

3758

## Interleaved B<sub>0</sub>-mapping during dynamic Creatine-CEST for correction of temporarily fluctuating B<sub>0</sub> inhomogeneities during plantar flexion exercise at 7T

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### Synopsis

Once the time resolution and specificity of Cr-CEST become comparable with 31P-MRS, it may replace it for the diagnosis of muscular disorders and treatment assessment due to its superior spatial resolution and sensitivity. The need of a complete Z-spectrum acquisition for B<sub>0</sub> inhomogeneity correction limits the achievable time resolution and is unable to track temporal  $\Delta B_0$  due to subject movement or B<sub>0</sub> field drifts that occur during a CEST experiment. Temporal B<sub>0</sub> field tracking allows independent B<sub>0</sub> inhomogeneity correction for each z-spectral point, which may substantially improve the reliability of spectral CEST asymmetry analysis.

### INTRODUCTION

Chemical Exchange Saturation Transfer (Cr-CEST) is a contrast mechanism that allows the detection of small amounts of metabolites with enhanced sensitivity. Creatine (Cr) is an endogenous metabolite with Amine protons (-NH<sub>2</sub>) involved in muscle energy metabolism, which can be altered under different disorders.<sup>1</sup>

Current CEST techniques are very sensitive to motion-induced bias in CEST quantification, which is unavoidable during dynamic muscle exercise studies. One of them arises from the physical variation in the B<sub>0</sub> field ( $\Delta B_0$ ) due to subject movement. The other one from the way the contrast is calculated in the spectral CEST asymmetry analysis, for each voxel along a number of MR images.<sup>2</sup>

Established B<sub>0</sub>-inhomogeneity correction methods for CEST can only correct static B<sub>0</sub> deviations (i.e., shift the frequency of the entire z-spectrum), but cannot compensate temporal B<sub>0</sub> changes that occur during a CEST experiment.

In this study, we propose and compare two alternative methods that allow a dynamic correction of B<sub>0</sub> changes for individual z-spectral points. These significant improvements in the acquisition and processing of CEST spectra are mandatory to translate Cr-CEST during exercise to a reliable tool for routine application.

### MATERIALS AND METHODS

The first approach (A) that we propose is to track temporal  $\Delta B_0$  by using the gradient echo images of the CEST scan itself having a certain echo time (TE) and assume a constant phase offset calculated from a previous double echo gradient echo (DE-GE) sequence.<sup>3</sup> The other option (B) that we propose is the use of an interleaved dual-echo navigator (NAV) prior to saturation.

These two dynamic correction approaches (A,B) were compared to three established static B<sub>0</sub> correction approaches: (C) Water saturation shift reference (WASSR)<sup>4</sup>, (D) minimum of CEST spectrum, and (E) application of one B<sub>0</sub> map obtained from a single DE-GE sequence<sup>5</sup> prior to the CEST experiment.

For this comparisons, the  $\Delta B_0$  in the x direction shown in Fig. 1 and 2 were calculated as the B<sub>0</sub> maps obtained after a manual increase in the voltage of the first order shimming coil in the x direction minus the B<sub>0</sub> maps obtained after optimum shimming. The measurements were performed on a commercially homogeneous spherical phantom for calibration from Siemens Healthcare, Erlangen, Germany.

The non-rigid diffeomorphic images registration were performed retrospectively in Matlab 2015b.<sup>6</sup> All the MRI scans were performed on a whole body 7T MR Magnetom system from Siemens Healthcare, with a 1H28-channel Tx/Rx knee coil from QED, Mayfield Village, Ohio, USA.

CEST images were acquired with five Gaussian saturation pulses of 100ms each separated by a 31ms delay and amplitude B<sub>1</sub>=1.2uT. The spectrum range was  $\pm 3.2$ ppm with a step size of 0.25 ppm (26 points).

WASSR images were obtained with the same parameters except for two saturation pulses of B<sub>1</sub>=0.2uT and a Z-spectrum between  $\pm 1.2$ ppm and a step size of 0.05 ppm (49 points). Phantom and volunteer's imaging were performed with imaging parameters of slice thickness=6mm, FA=5° and FOV=225x225mm.

The DE-GE images parameters were pixel BW =600 Hz, TR=12ms TE<sub>1</sub>=2.0ms TE<sub>2</sub>=5.1ms and 30 averages.

The Navigator EPI images parameters were pixel B<sub>1</sub>=2790 Hz, TR=1ms TE<sub>1</sub>=6.1ms TE<sub>2</sub> 9.2ms and EPI factor=3.

### RESULTS AND DISCUSSION:

In phantom studies the spatial  $\Delta B_0$  calculated from NAV shows the same slope and similar variability as the reference DEGE. On the other hand, the one determined from WASSR presents variability within the range of  $\pm 15$  Hz (Fig.1), which can only be compensated by scanning additional spectral points and hence further increasing scan time.

The alternative of calculating the  $\Delta B_0$  directly from each of the CEST images provides good results except for those images partially or totally saturated (i.e. acquired after saturation around 0 ppm, Fig 2.c).

The fact that exercise is performed during CEST images acquisition, with intrinsic deformation between consecutive images and that the data post-processing is done voxel-wise, elastic registration of CEST images and Field Maps (FM) become necessary for a reliable quantification in dynamic

exams.

The advantage of the NAV images is that a displacement field can be determined even for saturated CEST images, as those shown in Fig 3. The preliminary results in vivo (Fig4) show how the static B0 map in the ROI selected vary up to 25 Hz during plantar flexion exercise.

## CONCLUSION

This study shows the feasibility to map the B0 field repetitively during exercise prior acquisition of each z-spectral point, which can ensure accurate B0-correction for dynamic Cr-CEST experiment in vivo.

In comparison with the static standard methods such as WASSR, which assume constant B0 and no movement, dynamic correction methods (in particular interleaved NAV-based acquisition) can compensate for temporal B0 fluctuations and subject deformation/movement.

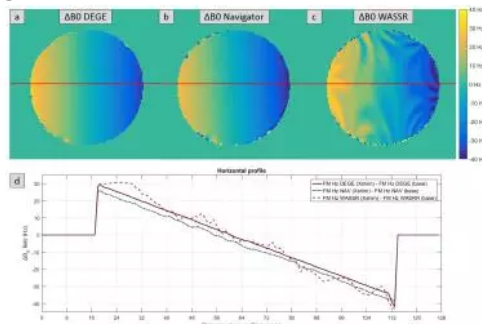
## Acknowledgements

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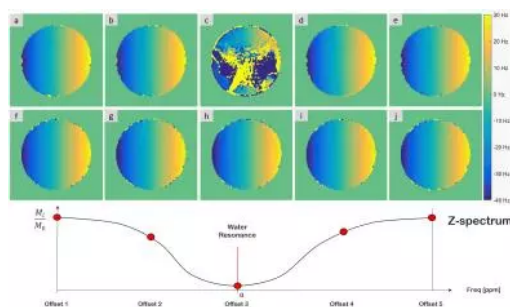
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## Figures



**Fig. 1:  $\Delta B_0$  profile comparison: DE-GE VS Navigator VS WASSR**

Spatial  $\Delta B_0$  in the x direction measured with (a) single DE-GE sequence prior to the CEST experiment, (b) interleaved dual-echo navigator (NAV) prior to saturation and (c) single WASSR sequence prior to the CEST experiment. The  $\Delta B_0$  profile along the horizontal red line is given in (d).  $\Delta B_0$  were calculated as the B0 maps obtained after a manual increase in the voltage of the first order shimming coil in the x direction minus the B0 maps obtained after optimum shimming for each of the methods.



**Fig. 2:  $\Delta B_0$  comparison: DE-GE & CEST VS Navigator**

Spatial  $\Delta B_0$  in the x direction calculated (a-e) from the gradient echo images of the CEST scan and (f-j) from the interleaved dual-echo navigator (NAV) images prior to saturation. Each saturation train of pulses are applied at the Z-spectrum offsets frequencies [1-5], being 0 at water resonance frequency. For the calculation of the  $\Delta B_0$  maps from CEST images at a certain TE, the phase offset calculated from a single DE-GE sequence prior to the CEST experiment is assumed constant.

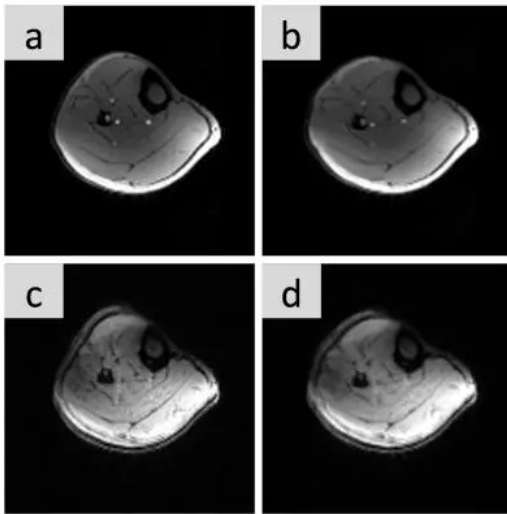
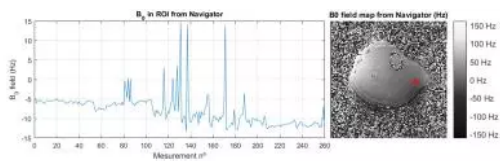


Fig. 3: Non-rigid registration of images from CEST (top row) and Navigator (bottom row) sequences.

Deformed GE magnitude images from CEST sequence acquired before elastic registration and (b) after registration. (c) Deformed EPI magnitude image used before and (d) after elastic registration. The images from the CEST scans don't show full contrast due to partial water saturation, the EPI images Navigator are acquired just before saturation is applied.



**Fig. 4: B<sub>0</sub> field evolution during plantar flexion exercise (measures=79-208)** Evolution of B<sub>0</sub> field measured from images obtained with the interleaved Navigator sequence. The values correspond to the mean of the red ROI located on the medial gastrocnemius.