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Aims and objectives

Since to the start, Diffusion Weighted images in mp-MRI showed its potential in Prostate Cancer (PCa) detection. Especially, many studies demonstrated correlation of post-processing Apparent Diffusion Coefficient (ADC) to tumour aggressiveness expressed as Gleason Score (GS) [1]. On the other hand, the use of contrast introduced and standardized by the Pi-RADS v1 has been recently reviewed in Pi-RADS version 2, changing the interpretation of contrastographic behaviour of suspected lesions [2]. Nowadays there isn't a quantitative parameter on Dynamic Contrast Enhanced (DCE-MRI) that strongly relates to GS similarly to ADC [3].

Moreover, due to the rising incidence of PCa, some study groups started theorizing the feasibility of a biparametric protocol omitting DCE, since it seems only to confirm what has already seen on DWI and T2WI [4]. The aim of this study is to compare ADC and Time To Peak (TTP) to aid in discriminating neoplastic lesion according to different GS and quantitatively evaluate the usefulness of DCE-MRI for aggressiveness assessment of prostate cancer.
Methods and materials

Patient selection *Fig. 1 on page 5*

84 patients suspected to have PCa on the basis of clinical or laboratory data were enrolled in this retrospective study. The median age of the patients was 69.4 (64.2-72.3) and the median serum PSA level was 11.2 ng/mL.

All recruited patients underwent a mp-MRI and a TRUS-biopsy was performed with a time gap not exceeding 2 months or within at last 6 weeks before mp-MRI. No one of the enrolled patients had a MRI/TRUS-fusion biopsy.

Patients under pharmacological treatment for Benign Prostate Hypertrophy (BPH) with 5-alpha reductase inhibitors (Finasterid or Dutasterid) and #1-blockers (Tamsulosin) and patients under treatment for cardiovascular disease were excluded since these drugs can affect prostate vascularization and cellularity, distorting TTP and ADC measurements, respectively. They were also excluded if the images were not satisfactory (multiple artifacts from, for example, total hip replacements, patient movements).

Acquisition Protocol *Fig. 2 on page 5*

Each patient underwent mp-MRI on a 3T MRI scanner (Signa EXCITE®HDxT, GE, Milwaukee, USA) according to *Prostate Imaging and Reported Data System Version 2 (Pi-RADS v2)* guidelines of 2015 with a pelvic coil (Phased Array, 8 channels). To suppress peristalsis of the bowels, intravenous injection of hyoscine butylbromide (Buscopan®, 20 mg, Boehringer, Taiwan) was administered immediately before the examination started.

All patients underwent para-axial T2-WI (Fast Recovery Fast Spin Echo-XL 90) parallel to the short axis of prostate and sagittal and paracoronal T2-WI parallel to the long axis. The diffusion study was then done by acquiring a single-shot echoplanar imaging sequence (DWI EPI) using two different b values (0, 1000) in a single acquisition. T1 Spoiled Gradient Echo was acquired before and after contrast administration.

Bolus injection of Gd-DTPA (Prohance® 279.3 mg/ml, flac. 15 ml i.v., Bracco, Italy) was performed by a power injector (Medrad®) with an injection rate of 4 ml/sec. followed by a 20 ml flush with saline.

Image analysis *Fig. 3 on page 6*

Image interpretation was carried out simultaneously by a specialized radiologist and a resident in radiology with respectively 14 years and 3 years of experience in prostate MRI. Regions of Interest (ROIs) were settled on suspected foci and on contralateral
healthy tissue. Post processing quantitative data were recorded on DWI and DCE-MRI sequences: ADC and TTP were matched to GS after sextant biopsy and/or radical prostatectomy.

**Histological Evaluation**

All sample obtained at biopsy were fixed in paraffin and stained with Ematoxylin-Eosin (EE). Each lesion was graded according to the Gleason Score System. Only 7 patients, after TRUS-biopsy, underwent to Radical Prostatectomy and surgical specimens obtained were processed: gross histological sections were fixed in paraffin, stained with EE and then evaluated according to modified Gleason Score System.

**Measurements and Statistical Analysis**

Data from mp-MRI were matched with the prostate biopsy or radical prostatectomy, which were considered as the standard of reference. Each pathological sample was matched to a corresponding MR image on the basis of the location. A *one-way ANOVA* was used to analyse whether mean ADC and TTP values depend on clinical and histological features of the cancer. A *p value* of 0.05 or less was considered to indicate statistically significant difference between the three protocols. Statistical Analysis was performed using MedCalc® software, version 13.0.6.
### Table 1: Clinical-pathological features in the study population.

<table>
<thead>
<tr>
<th>Patients</th>
<th>84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean) [years]</td>
<td>69.4</td>
</tr>
<tr>
<td>PSA tot. (mean) [ng/ml]</td>
<td>11.2</td>
</tr>
<tr>
<td>Number of suspected foci</td>
<td>100</td>
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</table>

<table>
<thead>
<tr>
<th>Gleason Score</th>
<th>PZ</th>
<th>TZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>3+3</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>4+3 or 3+4</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>4+4</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>5+4 or 4+5</td>
<td>8</td>
<td>1</td>
</tr>
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</table>

**Fig. 1:** Clinical-pathological features in the study population.

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<table>
<thead>
<tr>
<th>SEQUENCE</th>
<th>TR</th>
<th>TE</th>
<th>FOV</th>
<th>NEX</th>
<th>MATRIX</th>
<th>B value</th>
<th>Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRFSE-XL 90 Ax</td>
<td>5020</td>
<td>102</td>
<td>24x24</td>
<td>3</td>
<td>512x352</td>
<td>3 mm</td>
<td></td>
</tr>
<tr>
<td>DWI-EPI</td>
<td>5875</td>
<td>70</td>
<td>36x24</td>
<td>6</td>
<td>128x128</td>
<td>0-1000</td>
<td>3 mm</td>
</tr>
<tr>
<td>T1 GRE SPGR Perfusion</td>
<td>4.4</td>
<td>2.1</td>
<td>32x32</td>
<td>0.65</td>
<td>256x256</td>
<td>3 mm</td>
<td></td>
</tr>
<tr>
<td>FRFSE-XL 90 Sagital</td>
<td>4860</td>
<td>93</td>
<td>352x256</td>
<td>3</td>
<td>352x256</td>
<td>3 mm</td>
<td></td>
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<tr>
<td>FRFSE-XL 90 Coronal</td>
<td>8500</td>
<td>102</td>
<td>32x32</td>
<td>2</td>
<td>512x512</td>
<td>4 mm</td>
<td></td>
</tr>
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</table>

**Fig. 2:** Acquisition protocol
Fig. 3: Example of imaging interpretation and data registration. A. DWI B. ADC map C. DCE-MRI D. Curve enhancement
Results

GS # 6 was considered as a cut-off for positive findings. A total of 100 suspected foci were observed: 76 of 100 analysed foci have a GS # 6.

66 (86,8%) foci were identified in Peripheral Zone (PZ), while only 10 (13,2%) were in Transitional Zone (TZ). Statistical data and distribution of lesions according to GS are showed in Fig. 1 on page 8

Within the examined group of patients ADC and TTP were significantly lower for cancer tissue than healthy tissue in PZ (p<0,001) [Fig. 4 on page 8]. However, while a statistical correlation between ADC and GS was showed (p=0,013) [Fig. 4 on page 8], a significant correlation between TTP and GS was not demonstrated (p=0,826) [Fig. 4 on page 8]. Moreover, there was also no significant statistical correlation between ADC and TTP (p=0,669). Fig. 5 on page 9

In TZ data doesn't show any statistically significant results due to the small sample.
**Fig. 1**: Clinical-pathological features in the study population.

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Fig. 4: Statistical analysis comparing Apparent Diffusion Coefficient (ADC) and Time To Peak (TTP) related with Gleason Score (GS).

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Fig. 5: Statistical analysis comparing Apparent Diffusion Coefficient (ADC) and Time To Peak (TTP).

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Conclusion

Our findings indicate that both quantitative parameters (ADC and TTP) can predict malignant histology and MRI is a valuable technique to identify high-risk suspicious lesions. However, DWI-based quantitative measurement exhibits a stronger association with biopsy findings than TTP. This means that, if compared to TTP, ADC values, due to its direct correlation with GS, is able to better define tumour aggressiveness. Since this study was not intended to investigate the primary detection rate of MRI but its grading ability, matching of imaging with prostatectomy specimens seemed to be best qualified for this aim. With the intent to fix this limit, lesions were matched on a subjective basis in consensus of the pathologist and radiologist to minimize these inaccuracies. Another limitation of our study might be related to the distribution of GS in our subgroup of patients, with the majority of identified foci (63,2%) being of low and intermediate risk. To address this issue, we dichotomized the score variable, leading to a binary target variable (GS < 6 representing indolent cancer and GS # 6 representing intermediate and high risk cancer). However, the numbers of GS=8 and GS=9 were still smaller comparing to GS=6 and GS=7. Moreover, the major parts of identified foci were in PZ, and only a smaller part in TZ.

In conclusion, our study is a quantitative and statistical demonstration of the reason why a mp-MRI could be favourably performed omitting DCE in the single indication of tumour detection, reserving contrast-enhanced sequences for other indications (i.e. detection of local recurrence). Further studies are needed to confirm our results and evaluate the possibility of favourable application of a biparametric protocol.
Personal information

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References

2.
3.
4.