Multi-pool CEST imaging of glioblastoma at 7 T

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Target audience: Researchers who are interested in the in-vivo CEST-contrast in human brain tumors

Purpose: Chemical Exchange Saturation Transfer (CEST) enables indirect imaging of metabolites *in vivo* via magnetization transfer between exchanging protons of functional groups and water protons. Several exchanging pools were reported in brain tissue, such as amides, amines but also Nuclear-Overhauser enhancements effects (NOE) of aliphatic protons [1-3]. To isolate these effects, Z-spectrum fitting algorithms were proposed and successfully applied in animal studies [4]. Here we propose a CEST sequence with high spectral sampling which allows for application of pixel-wise Z-spectrum fitting at 7 T. Our method allows multi-parametric CEST imaging by separation of direct water saturation, semi-solid magnetization transfer and different CEST-effects from each other. The method was applied in a glioblastoma patient where NOE-, amide-, amine-CEST maps as well as a semi-solid MT map could be generated.

Methods: In previous studies it was shown that small CEST-effects can be described by Lorentzian line shapes [4]. Thus we use a multi-Lorentzian fit for modeling of in-vivo Z-spectra. After including a baseline Z_{ini} the fit function has the form

$$Z = Z_{ini} - \sum_{i=1}^{5} \frac{A_i \cdot \Gamma_i^2/4}{\Gamma_i^2/4 + (\Delta\omega_{RF} - \delta\omega_i)}$$

yielding the amplitude A, the FWHM Γ and the frequency offset δω of each pool. For modeling an *in vivo* system we take 5 pools under consideration: direct water saturation, the CEST-effects of amides, amines, an aliphatic pool and the MT-effect. The pixel-wise fit was based on a Matlab built-in least-squares method (The MathWorks, Nattick, Massachuttes, USA). For each 16 parameters a start value, a lower and upper bound was chosen before fitting. After the fitting a nearest-neighbor interpolation was applied.

Spectral highly-resolved Z-spectra were obtained by a centric-reordered 2D-GRE-CEST sequence (FoV = 178x220, resolution = 1.71x1.72 mm², slice thickness = 5 mm, α = 10°) implemented on a MAGNETOM 7 T whole body scanner (Siemens, Erlangen, Germany) using a 24-channel head coil for reception. For saturation a pulse train with 150 gaussian pulses with the length t_p = 15 ms (DC = 60 %) and B_1 = 0.9 µT each was used. 65 adapted frequency offsets were acquired in the range from -300 to 300 ppm.

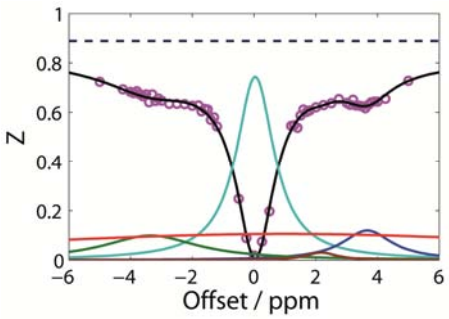

Figure 1: Z-spectrum of a patient within the tumor edge. Data points (purple circles) and fit (black line) are in good agreement. The isolated Lorentzians are identified as water (cyan), amide (blue), amines (brown), aliphatic NOE (green), MT (red).

Results: Figure 1 shows a fitted Z-spectrum within the tumor edge. The fit function (black) is in good agreement with the data points (purple circles). The Z-spectrum is decomposed in 5 Lorentzians (cyan: direct water saturation, blue: amides, brown: amines, green: aliphatic and red: MT) and a baseline (dashed black line). Figure 2 shows a gadolinium enhanced T_1-weighted co-registrated image together with the corresponding amplitude maps (A_i) of the different pools obtained by the pixel-wise fit. The T_1-weighted tumor enhancement is clearly hyperintense on A_{Amide} whereas MT and NOE signal intensity is isointense compared to the surrounding edema. Tumor necrosis is hypointense in all amplitude maps besides A_{Amine} which is in agreement with previous studies [1,4,5]. A central hyperintensity displays on A_{Amide} and less prominent also on A_{NOE}. Furthermore hot spots can be identified on A_{Amide} that do not display on the other amplitude maps. Contrast enhanced tumor satellite lesions can be identified on the T_1-weighted image that correspond with significant hyperintensities on A_{Amide} and hypointensities on A_{NOE} and A_{MT} compared to surrounding tissue.

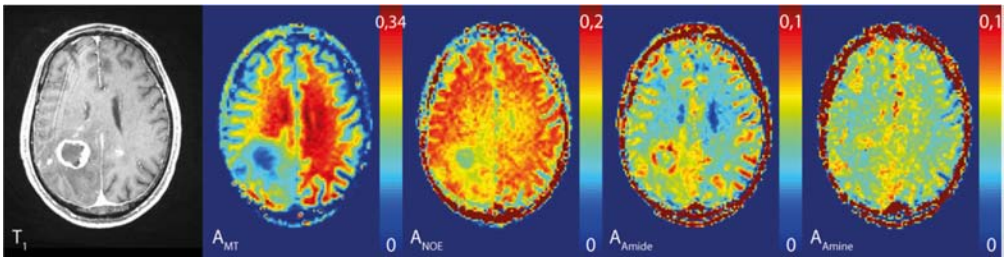

Figure 2: The Gd-enhanced T1-weighted image and the pixel-wise generated amplitude maps of the MT, NOE, amides and amines (left to right) are shown. The respective color map is displayed on the right side of each map.

Discussion: The proposed CEST sequence and evaluation method allowed separate detection of NOE-, amide- and amine-mediated CEST effects and MT simultaneously extending previous approaches [3,4]. Especially amide and NOE mapping provided distinct insights into glioblastoma substructure. The fast exchanging amines show no significant contrast in A_{Amine}, which might be due to the low labeling generated by the minor B_1.

Conclusion: Usage of highly-resolved Z-spectra and evaluation by a Lorentzian line shape model allows multi-parametric CEST imaging *in vivo*. The outcome of the fit is ready for continuative relaxation corrections[6,7]. The amplitude maps form a spectral specific CEST-MRI contrast providing information about healthy and pathologic tissue on a molecular level.

References:

1. Jones, C. et al. Magn Reson Med. 2006;56(3):585-592
2. Jin, T. et al. NeuroImage. 2012;59(2):1218-1227
3. Jones, C. et al. NeuroImage. 2013;77(15):114-124
4. Desmond, K. et al. Magn Reson Med. 2013; doi: 10.1002/mrm.24822
5. Kurki, T. et al. Magn Reson Imaging. 1995;13:501–511
6. Zaiss, M. et al. Jour Magn Reson. 2011;211(2):149-155
7. Zaiss, M. et al. NBM. 2013; doi: 10.1002/nbm.3054