3D mapping of Glutathione in the human brain via real-time motion corrected MEGA-LASER MRSI

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Target Audience:

MRS sequence developers; Neuroscientists and clinicians interested in antioxidants

Purpose:

Glutathione is the most important intra-cellular antioxidant in mammalian cells. GSH plays a vital role in the protection of neuronal cells from damage caused by reactive oxygen species such as free radicals. This makes GSH an excellent *in vivo* marker for oxidative stress, which is important in many neurological disorders.

MR Spectroscopy (MRS) is the only non-invasive method that allows the quantification of GSH. Unfortunately, GSH signals overlap with more abundant brain metabolites such as N-acetyl-aspartate (NAA), creatine, glutamate, lipids, and macromolecules and GSH is present in the brain only in relatively low concentrations of 1-2 mM.

The most popular MRS technique for unambiguous GSH detection is MEscher-GArwood (MEGA) editing [1], which provides the highest retained signal compared to other techniques. However, MEGA editing is a subtraction technique, and is, therefore, prone to scanner instabilities and motion artifacts. In addition to chemical shift displacement errors (CSDE) that are common with traditional MEGA-PRESS and which reduce editing efficiency, other technical limitations exist [2]. Most commonly, the measurements are limited to rather large single-voxels placed in the brain region of interest [3]. Few preliminary reports on 2D mapping of GSH exist [4].

Recently, a new 3D-MRSI sequence for robust and efficient GABA imaging was presented that integrates: i) adiabatic J-difference MEGA-LASER, ii) spiral acquisition, and iii) real-time motion and shim correction in one sequence [5]. Using this sequence, we have tested the feasibility of robust 3D mapping for GSH in the human brain.

Methods:

Five volunteers were scanned on a 3T TIM Trio MR Scanner (Siemens, Erlangen, Germany) using a 32-channel head coil (Siemens, Erlangen, Germany). Gradient Offset Independent Adiabatic GOIA-W(16,4) pulses, with 3.5 ms duration and 20 kHz bandwidth were used for LASER selection. Two 60 Hz Gauss refocusing pulses were used for MEGA editing (Fig.1)[5]. In order to minimize subtraction errors we used a combination of Reacquisition, Shim, frequency, and Motion Correction (ReShMoCo). For this, a dual-contrast, multi-shot 3D-EPI navigator was inserted prior to water suppression to provide real-time motion, shim, and frequency correction. Any data which happened to be corrupted by motion in between the updating of two consecutive navigators were selectively discarded and reacquired. Anatomical reference data (MPRAGE with 1mm³ isotropic resolution) and two 3D-MRSI scans with MEGA-editing for 3D mapping of GSH with two different resolutions were acquired (Fig.2). *In vivo* MRSI parameters were: TR/TE 1600/68ms; 8cc and 3cc isotropic; matrix size of 10×10×10 and 14×14×12 interpolated to 16×16×16; FOV 20×20×20cm and 20×20×17cm; VOI 10×8×5.5cm; spectral bandwidth 1.1kHz and 1.25kHz; 20 and 16 averages (acquisition weighted in z-direction); two-step phase cycling; TA 19:44min and 9:55min. Localization and spectral quality were evaluated qualitatively and quantitatively (i.e. linewidth, SNR) for MEGA-OFF and difference spectra. Simulations to find the optimum MEGA-LASER editing scheme were performed using GAMMA and results were used for creating suitable LCmodel basis sets. LCmodel processing was performed for both MEGA-OFF and subtraction spectra.

Results:

The weighted stack-of-spirals MEGA-LASER 3D-MRSI sequence provided accurate localization, high spectral quality, and editing efficiency (Fig. 2,3). In particular, the use of ReShMoCo ensured excellent data quality over a prolonged scan duration. (Fig. 2,3). The average SNR of GSH was 10±5 and 7±3 for the 8cc and 3cc resolution data. The confidence intervals for the local frequency deviation over the VOIs were ±8 Hz and temporal frequency drifts of 8±2 Hz and 15±3 Hz were measured and corrected online for the longer ~20min and the shorter ~10min scan, respectively.

Discussion/Conclusions:

Spiral accelerated MEGA-LASER 3D-MRSI with real-time ReShMoCo significantly improved editing efficiency and spectral *in vivo* quality in the presence of motion or scanner instabilities. Therefore, with ~10-20 min acquisition time, this sequence allows robust 3D mapping of GSH in the brain with possible application for neurological studies at 3T.

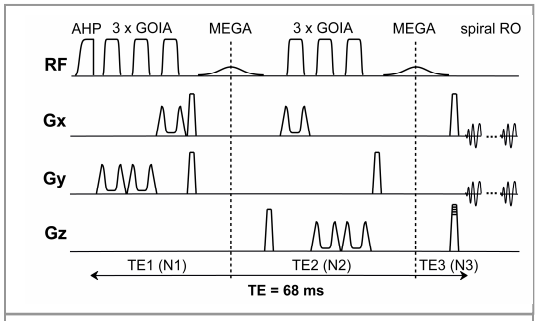

Fig. 1: Sequence schema of the MEGA-LASER sequence with 3D stack of spiral encoding. AHP excitation and three pairs of GOIA-W(16,4) selection pulses. Two frequency-selective Gauss pulses and spoiler gradients are used for MEGA editing. Preceding water suppression and volumetric navigator modules are not shown.

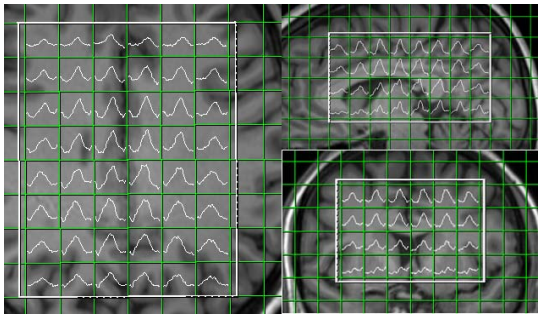

Fig. 2: Grid of spectra for the frequency range 2.8-3.1 ppm (containing the GSH peak) displayed in three orthogonal planes as overlay on anatomical reference data. The VOI (10×8×5.5cm³) is illustrated by a white rectangular box.

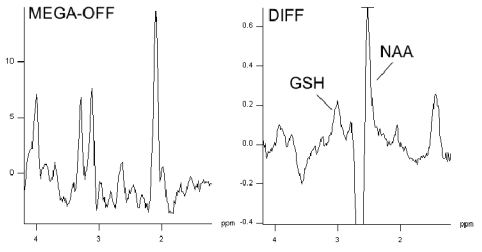

Fig. 3: Sample spectra from the same 8cc voxel for the spectrum obtained without MEGA editing (MEGA-OFF) and the difference spectrum (DIFF) obtained after subtraction of MEGA-ON and MEGA-OFF spectra. The position of GSH at 2.95ppm is indicated along with coedited NAA signal.

References:

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