Metabolic specificity analysis of CEST techniques at high and ultra-high magnetic fields

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Introduction: Chemical Exchange Saturation Transfer (CEST) imaging enhances the sensitivity of metabolites by detecting them via the rapid chemical exchange between a group of labile protons and bulk water, hence allowing their spatial distribution mapping. Advantages of using high and ultra-high field strengths for CEST include increased SNR, longer T_1-relaxation times for more efficient saturation periods and larger chemical shift dispersion. Yet, an important challenge using CEST methods is the selectivity towards the metabolite of interest, due to overlapping resonance peaks. In this study, we investigated CEST's selectivity by parameter optimization for various metabolites of interest and at two field strengths B_0.

Methods: CEST-PRESS experiments were performed on 17.2 T and 7 T Bruker BioSpec preclinical scanners using four phantoms with the following solutions: i. 40 mM lactate, ii. 20 mM glutamate, iii. 20 mM glucose and iv. a mix of i.-iii. at identical concentrations. All samples had pH=7 and were scanned at room temperature. In addition, glu-and glucoCEST-experiments with PRESS and RARE were performed on a cherry tomato (*S. lycopersicum*).

Results and Discussion: Using parameter optimization, the CEST-contrast can be tuned to the metabolite of interest, i.e. its contribution to the asymmetric Magnetization Transfer Ratio (aMTR) can be maximized. As shown by the *in vitro* Z-spectra obtained at 17.2 T, it is possible to maximize the contribution of glutamate to aMTR at the saturation chemical shift of 3 ppm (Fig 1A) while reducing the glucose contribution to 26% using optimal parameters. In comparison, the specificity of aMTR decreases at 7 T presenting a 32% glucose contribution and a lower resolution of the individual metabolites (Fig 1B). At both magnetic fields, there was no significant lactate contribution to the gluCEST signal when saturating at 3 ppm. By changing the B_1-field intensity used for saturation, a shift in the maximum aMTR contrast from the glucose chemical shift (1.2 ppm) to the glutamate chemical shift (3 ppm) was observed (Fig 1C) on a voxel in the tomato outer pericarp. A stark difference between the gluco- and gluCEST images can be readily observed (Fig. 1D) stemming, most likely, from the different distributions of glutamate and glucose in the tomato. As expected, lower values were observed for glucoCEST contrast compared to gluCEST.

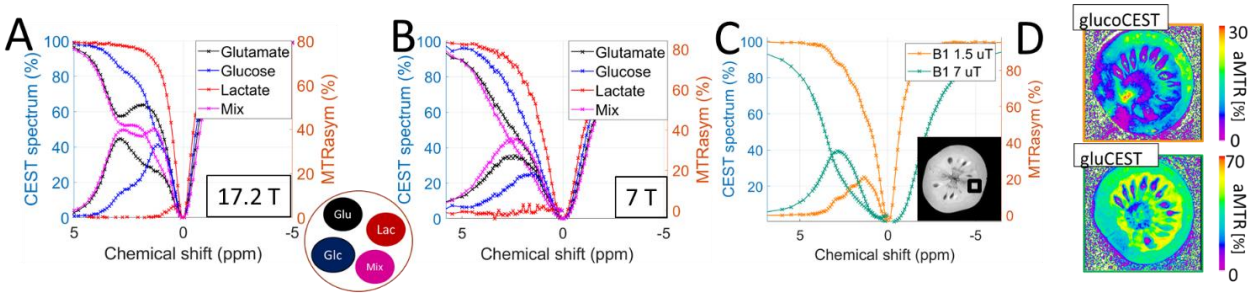

Fig. 1: Z-spectra acquired on the four solutions (see scheme) at A) 17.2 T and B) 7 T using a B_1-field strength of 7 µT. C) Z-spectra of a tomato pericarp at 17.2 T at B_1-field strengths of 1.5 µT (glucoCEST) and 7 µT (gluCEST). D) glucoCEST and gluCEST contrast images acquired with a CEST-RARE sequence (resolution 156µm x 156µm x 1mm; CEST T_{sat} 1.7s).

Conclusion: By carefully optimizing the CEST parameters, we can partially select for a compound of interest, i.e. glutamate or glucose. However, more sophisticated acquisition strategies and/or modelling approaches are necessary for the complete disentanglement of the different metabolite contributions (e.g. [1-2]).

References: [1] Yadav et al. Mag. Reson. Med. (2012) [2] Friedman et al. J. Am. Chem. Soc. (2010)