Multi-parameteric MRI and PI-RADS Scoring system: Our new inception in clinical practice with evaluation of the diagnostic performance of different Score combinations

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Aims and objectives

The heterogeneity and great variations among the studies performed to assess the diagnostic role of multiparametric MRI (mpMRI) in prostate cancer (Pca) may be explained by its complexity and sometimes the contradictory findings of the different single modalities which may result in a wide scope of possible interpretations of mpMRI findings leading to variations between different readers and different diagnostic centers [1-3].

To overcome these problems, the European Society of Urogenital Radiology (ESUR) recently has called a committee of experts and published a guideline providing recommendations for the performance of mpMRI investigations and a structured reporting scheme named Prostate Imaging Reporting and Data System (PI-RADS) [4]. This was inspired by the BI-RADS system for breast cancer detection which has proved great success in clinical practice [5].

Our aim is to evaluate the use of the ESUR-proposed PI-RADS scoring system for prostate cancer detection using multiparameteric MRI in our clinical practice and to compare the diagnostic performances of the single and combined PI-RADS scores.

Methods and materials

Patients:

76 prostatic lesions in 54 consecutive patients with clinical suspicion of cancer prostate (based on high PSA level or suspicious digital rectal examination) were prospectively assessed using 1.5T mpMRI including T2, DWI, DCE, MRS sequences. Confirmation of findings by laboratory and histopathological data obtained either from TRUS biopsy or radical prostatectomy.

MR Image Acquisition Protocol

The MR images were obtained with a 1.5-T system (Avanto; Siemens Medical Systems, Erlangen, Germany) by using phased array surface body coil (TORSO)-16 channels. Whenever possible, peristalsis was suppressed with an intramuscular injection of 20 mg of butyl scopolamine (Busvopan; Boehringer, Ingelheim, Germany) before the examination. The imaging protocol was as follows:
1- T2-weighted multiple-spin-echo images (in-plane spatial resolution of 0.55 × 0.55 mm, 3500-4400/132 [repetition time msec/echo time msec], 180° flip angle, 11-15 sections, 4-mm section thickness, echo train length of 15, 280-mm field of view, 240 × 512 matrix) were obtained in three orthogonal planes covering the prostate and the seminal vesicles.

2- DWI: (echoplaner sequence) TR 2100/TE 80, Matrix 128 x 128, field of view 220 (±20), slice thickness 3mm without gap in between and 3 different b values were used (0,400,800) . ADC maps were reconstructed on workstation for qualitative and quantitative assessment of DWI images.

3- A 3D MR spectroscopic imaging of the entire prostate is performed by using a section-selected box drawn closely around the prostate and a point-resolved spectroscopic sequence. The matrix size was 6 × 6 × 6 mm, the repetition time was 650 msec, and the echo time was 120 msec. volume of interest (VOI) aligned to axial T2WI; coverage of the whole prostate in the VOI; field of view at least 1.5 voxels larger than the VOI in all directions to avoid wrap-around or back folding; spectral selective suppression of water and lipid signals; positioning of at least six fat saturation bands close to the prostatic margin to conform to the prostatic shape as closely as possible.

4- DCE MR images were obtained using fast 3D T1-weighted gradient-echo images (T1-VIBE) (34/1.6, 14° flip angle, 10 transverse partitions on a 3D slab, 4-mm section thickness, 280-mm field of view, 77 × 256 matrix) were acquired during an intravenous bolus injection of a paramagnetic gadolinium chelate - 0.1 mmol of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) per kilogram of body weight-which was administered with a power injector at 2.5 mL/sec and followed by a 20-mL saline flush. With this sequence, the 3D volume was acquired every 15 seconds for 10 mins. Post processing includes ROI placement upon the suspected lesions as well as the normal gland.

Image Analysis:

For reporting and localization of findings, the prostate was divided into the apex, middle, and base of the gland and into 27 regions of interest (ROIs) as recommended by the ESUR guidelines according to a scheme presented by Röthke et al [6]. All T2-weighted, DWI, spectroscopic and dynamic MR data sets were prospectively evaluated and scored. In a first step single-scores from (1-5) for T2, DWI, DCE and MRS for each lesion were defined according to the ESUR guidelines [4]. Since the diagnostic significance of the T2w-TSE sequences differs for the peripheral and central glandular zone, two separate schemes were recommended by the ESUR for the two regions which were used at the current study. For MRS the consensus described two methods a quantitative and a qualitative one, the latter was employed at the current study. Then a PI-RADS sum (PS sum) score (scale from 4 to 20) was calculated by summation of the 4 previous single-scores.
Statistical Analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Agreement of the different predictives with the outcome was used and was expressed in sensitivity, specificity, positive predictive value, negative predictive value and accuracy. Receiver operating characteristic curve (ROC) was plotted to analyze a recommended cutoff based on Youden selected thresholds, the area under the ROC curve denotes the diagnostic performance of the test. A p value of p < 0.05 was considered as statistically significant.

Results

In the current study 76 lesions were identified, 15 lesions were confirmed to be non cancerous in origin and 61 lesions were confirmed to be foci of prostate cancer. Gleason score was histopathologically assigned for each malignant focus either after TRUS biopsy (for 49 lesions) or radical prostatectomy (for 12 lesions in 7 patients). 20 lesions showed Gleason score of <7 while 41 lesions showed Gleason #7.

Peripheral zone lesions (n=54) as well as central gland lesions (n=12) were assessed separately on T2, DWI, DCE and MRS with the exclusion of lesions involving both zones.

Diagnostic performance of mp-MRI for prostate cancer detection in Peripheral zone lesions and central gland lesions:

Analysis of receiver operator curve for the single PI-RADS score of each sequence as well as the summed PI-RADS score (PS sum) for detection of prostate cancer in peripheral zone lesions (Figure 1 and Table 1) showed:

- The summed PIRADS score of all the four sequences showed the highest AUC for cancer detection (Az= 0.923) And on using recommended Youden threshold of 12 for the summed score, it showed the highest sensitivity of 83.72% and highest specificity of 100%.
- The use of single MR sequences in detection of cancer in the peripheral zone led to lower AUC for prostate cancer detection.
- And as regards to the single PI-RADS scores the AUC was highest for DCE (0.921) followed by MRS, T2 and then DWI. On using a selected threshold of 3 for each of the single scores, the DWI showed highest sensitivity of (90.70%) and lowest specificity of (45.45%), while each of T2, DCE , MRS showed lower sensitivity with significant higher specificity than DWI. Detailed ROC evaluations of each score for all lesions shown in Figure 1 and Tables 1-2.
While Analysis of receiver operator curve for the single PI-RADS score of each sequence as well as the summed PI-RADS score (PS sum) for detection of prostate cancer in central gland lesions (Figure 1 and Table 1) showed:

• The only single PIRADS score that showed statistically significant AUC value was for the T2 score with (Az= 0.875) so it performed as the best single score in the central gland lesions.
• However the summed PIRADS (PS sum) score of all the four sequences combined still showed higher AUC for cancer detection (Az= 0.923) compared to the T2 score.
• While Single PIRADS scores for DW, DCE and MRS each alone was statistically insignificant in cancer detection of central gland lesions.
• Sensitivity and specificity was detected according to the selected thresholds and shown in Table 2.

![ROC curve](image)

**Fig. 1**: ROC curve of single PI-RADS scores for T2, DW, DCE , MRS and for summed PIRADS score for cancer detection in peripheral zone (on left) and in central gland (on right)

**References**: Radiodiagnosis, Alexandria university, Alexandria university hospital - Alexandria/EG
Table 1: ROC curve analysis of single PI-RADS scores for T2, DW, DCE, MRS and for summed PIRADS score for cancer detection in peripheral zone and in central gland.

References: Radiodiagnosis, Alexandria university, Alexandria university hospital - Alexandria/EG

Table 2: Agreement (sensitivity, specificity, PPV, NPV, and accuracy) in peripheral and transitional zones.

References: Radiodiagnosis, Alexandria university, Alexandria university hospital - Alexandria/EG

Analysis of receiver operator curve for T2 score with combinations of single PI-RADS scores as well as the summed PI-RADS score (PS sum) for detection of prostate cancer in peripheral zone lesions (Figure 2 and Table 3) showed:
• The AUC for peripheral zone lesions showed higher values for combined T2+DWI scores (Az= 0.855) when compared to single T2 score (Az= 0.805).
• Also on adding DCE score, the combined score for T2+DWI+DCE showed higher AUC values (Az= 0.918) than of the T2+DWI scores only (Az= 0.923) denoting better diagnostic accuracy.
• Still the summed PI-RADS score (PS sum) of all (T2+DWI+DCE +MRS) sequences showed the highest AUC (Az= 0.923) for detection of prostate cancer in peripheral zone lesions.
• When using the recommended Youden threshold of 3, 7, 10 as well as 12 for the single T2 score, combined T2+DWI, combined T2+DWI+DCE and for the PS sum respectively, it showed increased sensitivity and ascending trend towards better diagnostic performance on increasing combinations between scores, where sensitivity was 58% for T2 score, 65% for combined T2+DWI score, 76% for combined T2+DWI+DCE score, 83% for PS sum (T2+DWI+DCE +MRS) and showed a specificity of 100% for all. This indicates increased diagnostic performance and accuracy on using more score combinations reaching the highest when using the summed PI-RADS score for all the sequences together. Detailed ROC evaluations of each score for detection of peripheral zone lesions are shown in Figure 2 and table 3-4

Analysis of receiver operator curve for T2 score with combinations of single PI-RADS scores as well as the summed PI-RADS score (PS sum) for detection of prostate cancer in central gland lesions (Figure 2 and Table 3) showed:

• Adding DW score to T2 score had improved diagnostic accuracy and performed as the best combination score in detection of central gland lesions where it showed the highest AUC (Az= 0.969) which is significantly higher than that of T2 score alone (Az= 0.875) which performed as the best single score.
• On adding DCE score to T2+DW, it showed decrease in the AUC to (Az=0.938)
• On calculating the summed PIRADS (PS sum) score of all the four sequences combined the AUC (Az=0.953) was also less than that of T2+DW scores but higher than that of T2+DW+DCE scores.
• Sensitivity and specificity was detected according to the selected thresholds and shown in Table 4.
**Fig. 2:** ROC curves for T2, T2+DW, T2+DW+DCE and PS sum scores in cancer detection in peripheral zone (on left) and in central gland (on right)

**References:** Radiodiagnosis, Alexandria university, Alexandria university hospital - Alexandria/EG

**Table 3:** ROC curve analysis for T2, T2+DW, T2+DW+DCE and PS sum scores in cancer detection in peripheral zone and in central gland

**References:** Radiodiagnosis, Alexandria university, Alexandria university hospital - Alexandria/EG
Table 4: Agreement (sensitivity, specificity, PPV, NPV, and accuracy) in peripheral and transitional zones

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References: Radiodiagnosis, Alexandria university, Alexandria university hospital - Alexandria/EG

Thus the PI-RADS sum score in both PZ lesions and CG lesions showed no false positive results with 100% specificity for scores above 12.

More of the PI-RADS scores combinations were analyzed in order to identify the best single score that should be added to the T2 score as a first priority when there is no availability for all sequences to improve the diagnostic performance of T2 in both peripheral zone as well as central gland lesions. The DCE score was the best combination for the T2 score regarding the peripheral zone lesions with an Az=0.921 for T2+DCE combination, while regarding the central gland lesions as expected form the above results the DWI was the best combination for the T2 score with an Az=0.969. At the selected Threshold of 6; the T2+DCE combination at PZ showed sensitivity of 74.42% and specificity of 100% while the T2+DW combination at CG showed sensitivity of 100% and specificity of 75%. Detailed AUC values for different combinations was shown at Table 5.
Table 5: AUC values for T2 PIRADS score and its combinations for cancer detection in the peripheral zone and central gland

References: Radiodiagnosis, Alexandria university, Alexandria university hospital - Alexandria/EG

Images for this section:
Fig. 3: Case(1): A 74-year-old male patient presented with LUTS and high PSA (28 ng/ml), DRE was inconclusive revealing enlarged prostate gland. Multiparametric MRI:

- The prostate gland shows ill defined hypointense lesion at the inferior aspect of the left central zone (segments 11a and 11p): a) T2 axial sequence shows ill defined hypointense lesion at the inferior aspect of the left central zone (segments 11a and 11p) with the indeterminate appearance of the lesion T2 score considered = 3. b) The described lesion was hyperintense of DWI at high b value (800 s/mm2). c) ADC map showing very low
ADC value of the lesion measuring around 0.5 x10^-3.cm sec2. (DW score = 5) (d-e)DCE-MRI showing focal early enhancement and delayed washout of contrast of the described lesion.

Fig. 4: Case(1): (e)DCE-MRI showing delayed washout of contrast of the described lesion. (f)DCE-MRI ROI placement in post contrast T1WI (g)DCE-MRI regenerated curves with type 3 curve (in solid line) of the described lesion. (DCE score = 5 where 3 points for type 3 curve +2 points for focal asymmetrical enhancement) (h)MRSI showing
abnormal spectroscopic pattern of the described focus with very high Cho relative to Ci and Cr levels (Cho >> Ci) (MRS score = 5). Conclusion: PIRADS sum score of 18 which is consistent with a neoplastic focus of prostatic carcinoma at inferior aspect of the central zone along its left side. Histopathology: TRUS biopsy showed Left prostatic adenocarcinoma with Gleason score 6(3+3).
Fig. 5: Case(2): 68-year-old male patient had LUTS and anal pain with right basal hard gland on DRE and PSA of 8.5 ng/ml. Multiparametric MRI: •The prostate show a focal T2 hypointense nodule at the peripheral zone on the right side, at (Segments 4p and 6p). (a) Axial T2 FSE sequence showing well-defined focus displaying hypointensity. (T2 score = 4) (b) The described lesion was hyperintense of DWI at high b value (800 s/mm²) (c) ADC map showing low ADC value of the corresponding lesion measuring around 0.6 x 10⁻³ cm² sec⁻¹. (DW score = 5) (d) MRS of the described lesion shows high Cho relative to Ci and Cr levels (Cho > Ci). (MRS score = 4)
Fig. 6: Case (2): (e-f) DCE-MRI showing early focal enhancement and delayed washout of contrast of the described lesion. (g) DCE-MRI ROI placement in post contrast T1WI (h) DCE-MRI regenerated curves with type 3 curve (in solid line) of the suspicious focus. (DCE score = 5 where 3 points for type 3 curve +2 points for focal asymmetrical enhancement) Conclusion: Mp-MRI showed a PIRADS sum score of 18 which is in favor of neoplastic nodule of prostatic adenocarcinoma located in the right lobe, at its mid
&basal segments (segments 4p&6p). Histopathology TRUS biopsy was performed and proved to be adenocarcinoma Gleason score 7 (4+3).

**Fig. 7:** Case (3): 66-year-old male patient had LURTS and right hard nodule on DRE (right T2a and PSA was 24 ng/ml. Multiparametric MRI: The prostate showed a focal T2 hypointense nodule is noted at the central zone on the right side anteriorly (segment 3a and 1a): (a-b) Axial and sagittal T2 FSE sequence showing a suspicious lesion at the basal and midzonal regions of the right central zone displaying hypointensity with "erased charcoal appearance" (T2 score =4). (c) The described lesion was hyperintense of DWI at high b value (800 s/mm2) (d) ADC map showing low ADC value of the lesion measuring around 0.6 x10-3.cm sec2. (DW score = 5)
Fig. 8: Case (3): (e-f) DCE-MRI showing focal early enhancement and delayed washout of contrast of the suspicious focus. (g) DCE-MRI regenerated curves with type 3 curve (in solid line) of the suspicious focus. (DCE score = 5 where 3 points for type 3 curve + 2 points for focal asymmetrical enhancement) (h) MRSI showing abnormal spectroscopic pattern of the described focus with high Cho relative to Cr and Ci levels (Cho > Ci). (MRS score = 4) Conclusion: Mp-MRI showed a PIRADS sum score of 18 which is in favor of focal prostatic carcinoma along the left peripheral zone of mid and basal gland (segments 3a-1a). Histopathology TRUS biopsy was done and revealed right adenocarcinoma Gleason score 3+1, then Robotic radical prostatectomy was performed and confirmed the histopathology.
Fig. 9: A 75-year-old male patient had nocturia with highly elevated PSA of 239 ng/ml, the DRE was suspicious with firm right lobe. Multiparametric MRI: (a) Axial T2 FSE sequence showing sizable hypointense lesion noted at the peripheral zone on the right side involving segments 2p, 3p, 4p. (b) Axial T2 FSE sequence showing the described lesion is widely based on the prostatic capsule. It transgresses the prostatic capsule with invasion of the seminal vesicle. (T2 score = 5) (c-d) DWI and ADC map; the lesion shows hyperintensity on DWI and Low ADC with value measuring ($0.6 \times 10^{-3}$ mm$^2$/sec). (DW score = 5)
Fig. 10: Case (4): (e-f) DCE-MRI showing early enhancement of the described lesion with rapid washout of contrast in comparison to normal prostatic tissue. (g) DCE-MRI regenerated curves with type 3 curve (in solid line) of the described lesion. (DCE score = 5 where 3 points for type 3 curve +2 points for focal asymmetrical enhancement) (h) MRS showing border line spectroscopic pattern of the described lesion with Cho nearly equal to Ci levels (Cho = Ci). (MRS score=3) Conclusion: Mp-MRI showed a PIRADS sum score of 18 involving the right peripheral zone at the base and midzone of the prostate with ECE and SVI on the right side vesicle which is in favor of prostatic adenocarcinoma. Histopathology: TRUS guided targeted biopsy was performed and revealed right base and midzonal prostatic adenocarcinoma Gleason score 7(4+3).
Fig. 11: Case (5): 56-year-old male patient had LUTS with PSA of 5.8 ng/ml and enlarged prostate on DRE. Multiparametric MRI: (a) Axial T2 FSE sequence showing a small 1.4cm nodule at the right PZ segments 3 and 4p. (T2 score = 3) (b) The described lesion was isointense on DWI at high b value. (c) ADC map showing low ADC value of the lesion measuring around 0.8 x10-3.cm sec2. (DW score = 4) (d) MRS showing normal spectroscopic pattern of the described lesion with high Ci and low Cho levels (Ci >>Cho). (MRS score = 1)
Fig. 12: Case (5): (e) DCE-MRI ROI placement in post contrast T1WI (f) DCE-MRI regenerated curves shows type 1 curve (in solid line) of the described lesion. (DCE score = 1) Conclusion: Mp-MRI showed a PIRADS sum score of 9 which lowers the risk of being prostatic neoplastic lesion. Histopathology TRUS guided biopsy was performed and revealed chronic prostatitis with no malignant cells.
Fig. 13: Case (6): A 76-year-old male patient presented with LUTS and high PSA (84 ng/ml), DRE showed firm left lobe with enlarged seminal vesicle. Multiparametric MRI: The prostate gland shows post TURP central defect with bilateral hypointense lesions involves the peripheral zones: (a) T2 axial sequence shows an ill defined hypointense lesion at the right PZ (segment 3p) averaging 1.7cm with intact prostatic capsule. (T2 score = 3) (b-c) T2 axial sequence shows another larger hypointense lesion at the left PZ (segment 7 and 9p) averaging 3.8cm with invasion of the prostatic capsule and left NVB as well as left SVI. (T2 score = 5) (d) T2 coronal sequence shows the left sided lesion with SVI as well as bony deposits involving the pelvic bones.
Fig. 14: Case (6): (e-f) The left sided lesion is hyperintense on DWI with low ADC measuring (0.6 x 10^{-3} mm^2/sec). (DW score=5) (g-h) The right sided lesion is isointense on DWI with low ADC measuring (0.9 x 10^{-3} mm^2/sec). (DW score=4)
Fig. 15: Case (6): (i) DCE-MRI ROI placement in post contrast T1WI (j) DCE-MRI regenerated curves shows type 2 curve (in solid line) for the left sided lesion. (DCE score = 4 where 2 points for type 2 curve + 2 points for focal asymmetrical enhancement), while it shows type 1 curve (dashed line) for the right sided lesion with no focal enhancement (DCE score = 1) (k-l) MRS showing abnormal spectroscopic pattern of the left sided lesion with very high Cho relative to Ci and Cr levels (Cho >> Ci) (MRS score = 5). While it shows preserved spectroscopic pattern of the right sided lesion with normal Ci levels (Ci >> Cho) (MRS score = 1) Conclusion: Mp-MRI showed a PIRADS sum score of 19 for the left sided lesion which is consistent with a neoplastic focus of prostatic carcinoma; while it showed a PIRADS sum score of 9 for the left sided lesion which lowers the risk of prostatic cancerous lesion on this side. Histopathology: TRUS biopsy showed left prostatic adenocarcinoma with Gleason score 7(4+3) and left seminal vesicle involvement while it shows no cancerous lesions on the right side.
### Table 2: Agreement (sensitivity, specificity, PPV, NPV, and accuracy) in peripheral and transitional zones

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Table 4: Agreement (sensitivity, specificity, PPV, NPV, and accuracy) in peripheral and transitional zones
Conclusion

PI-RADS scoring system and mp-MRI has a promising role in Pca detection. Our data showed that the PI-RADS scoring system is a good tool to differentiate Pca from non cancerous lesions showing higher probability of Pca with higher PI-RADS scores. The use of single different scores resulted in lower diagnostic accuracy with improved accuracy for combined scores.

Our results regarding peripheral zone (PZ) lesions revealed that; The PI-RADS sum score for T2, DWI, DCE and MRS showed the highest AUC for Pca detection (Az=0.923) and on using a cut-off of 12, it showed the highest sensitivity of 83.72% and highest specificity of 100%. As regards Single PI-RADS scores the highest AUC was for DCE score (0.921). However, the DWI showed highest sensitivity of (90.70%) on using a selected threshold of 3 for single scores. Best combined score following the PI-RADS sum score was for the combination of T2+DCE scores.

These is matching with the results of previous studies which have already evaluated the PI-RADS scoring system using the results of MRI/TRUS fusion biopsy [7], MR-guided biopsy [8], and radical prostatectomy as a reference standard [9]. All of these studies found the PI-RADS scoring system to have a good diagnostic performance with high sensitivities and high accuracies; the interobserver agreement was good as well. In the previously mentioned studies, a sum score has been used to combine the individual scores for each sequence in an overall score for a lesion. However, the optimal cutoff values for a sum score were found to range from 8 to 10 compared to 12 at the current study this is because they only included T2,DW and DCE scores without using the MRS score which was considered optional by the ESUR [4]. Still our results is matching with these studies when we calculated the sum score for only T2, DW and DCE as the cut-off value was 10 when MRS was excluded.

Meanwhile, our mpMRI results in the central gland still show some controversy and needs more evaluation in the future. Where as for central gland (CG) lesions; PI-RADS sum score showed high AUC of 0.953; however the combination of T2+DWI score showed numerically the highest AUC of 0.969. The only single score that showed statistically significant AUC was the morphological T2 score (A那个时候 = 0.875). While adding DCE score resulted in slight reduction of the AUC score with no improvement of the diagnostic performance for Pca detection.However, still statistical analysis of our data regarding the CG cancer is limited by the small number of patients with CG lesions.

This goes along with the findings by Schimmoller et al. [10] where they analyzed Pca detection in CG and stated that the combination of T2WI and DWI Scores achieved the highest test accuracy while they showed low accuracy for DCE score in the CG lesions.

The PI-RADS scoring system distinguishes PZ and CG lesions on T2WI only, Since there is significant difference regarding the results in PZ and CG ;this urges the need of
assigning different scoring system for the CG for every score similar to what has been done for the T2 score to optimize the CG cancer detection.

Our results regarding the DCE score showed good diagnostic accuracy for Pca detection at the PZ with reduced accuracy at the CG, this matching with the results of Junker et al. [11] who showed good diagnostic accuracy of the DCE at the PZ with very low diagnostic accuracy regarding the CG lesions. However, Kuru et al. [12] stated that DCE doesn't add significant value to diagnosis of Pca while other studies showed high sensitivity and specificity for DCE in detection of Pca [13].

Due to this contradictory findings we recommend further modification of the DCE score by the ESUR as it is quite complex, because it combines a three point score for different curve types with additional points derived from morphological information regarding the symmetry and focality which is not clearly outlined by the current ESUR guidelines thus leading to significant differences between various studies.

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