MRI SURROGATES OF BLOOD FLOW ESTIMATES IN THE MALIGNANT PROSTATE GLAND

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Objective: Intrinsic susceptibility-weighted MRI (ISW-MRI) when coupled with dynamic susceptibility-contrast enhanced MRI (DSC-MRI) for relative blood flow estimation has been shown to detect radiobiologically relevant prostate cancer hypoxia with adequate sensitivity and specificity [1,2]. Unfortunately DSC-MRI has relatively poor signal-to-noise ratio, uses large doses of intravenous gadolinium contrast medium and is unable to image the entire prostate gland at adequate time and spatial resolution using gradient echo sequences, making it impractical for incorporation into radiation therapy planning procedures. The purpose of this study was to assess alternative, more clinically useful, MRI derived kinetic parameters as surrogates for prostate blood flow that could then be incorporated into a combined protocol with ISW-MRI for hypoxia detection.

Methods: 20 patients with prostate cancer (age 57-78, Gleason 6-9, PSA 3.7-34.0ng/ml) that were due to be treated with radical radiotherapy underwent two MRI investigations on consecutive days prior to the commencement of their neo-adjuvant androgen deprivation. Patients were imaged in a 1.5T MRI scanner using phased array pelvic coils. T_2-weighted images perpendicular to the urethra were used to identify tumour slice locations. T_1W spoiled GRE sequences (TE 5ms, TR 74ms, flip angle=70°, 3 slices) were acquired before and after the bolus administration of 0.1 mmol/kg b.w. of Gd-DTPA with 40 time points over 8 min, through the prostate. ROI were placed around the whole gland and tumour to calculate pixel-by-pixel values of K^{trans}, v_e, k_{ep} and the initial area under the gadolinium curve over the first 60 seconds ($IAUGC_{60}$) using the methods of Tofts [3] using MRIW software [4]. To acquire relative blood flow (rBF) data a T_2*-weighted sequence was used. For this the prostate was imaged every 2 seconds over 2 minutes (TE 20ms, TR 30ms, flip angle = 40°, one slice of eight millimetre thickness). A bolus of 0.2 mmol/kg b.w. of Gd-DTPA was administered at 4ml/s after 20 seconds. A gamma variate fitting function to the changing SI data was used obtain rBF measurements. Mean values for the two MRI investigations for each parameter in each patent were calculated. Spearman's ρ (rho) was calculated to determine the correlation between the various kinetic parameters.

Results: Correlation between the kinetic parameters is outlined in the table and illustrated for one patient in the figure. Significant correlations between rBF and the T_1-weighted parameters K^{trans}, k_{ep} and $IAUGC_{60}$ were demonstrated. The strongest correlation in tumour was noted for $IAUGC_{60}$ ($\rho = 0.62$, p=0.006) and for the whole prostate was for k_{ep} ($\rho = 0.70$, p=0.001). v_e did not correlate with rBF with statistical significance.

Conclusion: Parameters derived from T_1-weighted DCE-MRI correlate significantly with rBF in the malignant human prostate. It is therefore likely that these could be substituted for rBF and be combined with ISW-MRI for the purpose of hypoxia detection in a clinically feasible, multislice, whole gland imaging protocol. Further research is currently underway to determine the diagnostic accuracy for combinations of ISW-MRI with K^{trans}, k_{ep} and $IAUGC_{60}$ for prostate tumour hypoxia identification.

Table: The correlation between rBF and K^{trans}, k_{ep}, v_e and $IAUGC_{60}$

		K^{trans}	k_{ep}	v_e	$IAUGC_{60}$
Whole Prostate	ρ	0.66	0.70	0.31	0.67
	p-value	0.002	0.001	0.179	0.002
Tumour	ρ	0.59	0.59	0.35	0.62
	p-value	0.009	0.008	0.145	0.006

Figure: Illustration of the correlation between rBF and K^{trans}, k_{ep}, v_e and $IAUGC_{60}$
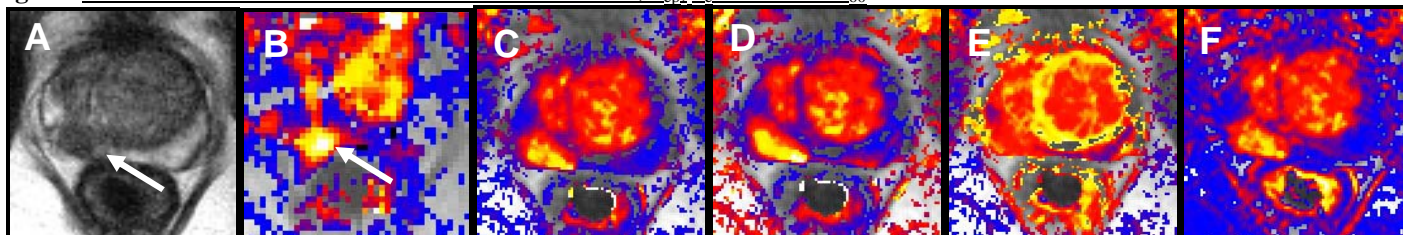
A 67 year old patient with T3b, Gleason 5+4 Carcinoma of the prostate which can be seen on the T_2-weighted MRI image as a region of low signal intensity within the otherwise bright peripheral gland (arrow, panel A). The T_2* derived rBF map demonstrates high blood flow in the tumour (arrow, panel B). The maps of K^{trans}, k_{ep} and $IAUGC_{60}$ (panels C, D and F respectively) clearly demonstrate high kinetic parameter values in the tumour, correlating with the rBF map. This is not the case for v_e (panel E).

References [1] Hoskin PJ, Carnell DM, *et al*. Int J Radiat Oncol Biol Phys, 2007 [2] Alonzi R, Padhani AR, *et al*. proc. ISMRM 2008 (abstract) [3] Tofts PS and Kermode AG. Magn. Reson. Med. 1991 [4] d'Arcy JA, et al. Radiographics. 2006;26(2):621