23Na Chemical Shift Imaging and Late Gadolinium enhanced (LGE) MRI of acute ischemia reperfusion myocardial injury

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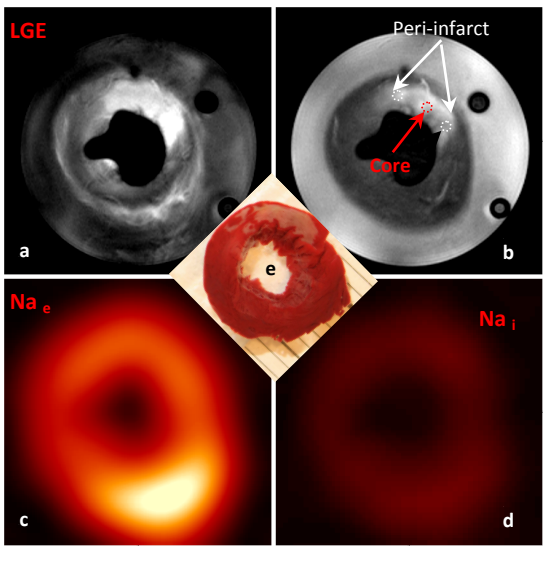
Abstract

Introduction – Late Gadolinium Enhancement (LGE) MRI is commonly used to estimate the infarct after reperfusion. However, accurate assessment with LGE MRI is complicated by the presence of edema and its ability of discriminating reversible from irreversible injured myocardium. Imaging of Sodium is known to provide valuable information on cellular integrity and ion homeostasis of different myocardial pathological states. We have previously shown that during reperfusion after ischemia induced by application of low coronary flow in an isolated rat heart model, the elevated intracellular sodium (Na_i) signal intensity correlated to the severity of ischemia [1]. Furthermore, we have shown that a higher level of interstitial edema in isolated heart model also increases extracellular volume distribution in LGE MRI and ^{23}Na CSI [2]. However, the complex physiological changes after acute IR myocardial injury in vivo remain to be addressed.

Therefore, the **aim** of this study was to investigate the ability of ^{23}Na CSI complemented by ^{1}H LGE MRI in isolated rat heart to characterize the injured myocardium as soon as 2 hours after the IR injury, which was induced while the rats were still alive.

Method – Male Wistar rats (n= 7) underwent 50 minutes ischemia, followed by 60 minutes of in vivo reperfusion. Subsequently, hearts were isolated and perfused in a Langendorf setup where LGE MRI and ^{23}Na CSI scans were initiated to assess injured myocardium. TmDOTP and Gadovist were added to the buffer for ^{23}Na CSI and LGE MRI, respectively. ^{23}Na CS images were obtained with TR = 30ms, FOV = 20mm, matrix = 16x16 for the spatial domain and 128 points for the spectral domain, slice thickness = 5mm, and acquisition weighted k-space filtering. LGE MRI scans were performed with a prospectively cardiac gated T_1-w short-axis multi-slice FLASH sequence during continuous Gd perfusion and after washout, with the following parameters: TR = 63 ms, TE = 2.8 ms, FA = 75^0, NA=8, 6 slices of 2.5 mm thickness, matrix = 256×256, FOV = 2×2 cm^2. At the end of the MR scan, hearts slices were stained for viability with TTC. The Na image signal intensity (SI) was measured in three different regions; remote, peri-infarct, and infarct core of the myocardium based on the LGE images. The enhanced area of the LGE was quantified with a semiautomatic algorithm (segment, Sweden) based on signal-intensity thresholds (2, 4, and 6 SDs above remote myocardium).

Result – Figure 1 presents a mid short-axis of LGE, extracellular (Na_e) and intracellular (Na_i) CS images, and TTC of an isolated rat heart after IR injury. LGE MR images delineated the infarct and correlated well (0.99, Pearsson correlation) to the TTC unstained region. The Na_e/Na_i ratio is 8.77±0.78 in the remote region, whereas it is 6.61±0.66 and 7.43±0.66 ($p<0.05$) in the core of the infarct and peri-infarct regions, respectively, indicative for the disturbed Na^+/K^+ balance. The Na_e normalized SI was higher (1.51±0.06) in the core of the infarct as compared to the peri-infarct region (1.32±0.05, p=0.02). Similarly the normalized Na_i was higher in the core of the infarct (0.25± 0.04) as compared to the peri-infarct region (0.18±0.01, p=0.02). These changes are consistent with the irreversible cellular damage in the anterior wall, confirmed by the TTC staining. Figure 2 shows infarct size estimations for different segmentation cutoff thresholds, based on the SD of the signal in the remote region. Using a threshold of 4 SD resulted in the best agreement for LGE, Na images and TTC.



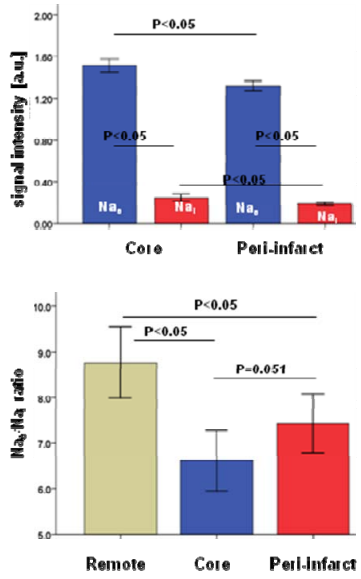


Fig 1 – (left) An example of isolated rat heart slice with inferior infarction. LGE images (top) during perfusion with Gd (a) and after Gd washout (b). Extracellular (c) and intracellular (d) Na CS images (bottom) and (e) corresponding TTC staining (center). **(Right) -**Normalized signal intensity of the extracellular and intracellular Na in the core and the border zone of the infarct (top), and the ratios of Na_e/Na_i (bottom).

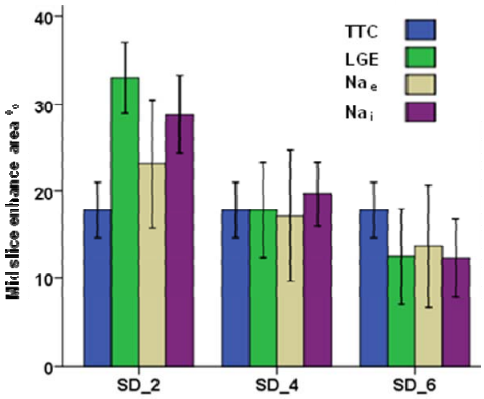


Fig 2 – Enhanced area delineation based on signal-intensity thresholds (2, 4, and 6 SDs above remote normal myocardium.

Discussion and conclusion – LGE MR images showed a higher contrast between remote and infarct than Na MR images. The increase of Na_e suggests the presence of extracellular edema. In contrast, the elevated Na_i signal, as a result of the reduced rates of Na^+_i removal via Na^+/K^+ ATPase, makes Na_i a marker of irreversible injured cell, confirmed by the TTC. The significant difference of Na^+ signal intensity between the infarct core and the peri-infarct region combined with LGE is more sensitive tool of cell injury than either of them alone. Similarly, infarct size estimation with LGE and Na MRI are influenced by the selected threshold SD method. These results may prove ^{23}Na CSI to be a unique and valuable post-MI predictor and demonstrates the importance of Na MRI as promising tool for accurate myocardium viability assessment.

References – *1) M. A. Jansen et al, Circulation-2004; 110: 3457-3464. 2) E. Aguor et al, Proc. 19th ISMRM (2011), abstract 1353, Montréal, Canada.*