Relationship between cell turnover and density in normal prostate regions: correlating quantified choline and citrate with apparent diffusion coefficient from high resolution DWI

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Purpose

Magnetic Resonance Spectroscopic Imaging (MRSI) and Diffusion-Weighted Imaging (DWI) increase the sensitivity of detection of prostate cancer because malignant prostate tissues have a higher metabolite ratio (choline + polyamines + creatine)/citrate and lower apparent diffusion coefficient (ADC) than non-malignant tissues. The relationship between these parameters however is poorly established, although previous data indicate that citrate concentrations and ADC values are independently correlated to tissue cellularity. [1] In this study, short echo-time spectroscopy (TE=32ms) is investigated for its improved depiction of metabolites by reducing T2-decay compared to standard long-TE implementations. Choline and citrate concentrations are calculated for peripheral zone (PZ) and central gland (CG) and correlated with ADC values from these voxels in order to determine the relationship between these parameters indicative of cell turnover and density.

Methods

13 prostate cancer patients referred for clinical evaluation using MRI were examined at 3.0T (Achieva, Philips Medical Systems, Best, The Netherlands) using an endorectal coil (MEDRAD, USA) inflated with 60ml of perfluorocarbon in combination with a phased-array surface coil. T2W-MRI, short- and long-TE ^{1}H-2D-Chemical Shift Imaging (CSI) and single-shot EPI DWI examinations were performed on all patients. Water-suppressed ^{1}H-2D-CSI was performed with PRESS using TR/TE=1400/32ms,100ms; FOV=120mm×120mm× 15mm; 12×12 reconstruction matrix; outer-volume suppression using REST. Equivalent scans without water suppression provided water signal as an absolute concentration reference. Metabolite quantification was accomplished using QUEST[2] which fits peaks to simulated basis sets. Citrate and *myo*-inositol basis sets were modelled with J-evolution whilst all other peaks were modelled as singlets; no relaxometric corrections were made. DWI was performed using b-values 0 and 800 s/mm^2. ADCs were computed with the scanner software using a mono-exponential fit.

Results

Example spectra with QUEST fitting are shown in Figure 1. Larger and additional peaks are seen in the TE=32ms spectra. Choline was separated from other metabolite resonances in 76 out of the 237 prostate voxels using TE=32ms, compared to in 13 voxels at TE=100ms. Two voxels were inspected by an experienced observer to contain tumour.

Table 1 Parameter values for healthy peripheral zone (PZ) and Central Gland (CG) voxels

(n=74)	choline/citrate	choline (mM)	ADC (10^{-3} mm^2/s)
PZ	0.070±0.068	3.67±2.20mM	1.56±0.15
CG	0.060±0.052	3.56±1.31mM	1.54±0.19

Absolute values for choline, choline/citrate ratios and ADCs derived from these 76 voxels are given in Table 1. The two partial tumour PZ voxels had choline/citrate, choline and ADC values of (0.057, 5.49mM, 1.24±0.45mm^2/s) and (0.106, 8.13mM, 1.03±0.52mm^2/s). No significant difference was found in either choline concentration or ADC between PZ and CG (p=0.40 and p=0.20 respectively). Plots for metabolites vs. ADC are shown in Figure 2a-c. Citrate T2 was 88±34ms in the PZ (n=34) and 90±50ms (n=86) in the CG, whilst choline T2 was 61±18ms (n=13) across both zones. The correlation of citrate to ADC from all 76 voxels was r^2=0.146 (Figure 2a).

Discussion

Choline and citrate T2s are shorter than literature values[3] which may be due to our shorter TE and suggest that short-TE spectroscopy is favourable for increasing prostate metabolite signal. J-evolution simulations ignoring T2-decay show that citrate has ~30% larger baseline-to-inner peak height at TE=100ms than at TE=32ms. However, *in vivo* the baseline-to-inner peak height is reduced by ~40%, i.e. a 58% reduction accommodating J-evolution; T2~78ms. The fitted singlet at 3.2ppm attributed to choline also decays considerably, but this may be partly due to spectral overlap with short-T2 metabolites. Choline and citrate have a large range of values in non-malignant tissues and did not distinguish PZ from CG; ADC is less variable. The weak positive correlation between citrate and ADC may relate to increased ductal volume in secretory glandular regions.

1. Wang et al. JMRI **29**:1360-1366 (2009) 2. http://www.mrui.uab.es/mrui/mrui_Overview.shtml
3. *Scheenen et al.* MRM **53**:1268-1274 (2005)

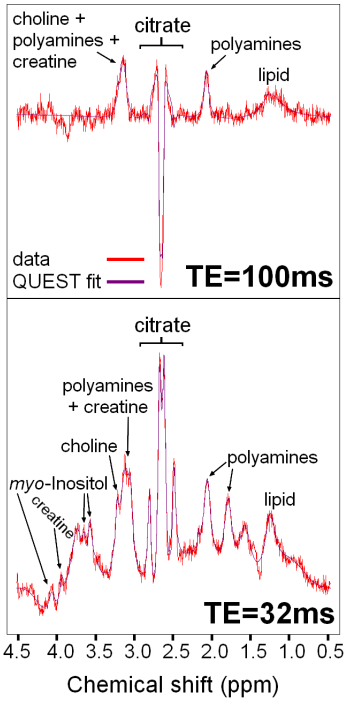

Figure 1 Short- and long-TE spectra from the same voxel with QUEST fit.

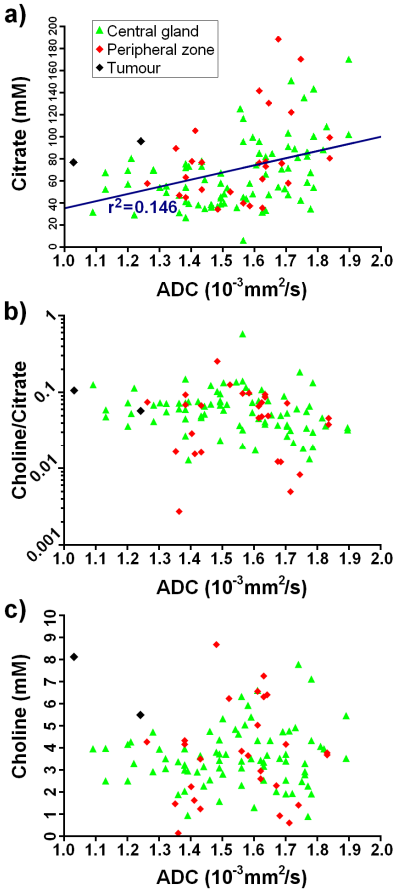

Figure 2 a) citrate vs. ADC b) choline/citrate vs. ADC c) choline vs. ADC in 76 prostate TE=32ms ^{1}H-2D-CSI voxels.