Breast Cancer Diagnosis Using Single-Voxel MRS Measurement of Apparent Diffusion Coefficient of Water

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Motivation: Quantitative single voxel MRS of choline-containing compounds (tCho) has been shown to increase sensitivity and specificity of breast cancer diagnosis[1] and provide an early indicator of chemotherapy treatment response[2]. However, measurement of tCho is fraught with technical limitations due to low signal to noise ratio (SNR), motion, lipid overlap, artifactual sidebands, and shimming[3, 4, 5]. The apparent diffusion coefficient of water (ADC_w) is an additional MR-accessible parameter which has already shown utility in cancer research[6, 7]. Diffusion weighted imaging (DWI) studies have demonstrated effectiveness in breast[8], although DWI has limitations as well. EPI-DWI is fast, but limited in resolution, prone to distortion and motion artifacts. It also has SNR limitations, and issues of image registration. Other imaging modalities overcome some of these limitations but require more precious magnet time. Each requires overlay, comparison, and perhaps post-processing to verify the region of interest (ROI). Single voxel ADC (SV-ADC) measurement, although lacking the ability to spatially resolve the ROI, offers the possibility of a rapid, simple, and high-SNR measurement.

Methods: We added a spin-echo ADC preparation sequence in front of a LASER[3, 9] localization sequence. LASER is an adiabatic spin-echo localization sequence implemented with pairs of hyperbolic secant pulses[9] for each of three orthogonal slices. Our ADC preparation uses adiabatic half-passage excitation and a BIR4 adiabatic pulse[9] for refocusing. Experiments were performed on a 4 T, 90 cm bore Oxford magnet with Siemens Sonata gradients and shims, Varian console, and custom designed transmit-receive quadrature coils designed for *in vivo* ^{1}H spectroscopy of the breast[10].

As part of our ongoing breast MRI/MRS protocols we studied subjects with suspected breast cancer or undergoing neoadjuvant chemotherapy. All subjects were consented under one of two IRB-approved protocols. After identification of the lesion by dynamic contrast-enhanced MRI a series of single acquisitions with ADC-LASER were performed. Seven b-values from 7.16×10^6 s/m^2 to 458×10^6 s/m^2 in geometric progression were used. In all cases a z-oriented gradient was used; echo time was 100ms and TR 3 s. The measurement of SV-ADC added roughly 30 s to the measurement protocol for each voxel. A non-linear least-squares fit was applied to the data points of each series; typical error sigma for SV-ADC was on the order of 10% or less. Accuracy and repeatability of the measurement was tested in pure water and agarose phantoms at known temperature.

Results: Two comparisons have been carried out. SV-ADC was compared to core biopsy results from a single lesion in each of 15 patients, and SV-ADC was compared to tCho concentration (mM/kg, with water as the internal reference) in 38 lesions, with data pooled over multiple patients, voxels, and measurement sessions. Figure 1. shows the distribution of SV-ADC values in lesions obtained from the population of patients with biopsy proven cancer, N=11, mean=1.29×10^{-9} m^2/s, std. dev.=0.29e-9, median=1.14. Two outliers (included in the analysis) had biopsy and/or image visible necrosis in the voxel. Figure 1. also shows the distribution of SV-ADC values from benign lesions N=4, mean=1.97×10^{-9} m^2/s, std. dev.=0.18e-9, median=1.94. The SV-ADC values of malignant lesions were significantly lower than those of benign lesions (one-sided t-test, $p<0.0001$). Figure 2. shows SV-ADC vs. measured tCho in a population of voxels (1-3 per patient). A model fit corresponding to $(\text{SV-ADC})^{-1} = 0.45 + 0.15\text{tCho}$ was obtained with $R^2=0.66$, N=38 voxels.

Discussion: For this small population of patients SV-ADC seems to have diagnostic potential, and given the correlation to tCho, may have potential for monitoring neo-adjuvant chemotherapy. Since b-value does not uniquely specify an ADC measurement in a multi-compartment system, with restriction, we anticipate the ability to tune the measurement parameters (b-value, echo time, q-value) to maximize specificity.

We gratefully acknowledge support from NIH R01CA92004 and P41RR008079, The MIND Institute, and The W. M. Keck Foundataion.

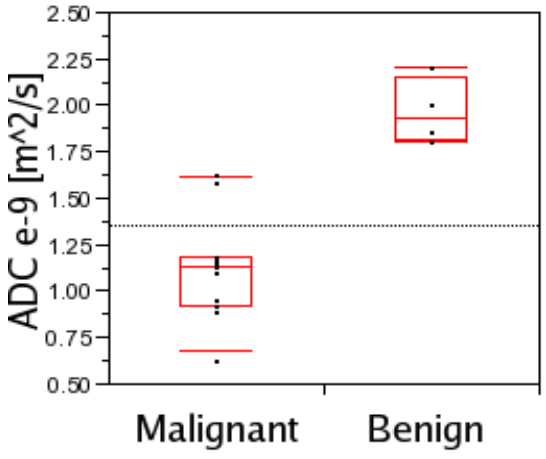

Figure 1. SV-ADC (10^{-9} m^2/s) from patients with biopsy proven cancer (N=11) and with benign pathology (N=4)

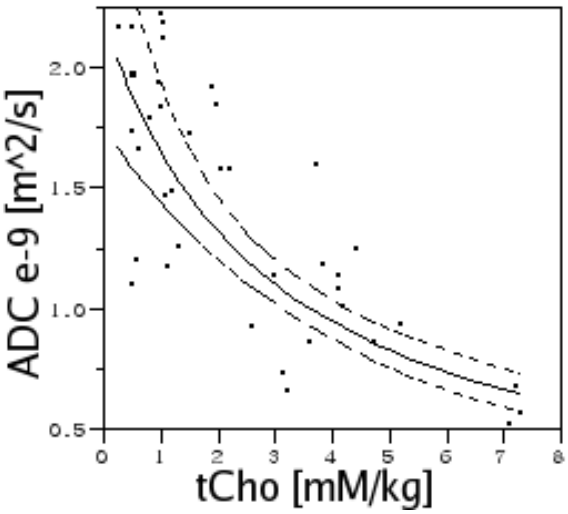

Figure 2. SV-ADC (10^{-9} m^2/s) vs. tCho concentration (mM/kg, N=38 voxels)

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