In vivo reproducibility of CEST-based pH maps in resting healthy leg muscles at 3T

Valentin Henriet[1], Pierre-Yves Baudin[1], Benjamin Marty[1], Marc Lapert[2], Harmen Reyngoudt1[1]

[1]*Institute of Myology, Neuromuscular Investigation Center, NMR Laboratory, Paris, France*
[2]*Siemens Healthcare SAS, Courbevoie, France*

INTRODUCTION:

Intramuscular pH has demonstrated to be a valuable biomarker in neuromuscular diseases, with ^{1}H Magnetic Resonance Spectroscopy (MRS) as the standard approach to determine pH *in vivo* [1]. MRS-based pH is highly sensitive and reproducible, but unlocalized and without spatial information in case of single voxel approaches or time consuming in case of MRS imaging applications. However, as creatine-CEST is an imaging modality that is inherently sensitive to pH, it can be used to obtain pH maps noninvasively, with a spatial resolution close to quantitative MRI-based maps water T2 and water T1 in muscle [2,3]. Here, we report results on tCr-CEST-based pH maps at 3T in leg muscles of healthy volunteers.

METHODS:

Experiments were performed using a 3T clinical scanner Magnetom Prisma^{FIT} (Siemens Healthineers, Erlangen, Germany) and a 15-channel transceiver RF coil.

A pulsed CEST-FLASH sequence was acquired at 41 frequency offsets regularly spaced between -4ppm and 4ppm, centered on the water frequency. A 600ms long saturation pulse train composed by a series of 99ms rectangular saturation pulses with a 1ms inter-pulse delay (duty cycle=99%) was run twice, with two different B1 values: 1.0µT and 1.5µT. The parameters of the FLASH readout were: matrix size = 128x128, FoV = 180mm², slice thickness = 9mm, TR = 7.4ms, TE = 3.9ms, FA = 10°, bandwidth = 520Hz, 1 excitation. WASAB1 images were collected for B0 and B1 corrections and were reconstructed with an open-source Matlab algorithm (Mathworks,Natick, USA) [4,5]. All other steps were carried out with in-house Python code, including z-spectrum denoising based on Singular Value Decomposition (7 components were kept with soft thresholding). The CEST-based pH was calculated based on the AREXratio method (y= -0.37x + 3.33, R^2 = 0.99).

As a gold standard for pH assessment, a Point Resolved Spectroscopy (PRESS) sequence was acquired in the *tibialis anterior* (TA), *soleus* (SOL) and *gastrocnemius medialis* (GM) muscles with the following parameters: voxel size = 20x20x20mm, TR = 3000ms, TE = 30ms, 64 excitations, spectral bandwidth of 4kHz, 2048 data points [1]. MRS data were processed using jMRUI. The CEST-based pH were extracted in the same region of interest as for ^{1}H MRS-based pH. One healthy volunteer (27.0 years; F) was scanned at rest three times to assess reproducibility. Then, we looked at a cohort of 10 healthy volunteers at rest (39.0±8.4 years; range 22.6-61.6; 6/5 M/F).

RESULTS:

Concerning the three experiments done within the same healthy volunteer, denoising led to a strong decrease in the CEST-based pH standard variation by a factor 6 to 10 depending on the muscle (Fig 1.**A.**). Inter-scan CV% for CEST-based pH were ≤0.5% and were close to CV% values for ^{1}H MRS-based pH. CEST-based pH did show a strong bias compared to ^{1}H MRS-based pH (Fig. 1.**A.** and 1.**B.**). Between the different healthy volunteers, inter-subject CV% values for CEST-based pH were, on average, 1.3% and were slightly higher than the MRS-based pH CV% of 0.6 (across all muscles). pH values did not correlate between both quantification methods (*P*=0.22 for Pearson correlation) in the pH range of interest (Fig 2).

DISCUSSION AND CONCLUSION:

We demonstrated preliminary results of CEST-based pH mapping in resting leg muscles at 3T. Future steps will include to further investigate (1) the pH bias between the different quantification methods; (2) the robustness to B_1^+ heterogeneities and water T_2 and water T_1 muscle alterations, (3) an extended pH range by measurements in healthy muscle (after exercise, pH<6.90) and pathological muscle (neuromuscular diseases, pH>7.10).

A.

	MRS ^{1}H		CEST RAW DATA		CEST DENOISED DATA	
	pH	CV%	pH	CV%	pH	CV%
GM	7.01	0.4%	8.33 ± 0.30	0.7%	8.37 ± 0.05	0.5%
SOL	7.00	0.3%	8.28 ± 0.61	0.4%	8.35 ± 0.06	0.3%
TA	7.01	0.3%	8.34 ± 0.86	1.7%	8.45 ± 0.09	0.5%

B.

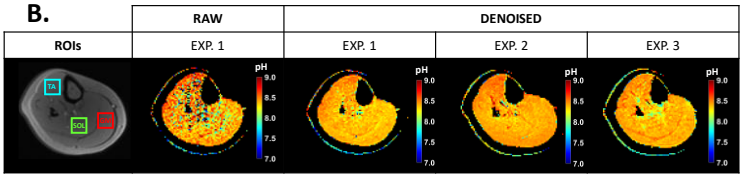

Fig 1. **A.** ^{1}H MRS-based pH and CEST-based pH before and after denoising, in GM, SOL and TA over 3 experiments. **B.** Corresponding pH maps.

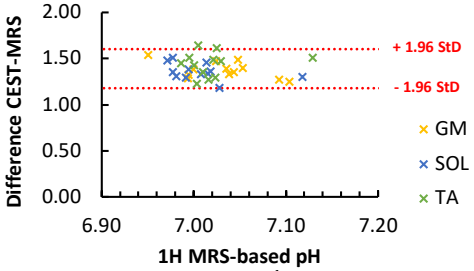

Fig 2. Bland-Altman plot with ^{1}H MRS-based pH and CEST-based pH measured in ten healthy volunteers.

ACKNOWLEDGMENTS:

This project received funding from the Agence Nationale de la Recherche (ANR), under agreement n°ANR-22-CE19-0019.

REFERENCES:

[1] Reyngoudt et al. NMR Biomed. 2018;31:e3839. [2] Rerich et al. NMR Biomed. 2011;28:1402-12. [3] Marty et al. Radiology 2021;300:652-60. [4] Schuenke et al. MRM 2017;77:571–580. [5] Zaiss et al. NMR Biomed.2014;27: 240–252