Diagnostic modelling of multi-parametric MRI as a radiological tool to predict transition zone prostate cancer

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Purpose: Multi-parametric MRI has a reported sensitivity of 73% and specificity of 89% for detection of tumour within the peripheral zone of the prostate [1]. However, benign prostatic hypertrophy as commonly found in the transition zone produces signal changes that make the radiologists detection of anterior gland tumour more difficult [2]. Our study derived a predictive model for classification of suspected sites of anterior gland disease based on clinical (age, postive specific antigen [PSA]), gland volume, PSA density), quantitative MRI parameters (apparent diffusion coefficient [ADC], contrast enhanced, T2 image signal) and textural features of MR images (entropy, contrast, co-occurrence); and compared the performance of this model for detection of tumour against a consensus radiologist opinion.

Methods: Our local hospital database was searched for men that had pre-biopsy multi-parametric MRI performed between 2007 and 2010, and a subsequent template mapping biopsy of the prostate within 6 months following the MRI. In total 73 men (42-78 years old, mean 61 yrs) with mean PSA of 8.39ng/ml (1.2-40) and mean prostate gland volume of 44.06ml (18.9-101) were identified. Anterior gland tumour was diagnosed on template mapping biopsy in 43.8% (32/73). All multi-parametric MRI datasets included axial T2 weighted (T2w) images, ADC and arterial phase contrast enhanced (aCE) images.

Two experienced radiologists (5 and 8 years of prostate MR experience, each reporting 400-600 prostate MRI reports per year) in consensus unaware of the histological diagnosis prospectively assessed each MRI study and graded the likelihood of clinically significant tumour (≥0.5cm³ or likely to contain a Gleason grade 4 component) within the anterior gland (1-definite normal, 2-tumour unlikely, 3-indeterminate, 4-tumour likely and 5-definite tumour). Where an area was identified as MR grade 3 to 5 the radiologists contoured the region on T2w, ADC and aCE image containing the largest diameter of the suspected area. Where no tumour focus was suspected the radiologists contoured a 1 cm diameter circular region within the transition zone at the mid-gland level. Subsequently, template mapping biopsy results were reviewed and the radiologists matched the biopsy location to the region of interest (ROI) thereby classifying the region as positive or negative for tumour. Mean signal intensity (SI) and the SI ratio to internal oblique muscle was calculated for each ROI on T2w, ADC and aCE images. Textural analysis for each ROI on T2w, ADC and aCE images was performed with histogram (i.e. mean and entropy) and grey level co-occurrence matrix (i.e. contrast, energy and co-occurrence) analysis.

Linear discriminant analysis and leave-one-out cross validation was used to derive and test a predictive model based on clinical, quantitative MRI parameters and textural features of MR images. The significance of individual parameters was assessed by Wilks’ Lambda (Λ) [0,1], Independent variables that significantly contribute to the discriminant function have smaller Λ than the variables that contribute less. Receiver operator characteristic (ROC) area under curve (AUC) was calculated for the LDA (and the mean AUC of 1000 sub-samples (Bootstrapping)) and consensus radiologist opinion (MR grade).

Results: Table I illustrates the distribution of patients by radiologist assigned MR grade and the percentage in each group with tumour at the ROI site. Where radiologists were uncertain of disease (MR grade 3) 47.8% (11/23) patients had significant tumour. The ROC AUC for radiologist MR grade for classification of tumour presence was 0.845 The LDA bootstrapped predictive model had a ROC AUC of 0.971. When separated into individual patient groups (as per the MR grade) the ROC AUC was 0.96, 0.987 and 0.93 for Group A, B and C respectively. The three most significant variables of the LDA model were ADC value, T2 SI ratio and gland volume (figure 1). Overall the LDA model was able to correctly classify 74% of regions correctly using leave-one-out cross validation of independent samples.

Table I: Distribution of patients by radiologist assigned MR grade

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of patients</th>
<th>Number of patients with significant tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (MR grades 1 and 2)</td>
<td>28</td>
<td>3</td>
</tr>
<tr>
<td>B (MR grade 3)</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>C (MR grades 4 and 5)</td>
<td>22</td>
<td>19</td>
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Figure 1: Wilks Λ for the independent variables of the diagnostic model. Contribution with Λ>0.95 were not included in the figure.

Figure 2: Receiver operator characteristic (ROC) curves for the LDA model based on MR grade (black curve) and the model based on clinical and MR derived parameters (grey curve).

Conclusion: Ascribing tumour within the transition zone is a difficulty for radiologists and almost one third of our patients within this study were classified as indeterminate (MR grade 3) despite the fact that both our study radiologists were very experienced. Furthermore 47.8% of patients within the MR grade 3 group had clinically significant cancer.

Our LDA model built on quantitative clinical, MR parameter and textural analysis features had a high predictive ability for assignment of tumour status (ROC AUC 0.971; figure 2). Indeed, the bootstrapped AUC for those patients identified as MR grade 3 by the radiologists was also high (0.987). When applied to independent samples the LDA model was able to correctly classify approximately ¾ of our patient population.

In summary, our results suggest that the LDA model derived in this study may aid radiologists classify indeterminate areas (MR grade 3) within the transition zone. Prospective application to a separate cohort of patients is planned.