Derivation and comparison of site specific peripheral and transition zone quantitative DCE MRI logistic regression models for prostate cancer detection: does cancer location matter?

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Target audience: Clinicians, medical image computing, physicists involved in application of quantitative DCE parameters for disease classification

Purpose: Dynamic contrast enhancement (DCE) MRI has been advocated for detection of prostate cancer, but studies predominantly concentrate on peripheral zone tumours [1]. Biological differences are known to exist between tumours within transition and peripheral zones due to their different microenvironments [2, 3]. This study aims to compare and contrast quantitative DCE MRI parameters of prostate PZ and TZ cancer and non-cancer regions; to identify those best able to classify cancer tissue at each site and thereby improve DCE MRI based diagnostic models used within computer aided detection software.

Methods: Retrospective data-analysis was performed on a cohort of patients that were imaged with prostate multi-parametric (mp) MRI (T2, diffusion, DCE). DCE-MRI was performed with a temporal resolution of 16 seconds, TR/TE 5.61/2.5 ms, flip angle 15°, field of view 269 mm, slice thickness 3 mm, number of time points 35. All patients underwent subsequent transperineal template mapping biopsy (TTMB) of the gland at 5 mm intervals at apical and basal levels with biopsy cores segregated into 20 sectors by Barzell zone. A total of 146 patients were included. Two experienced radiologists, in consensus, performed region of interest (ROI) placement on early arterial contrast enhanced images using the remainder of the multi-parametric MRI dataset in combination with cognitive matching with TTMB data to guide ROI placement at the location of significant cancer. Where there was no significant (Gleason ≥3+4, or ≥4mm cancer core length (CCL) [4]) cancer on TTMB the radiologists contoured an ROI in a location corresponding to a non-cancer biopsy result on TTMB. Where there was more than one significant cancer location the radiologists contoured the site with the longest CCL. In total 76 PZ ROIs (56 normal, 20 significant cancer), and 70 TZ ROIs (42 normal/BPH, 28 significant cancer) were drawn. For each patient an additional ROI was placed within the right obturator internus muscle for comparison of normalised signal intensity (SI) across patients (*DCE nSI*) on early arterial contrast enhanced images. Initial slope of enhancement (*SoE*); maximum enhancement (*ME*); curve type (E_{type}); and total area under the time-intensity curve (TIC) (*Area*) were derived based as previously described [5]. Pharmacokinetic analysis was performed using the Toft model [6] fitted with the modified Bayesian algorithm suggested in [7] and blood plasma volume, v_p; transfer constant between plasma and interstitial space, K_{trans} (min^{-1}); rate constant between interstitial space and plasma, k_{ep} (min^{-1}) were derived. The Mann-Whitney U test was used to compare median values (significance level 0.05) of individual DCE MRI derived parameters between PZ and TZ cancer and PZ and TZ non-cancer ROIs. A logistic regression (LR) analysis followed by receiver operator characteristic (ROC) area under curve (AUC) estimation was performed for each DCE MRI parameter for TZ and PZ cancer classification.

Results: Table 1 illustrates the median values (MV), the interquartile range (IQR) and Mann-Whitney U significance test (MWU) of DCE parameters for comparison of PZ and TZ cancer ROIs and PZ and TZ non-cancer ROIs. K_{trans}, k_{ep}, and *SoE*, *DCE nSI* and *ME* were significantly greater in TZ than PZ non-cancer ROIs. There was no significant difference in the remainder of the DCE MRI derived parameters between TZ and PZ for non-cancer ROIs; and no difference in *any* DCE MRI derived parameter between TZ and PZ cancer ROIs (table 1).
The majority of DCE MRI derived parameters showed significant ($p<0.05$) discriminatory ability to differentiate cancer from non-cancer ROIs within the PZ; but only *ME* had discriminatory power within the TZ. Table 2 illustrates a univariate ROC analysis of the parameters with significant discriminatory ability.

Table 1: Median values (MV), interquartile range (IQR), and Mann-Whitney U test (MWU) of the DCE parameters that were significantly different between cancer PZ and TZ and non-cancer PZ and TZ ROIs.

	non-cancer					cancer				
	PZ		TZ			PZ		TZ		
DCE parameters	MV	IQR	MV	IQR	MWU	MV	IQR	MV	IQR	MWU
K_{trans}	0.21	0.16	0.35	0.19	<0.01	0.29	0.17	0.29	0.13	0.72
k_{ep}	0.35	0.30	0.46	0.29	0.02	0.50	0.33	0.38	0.20	0.22
DCE nSI	1.18	0.29	1.72	0.51	<0.01	1.62	0.35	1.45	0.38	0.46
SoE	30.62	21.5	58.04	23.76	<0.01	49.79	21.02	54.10	21.30	0.68
ME	1.24	0.31	1.77	0.42	<0.01	1.54	0.55	1.36	0.50	0.52
E_{type}	2	1	3	1	<0.01	3	1	3	1	0.70
Area	910.22	413.4	1477.68	498.52	<0.01	1178.84	432.96	1350.07	320.15	0.18

Table 2: Univariate ROC analysis of the parameters with significant discriminatory ability between cancer and non cancer ROIs.

DCE parameters	AUC	Std	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
Transition zone				
ME	0.72	0.07	0.60	0.85
Peripheral zone				
K_{trans}	0.71	0.07	0.58	0.84
k_{ep}	0.69	0.07	0.55	0.83
DCE nSI	0.79	0.06	0.68	0.90
SoE	0.70	0.7	0.57	0.83
E_{type}	0.65	0.07	0.52	0.79
Area	0.67	0.07	0.54	0.79

Discussion: There was no significant difference in DCE MRI parameters between PZ and TZ tumour ROIs; suggesting that the potential biological differences between tumours [8,9] may not affect DCE radiological phenotype. There was a significant difference in the majority of DCE parameters between PZ and TZ non-cancer ROIs likely reflecting the presence of benign prostatic hypertrophy (BPH) with adenoma formation within non-cancer transition zone and the consequent increased permeability and capillary density. The presence of BPH within the transition zone is also likely to account for the different DCE MRI parameter discriminatory ability between cancer and non-cancer; more specifically the majority of DCE MRI parameters were able to classify cancer PZ ROIs; but only *ME* was useful for classification of cancer TZ ROIs and its discriminatory utility was based on a relatively ***reduced*** enhancement within TZ cancer ROIs compared with TZ non-cancer ROIs.

Conclusion: The ability of DCE-MRI parameters to localise tumour is reduced in TZ, likely due to presence of adenoma. Whereas the increased permeability/microvascular density of cancer relative to surrounding non-cancer areas facilitates the localization of disease within the peripheral zone; it is the decreased enhancement (*ME*) of cancer relative to the surrounding non-cancer areas that aids tumour localisation within the TZ. Our results have clinical utility for the improvement of computer aided diagnostic tools by providing zone specific data for improving classification of tissue type.

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