Lineshape and Susceptibility in a Rat Glioma Monitored by Echo Planar Spectroscopic Imaging

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Introduction

Echo planar spectroscopic imaging (EPSI) is an improvement over conventional magnetic resonance spectroscopic imaging (MRSI), especially for studies where S/N is not limiting. EPSI allows monitoring of the intensity, susceptibility shift, and linewidth as a function of position. It results in shorter acquisition times as *k*-space is rapidly traversed, but so far has been only used at lower fields. This work describes EPSI at 4.7 T based on previous implementations of EPSI. We implemented EPSI with two spatial dimensions (1, 2) without water- and outer volume suppression. This is the first time that this sequence has been developed for this field strength. We applied this sequence to time-resolved *in vivo* ^{1}H spectroscopy to observe the pharmacokinetics of contrast reagent (CR) in a rat C6 glioma at high spatial resolution.

Materials and Methods

An EPSI sequence was implemented for the first time on a 4.7 T Bruker Biospec. The pulse sequence was written in the Bruker pulse programming language augmented with C source-code routines for dynamically calculating acquisition parameters (IMND) for Paravision 2.1.1. Validation was performed with sealed syringe and plunger phantoms to assess the quality of the reconstructed projection images as well as the quality of the proton spectra. The gradients were trapezoidal and the RF excitation was a single 90° pulse. The bandwidth of the digitizer was set at 152 kHz, resulting in a spectroscopic bandwidth of 592 Hz (3.0 ppm). The spectroscopic resolution was 4.6 Hz/pt. Fat suppression was not used as the brain slices contained very little fat.

Infusion experiments were carried out on rats implanted with C6 glioma cells. C6 cells (~10^5 cells in 10 µl) were injected stereotaxically in the right caudate nucleus of the brain. A 73 mm inner diameter volume coil was used for excitation, while an 18 mm diameter surface coil, placed above the rat brain, was used for signal reception. After acquisition of pre-contrast data sets, an Omniscan bolus of 0.1 mmol/kg was injected and followed by infusion at a rate of 2 mmol kg^{-1} hr^{-1}. The intensity and the perfusion of the CR were followed by interleaving the EPSI acquisitions (TE = 5 ms, TR = 1 s) with T_1-weighted spin-echo experiments (TE = 6.4 ms, TR = 80 ms). For EPSI data of 256^3 points, the time resolution of a single experiment was determined by the time necessary to complete all phase encoding scans, which was 7.4 minutes. The resulting in plane spatial resolution was 125 µm/pt on each side with 1 mm slice thickness.

Results and Discussion

The image in Figure 1 demonstrates that a high spatial and spectroscopic resolution has been achieved. Representative time-series spectra are depicted on the outer edges of the image and demonstrate that the dynamic contrast enhancement also affects the lineshape due to CR induced changes in the magnetic environment. These changes are clearly resolved on the timescale of the EPSI experiment.

In EPSI datasets, resonance frequencies are sensitive to local field and hence can yield a B_0 image that is affected by local susceptibility. Both the intensity and linewidths were affected by Omniscan and were used to follow pharmacokinetics. Furthermore, at high resolution, we observed multiple water resonances near the edge of the tumor. Multiple peaks have recently been observed in a bioreactor (3), where the intracellular water component has been resolved. Also, diffusion tensor imaging (DTI) studies of rat C6 gliomas have reported high planar anisotropy in the areas near the brain-tumor interface (4). Histology showed the existence of flattened cells surrounding the tumor, which suggests that the high diffusion anisotropy measured may be due to the flattening of peritumoral glial cells, resulting in a non-spherical shape. This kind of geometrical changes may induce shifting and/or broadening in the water signal due to a susceptibility effect based on the Sphere of Lorentz theory (5). Hence, the multiple resonances, that we observed, may represent distinct multi-compartment environments in anisotropic peritumoral tissue. We believe that analysis of peak multiplicity using high resolution EPSI provides an important window characterizing susceptibility effects in these anisotropic tissues, with high spatial, spectroscopic, and temporal resolution.

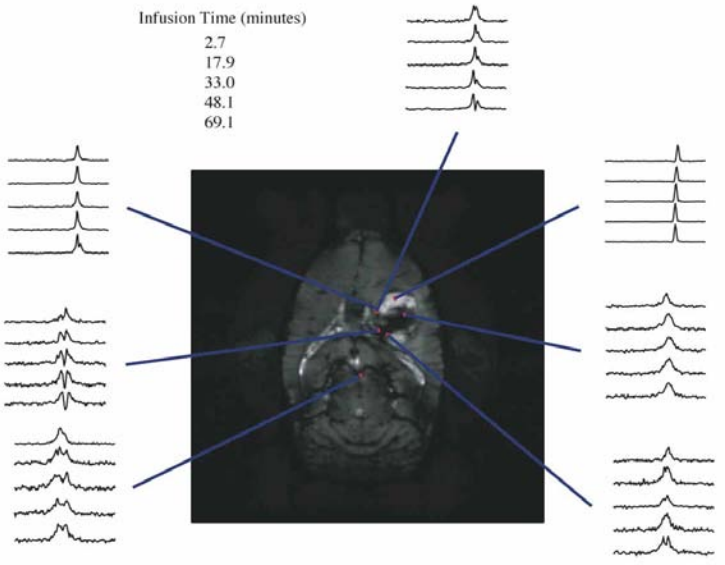

Figure 1. Representative infusion time-series stack-plots. Each stack-plot depicts increasing infusion time going from top to bottom for a particular voxel. The infused CR was Omniscan, and was performed for a total of 76.4 minutes. The image is derived from the final EPSI 3-D data set in the series and is a projection created by using the maximum intensity values. The in plane spatial resolution is 125 µm/point with 256 points on a side. The spectral bandwidth is 3.0 ppm.

References

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