Visualizing Regional Changes in Metabolism in a Rat Model of Acute Myocardial Infarction Using Hyperpolarized 13C MR

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Introduction: Metabolic magnetic resonance imaging using hyperpolarized [1-13C]pyruvate has previously been used to image cardiac metabolism in vivo [1]. The aim of this study was to investigate if this technique could be used to visualize regional changes in metabolism after myocardial infarction in rats. Our hypothesis was that the decrease or absence of the pyruvate metabolites lactate, alanine and/or bicarbonate could be used as markers of severe ischemia and infarction.

Methods: Regional metabolism was studied by MRS in the heart of 3 Sprague Dawley rats by injecting 1 mL 80 mmol/L hyperpolarized [1-13C]pyruvate over 7 s via a tail vein catheter before and after inducing a left ventricular myocardial infarction. An established rat model of acute myocardial infarction was used [2]. The rats were anesthetized and intubated for artificial respiration before the experiment. After a left thoracotomy and a pericardiectomy, the left anterior descending artery was occluded by placing a ligature around the branch. The ligature was placed to get an infarct of approximately half the size of the anterior wall of the left ventricle. The ligature was released 30 min later for reperfusion. The infarct was confirmed visually and by measuring blood levels of the cardiac ischemia marker Troponin I, before and after infarction. Scanning was performed using a 4.7 T preclinical MR-scanner (Varian Inc., USA) with a 13C/1H radiofrequency (RF) volume coil and a 13C receive surface coil (RAPID Biomedical GmbH, Germany) placed over the heart. ECG, respiration rate, and body temperature were monitored throughout the experiment (SA Instruments, USA). Anatomical images were acquired prior to 13C-imaging for spatial localization of the heart and correct coil positioning. Proton long axis MR images were acquired using a cardiac and respiratory-gated cine pulse sequence. Before acquiring the MRS-images, a time series of the metabolism was generated to verify correct timing for starting the CSI pulse sequence. The dynamic time series were acquired by collecting 13C spectra every 2 s after injection of hyperpolarized [1-13C]pyruvate, using a non-gated slice-selective sequence and 10º flip angle. The MRS-images with hyperpolarised [1-13C]pyruvate were acquired in a long-axis view of the heart using a cardiac- and respiratory-gated CSI pulse sequence (FOV 25 mm, slice thickness 5 mm, FA 10º). The CSI-scan was initiated 7 s after end of injection. Metabolite maps were calculated using time-domain fit (jMRUI). [1-13C]pyruvate was hyperpolarized using a HyperSense polarizer (Oxford Instruments, UK). In the liquid state the C-1 polarization of pyruvate was ~25 % at pH ~7.6, temperature ~30 ºC and isotonic osmolality.

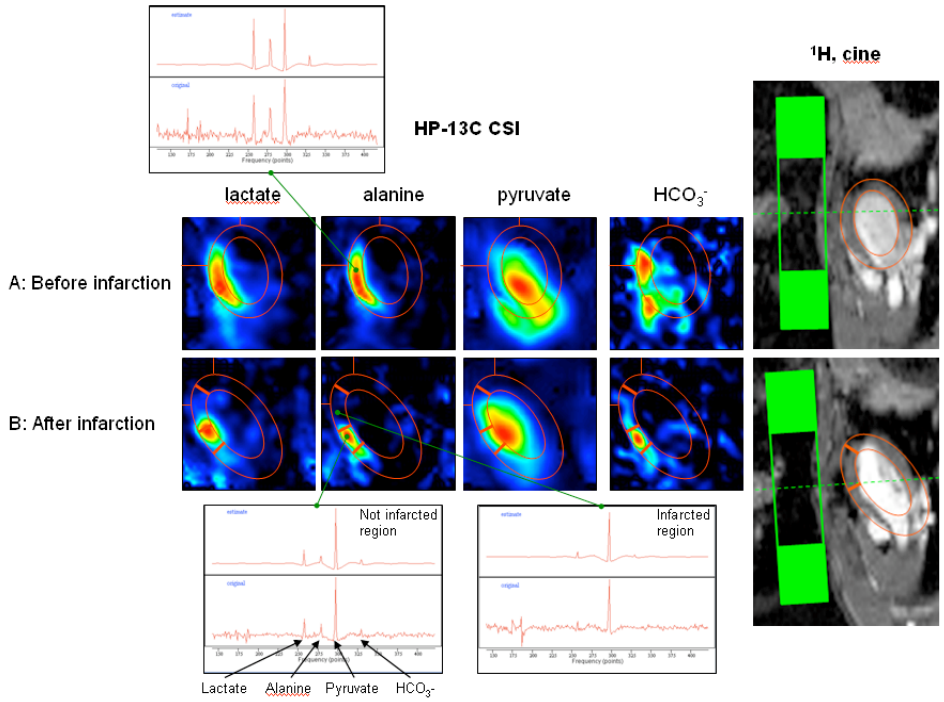

Fig 1. Metabolite maps of lactate, alanine, pyruvate and bicarbonate measured using hyperpolarized 13C MRS over the anterior wall of the left ventricle of a rat heart before (A) and after (B) an induced infarction. After infarction, the metabolism was absent in the infarcted region whereas in the not infarcted region the metabolism was preserved.

Results: Before infarction, a uniform and myocardium specific distribution of the lactate and alanine signal was detected in the metabolite maps over the anterior wall of the left ventricle (Figure 1A). After infarction the signal from lactate, alanine, and bicarbonate were absent in the infarcted region of the myocardium (Figure 1B), whereas, in the region not affected by infarction, the signal levels were comparable to the levels before infarction. Due to lower signal levels of bicarbonate there was a greater contribution of noise in these maps (see spectrum insert in figure 1B).

Conclusion: This study demonstrates that hyperpolarized 13C MRS can be used to visualize regional changes in cardiac metabolism in rats after myocardial infarction. Further studies will determine if the model is sufficiently sensitive to visualize metabolic changes after shorter ischemic periods.

References: [1] Golman K, *et al.* Magn Reson Med, 2008, 59: 1005-1013, [2] Thomas N.P. *et. al.* Annals of Surgery , November 1954, 675-682.