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Delineating malignant and normal tissue in prostate cancer using DCE-MRI modeling to quantify Perfusion, Capillary Permeability and Dispersion

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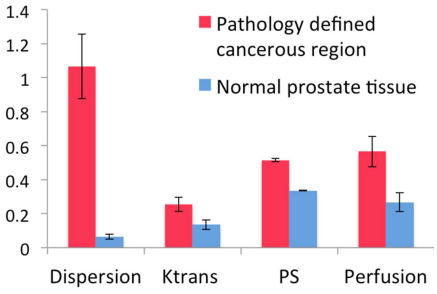
Target Audience: This work is targeted at physicists and clinicians interested in detection and localization of cancer using DCE-MRI.
Purpose: Distinguishing between prostatic carcinoma and non-cancerous prostate disease presents a significant challenge. MRI offers a non-invasive imaging method that fully visualizes the prostate *in-vivo*, and dynamic contrast-enhanced MRI (DCE-MRI) has great potential to improve specificity in the diagnosis of prostate cancer. Tumor growth is dependent on the recruitment of vascular supply and changes in the vasculature due to cancer are often measurable with DCE-MRI. In this work, we assess and evaluate pharmacokinetic modeling of DCE-MRI using 6 prostate patient cases available with the whole-mount histopathology. We use the histological analysis to evaluate the ability of DCE-MRI parameters to delineate between cancerous and normal prostate tissues.
Methods: DCE-MRI data was acquired in 6 patients who later underwent radical prostatectomy on Siemens 3T systems. The DCE-MRI protocol consisted of a 3D spoiled gradient echo acquisition with temporal resolution of 4.2s, TE of 1.5ms and TR of 3.9ms. T_1 maps were measured using variable flip angle (VFA) imaging (flip angles 2°, 5°, 10°, and 15°) for the conversion of signal intensity to contrast agent concentration. A population averaged arterial input function (AIF) was utilized [1]. We implemented three pharmacokinetic models that were fitted to the time course data: The extended Tofts model (ETM) [2] to measure Ktrans, ve, vp and delay time of bolus arrival, *Tdel*. The adiabatic approximation to the tissue homogeneity (AATH) model [3] to measure perfusion (F), Extraction fraction (E), PS, ve, Tdel and mean capillary transit time *tau*. Finally an intravascular dispersion model was implemented [4] to measure dispersion sensitive parameter Kappa. Histopatalogical analysis was meticulously carried out such that accurate correlation could be achieved between cancerous regions of prostate identified from pathology and the imaging slices. ROI's containing cancerous tissue derived from the histology were drawn onto the corresponding imaging slices (figure2). Reference ROI's in normal non-cancerous tissue were used for comparison in order to assess how well the modeled parameters delineate between cancerous and normal tissue. For each measured parameter the mean and standard deviation over the cohort of 6 patients are plotted in cancerous and normal tissue.

Results: The parameters that showed the most difference between normal and cancerous tissue are plotted in figure 1. Dispersion (Kappa) gives the clearest delineation and highest specificity between cancerous and normal tissue. Measured dispersion is approximately 17 times larger in cancerous tissues than non-cancerous tissue (17000% increase) (figure 1). Ktrans shows a 88% increase in cancerous tissues, PS a 53% increase and Perfusion a 110% increase. Figure 2 shows maps generated from the model fitting compared with Histo-pathology and T2-Weighted imaging. The increased specificity in delineation between normal and cancerous tissue from the dispersion map is clearly visible.



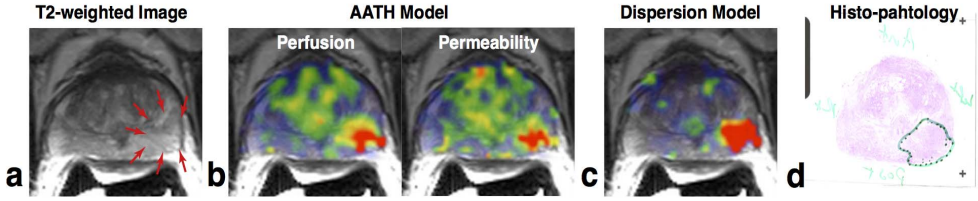


Fig 1 (Left): Mean and SD of dispersion, Ktrans, PS and Perfusion in normal and cancerous tissue are plotted. Dispersion clearly shows the greatest difference between tissues
Fig 2 (Above): Example of typical dataset showing a) T2 weighted image with region taken from pathology outlined. The image is overlaid with (b) Perfusion and Permeability map generated using AATH model (c) Dispersion map and (d) Histo-pathology with cancerous ROI shown.

Discussion: Figure 1 shows that Ktrans, F, PS and Dispersion all delineate between cancerous and normal prostate tissue over the group. The dispersion model shows the greatest specificity for delineation of cancerous tissue by an order of magnitude suggesting the method may be particularly powerful for prostate cancer detection. The method benefits from not requiring an AIF increasing its attractiveness. Mean perfusion in normal prostate tissue measured over the patient group using the AATH Model was 26.7±5.7 ml/100ml/min, within the range of reported literature values [5]. The AATH model shows an increase in F and PS in cancerous tissue. This is valuable additional information that the extended Toft's model cannot distinguish and may be especially useful in the assessments of anti-angiogenic therapies. Also, directly measuring physiological parameters such as F and PS from MRI data is a positive step that will make MRI measurements more intuitive for clinicians and perhaps promote wider use of the techniques.
Conclusion: Dispersion shows a dramatic increase in specificity for prostate cancer detection compared to F, PS or Ktrans. This method warrants further investigation in the prostate and in other cancer tissues. Quantification of physiological parameters F and PS using the AATH model allows Ktrans to be decoded and a greater understanding of true tissue physiology to be had. Combining such measurements will allow greater understanding of vasculature changes in cancer and more powerful detection and surveillance methods.
References: [1] Parker et al MRM (2006) 56(5):993-1000. [2] Tofts et al JMRI (1999) 10:223-232. [3] St Lawrence et al JCBFM (1998) 18: 1365-1377. [4] Mischi et al Proc Intl Soc MRM (2013) 0095. [5] Li et al NMR Biomed (2013); 26 51-57