Development of a 3D CEST Pulse Sequence with Embedded Field Map and Low SAR for pH-Weighted Contrast in Stroke Patients

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Introduction

Chemical exchange saturation transfer (CEST) permits the detection of dilute labile proteins to allow pH-weighted imaging. It is of great interest in stroke studies to reveal ischemic acidosis. However, clinical applications of the technique are currently limited due to time and specific absorption rate (SAR) restrictions. Successful CEST experiments require long radiofrequency (RF) pulse trains to reach the steady state, which leads to a high SAR and a long examination time. Additionally, the saturation frequency is often shifted due to the inhomogeneity of the main magnetic field. For correction, a separate field-map scan is usually acquired. In this study, we developed a three-dimensional (3D) pulse sequence with low SAR and embedded field map information. Potential application for detecting ischemic acidosis is demonstrated in a stroke patient imaged on the second day after symptom onset.

Materials and Methods

Sequence Design: The sequence was implemented on a 3T scanner (TIM Trio, Siemens, Erlangen, Germany). As shown in Fig. 1, the sequence has two parts: *(a)* the reference image acquisition without saturation pulses; *(b)* the CEST image acquisition with off-resonance saturation pulse. To optimize the total acquisition time, a multiple gradient-echo readout was implemented in part *(a)* for measuring T_2* and computing the field map (Fig. 1a). Since there is a hard limit of the duty cycle (< 50%), the repetition time (TR) has to be at least twice as long as any RF pulse included. A segmented turbo FLASH readout was implemented in the CEST part *(b)* to save measurement time by reducing the number of repetitions. A turbo factor of 4 is shown in the Fig. 1b. The partition-line *k*-space was acquired in the order from the longest distance to the center to the shortest one, so that the central lines were recorded when the system had reached the steady state (see Fig. 1c). *Phantom:* A phantom with six tubes of 100mM creatine in 100 mM phosphate-buffered saline (PBS) at different pH values (5.6, 6.0, 6.3, 6.6, 6.8, and 7.2) was used. To adjust relaxation times toward physiologic ranges, 0.2% v/v Magnevist was added to the solution. *Patient:* A patient (male, 65y, 75 kg) with PCA infarct was measured on the second day after symptom onset. Sequence parameters included TR, 200ms; TE, 5ms; Sat pulse duration, 100ms; Sat flip angle, 500°; Sat frequency offset, ±3, ±3.25, ±3.5, ±3.75, ±4ppm; voxel size 2×2×5mm; partition 12; examination time 6 mins. *Data Processing:* The field map was calculated from the phase contrast of the multiple gradient echoes. For each voxel, the *Z*-spectrum was interpolated and corrected according to the field map. The pH-weighted contrast was defined as asymmetric magnetization transfer ratio $MTR_{asym} = S_{sat}(\text{neg. offset})/S_0 - S_{sat}(\text{pos. offset})/S_0$, where S_{sat} and S_0 are the imaging signal intensities measured with and without RF saturation, respectively.

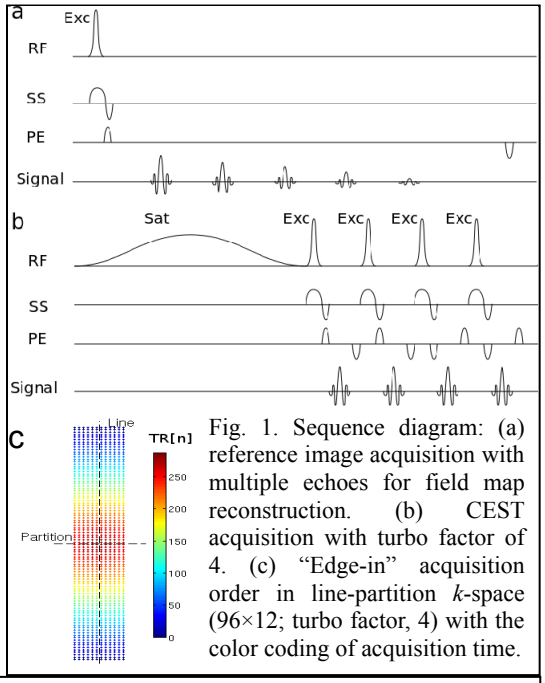

Fig. 1. Sequence diagram: (a) reference image acquisition with multiple echoes for field map reconstruction. (b) CEST acquisition with turbo factor of 4. (c) "Edge-in" acquisition order in line-partition *k*-space (96×12; turbo factor, 4) with the color coding of acquisition time.

Results

Phantom: Fig. 2a shows *Z*-spectra and MTR_{asym} of the creatine solution at different pH values. Peak with different amplitudes are observed at ~1.9 ppm downfield from water, where the amide protons of creatine resonate. The corresponding MTR_{asym} map in Fig. 2b demonstrates a consistent change of MTR_{asym} with the change in pH. *Patient:* In right posterior cortex around the infarction (Fig. 3), the hypointensity of MTR_{asym} (3.5 ppm) matches the perfusion mean transit time (MTT) deficit. This indicates that the tissue receives blood supply and is at risk of infarction. The SAR level was 3% for the patient scan.

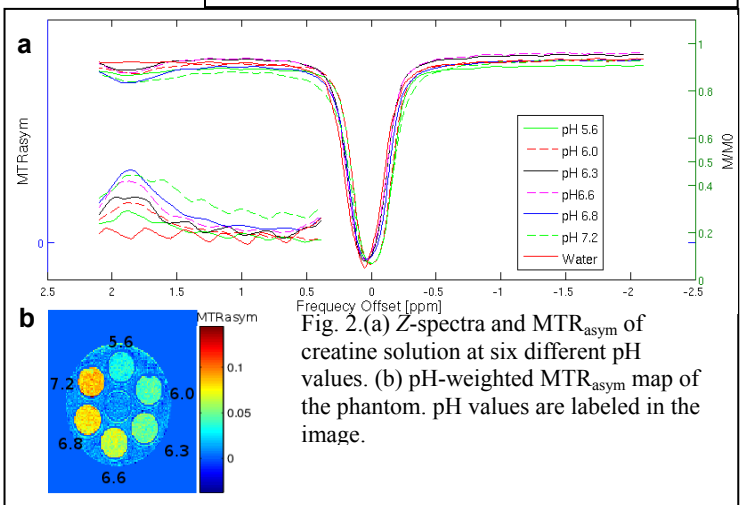

Fig. 2.(a) *Z*-spectra and MTR_{asym} of creatine solution at six different pH values. (b) pH-weighted MTR_{asym} map of the phantom. pH values are labeled in the image.

Discussion

Clinical application of CEST has been limited, since it requires multiple scans with off-resonance saturation, which leads to a long measurement time and high SAR. In our study, we integrated a field map measurement in the reference scan and introduced a turbo factor to accelerate the data acquisition during the RF off-duty time after the saturation. The edge-in sampling scheme ensured that the central portion of *k*-space was acquired during steady state.

Preliminary hypointensities of MTR_{asym} observed in the ischemic tissue, rather than in the infarction, indicated a lower pH value, which match previous animal results [1]. This might be explained by accumulated lactate under ischemic conditions with abnormal blood supply. Comparison with a FLAIR image at day 5 suggests that the reduced pH did not indicate a tissue fate of infarction. Further studies are necessary to explore the ischemic acidosis in more detail.

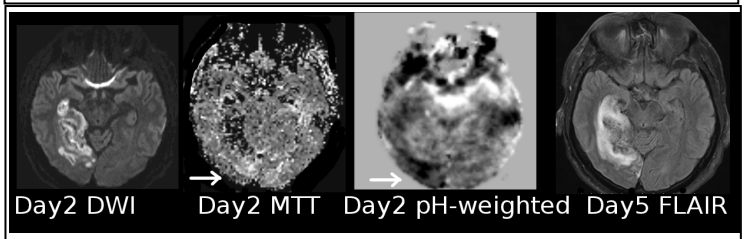

Fig. 3. Imaging results in the stroke patient

Reference: [1] Zhou et. al. Nature Med. 9, 1085 (2003).