Functional MR Parameters of Histopathologically Indentified Prostate Tissues

S. F. Riches[1], V. A. Morgan[1], G. S. Payne[1], C. Fisher[2], S. Sandhu[2], D. J. Collins[1], and N. M. deSouza[1]

[1]CRUK Clinical Magnetic Resonance Group, Royal Marsden NHS Trust & Institute of Cancer Research, Sutton, Surrey, United Kingdom, [2]Department of Pathology, Royal Marsden NHS Trust, London, London, United Kingdom

Introduction: MRI is increasingly being used in the pre-treatment evaluation of prostate cancer. High resolution T2-weighted imaging (T2W) alone has a low sensitivity and specificity (around 70%) for tumour detection, which is reduced further when tumours of less than 1cm in diameter are considered. Contrast mechanisms other than T2W imaging are therefore being sought to improve tumour detection. Previous studies have determined tumour values for apparent diffusion coefficients (ADC) [1, 2] from diffusion weighted imaging (DWI), area under the contrast uptake curve (AUC_{Gd}), volume transfer constant (K_{trans}) and reflux rate constant (K_{ep}) from dynamic contrast enhanced imaging (DCE-MRI) [1,3,4] and the ratio of choline to citrate (Cho/Cit) metabolites from ^{1}H spectroscopy [2-4], but no single study has determined all parameters for histologically-defined TU and non-TU regions in one population. The purpose of this study was to establish the values for histopathology-defined regions of tumour, normal peripheral zone and normal central gland tissue from T2W imaging, DWI, DCE-MRI and ^{1}H spectroscopy.

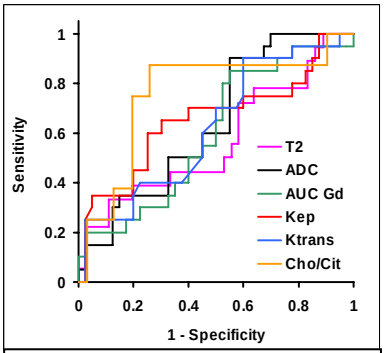
Method: Twenty patients referred for routine clinical evaluation prior to prostatectomy at our MR centre were studied on a Philips Intera 1.5T scanner with an endorectal balloon coil inflated with 55mls of air. Patient characteristics were: mean age 60 yrs, (range:47-76yrs), stage T1 (n=13) or T2 (n=7), Gleason Grade 3+3 (n=11), 4+3(n=3), 3+4(n=6), PSA=7±3 ng/mL (mean ± sd). Following standard 3-plane imaging (FSE, TR/TE=2000/90, 20 slices, 3mm thickness, 512x512 matrix, 140mm FOV), 12 axial slice DWI (TR/TE 2500/69, 4mm thickness, 200mm FOV, 128x128 matrix, 4 b-values 0,300,500,800 s/mm2 in three directions) were acquired and isotropic ADC maps generated with all b-values using scanner software. An axial ^{1}H 2D-CSI (TR/TE 1200/120, 15mm thickness, 200mm FOV, 16x16 matrix) was acquired, grid-shifted to align the voxels with regions of tumour, and processed using LCModel [5] to obtain ratios for Cho/Cit for each voxel. An axial DCE-MRI series (TR/TE 4.1/1.77ms, 5mm slices, 8 slices, 128x128 matrix, 300mm FOV, 90 timepoints) was obtained with 0.4ml/kg of Magnevist and parametric maps for AUC_{Gd}, K_{trans} and K_{ep} generated in MRIW [6].

The fresh whole mount prostate was cut and digitally photographed [7]. Areas of tumour outlined on histology sections by an experienced histopathologist were also digitally photographed. Regions of interest (ROIs) were drawn around the whole prostate and the central gland on all slices of the T2W axial scans, and around the whole prostate on the ADC maps by an experienced radiologist. Tumour regions were transferred from the histopathology slides to the corresponding T2W axial scans using a 2 step non-rigid registration of landmarks based on the prostate outline and internal structures on the fresh slice photographs, histopathology photographs and axial T2W images [8], to obtain regions of histologically derived tumour (TU), central gland (CG) and peripheral zone (PZ, whole prostate minus TU and CG). For DCE-MRI parameters (AUC_{Gd}, K_{trans} and K_{ep}), ROIs were directly transferred to the corresponding DCE-MRI slices; for ADC values, ROIs were shifted by matching the centre of mass of the whole prostate outlines on the T2W images and ADC maps to correct for a rigid-body EPI shift; for Cho/Cit ratios, voxels whose volume was more than 70% within the prostate outline were classified as either TU (>30% TU), PZ (0% TU, <30%CG), CG (0% TU and >70%CG) or mixed (all other voxels). Differences between TU and combined non-TU (CG or PZ), TU and PZ, and TU and CG were tested using non-parametric tests for related samples at a 5% significance level. The analysis was performed including all TU ROIs and repeated excluding TU ROIs with an area <1cm^2.

Parameter	Signal Intensity on T2	ADC	AUC_{Gd}	K_{trans}	K_{ep}	Cho/Cit*
TU	159±85	1343±193	30±12	0.17±0.06	0.54±0.17	0.25±0.20
Non-TU	152±68	1419±154	26±10	0.15±0.06	0.42±0.12	0.13±0.06
TU vs Non-TU (PZ + CG)	0.455	**p<0.001**	**p=0.007**	**p=0.008**	**p=0.005**	**p=0.002**
PZ	164±77	1458±135	24±8	0.13±0.05	0.42±0.12	0.12±0.03
CG	141±58	1381±165	29±11	0.16±0.06	0.47±0.17	0.14±0.03
TU vs PZ	0.455	**p<0.001**	**p=0.006**	**p=0.003**	**p=0.004**	**p=0.002**
TU vs CG (all ROIs)	0.191	p=0.433	p=0.441	p=0.288	p=0.065	p=0.251
TU vs CG (>1cm2)	**p=0.044**	**p=0.017**	**p=0.002**	**p=0.018**	**p=0.032**	p=0.251

*Parameters (mean ± sd) for TU and non-TU (CG, PZ and CG+PZ) regions. Significant differences in the population are shown in bold typeface. *n=14 tumour voxels originating from 8 patients.*

Results: Mean values (± standard deviation) for the parameters calculated are shown in the table. No difference was found in the T2 signal intensity values of TU and non TU, or between PZ and CG. ADC was significantly lower in TU than non-TU (p<0.001) and Cho/Cit metabolite ratio was lower in voxels containing >30% TU than those with no TU (p=0.002). AUC_{Gd}, K_{trans} and K_{ep} were all significantly higher (p=0.007, 0.008 and 0.005 respectively) in TU. When non-TU PZ and CG are considered separately, TU is significantly different from the PZ for all parameters except the T2 signal intensity, whilst the CG is not significantly different with any parameter. When only TU with an area larger than 1cm^2 are included in the analysis, the TU is different from the CG for the ADC, AUC_{Gd}, K_{trans} and K_{ep}. ROC analysis showed AUC for these parameters were; T2 signal intensity: 0.571, ADC: 0.644, AUC_{Gd}: 0.60, K_{trans}: 0.623, K_{ep}: 0.657, Cho/Cit: 0.758.



ROC curves showing the ability of each parameter to identify TU from non-TU.

Discussion & Conclusion: Functional changes in TU tissue are more useful than T2W changes for determining the true extent of TU in the prostate. The inability of functional parameters to distinguish between TU and CG is due to increased variation of all parameters in the CG compared with the PZ. Improvement of the resolution of the functional techniques should improve the discrimination of TU and CG.

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