Optimal combined functional MR parameters to correctly identify tumour in the prostate.

Sophie F Riches[1], Geoffrey S Payne[1], Charlie Jameson[2], Christopher Ogden[3], Mike Partridge[4], Veronica Morgan[1], Sharon Giles[1], and Nandita M deSouza[1]

[1]CR-UK and EPSRC Cancer Imaging Centre, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sutton, Surrey, United Kingdom, [2]Department of Histopathology, University College London Hospitals, London, London, United Kingdom, [3]Department of Surgery, Royal Marsden NHS Foundation Trust, Sutton, Surrey, United Kingdom, [4]Gray Institute for Radiation Oncology and Biology,Department of Oncology, University of Oxford, Oxford, Oxfordshire, United Kingdom

Target Audience Clinicians and physicists investigating prostate cancer and MRI for radiotherapy planning

Purpose Improvements in radiotherapy techniques allow contouring of doses to a target of interest and delivery of a radiation boost to the dominant intraprostatic nodule (DIL) in the prostate potentially would improve treatment efficacy. The purpose of this study was to investigate the ability of different functional MR parameters to correctly classify tissue types in the prostate defined on whole-mount histology and determine the optimal combination of multiple parameters required to identify tumour.

Methods In 24 patients, diffusion-weighted imaging (DWI), dynamic contrast-enhanced imaging (DCE-MRI), T_2-maps and 3D proton MR spectroscopic imaging (MRSI) were acquired. Tissue types (normal peripheral zone (PZ), normal central gland (CG) and tumour (TU)) defined on histological specimens after prostatectomy were mapped onto the matched parametric maps. All functional parametric maps were resampled to the MRSI resolution (6x6x6mm) and the apparent diffusion coefficient (ADC), T_2, choline+creatine/citrate (Cho+Cr/Cit) ratio, and the vascular parameters K^{trans}, K_{ep}, V_e, and initial area under the gadolinium curve (IAUGC) were determined for each tissue class. Differences in the populations in tissue classes were tested using ANOVA and Bonferroni corrected post-hoc tests. Receiver operator curves (ROCs) were generated for each parameter to determine the ability of each parameter to discriminate between non-malignant and malignant tissue. Multiple functional MR parameters were combined using linear discriminant analysis and ROCs generated for the optimal discriminant functions. The ability of the model to predict tissue type at a voxel resolution was investigated by applying the discriminant function cut-off at the 90% specificity point in the same cohort of patients. The sensitivity and specificity of the model at predicting the tissue class of each voxel compared with histopathological findings was calculated for each patient and the mean value found.

Results ADC, Cho+Cr/Cit, K^{trans}, K_{ep}, and IAUGC for the TU tissue class was significantly different to those for PZ and CG (all $p<0.001$). V_e and T_2 for TU were significantly different to PZ ($p<0.001$), but not CG ($p=1$). Fig 1 shows the ROCs for discriminating TU from PZ (left) and CG (right). The optimal combined model for TU vs. PZ did not include T_2 or V_e and for TU vs. CG it did not include V_e, Cho+Cr/Cit or IAUGC. The area under the ROC curve of the combined model was significantly greater ($p<0.001$) than any individual parameter for discriminating TU from both PZ and CG. The combined model was stable when different subgroups of both random voxels and random patients were used to generate the discriminant function. When cut-off values extracted from the combined model ROC at 90% specificity were applied to individual patients, the sensitivity for prediction of tissue type at the MRSI resolution ranged from 79% (larger tumours) to 0% (small tumours), but with high specificity (98 ± 9 [93 – 100] %).

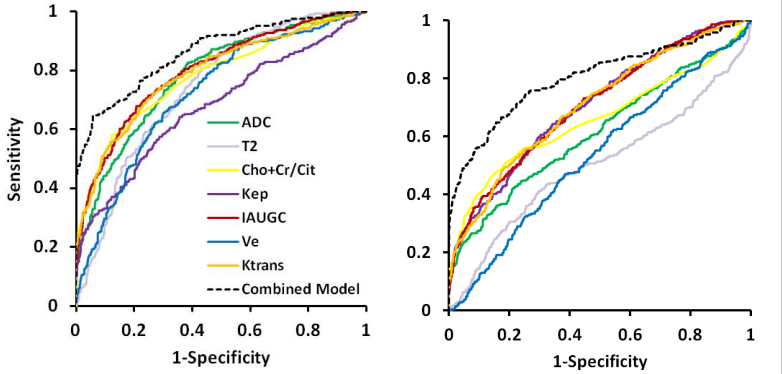

Fig 1. ROCs for individual functional parameters and the optimal combined model for discriminating between TU and PZ (left) and TU and CG (right).

Discussion The greater diagnostic power of the combined model compared with the individual parameters suggests information contained in multiple parameters is complementary. Validation of the combined model by comparison of the predicted tissue class of each voxel with the true tissue class gave a substantially lower average sensitivity and specificity for individual patients than expected from the population ROC; previous studies have used ROCs as the endpoint and have assumed that they indicate the accuracy of predicting tumour in prospective patients. This study demonstrates that the relationship between the ROC and the accuracy of locating tumour in a patient is not simple; the accuracy of the ROC is the highest achievable accuracy and if there is large inter-patient variability in the data some patients may have very low sensitivities for identifying the DIL. The low number of tumour voxels compared with normal voxels also makes selection of the optimal discriminant function cut-off difficult as sensitivity and specificity measures are problematic with low numbers of true positives.

Conclusion This study shows that a combined model gives greater accuracy in discriminating between tumour and normal prostate tissue types due to complementary information in the functional techniques and that the optimal model includes parameters from DWI, DCE-MRI, T2, and MRSI. Accuracy of prediction of tumour within a patient is lower than that expected by the ROC curves due to high inter-patient variability within the population.