Assessment of abnormal ADC matched voxels with DCE parameters for characterization of prostate cancer at 3T

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Introduction: Apparent Diffusion Coefficient (ADC) values, derived from Diffusion Weighted Imaging (DWI), have been shown on multiple occasions to correlate with Gleason score and prostate tumor aggression (1-2). Pharmacokinetic (PK) analysis of Dynamic Contrast Enhanced (DCE) MRI data has also been shown to correlate with specific histological components associated with malignancy (3). However, DWI often suffers from spatial distortion (particularly at high b values) and so without inter-sequence registration to DCE, it is difficult to determine if tumor-suspicious PK parameters are in the same tissue location as tumor-suspicious ADC values, and if PK analysis offers any additive value to ADC maps in prostate cancer detection. Through registration of ADC maps to raw DCE images, we sought to determine if the PK parameters K^{trans} (forward value transfer constant), and v_e (volume fraction of extracellular extravascular space) differed within regions of tumor and normal tissue as defined by ADC within the prostate peripheral zone (PZ), as confirmed by pathology at radical prostatectomy. We also attempted to determine if there is an association between the PK parameters and ADC maps in regions suspicious for prostate cancer and if they have a role in cancer detection when used in conjunction with ADC maps.

Materials and Methods:

Table 1: Characteristics of Study Cohort

Characteristic	Value
Age (years)	
Mean ± SD	57±7
Range	42-66
PSA (ng/ml)	
Mean ± SD	9.6 ±11.1
Range	1.9-38.6
Time from PSA to MRI (days)	
Mean ± SD	71±92
Range	7-312
Time from MRI to Surgery(days)	
Mean ± SD	79±95
Range	4-381
Gleason score	
≤6	n=2
7	n=9
≥8	n=2

18 patients were enrolled in a prospective study approved by the institutional review board. They underwent endorectal prostate MR using a 3.0T Signal HDx scanner (GE Healthcare). Of those, 2 patients were excluded due to non-adherence to the DCE protocol, 2 due to failure of registration of ADC maps to DCE, and one due to significant artifacts rendering MR non-diagnostic. Characteristics of the remaining 13 patients are outlined in Table 1. Subsequent to radical prostatectomy, a detailed tumor location report was available to us at the time of analysis.

DCE was performed with 3D-Fast spoiled gradient (FSPGR) images using FOV: 26 cm; slice thickness: 6mm; spacing: 6mm; Matrix: 256x160; contrast (Gadolinium gadopentetate (Gd)) injection rate of 3ml/sec; slab thickness 16-20 slices, 5 sec/volume, repeat 60 times, with a total scan time of 5 minutes. Single shot echo planar DWI was performed using b values of 0 and 500, and 0 and 1400 with trace ADC maps generated at all b values.

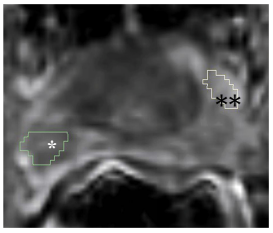

Figure 1. (b0-500)ADC map outlining tumor area in the right PZ (*) and normal tissue (**) in the left PZ.

Regions of Interest (ROIs) suspicious for tumor (n=16) and normal tissue (n=6) were contoured (Figure 1) on (b0-500) ADC images using 3D Slicer (www.slicer.org), after review of all ADC maps, T2 WIs, raw DCE images, and of the tumor location on pathology. (The reader was blinded to the PK maps during ROI determination). A deformable registration technique was used to recover image distortions on DWI by registering baseline DWI to T2w image, which in turn was registered to T1w pre- or post-contrast image that was aligned with DCE series. Subsequently, PK analyses of all voxels within the contoured ROIs were performed using a custom research tool (OncoQuant, GE Global Research) using a population averaged bi-exponential arterial input function augmented with a first pass peak (4). For each outlined ROI, the mean initial T_1 of the prostate was assumed to be 1597 msec (ref) and the mean signal intensity change from the DCE images was used to calculate the estimated Gd concentration as a function of time. PK analysis was done on a total of 1162 tumor voxels (mean 75 voxels/ROI) and 337 benign voxels (mean 67/ROI).

Table 2: Average values per voxel (mean±SD)

	ADC (10^{-3}mm^2/sec)	K^{trans}(min^{-1})	v_e
PZ Tumor	1.232±.318	0.28±0.2	0.21±0.1
PZ Normal	2.055±.274	0.19±0.1	0.19±0.2
Wilcoxon Signed Rank	p<0.001	p<0.001	p<0.001

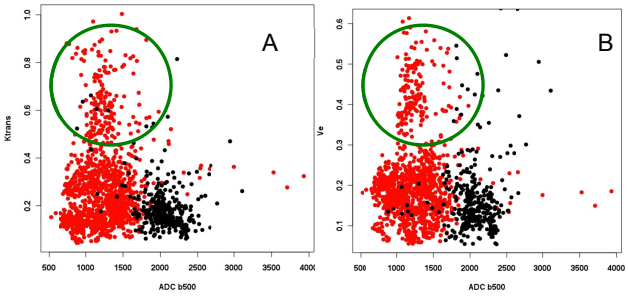

Figure 2: Scatterplots demonstrating weak correlations between ADC and (A) K^{trans}(ρ=-0.07), and (B) v_e(ρ=-0.14) in areas of tumor (red) and normal (black) tissue, as outlined according to ADC maps. Green circles highlight a subset of measurements where PK parameters are sufficient to differentiate between normal and cancerous tissue.

Results:

The mean±SD for tumor and normal tissue are summarized in Table 2. Non-parametric Wilcoxon signed rank test showed a significant difference between tumor and normal tissue for all 3 parameters. Correlations between the ADC, K^{trans} and v_e were investigated using Spearman rank correlation coefficient, and a moderate correlation between K^{trans} and v_e (ρ=0.45) was found, in addition to a weak negative correlation between ADC and K^{trans} (ρ=-0.07), and ADC and v_e (ρ=-0.14) (Figure 2). Logistic regression was used to investigate the value of K^{trans} and v_e parameters in differentiating between ADC-defined tumor and normal tissue. We found that the regression coefficients for both K^{trans} and v_e were significantly different from 0 (p<0.008 for v_e, and p<0.0001 for K^{trans}). A logistic regression model that combined ADC, K^{trans} and v_e parameters also produced non-zero coefficients for all three parameters (p<0.05). However, analysis of variation with χ^2 test showed that v_e parameter does not contribute significantly to the model (p>0.05) and can be removed.

Conclusion:

We observed statistically significant differences between the normal and tumor regions in the values of K^{trans} and v_e, when analyzed on a per-voxel basis. Clearly, this difference in the investigated PK parameters alone will not allow reliable identification of cancer for all of the image locations we considered. However, considering the variability in the appearance and function of the cancer-affected tissue within the tumor and across the different patients, our observation confirms that PK parameters may play a complementary role in cancer detection. The weak correlations between both K^{trans} and v_e and the ADC values underscore the fact that different pathophysiological processes are being assessed with DWI and DCE. Therefore we hypothesize that these parameters may play a contributory role in cancer detection, in particular when used in conjunction with ADC maps. Voxel-wise analysis techniques that integrate multiple parameters by means of deformable registration, like the one employed in this study, have the potential to improve quantitative assessment and characterization of tumor heterogeneity based on mpMRI, which is particularly important for the measurement of tumor volume and evaluation of cancer treatment response.

(1) Itou at al, JMRI 2011. (2) Vargus et al., Radiology 2011. (3) Langer at al, Radiology 2010. (4) Morgan at al., Br J Cancer 2006

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