Crushed Early Acquisition Spin Echo (CEASE): a novel technique for positive contrast and spectroscopic imaging of superparamagnetic particles

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Introduction

There has been increasing interest in using micron-sized iron oxide (MPIO) particles for cell tracking[1]. Traditionally, T2* weighted images have been used to provide negative contrast; however hypointense regions that are not due to iron oxide particles are likely to be present in biological samples. Positive contrast techniques have been shown to be more specific to contrast generated by iron oxide[2] Here, we present a novel positive contrast sequence that consists of an excitation pulse, a crusher, and an early spin-echo acquisition; leading to the name Crushed Early Acquisition Spin Echo or the CEASE sequence.

Method

A simplified schematic of the CEASE sequence developed is presented in Figure 1. Over macroscopic distances with uniform magnetization, the gradient G_c completely dephases magnetisation ($\Delta\varphi=\gamma\Delta\mathbf{r}\mathbf{G}t$, where $\Delta\varphi$ is the phase difference between 2 spins separated by distance $\Delta\mathbf{r}$, G is gradient strength, and t is the gradient duration). Even with a voxel length of 100 microns, a gradient of 5G/cm for 0.5ms would dephase spins by 13.4 radians across the voxel length. However, spins *local* to microscopic deposits of iron oxide are dephased in the time between the excitation pulse and the beginning of the gradient G_c. The gradient then acts to rephase these spins which are sampled at time τ_d before the normal spin-echo. In practice, there will be a distribution of frequencies surrounding the iron oxide. The spectra of all voxels can be obtained by acquiring a set of images at a range of τ_d and taking the Fourier transform with respect to τ_d.

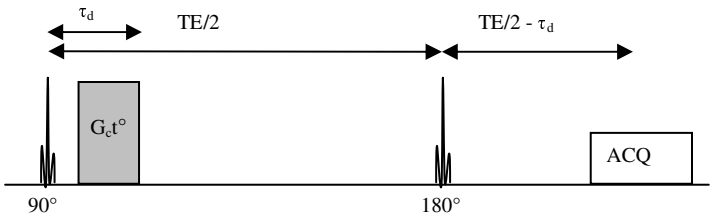

Figure 1 Schematic of CEASE sequence developed

The CEASE sequence was implemented on a Varian, Inc. 7T imaging system equipped with a 72mm (for a phantom) and a 39mm diameter (for ex-vivo sample) r.f. coils (RAPID Biomedical GmbH) and using a conventional single echo acquisition. Rat mesenchymal stem cells (MSC) were incubated with 1.63 micron MPIO particles (Bangs Laboratories, Inc.) at a concentration of 10 µl/ml complete medium. 20 hours later, excess iron particles were removed with fresh complete medium, and the cells were harvested and resuspended in complete medium. A 1% agarose phantom containing 9 wells of labelled MSC was constructed by half filling a 38mm diameter plastic container with agarose, creating small wells in the set agarose and then filling the wells with 0.2-2 µl labelled MSC. Finally the container was fully filled with agarose. An ex-vivo Wister rat brain sample was prepared by injecting 1 µl of 15.8mM Ibotenic acid (IBA) into both hemispheres in a live animal on postnatal day 5 (P5) to create a brain legion. Labelled MSC were injected into the periventricular lesioned area on the right side only at P6. The animal was perfused with fixative at P56, the brain removed and suspended in agarose gel. Images were acquired with the following parameters: TR = 7s, TE = 59.6ms, $G_c t$ = 12 G/cm and 10 G/cm for 0.5ms (ex-vivo sample and phantom respectively), 17 values of τ_d starting at 0.6ms and in 2ms steps, 96x32 matrix. Images were Fourier transformed with respect to τ_d.

Results

Figure 2 demonstrates that the CEASE sequence provides positive contrast and that spectroscopic imaging can be achieved. Regions of positive contrast in CEASE images match up well with hypointense regions in T2*W images. The variation in intensity at different frequencies show that there is a distribution of frequencies within each voxel. The CEASE images from the ex-vivo sample clearly shows migration of labelled MSC near to the lateral ventricles in both hemispheres.

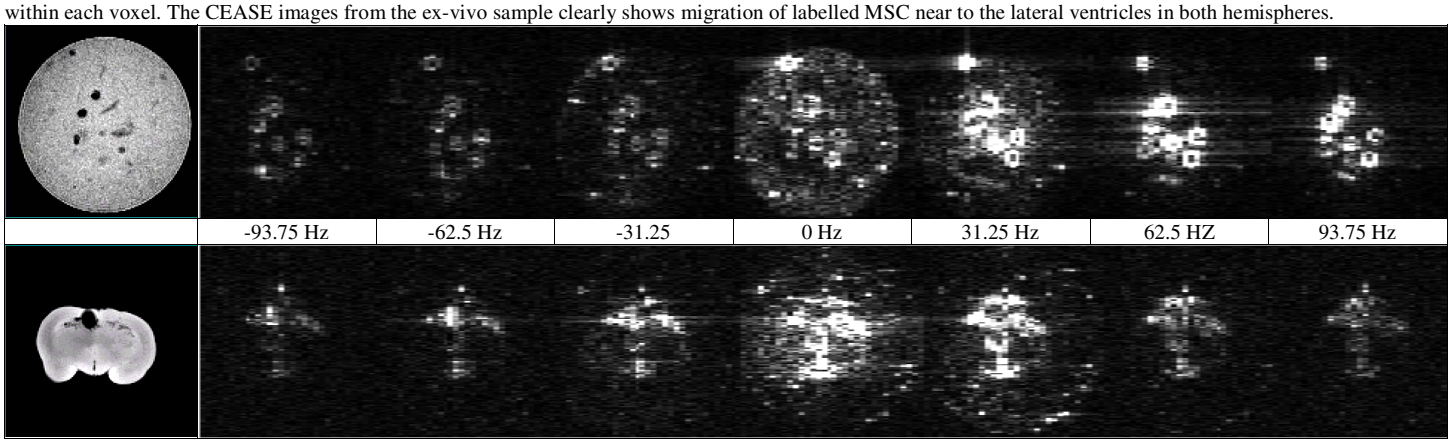

Figure 2 Positive Contrast Spectroscopic Imaging with CEASE. Left: Equivalent T2*W 3D GE image; Right: CEASE images Fourier transformed with respect to τ_d and scaled to 8 times normalised intensity. Top: Phantom containing 9 wells of varying amounts of MPIO labelled MSC. Bottom: ex-vivo sample.

Conclusion

We have demonstrated that the CEASE sequence provides positive contrast and spectroscopic imaging in a phantom and an ex-vivo sample.

Discussion

In this study single slice single spin echo readout was used. Total scan time for CEASE spectroscopic imaging was about 64 minutes. In principle, multi-slice and EPI readout could be used, dramatically reducing scan times. The frequency distribution data potentially provides quantitative information on regional iron oxide concentration, but this requires further investigation. Further data acquired in this study indicates that 3d shape of susceptibility gradients can be elucidated by taking several directions of gradient G_c. Varying gradient strength coupled with τ_d would also probe different susceptibility gradients.

References

1. Shapiro, E.M., S. Skrtic, and A.P. Koretsky, *Sizing it up: Cellular MRI using micron-sized iron oxide particles.* Magnetic Resonance in Medicine, 2005. **53**(2): p. 329-338.
2. Cunningham, C.H., et al., *Positive contrast magnetic resonance imaging of cells labeled with magnetic nanoparticles.* Magnetic Resonance in Medicine, 2005. **53**(5): p. 999-1005.