is only available in few centres and need long procedure time (13).

When regarding the overall diagnostic accuracy by patient of 94% for DW-MRI an 100% for T2W-MRI and combined imaging and by lesion of T2W-MRI (76%); DW-MRI (86%) and combined imaging (89%) of this study it should be valuable to report the urologists areas suspicious for PCa on MRI to directly guide the biopsy needle there. Our data has slightly better results than other studies probably due to investigating biopsy confirmed PCa patient in the high-risk group with relatively larger tumors.

A recently published paper of Vilanova et al. investigated MRI before biopsy and reported diagnostic accuracies of 73.5% % for T2W-MRI alone, of 81.8% for DW-MRI alone and of 84.8 % for combined imaging (14). They also recommended combining at least one functional technique with free-to-total PSA ratio to raise diagnostic accuracy. Beside these high detection rates, the authors stated that functional MRI has the potential to help avoid a large number of negative biopsies.

Also Choi MS et al. described the usefulness of pre-biopsy and post-biopsy MRI (15) with sensitivities of 84.8% and 92.4%, PPVs of 75.7% and 92.4%. The MRI location match percentage before and after biopsy was 89.3% and 94.1%. The authors concluded that MRI before prostate biopsy can provide

<table>
<thead>
<tr>
<th>Table 3. Detection of prostate cancer by lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
</tr>
<tr>
<td>Specificity</td>
</tr>
<tr>
<td>Positive predictive value</td>
</tr>
<tr>
<td>Negative predictive value</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
</tr>
</tbody>
</table>
more information by which to identify prostate cancer during prostate biopsy and thus reduce the false-negative rate.

Kpandemiau Abu V. reports of a growing interest in the use of imaging techniques like MRI as first-line specialist investigation for suspicious PCAs (15). This is an interesting idea, but MRI screening for PCAs is not practicable in our country.

In future we tend to implement endorectal MRI for patients with previous negative biopsies but ongoing suspicion of cancer to avoid biopsy in case of negative findings or in case of positive findings to directly guide the biopsy needle towards suspicious areas.

ECE was suspected in 8(47%) of the patients while 7(41%) men were suspected of SVI and in total 6(33%) men had both ECE and SVI. Our urologists took in consideration the MRI report and together with the age, PSA serum levels and Gleason score the treatment plan was decided. As a result none of this patients underwent radical prostatectomy and instead was treated with palliative cryotherapy, radiotherapy and hormone therapy.

Jager GJ et al. analysed the usefulness of preoperative MRI for moderate or high risk of ECE and concluded that preoperative MRI in this group of patients is cost-effective (17).

Ren j et al. evaluated the usefulness of DWi-MRI in the detection of SVI and he reported the AUC for T2W-MRI in combination with DW-MRI (0.897) was significantly higher accuracy than T2W-MRI alone (0.779) in the detection of SVI (18).

Prostate cancer remains a national healthcare problem with increased prevalence (19) a larger well-designed study should be performed in the future to obtain normative references for signal intensity characteristics and ADC values of normal prostate tissue and cancer.

We have to state several limitations: (1) we used systematic biopsy as the reference standard, even though it may miss a substantial percentage of prostate cancers. However, it is the method of choice for cancer detection. (2) Our study population was relatively small. (3) We did not use MR spectroscopy and dynamic contrast enhanced MRI, even we know the improved PCa detection rates and local staging using all 4 MRI techniques. (4) we do not have data on intra-observer and interobserver variability.

Conclusions

The combined use of T2W-MRI and DW-MRI endorectal MRI yields highly accurate PCa detection rates in the high risk group men. In our study endorectal MRI seems to have an important role in local staging and treatment planning. Further studies with a prospective design and in comparison to prostatectomy specimen should be done to reevaluate MRI for prostate cancer diagnosis in our population.

References