# Isolating CEST and MT in the Human Calf Muscle at 7T

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**TARGET AUDIENCE:** Those interested in chemical exchange saturation transfer (CEST) and magnetization transfer (MT) methodology for studying muscle biochemistry, metabolism and function.

**PURPOSE:** CEST is a molecular imaging technique that allows the indirect detection of protons associated with chemically exchangeable functional groups such as amines ($NH_2$), amides (NH) and hydroxyls (OH). Alterations in the kinetics of such chemical exchanges in skeletal muscle have been associated with several common diseases such as insulin resistance, myopathies, and type 2 diabetes[1]. However, it is often very challenging to isolate genuine CEST contrast from MT effects that can demonstrate asymmetries with respect to the main water resonance, and can affect quantification of CEST measurements. We have recently developed a framework under which such overlapping signatures can be separated with the use of a simultaneous two-frequency RF irradiation method that enables the removal of MT asymmetries[2], resulting in uniform MT (uMT) effects. In this work we demonstrate the in vivo application of this uMT CEST method for imaging the human calf muscle at 7T and compare it with conventional single-frequency CEST.

**METHODS:** We imaged three healthy male volunteers. We used a two dimensional GRE imaging sequence (flip angle = 10°, TR = 24s, TE = 3.5ms, FOV = 160 x 160 $mm^2$, matrix size = 196 x 196 and slice thickness = 5 mm). The presaturation module consisted of a train of 10 Gaussian (in the conventional CEST), or a train of 10 cosine-modulated Gaussian pulses (in the uMT CEST), each 100 ms long. We varied the offset frequencies of the presaturation pulses from -3600 Hz to 3600 Hz in 100 Hz steps. Their nominal flip angles were 1800° ($B_{1,rms}$ = 0.53 μT) and 3600° ($B_{1,rms}$ = 0.76 μT) for the conventional and uMT CEST respectively, while we modulated the cosine pulse at a frequency of 1.8 kHz. For the conventional CEST experiment, we obtained $B_0$ maps using the WASSR method[3] (presaturation using two 100 ms-long 180° Gaussian pulses, with the offset frequency varying from -720 Hz to 720 Hz in steps of 20 Hz). For the uMT CEST experiments, we obtained $B_0$ maps from the middle positions of the two minima at ±1800 Hz in the Z spectra.

**RESULTS:** An anatomical cross-section of the calf muscle of one volunteer can be seen in Fig.1a. Conventional CEST maps before and after $B_0$ correction are shown in Fig.1b-c, while uMT CEST maps before and after $B_0$ are shown in Fig1.d-e. MT asymmetry plots in segmentations of the soleus (S), and the gastrocnemius medial (GM) muscles are shown in Fig.2. Asymmetry in the skeletal muscle can result from multiple exchangeable sites such as glycol-CEST (0.75-1.25ppm), Cr-CEST (1.8-2.0ppm), PCr-CEST (~2.5ppm) and APT-CEST (~3.5ppm).

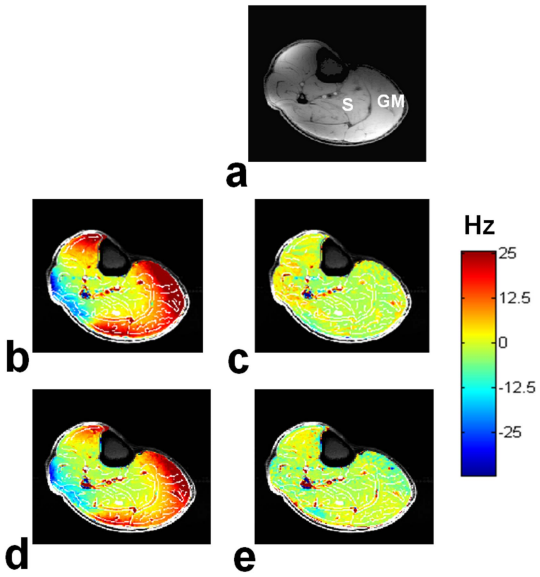


**Fig. 1. CEST maps in human calf muscle before and after $B_0$ correction (integral 0-2 ppm range.) a) Anatomical cross-section, where the soleus (S) and the gastrocnemius medial (GM) muscles are identified. b-c) conventional CEST contrast before/after WASSR $B_0$ correction. d-e) uMT CEST contrast before/after $B_0$ correction.**

**DISCUSSION:** MT asymmetries at large frequency offsets (4-6ppm) were close to zero in the uMT CEST method in all healthy volunteers, while conventional CEST was less successful in removing those asymmetries, as it can be seen in Fig.2, which suggests that uMT CEST has the potential of providing more accurate CEST measurements at smaller frequency offsets.

**CONCLUSION:** The results of this work suggest that uMT can become an important tool for studying muscle chemical exchange processes that are related to several common diseases such as diabetes, peripheral vascular disease, and neuromuscular disorders, more accurately compared to existing CEST methods.

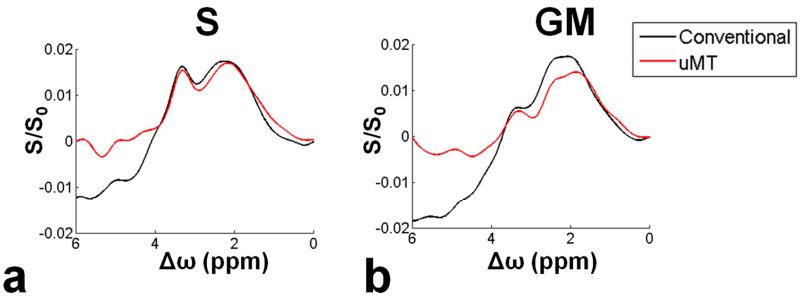


**Fig. 2. MT asymmetry plots with conventional and uMT CEST, a) in the S and b) in the GM muscles. MT asymmetries are close to zero when using the uMT CEST method.**

**REFERENCES:** **1**. Nikoulina SE, Ciaraldi TP, Mudaliar S, *et al*. Potential role of glycogen synthase kinase-3 in skeletal muscle insulin resistance in type 2 diabetes. Diabetes 2000;49(2): 263-271. **2**. Lee JS, Regatte RR, Jerschow A. Isolating chemical exchange saturation transfer contrast from magnetization transfer asymmetry under two-frequency rf irradiation. J. Magn. Reson. 2012;215:56-63. **3**. Kim M, Gillen J, Landman BA, Zhou J, van Zijl PCM. Water saturation shift referencing (WASSR) for chemical exchange saturation transfer (CEST) experiments. Magn. Reson. Med. 2009;61(6):1441-1450.