Increased sensitivity to tumor oxygenation in mice using high resolution echo-planar spectroscopic imaging

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Introduction: Tumor oxygenating (TOX) treatments are being developed to increase tumor pO_2 and thus increase response to radiotherapy. BOLD (blood oxygen level dependent) MRI provides non-invasive spatially resolved evaluation of response to TOX's. Previous work in this laboratory demonstrated that high spectral and spatial resolution MR imaging optimizes sensitivity to effects of TOX's by increasing sensitivity to small changes in water signal linewidth and lineshape. However, this work was based on the use of conventional spectroscopic imaging methods, and spatial, spectral, and temporal resolutions were not optimal. Here we demonstrate that high resolution EPSI can be used to acquire data with increased spatial and temporal resolutions and minimal distortion of the spectral lineshape.

Method: Nude mice (n = 5) were inoculated in the hind leg with AT6.1 tumor cells. EPSI was performed with $195 \times 195 \mu m^2$ in-plane resolution, slice thickness of 400μm, and ~7.8 Hz spectral resolution (TR = ~ 1.5 second, spatial/spectral matrix = 128x128x64) on a 4.7T scanner. Data were acquired during a control period (5-10 images) followed by carbogen (18-21 images) with a time resolution of ~3 minutes. The scans were both respiratory and cardiac gated. Three-dimensional EPSI data were Fourier transformed to produce detailed water spectra associated with each small image voxel. Spectra were phase corrected to produce a pure absorption water peak in each voxel, and water peak-height (PH) images were produced. An average baseline PH image was subtracted from PH images acquired during the carbogen period. A region growing algorithm identified areas where the water peak-height changes were highly statistically significant ($p<0.01$). Changes in PH over time were evaluated.

Results: The EPSI sequence produced water peak height images with excellent contrast. The water spectra in muscle were generally Lorentzian and narrow, and showed no evidence of distortion due to eddy currents. In four of the five experiments the water peak-height increased significantly in 12-28% (average = 15%) of the pixels in the tumor, and decreased in all five experiments in 3-36% of the pixels in the tumor (average=11%). Representative results are shown in Figure 1. Water PH images are shaded red in regions of positive enhancement and blue in regions of negative enhancement. The tumors are the regions with greatest intensity in the PH images. The changes were often spectrally inhomogeneous – different components of the water resonance in individual voxels responded differently to carbogen. The greatest changes in water peak-heights were near the edges of tumors. Time series data in Figure 1 show representative time dependent changes in peak-height as carbogen is introduced. Plots are for individual voxels located where the arrows are pointing. The dashed lines are the time series data and the solid lines are the average of the baseline (its length equal to the number of baseline scans performed). Changes in peak height often continued throughout the carbogen breathing period.

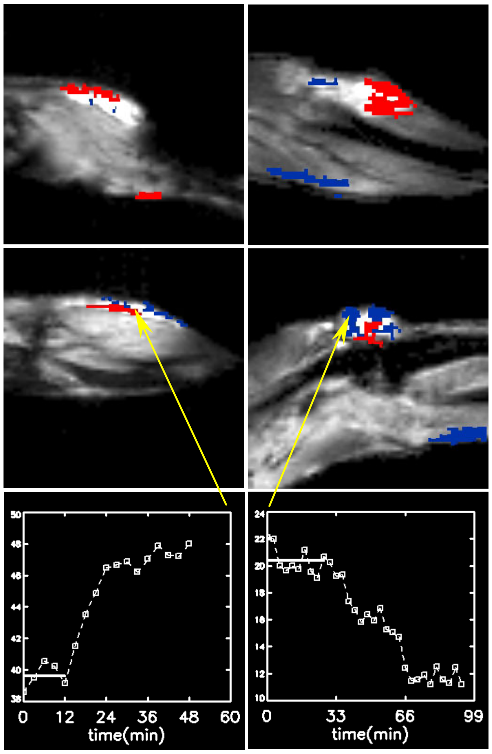

Figure 1

Discussion: EPSI allowed acquisition of spectral data with much higher spatial and temporal resolutions than were achieved in previous work (1). This is advantageous because of the spatial, spectral and temporal heterogeneity of tumor response to carbogen. The results suggest that high resolution EPSI is very sensitive to changes in BOLD contrast. Because this method is non-invasive and uses standard clinical MRI equipment, it could allow physicians to identify optimal tumor oxygenating therapy for individual patients.

References:

1. Al-Hallaq HA, et al. NMR in Biomedicine **15:** 28-36, 2002