FISPCEST: A Rapid, Acquisition for Dynamic Detection of CEST/PARACEST Activity

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Abstract

We have developed a new FISP Chemical Exchange Saturation Transfer (FISPCEST) pulse sequence to dynamically monitor CEST contrast changes with high sensitivity. The FISPCEST technique provides <3sec acquisition times providing an order of magnitude improvement over current CEST techniques. The FISPCEST acquisition combines a single, ~2sec, nonselective CEST preparation followed by a ~500ms FISP acquisition. The dramatically improved temporal resolution is obtained with only a 15% loss in CEST sensitivity compared to standard spin echo acquisitions. The FISPCEST technique is adaptable to endogenous and exogenous (PARA)CEST applications enabling the rapid acquisition of CEST spectral maps and multislice CEST images.

Introduction:

Many examples of both endogenous and exogenous Chemical Exchange Saturation Transfer (CEST) have been demonstrated.[1,2,3] However, the temporal resolution of the CEST MRI acquisitions in these previous studies is quite low (10-30mins per time point) and primarily restricted to single slice acquisitions. The long acquisition times have limited the applications of *in vivo* CEST studies as some physiologic changes (metabolism, local temperature, blood flow) occur much faster than the standard acquisition timescales, especially in animal models. Recent FLASH-CEST developments have reduced the acquisition time to 30-60seconds[4]. However, these acquisitions are still somewhat slow, especially for multi-slice applications, and can result in a substantial loss of CEST sensitivity.

Methods:

A FISP (Fast Imaging with Steady-State Free Precession) pulse sequence was modified for a Bruker Biospec 9.4T scanner to include a CEST preparation scheme (Fig. 1). The CEST preparation consisted on 1000, non-selective Gaussian pulses (2.25ms, 20uT) with a tunable off-resonance frequency. The FISP sequence (TR/TE=4/2ms, res=230umx230umx1mm tip angle=60deg) then acquired all 128 lines of k-space following an alpha/2-TR/2 preparation and 10 dummy scans to reduce steady-state transitional effects. A FISP sequence was selected instead of True FISP to avoid severe banding artifacts at 9.4T. A 40mM Eu(III)DOTAM-Gly^2 PARACEST agent sample was synthesized and scanned with a PBS sample. A FISPCEST spectra was obtained by adjusting the center frequency of the CEST pulse train. CEST-spin echo (SE-CEST) images were also obtained to determine the relative PARACEST sensitivity of the FISPCEST sequence.

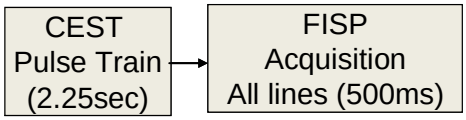

Fig. 1: Schematic of FISPCEST acquisition

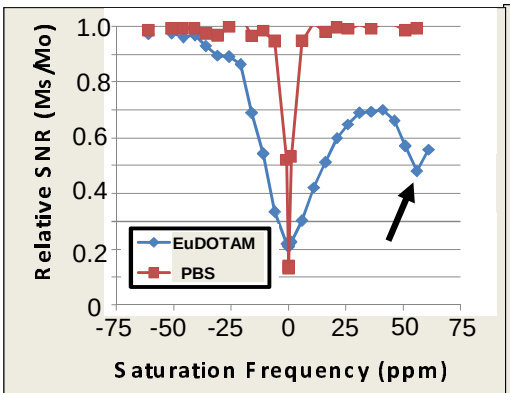

Fig. 2: In vitro FISPCEST spectra from a 40mM EuDOTAMGly PARACEST agent and PBS control. The PARACEST agent shows 50% CEST effect at 56ppm.

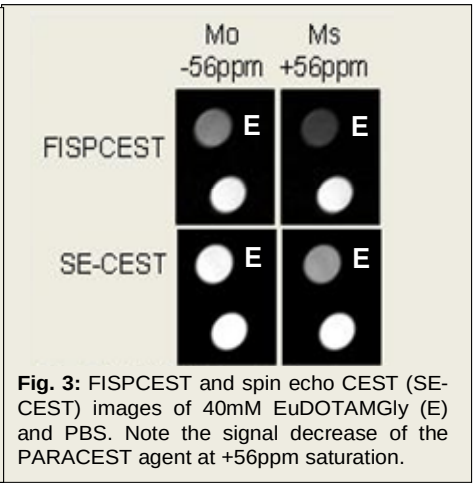

Fig. 3: FISPCEST and spin echo CEST (SE-CEST) images of 40mM EuDOTAMGly (E) and PBS. Note the signal decrease of the PARACEST agent at +56ppm saturation.

Results

The FISPCEST spectra shows a dramatic ~50% CEST sensitivity at 56ppm for the EuDOTAMGly PARACEST agent (Fig. 2, arrow). This FISPCEST effect was only 15% lower than the CEST effect from an 11min, spin echo CEST acquisition (SE-CEST) with one saturation pulse/K-space line (TR/TE=5000/8ms, same CEST pulse design). Images from the FISPCEST and SE-CEST acquisitions at +56ppm (CEST) and -56ppm (No CEST) are shown in Fig. 3. The EuDOTAMGly sample is labeled with an E.

Discussion

This work demonstrates the first results from a FISP-CEST acquisition that provides a means to dynamically acquire CEST images for both endogenous and exogenous CEST experiments in under 3seconds. This temporal resolution is obtained with little or no loss of CEST sensitivity by combining the rapid FISP acquisition with a long CEST saturation pulse train. This new FISPCEST acquisition enables truly dynamic, multi-slice, highly sensitive CEST imaging for detecting exogenous PARACEST agents *in vivo*. In addition, this method can be used to generate FISPCEST spectra for each voxel for endogenous CEST activity (ex. glycoCEST[2]) in under 1 minute. In this way, the FISPCEST provides a more thorough quantitative analysis allowing the CEST effect to be distinguished from other factors that can confound CEST results (i.e., Magnetization Transfer, off-resonance artifacts, etc).

References:

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