Application of the PI-RADS score system by radiologists in training on the multiparametric MRI studies performed to patients under biochemical suspicion of prostatic cancer and previous negative biopsies before a new targeted biopsy.

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Purpose

Multiparametric MRI (mpMRI) provides a noninvasive approach to the characterization of prostate anatomy, angiogenesis, cell density and metabolism (T2 weighted image (T2w), dynamic contrast enhance (DCE) sequences and diffusion weighted image (DWI) and spectroscopy respectively) not just for local staging, but also for the initial diagnosis of prostatic carcinoma [2], having emerged as a new and important tool in the field.

Even though there is supportive evidence for the use of mpMRI, the lack of standardization of diagnostic criteria has stalled the wide application of this tool. This issue has been addressed as of 2012 by the European Society of Urogenital Radiology (ESUR) with the publication of a unified scoring system for the mpMRI, known as the Magnetic Resonance Prostate Imaging Reporting and Data System (MR PI-RADS) in an effort to emulate similar systems like the one used by breast radiologists (BI-RADS), in order to reduce the interobserver variability while increasing the diagnostic value of the technique [3, 4, 5].

The PI-RADS is currently being validated in several studies, such as the multicentric prospective study from Daniel Portalez et al [3], showing promising results.

The purpose of our study is to evaluate the role of prostate mpMRI using the PI-RADS system in patients with biochemical suspicion of prostatic cancer and at least one previous negative biopsy using the subsequent targeted biopsy as gold standard. Evaluating:

- The interobserver reliability
- The relationship between PI-RADS scores and histological results

Methods and Materials

Patients: In 2008 our institution began routinely performing mpMRI of the prostate. The gross of the studies were acquired for local staging, restaging and postsurgical evaluation. We reviewed our hospital records for:

- Patients referred by urologists under suspicion of prostatic carcinoma (elevation of PSA) and at least one previous TRUS biopsy in which a new targeted biopsy was considered. [Following mpMRI, all patients
underwent targeted TRUS biopsies performed by the urologists, who were aware of the imaging findings.]

- 14 patients met the inclusion criteria.

**mpMRI protocol:**

- T2w images (fast spin-eco) acquired in the three planes.
- DWI using different b-values with an apparent diffusion coefficient (ADC) map in the axial plane.
- DCE MRI obtained by fat saturated T1w (fast field echo sequence) following intravenous bolus injection of 0.1 mMol/kg of Gadobutrol.
- 3D MR spectroscopic imaging of the entire prostate using a section-selected box drawn closely around the prostate and a point-resolved spectroscopic sequence.

**Scoring and evaluation of image data:**

- mpMRI data sets were retrospectively evaluated and scored according to the 5-point PI-RADS scale (as depicted in the ESUR 2012 guidelines) without prior knowledge of the prostate-specific antigen level or biopsy results.
- Radiologists 1 (D.G.R) and 2 (O.C.C) independently interpreted and scored all five data sets. The two radiology residents (third year) had similar levels of experience in evaluating prostate MR images.

**Data analysis:** The elementary units for analysis were the prostate mpMRI results represented in PI-RADS scores (5 subscores and a total sum score), and the presence or absence of prostate cancer in the targeted biopsy result.

- **The interobserver reliability:** we used a linear weighted Kappa in order to take into account the degree of disagreement between observers.
- **The relationship between PI-RADS scores and histological results:** were assessed by the U Mann Whitney test.

Results are given for each observer and in a conjunct manner. All p values reported were derived at two-sided tests; P< 0.05 was considered to indicate statistical significance.
Results

Population:

• 14 patients with a mean age of 66.78 +/-6.38 (range 54-76 years)

• At least one previous negative TRUS biopsy. Mean number of biopsies 3.64 (range 1-6).

• PSA previous to the mpMRI was elevated in all the patients. Mean value 20.59+/-10.67 (range 7.77-52.61).

• All patients underwent biopsy following MRI with a median interval of 94.71 days +/-90.67 (range 8-287).

The biopsy was positive for cancer in 6 patients (42.85%). The maximal Gleason score was 4+5 (n=1), 4+3 (n=2), 3+4 (n=1), 3+3 (n=2). Patients with negative biopsies continued clinical follow up, with a control mpMRI in two of them.

MULTIPARAMETRIC MRI

Figure 1 depicts a mpMRI study with a high PI-RADS score and positive biopsy for prostatic carcinoma.

Figure 2 depicts a mpMRI study with a low PI-RADS score and positive biopsy for prostatic carcinoma. Please refer to the annotations for further information.

PI-RADS SCORE AND INTERRATER RELIABILITY: The highest interrater reliability was found to be Kappa = 0.778 for the T2w score and Kappa= 0.644 for the DCE sequence. The Kappa for the total score was 0.526 (95% CI 0.355, 0.697).

<table>
<thead>
<tr>
<th>MRI sequence</th>
<th>Weighted kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2w image</td>
<td>0.778</td>
</tr>
<tr>
<td>DWI</td>
<td>0.417</td>
</tr>
<tr>
<td>DCE</td>
<td>0.644</td>
</tr>
<tr>
<td>Spectroscopy</td>
<td>0.596</td>
</tr>
<tr>
<td>Total score</td>
<td>0.526</td>
</tr>
</tbody>
</table>
**PI-RADS SCORE AND RELATIONSHIP WITH BIOPSY:** The data from the two readers was analyzed independently as well as pooled. Higher PI-RADS scores were observed in positive biopsies for the T2 and DWI score (P<0.05), with a tendency in the total score (P=0.071) No statistically significant difference was observed in the other subscores.

**Pooled data**

Multiparametric magnetic resonance imaging characteristics of 14 biopsies, as a function of the presence or absence of prostate cancer

<table>
<thead>
<tr>
<th></th>
<th><strong>Negative biopsies</strong></th>
<th><strong>Positive biopsies</strong></th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2 score (1-5)</td>
<td>2 (95% CI 2, 3)</td>
<td>4.25 (95% CI 2.38, 5)</td>
<td><strong>0.0146</strong></td>
</tr>
<tr>
<td>DWI score (1-5)</td>
<td>2.5 (95% CI 1, 3.68)</td>
<td>4.5 (95% CI 3.19, 4.9)</td>
<td><strong>0.0136</strong></td>
</tr>
<tr>
<td>DCE score (1-5)</td>
<td>2.25 (95% CI 1.9, 4)</td>
<td>3.75 (95% CI 1.29, 4)</td>
<td>0.327</td>
</tr>
<tr>
<td>Spectroscopy score (1-5)</td>
<td>2.25 (95% CI 1.4.09)</td>
<td>2.5 (95% CI 1.4.3)</td>
<td>0.8968</td>
</tr>
<tr>
<td>Sum of scores (4-20)</td>
<td>9.75 (95% CI 8.31, 11.16)</td>
<td>14.5 (95% CI 8.1, 17.5)</td>
<td><strong>0.0704</strong></td>
</tr>
</tbody>
</table>
Fig. 3: Pooled data
References: Diego Gutierrez

Independent data

Fig. 4: Independent data
References: Diego Gutierrez
Fig. 1: A. T2w image depicting a low signal intensity focus with bulging of the capsule, located in the transitional zone as well as the anterior horn of the peripheral zone (arrow). This lesion was classified as PI-RADS 5 by both readers. B and C. DWI (high b value) and corresponding ADC map, showing a focal area of hyper SI with reduced ADC (arrows). Classified as PI-RADS 5 by both readers. D and E. DCE sequence and selected still image depicting a type 3 curve of the focal lesion. Classified as PI-RADS 4 by both readers. F. Qualitative spectroscopy. The creatine peak is higher than the Citrate peak. This finding was classified as PI-RADS 4 by one of the readers and 3 by the other. In this case the biopsy of the suspicious area was positive for carcinoma, Gleason 3+4.
Fig. 2: A. T2w image depicting an area of homogeneous low SI, well marginated, originating from the TZ (arrow). This finding was classified as PI-RADS 2 by both readers. B and C. DWI (high b value) and corresponding ADC map. Classified as PI-RADS 2 by one of the readers and 4 by the other. D. DCE sequence of the area identified in the T2w image (continuous line). Classified as PI-RADS 2 by both readers. E. Qualitative spectroscopy. The citrate peak is more than two times de high of the creatine peak. This finding was classified as PI-RADS 1 by both readers. The biopsy of the suspicious area was positive for carcinoma. Gleason 3+3.
**Fig. 3:** Pooled data

**Fig. 4:** Independent data
Conclusion

The recommended use of MRI in prostate cancer is multiparametric. The integration of technics such as DWI, DCE and spectroscopy has been shown to increase the sensibility and specificity of prostate cancer detection [4], reaching predictive values of up to 80% [6].

We found the PI-RADS score system to be a reliable reporting system for the mpMRI with fairly good interobserver agreement, with the highest kappa for the T2w image and DCE sequence. A positive relationship not only between the T2w image and DWI scores, but also the total score, and the presence of carcinoma in the targeted biopsies was found.

Is it important to note that the readers, despite being trained in prostate mpMRI, are by no means considered experts. Nonetheless, the promising results obtained not only in this, but also in other studies [3] put in evidence the need for a further large-scale prospective validation of the PI-RADS.

Given the current management of prostatic carcinoma, the gold standard used in our study was the targeted biopsy in all but one patient (who underwent a radical prostatectomy, confirming the biopsy results), and in the same manner, negative biopsies could not be verified for the absence of cancer, amounting to a classic verification bias. It would also be beneficial to dispose of a larger sample, which would probably be needed in order to achieve a significant statistical difference in other PI-RADS subscores.

References


**Personal Information**