Title:
Logistic regression models may predict Gleason grade of prostate cancer in the peripheral zone but not the transition zone

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Target audience: Radiologists, Urologists, Physicists, Engineers and Oncologists

Background:
Multiparametric MRI has emerged as a useful tool in the detection, staging and surveillance of prostate cancer, and multiple studies have demonstrated that quantitative MRI metrics correlate with Gleason grade (1–3).

We aim to develop logistic regression (LR) models using quantitative parameters derived from multiparametric (mp) prostate MRI to predict the presence of Gleason 4 disease. Separate models were built for the transition zone and peripheral zone and model performance was compared against the opinion of two experienced radiologists.

Methods:
176 men were identified from an existing clinical trial database between February 2012 and April 2014. Patients had lesions on mpMRI with subsequent MRI targeted biopsies, which acted as the reference standard. See table 2 for baseline patient characteristics.

MRI was performed using a 3T scanner (Achieva, Philips Healthcare, Netherlands) with a cardiac phased-array coil. A full description of MR parameters is provided in Table 1.

Two experienced radiologists (HS and SP) reporting >500 prostate MRIs/year recorded the location of index lesions and qualitatively assessed the presence of a Gleason 4/5 component.

MR datasets were analysed with MIM Symphony Version 6.1 (MIM Software Inc, USA). Rigid translational co-registration of T2W, ADC and DCE images were performed semi-automatically, with subsequent manual refinement. A board certified radiologist (EJ) manually contoured a volume of interest (VOI) for each index lesion. The mean signal intensity of each VOI on T2W, ADC and DCE images at all time points were measured. In order to standardize signal intensity between subjects, T2 and ADC metrics were normalized to the bladder and DCE metrics to the obturator internus muscle. Quantitative and semi-quantitative DCE parameters were also derived.

LR model development
Individual logistic regression models were derived separately for the peripheral zone (PZ) and transition zone (TZ), to predict a Gleason 4/5 component. A score

test was used to select the mp-MRI parameters most likely to contribute significantly ($p<0.05$) for inclusion in each model.

Internal validation of LR models was performed and receiver operator characteristic area-under-the-curve statistics (ROC AUC) were calculated for the models prior to and following leave-one-out analysis (LOOA), as previously described (4). Performance of single parameter LR models was compared with the multi-parametric LR model.

Results:

Peripheral zone

The optimal combination of parameters in the PZ proved to be T2nSI, ADCnSI and Maximum Enhancement (ME), with univariate AUCs of 0.670, 0.783 and 0.732 respectively. A combination of all three parameters gave an AUC of 0.828 (CI 0.756 to 0.899), which fell to 0.803 (95% CI 0.727 to 0.880) following LOOA.

Using a threshold of 0.5, the MRI derived model had a sensitivity of 0.83 and a specificity of 0.6935, whereas the radiologists had a mean sensitivity of 0.85 and a specificity of 0.60.

Transition zone

The optimal combination of parameters in the TZ proved to be T2nSI and ADCnSI, with univariate AUCs of 0.632 and 0.688 respectively. Combining these two parameters gave an AUC of 0.674 (CI 0.501 to 0.846), which fell to 0.579 (95% CI 0.394 to 0.763) following LOOA.

Using a threshold of 0.5, the MRI derived model had a sensitivity of 0.792 and a specificity of 0.500, whereas the Radiologists had a mean sensitivity of 0.875 and a specificity of 0.667.

Discussion:

In this study, we were able to successfully build a model to predict the presence of a Gleason 4 component in the PZ, using a combination of mean T2-nSI, ADC-nSI and ME-DCE, which are the robust quantitative MRI-derived parameters. The performance of the model was similar to two experienced radiologists.

The TZ model classifiers provided only a moderate ROC-AUC; with the radiologist's opinion giving a higher performance. This zonal discrepancy confirms that LR models for characterization should be zone specific, as is the case for tumour detection (4).

Another group developed mp-MRI based models for the characterization of Gleason 4 disease in a smaller cohort of 54 patients, although their cutoff of tumours >0.5cc makes their data less generalizable (5). The lack of a size cutoff was a strength of our study as smaller lesions can be characterized using our model.

This PZ model could be applied clinically using a sensible diagnostic threshold to trigger a biopsy and fully characterize the Gleason grade, or avoid biopsy in lesions with high probability of benignity. LR models could prove useful as a training tool for less experienced radiologists, or for radiologists looking for a second opinion regarding Gleason grading.

Conclusion:

Logistic regression models using conventional mp-MRI sequences could prove to be a useful tool in prostate cancer characterisation, but should be zone specific and perform better for peripheral zone tumours.

References:

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Multi-parametric MRI phasing details for prostate detection scan 3 T

Sequence	Coil	TR	TE	FA degrees	WFS (pix)	BW Hz/Px	FoV mm	Slice thickness mm	Gap	TSE factor	Phasing direction	FS	ACQ matrix			To du
T2 TSE coronal	Dual	6128	100	90	2.704	160.7	180	3	3	16	R > L	No	300 × 290			05
T2 TSE axial	Dual	5407	100	90	2.704	160.7	180	3	0	16	R > L	No	300 × 290			05
T2 sag REF	Dual	1579	100	90	1.999	217.3	240	5	5	20	A > P	No	120 × 89			00
T1W TSE	Sense XL Torso	487	8.0	90	1.997	217.6	240	3	3	4	R > L	No	184 × 184			03
VISTA sense	Dual	2000	200	90	1.108	392.0	200	3	3	66	R > L	No	248 × 187			04
DWI 0 150 500 1000	Dual	2753	80	90	40.353	10.8	220	5	0		A > P	SPAIR	168 × 169			05
DWI sFOV	Dual	2824	89	90	23.048	18.9	90	5	0		A > P	SPIR	68 × 61			05
DWI b2000	Dual	2000	78	90	44.108	9.9	220	5	0		A > P	SPIR	168 × 169			03
										TFE factor				TFE shots	TFE shot interval (ms)	
DCE 2 dyn mod sense	Dual	5.8	2.8	10	1.766	246.1	180	3	0	38	R > L	SPAIR	140 × 177	49	280	00
DCE 20 dyn mod sense	Dual	5.8	2.8	10	1.766	246.1	180	3	0		R > L	SPAIR	140 × 162	45	280	04

Description of mpMRI parameters.
DWI: Diffusion-weighted image. DCE: dynamic contrast enhanced.
0.2mg/kg (up to 20mg) of a spasmolytic agent (Buscopan; Boehringer Ingelheim, Germany) was also administered intravenously to reduce bowel peristalsis.

134 PZ tumours, 71 Gleason 4/5
42 TZ tumours, 24 Gleason 4/5
Median age 63.0 yrs (range 43.0 – 83.4)
Median PSA 7.21 (range 2 – 32)
Median prostate volume 37 cc (range 16 – 83)

Baseline patient characteristics