

Comparison of tissues characterized by CEST spectra at 7T

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Introduction: Chemical exchange saturation transfer (CEST) provides a wealth of potential endogenous biomarkers, including metrics related to cell density and rates of proton exchange (which are correlated with pH). The shapes of CEST spectra, acquired by measuring the influence of a saturation pulse applied over a range of off-resonance frequencies, are sensitive to the environment of exchanging protons such as those in amide and hydroxyl groups, as well as the presence of lipids [1]. CEST metrics typically involve measuring the amplitude of "peaks" in the CEST spectrum, or ratios between the amplitude of a peak and the corresponding negative offset frequency (proton transfer ratio, PTR). When one is interested in determining the changes in CEST spectra due to pathology or treatment, it is essential to first have a reliable baseline. Several properties of the peaks are of interest in addition to the amplitude, including the frequency offset and width. We present CEST spectra in 6 regions: white matter, grey matter, muscle (before and after sacrifice), bladder, and tumour (Lewis lung carcinoma, LLC).

Method: Animals (rats for neural tissue and mice for all other regions) were imaged on a 7T preclinical MRI (Bruker Biospin). The CEST imaging sequence consisted of a single rectangular off-resonance RF pulse, 490 ms in duration, followed by a single-slice spoiled gradient-echo (FLASH) readout with TR/TE = 500/3.1 ms at a resolution of 0.5x0.5x2mm. The saturation pulse amplitude was 0.57 μ T and the offset frequency ranged between -2000 and 2000 Hz (6.71 ppm) in increments of 50 Hz and with 5 reference images at 200000 Hz interspersed throughout the acquisition to allow retrospective correction for signal drift. The water peak was shifted to 0 Hz offset on a voxel-wise basis to correct for B₀ inhomogeneities across the image as well as shifts due to susceptibility differences between tissues. Fast spin-echo images with 8 echoes per TR were acquired at a resolution of 0.1x0.1x1mm with 5 slices as a reference to aid in definition of ROIs. Parameter maps were generated by using a peak-fitting algorithm [2] which decomposed the CEST lineshape into the sum of four Lorentzian functions. SNR was above 100 in all ROIs.

Results and Discussion: We present CEST spectra and parameter maps in several anatomical regions. Notable is the large amide peak in the LLC tumour as compared to nearby muscle (Figure 1.b), which is consistent with experiments which measured the amide proton transfer ratio (APTR) in tumours[3-5]. However, there is a large mobile lipid peak [6] existing at approximately -1000 Hz (Figure 1.a), which complicates the usage of APTR as a metric of amide proton concentration or exchange rate. In fact, it is differences in the extent of lipid peak that mainly distinguish differences between CEST spectra of grey and white matter (Figure 1.a).

Figure 1. CEST spectra in four tissues, emphasizing the amide and mobile lipid peak.

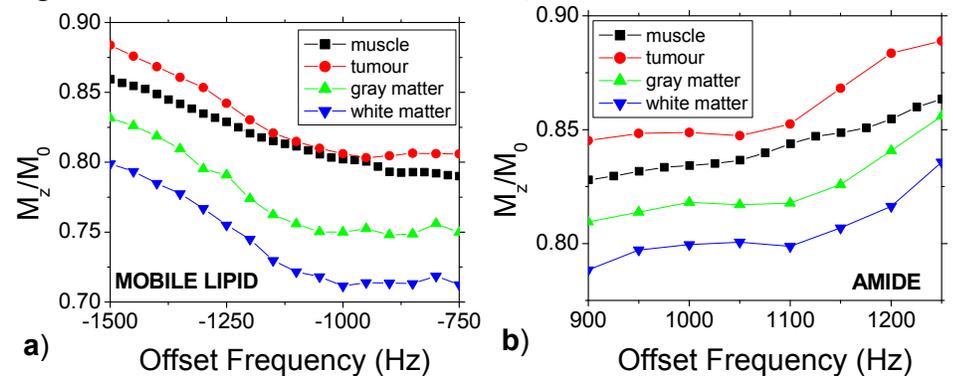


Figure 2.

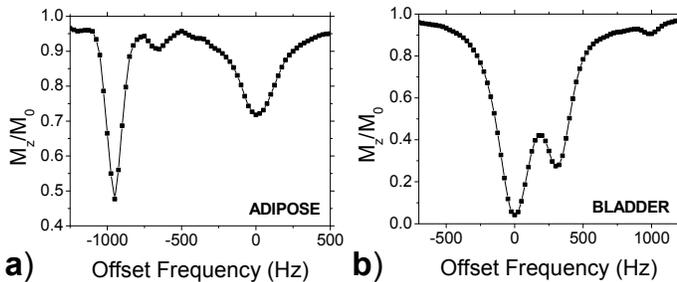
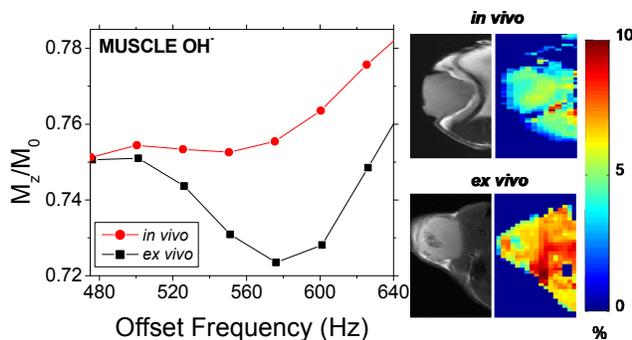


Figure 3.



Regions which have very high concentration of fat will also confound attempts to adjust the spectra for B₀ inhomogeneities. As evidenced in Figure 2.a, if spectra were shifted to place the minima of the spectrum at 0 Hz then this procedure would incorrectly center the spectrum on the lipid peak. As a point of interest we have included the CEST spectrum of urine within the bladder, which has a strong peak around 400 Hz due to the high concentration of urea which has -NH₂ groups contributing to CEST (Figure 2.b). There is an additional peak around 1050 Hz which we speculate is indicative of proteinuria since the animals were tumour-bearing [7]. In Figure 3 we note the large OH- effect in the tissue after sacrifice which was not present in-vivo, which we attribute to lactic acidosis. The broad MT effect is also present in all spectra, and visible in the fact that the spectra do not reach the maximum signal well beyond where the direct effect ends. It also causes an increase in the offset of the FWHM of the direct effect.

Conclusion: There are a wide range of features visible on the CEST spectra that can provide a valuable platform for further optimization of CEST experiments and exploration of CEST-related biomarkers.

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