Assessment of Chemical exchange saturation transfer effects in Myocardial Tissue at 7T

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Background:

It is important to distinguish non-infarcted viable myocardial tissue from infarcted tissue in order to determine preoperatively the benefit of a revascularization procedure. Dysfunctional, but viable myocardium has potential for contractile recovery after reperfusion. There are several non-invasive methods for assessing myocardial ischemia and viability including positron emission tomography, single-photon-emission computed tomography, dobutamine stress echocardiography, and cardiovascular magnetic resonance imaging (MRI). Developments over the past two decades have established MRI and MR spectroscopy (MRS) as powerful techniques for investigation of cardiac dynamics, morphology, and bioenergetics. Using ^{31}Phosphorus MRS, myocardial creatine kinase (CK) kinetics, high energy phosphate compounds are detected. Magnetization transfer (MT) imaging studies have shown less MT ratio in the infarcted region compared to non-infarcted region[1]. We hypothesize that chemical exchange saturation transfer (CEST) contrast arising from exchangeable protons (-NH, -NH2 and –OH) from different metabolites present in the myocardial tissue may vary between normal and infarcted regions and cardiac CEST MRI may be a viable new methodology for imaging of such pathology. In the current study, we used a combination of an experimental swine model of chronic left ventricular myocardial infarction and CEST imaging technique to demonstrate the feasibility of detecting infarcted and non-infarcted regions.

Materials and Methods:

The study was conducted under an approved Institutional Animal Care and Use Committee protocol at the University of Pennsylvania. Swine underwent a surgical procedure tethering the circumflex artery. Following sacrifice, at 4 weeks, tissue samples from chronic, left ventricular myocardial infarction swine heart tissue samples (n=3) were obtained and kept in normal saline. Infarcted and non-infarcted (less or negligible infarction) regions were identified on tissue samples. All the imaging experiments were performed on a 7T Siemens whole-body clinical scanner (Siemens Medical Solutions, Malvern, PA) with a custom built solenoidal coil. CEST images were acquired with a flash readout, using a Hanning windowed saturation pulse train of 10 pulses. Z-spectra from in-vitro creatine (Cr, 10mM) phantoms as well as the tissue samples (5 hours post sacrifice) were acquired at peak B1 of 200Hz and 1 second saturation pulse duration over a ± 4.5ppm range relative to the bulk water resonance frequency in steps of 0.25ppm, using the following parameters: slice thickness = 5 mm, GRE flip angle = 10°, GRE readout TR = 6.5 ms, TE = 3.2 ms, field of view = 100 × 100 mm^2, matrix size = 192 × 192 mm^2, and one saturation pulse and 64 acquired segments at every 12 s. We also acquired B0 and B1 maps. The total imaging time was about 15 min. CEST images were first corrected for the B0 to generate Z-spectra and CEST maps, which were further corrected for B1 inhomogeneity using the method described previously[2]. After defining the CEST asymmetry peak both in infarcted and non-infarcted regions, CEST maps were generated for the frequency offset of ±2.0ppm using the equation- ***CEST contrast=100%*[Mneg – Mpos] / Mneg***

where Mpos, Mneg are the acquired MR signals at +2.0ppm, -2.0ppm respectively. To minimize the contribution from direct saturation and magnetization transfer effect, we used ***Mneg*** instead of ***M0*** for normalization.

Results and Discussion:

CEST effect centered at 2ppm as well as asymmetry peak of Cr phantom and myocardial tissues at 7T were similar. Figure 1 shows the asymmetry plot from creatine, infarcted and non-infarcted region of the tissue sample as shown in figure 2A. In Cr phantom asymmetry peak was centered at ~2ppm and was narrower compared to myocardial tissue regions. The asymmetry curves both in infarcted and non-infarcted region show a broad CEST peak centered at ~2.0ppm. The broader CEST effect in myocardial tissue may be due to contribution from other metabolites and macromolecules; a detailed investigation is in progress. Figure 2 shows the anatomical image of tissue sample (A) and the corresponding CEST map (B) along with B0 and B1 map (C). B0 and B1 maps are quite homogenous and used to correct the CEST map. Two regions were detected on tissue sample as shown in figure 2A, these regions are distinguished as infarcted and non-infarcted regions. CEST map showed a clear difference in the CEST contrast between infarcted and surrounding non-infarcted zone. Reported metabolites present in myocardium in vivo are-creatine (Cr, 17.5mM), phosphocreatine (PCr, 10mM) and adenosine tri-phosphate (ATP, 5.5mM) and glutamate (Glu, 6.2mM). All these metabolites showed a significant CEST effect due to the presence of exchangeable amine protons (-NH2) with asymmetry peak detected at ~1.8ppm, ~2.5ppm, ~2ppm and ~3ppm respectively. It has been observed that the Cr, PCr and ATP –NH2 protons are in the slow exchange regime, while glu –NH2 protons are in the intermediate exchange regime. During infarction significantly decreased concentration of all these metabolites has been reported[3,4] which may be responsible for decreased CEST contrast from infarcted region. Further decrease in pH (~0-8-1 unit pH) has been shown in infarcted region, and it was observed that low pH result in decreased CEST contrast from Cr, PCr and ATP while glu showed higher CEST effect at low pH. Because glu concentration decreases during infraction so increased CEST effect due to low pH may cancel out and may contribute negligible to the observed CEST effect. Based on our initial observation, we suggest that the low CEST contrast in infarcted myocardial tissue is due to decreased concentration from Cr and low pH. We are in the process of implementing the heart CEST technique on left ventricular infarcted swine model in-vivo at 3T. Once this technique implemented successfully on the swine model, it is relatively straightforward to incorporate it in human heart imaging, to investigate the diagnostic potential of this method in staging the myocardial infarction and tissue in the border zone of the infarction.

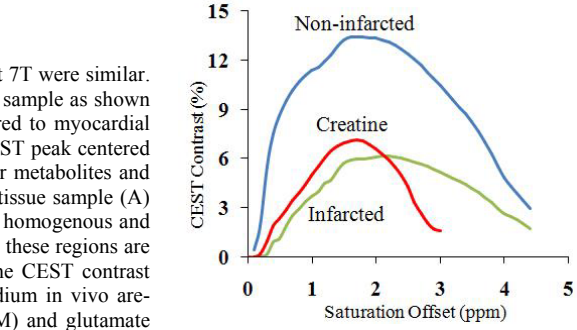

Figure 1. shows the Z-spectra asymmetry curves from infarcted (region 1) and non-infarcted (region 4) areas as shown in figure 2A and from creatine. All asymmetry curves peak at ~2.0ppm. Non-infarcted region shows higher CEST contrast than infarcted region.

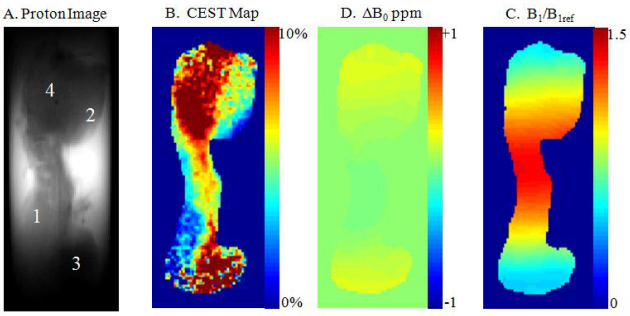

Figure 2. A. shows the anatomical image of tissue sample on which two regions are defined i.e. infarcted (1&2) and non-infarcted regions (3&4). B. The corresponding CEST map shows higher CEST effect in the non-infarcted zone compared to the infarcted region. Figures C and D are showing the B0 and B1 ratio maps, which are used to correct the CEST contrast.

References:

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