Early Diagnosis of Myocardial Infarction Areas on Rat Models using 2D ^{31}P CSI

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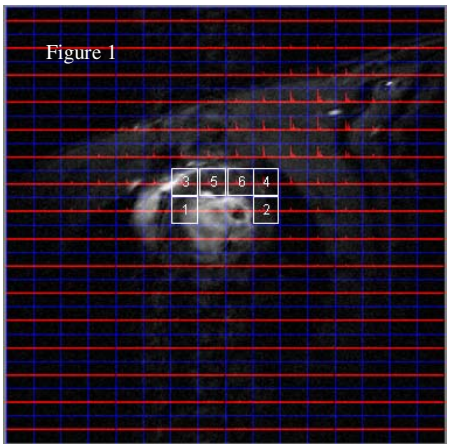
Introduction: Early diagnosis of myocardial areas at risk during acute myocardial infarction is important for both basic sciences and clinical applications (1, 2). Noninvasive cardiac MRI techniques, such as cine, for risk area assessment can generate high spatial and temporal resolution (3). However, energetic metabolism information in myocardium, which is important for early evaluation of myocardial viability, cannot be obtained using conventional cardiac MRI techniques. ^{31}P chemical shift imaging (CSI) techniques have been used for myocardial viability assessment both on humans and animals by measuring the relative concentrations of endogenous high energy phosphates (HEPs), such as phosphocreatine (PCr) and adenosine triphosphate (ATP) (4, 5). Previous multidimensional ^{31}P CSI studies on myocardial infarcts of rats and humans demonstrated that the PCr-to-ATP ratio is significantly lower in the risk area than that of the normal myocardial region (5, 6). The purpose of this study is to exploit sensitivity-enhanced ^{31}P CSI techniques for early diagnosis of risk areas during acute myocardial infarction on rat models.

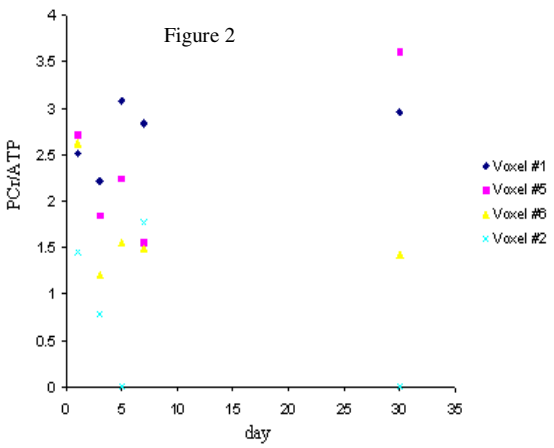
Methods: Animal preparation was performed in accordance with the animal care and use committee of the National Institutes of Health. Three Sprague Dawley rats with an average weight of 150 g were purchased from Harlan, Inc. Myocardial infarction in one of the rats was induced by completely occluding the left anterior descending artery (LAD). During the in vivo imaging experiments, the rats were anesthetized using 0.5% - 2.0% inhaled isoflurane in a 95% oxygen and 5% carbon dioxide gas mixture. The rats were restrained to the temperature controlled animal bed using paper tapes with the nose fitted into the nose cone. The heart and respiration rates were monitored using an ECG system (SA Instruments, Stony Brook, NY, USA) by pinning the ECG electrodes into one front paws and one hind paw and by placing the pneumatic pillow at the animal's lower abnormal position, respectively. The ECG signal was used to gate the MRI data acquisition. 0.5 mL of 9.6 nM SPIO dH_20 solution was injected intravenously to the treated rat on day 30 for contrast enhanced MRI.

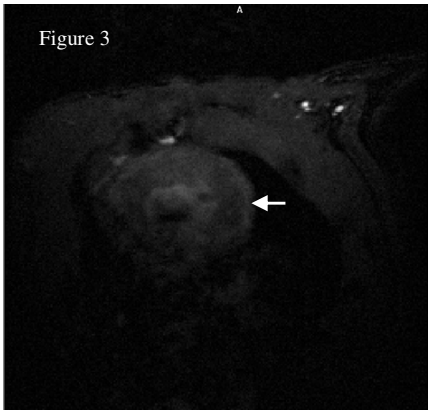
^{1}H anatomical and cine functional images were collected from both the control and the treated rats over a period of 30 days on a Bruker BioSpin 9.4 T horizontal bore (30 cm ID) magnet equipped with an actively shielded 116 mm gradient coil (gradient strength = 170 kHz/cm, rise time = 120 μs) and Paravision 4.0 console software. The operating ^{1}H and ^{31}P resonance frequencies were 400.32 MHz and 162.05 MHz, respectively. A ^{1}H-^{31}P transmit/receive double resonance surface coil (ID = 3 cm, maximum peak power = 50 W, maximum average power = 5 W) from Bruker was used for in vivo ^{1}H and ^{31}P CSI imaging. ECG-triggered cine images were collected using the FLASH pulse sequence from Bruker (imaging parameter: TE = 2.62 ms, TR = 176.74 ms, FOV = 40 mm, number of averages = 6, number of frames = 16, matrix size = 256 x 256, slice thickness = 1 mm, hermite excitation pulse (pulse length = 1 ms, bandwidth = 5400 Hz, flip angle = 30°, RF power = 16.5 dB), number of dummy scans = 10).

A single slice ^{31}P CSI was acquired in conjunction with the above ^{1}H imaging without ECG gating from the rat hearts (slice selective sech pulse (pulse length = 2 ms, R-factor = 20, bandwidth = 10 kHz, B_1(max) = 1.2 kHz, size of shape = 1000 points), slice thickness = 13 mm, FOV = 40 x 40 mm^2, Matrix size = 8 x 8, recon size = 16 x 16, spectral width = 8 kHz, central frequency offset = 1.5 kHz, TR = 260 ms, number of scans = 5000, type of signal = FID, experimental mode = weighted, number of dummy scan = 10, scan time = 21m42s600ms). The 2D ^{31}P CSI raw data were processed and analyzed using Topspin 1.5 in ParaVision 4.0.

Results: For the control rat heart, the PCr-to-ATP ratios for all the labeled voxels (Fig. 1) over the time course are above 2. For the LAD occluded rat heart, the myocardium energetic state varies by voxel locations. In particular, the PCr-to-ATP ratios for the voxels within and close to the occluded area decreased significantly over the time course, whereas the voxel far from the lesion area showed viable energetic state over the time course (Fig. 2). In the contrast enhanced image (Figs. 3), the PCr-to-ATP ratio was normal for the voxel far from the lesion area (pointed by arrow), decreased in voxels close to the lesion area, and dropped to zero in the center of the lesion area.







Discussion: Longitudinal study of the treated rat heart demonstrates that 2D ^{31}P CSI is sensitive to the ischemic risk areas. The PCr-to-ATP ratio reflects the decrease of the myocardial viability from the peripheral to the central areas of the injured myocardium. The deviation of the PCr-to-ATP ratio from 2 could be due to the sub-optimized adiabatic pulse power. Early and accurate diagnosis of myocardium at risk during acute ischemia is possible using sensitivity-enhanced 2D ^{31}P CSI techniques.

Reference and Acknowledgments: (1) Jennings RB et al, Circulation 1976; 53 (suppl I): I-26-I-29. (2) Gersh BJ et al, Circulation 1993; 88:296-306. (3) Simonetti OP et al, Radiology 2001; 218: 215-223. (4) Hansch et al, Eur Radiol 2005; 15: 319-323. (5) von Kienlin M M et al, Magn Reson Med 1998; 39: 731-41. (6) Steinboeck P et al, Herz 2003; 28: 461-5. The authors wish to thank Dr. Amir Abduljalil for helpful discussions.