Simultaneous creatine and phosphocreatine mapping of skeletal muscle by CEST MRI at 3T

Licheng Ju[1,2], Kexin Wang[1,3], Michael Schär[2], Su Xu[4], Joshua Rogers[4], Dan Zhu[1,2], Qin Qin[1,2], Robert Weiss[2,5], Jiadi Xu[1,2]

1. *F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, MD, USA*
2. *Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University, Baltimore, MD, USA*
3. *Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD, USA*
4. *Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland, Baltimore, MD, USA.*
5. *Division of Cardiology, Department of Medicine, Johns Hopkins University, Baltimore, MD, USA*

INTRODUCTION:

Phosphocreatine (PCr) and Creatine (Cr) are essential metabolites in muscle cells (1,2). This investigation is to evaluate the feasibility of simultaneous mapping of PCr and Cr at 3T by PLOF CEST method.

METHODS:

Five adult wild-type mice were scanned on a 3T Bruker Biospec system equipped with a 40 mm quadrature volume resonator for both transmission and reception. A Philips Ingenia Elition 3.0 T and a dStream Flex M Coil were used for CEST human experiments, which include five healthy subjects. The quantification of PCr in the calf muscle was achieved using pulse-acquire ^{31}P MRS spectra obtained through a single-pulse sequence.

RESULTS:

A comparison of the Z-spectra in mouse hindlimb before and after euthanasia indicated that CrCEST is a slow-exchanging process with exchange rate between 45.5 s^{-1} to 150.7 s^{-1} in muscle. This allowed us to simultaneously extract and assign PCr/CrCEST signals at 3T using the PLOF method. We determined optimal B_1 values ranging from 0.3-0.6 μT for CrCEST and 0.3-1.2 μT for PCrCEST in muscle. For the study on human calf muscle, we determined an optimum saturation time of 2 seconds for both PCr/CrCEST (B_1 =0.6 μT, Fig. 1D). The PCr/CrCEST using 3D EPI were found to be comparable to those obtained using TSE. (3D EPI/TSE PCr: (2.6 ± 0.3) % / (2.3 ± 0.1) %; Cr: (1.3 ± 0.1) % / (1.4 ± 0.07) %, Fig. 1E). The PCr to ATP ratio was determined to be 4.83 (n=3) from the ^{31}P MRS data, resulting in an average 39.58 mM PCr concentration in human calf muscle, which then is used for calibrating the PCrCEST concentration map.

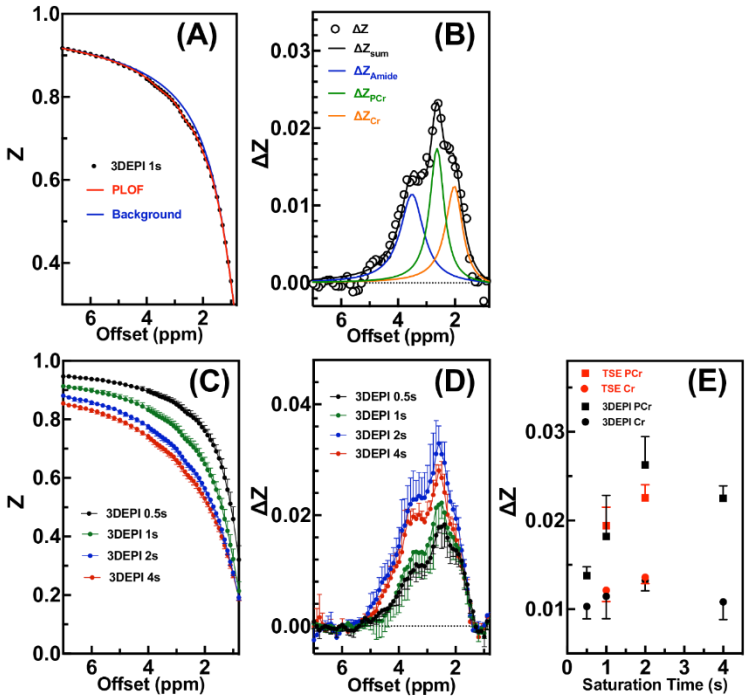

Figure 1 Illustration of PLOF fitting on human calf muscle, and a comparison of Z and ΔZ spectra acquired by 3D EPI

DISCUSSION:

The breakdown of creatine phosphate into creatine and inorganic phosphate, which is catalyzed by creatine phosphatase, occurs after death (1,3). Therefore, the PCr to Cr conversion during postmortem provides a suitable method for validating PCr and Cr CEST at 3T (4). Due to the slow-exchanging rate of CrCEST, the current study provides a three-peak PLOF method to simultaneously yield high-resolution amide, PCr and Cr maps at 3T. The extraction of Cr and PCr CEST signals also provides an opportunity to optimize the acquisition scheme for in vivo Cr and PCr CEST applications at 3T. Given the potential for PCrCEST and protein ArgCEST contaminations at 2 ppm, we refrained from conducting Cr concentration map calibration in this work.

CONCLUSION:

Our study unveiled a prominent CrCEST peak at 2.0 ppm in the mouse hindlimb post-euthanasia at 3T, indicating that CrCEST is characterized as a slow-exchanging process within muscle. Furthermore, we used the proposed PLOF method on human muscle at 3T to obtain high-resolution maps of amide, PCr, and Cr simultaneously. Comparison of 3D EPI and TSE approaches indicated that the 3D EPI method provided comparable PCr/Cr CEST maps in muscle for the two methods. These findings suggest that PCr/CrCEST has the potential to be a cost-effective and widely available method for measuring PCr/Cr in muscle at 3T, which could assist in the diagnosis of related diseases.

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REFERENCES:

1. Wyss M, et al. Physiol Rev 2000; 80:1107.
2. Andres RH, et al. Brain Res Bull 2008; 76:329-343.
3. Chung JJ, et al. Magn Reson Med 2019; 81:3476-3487.
4. Zu Z, et al. NMR Biomed 2021; 34:e4437.