^{23}Na Chemical Shift Imaging of myocardial edema

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Introduction – Distinction between viable and non-viable myocardium is essential for diagnosis and treatment of patients with coronary artery disease. Delayed contrast-enhanced (DCE) MRI has become the gold standard to determine the size of chronic infarcts. However, although T_2-weigthed MRI shows great promise to delineate the area at risk after the event related to the formation of edema, the accuracy of DCE-MRI to determine the size of acute infarcts has been questioned because of that same edema. As an alternative approach we would like to propose ^{23}Na Chemical Shift Imaging (CSI) with the aid of a shift reagent. In edematous, but viable tissue we expect the extracellular Na^+ signal (Na^+_e) to be increased but little change in the intracellular Na^+ signal (Na^+_i). In acute infarcts with cell membranes still intact, we expect Na^+_i to be very high, whereas in chronic infarcts Na^+_e should be very high and Na^+_i should be absent. To further explore this methodology, we have created an isolated, perfused heart model of extracellular edema based on different perfusion pressures, which has been characterized using ^{31}P MRS. Subsequently, we have characterized the formation of edema by both DCE ^{1}H MRI and ^{23}Na CSI.

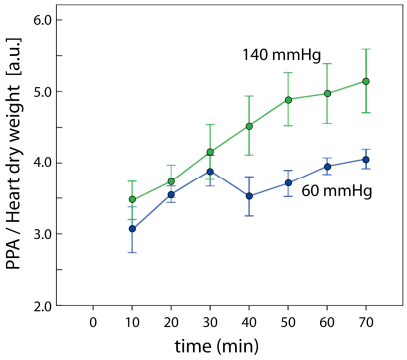
Materials and Methods – Isolated rat hearts were perfused with modified Krebs-Henseleit buffer according to Langendorff and MRI and MRS scans were performed with a 9.4T scanner (Bruker, Germany).

^{31}P-MRS: 5 mM Phenylphosphonic acid (PPA) was added to the buffer as a marker of the extracellular space (Fig. 1). After preparation at 60mmHg, hearts were perfused for 70min at 60mmHg, n=6 or at 140mmHg, n=5 to induce different levels of edema. To exclude extracardiac signals, hearts were not submerged. ^{31}P MRS-spectra were acquired following accumulation of 150 FIDs with a 45° pulse angle and a 2s repetition time. Peaks were quantified using JMRUI software and appropriate prior knowledge parameters.

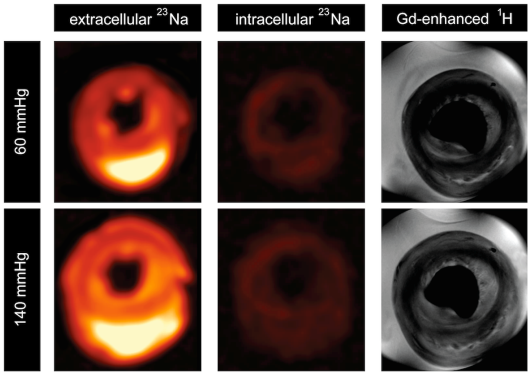
^{23}Na CSI: 3.5mM TmDOTP was added to the buffer as a shift reagent. Hearts (n=4) were perfused at 60mmHg for 60min and subsequently at 140mmHg for another 60 min. The extra-cardiac space was flushed with a Na^+-free, Li^+-containing buffer. Short-axis chemical shift images were obtained with a TR=30ms, FOV=20mm, a 16x16 matrix for the spatial domain and 128 points for the spectral domain, slice thickness of 5mm, acquisition weighted k-space filtering and a total acquisition time per CSI data set of 5min. Whole heart (WH) and left ventricle (LV) contours and average signal intensities of the entire LV were determined with Bruker Paravision software.

DCE-MRI: 1.3 mM GdDTPA was added to the buffer as contrast agent. Hearts (n=6) were perfused at 60mmHg for 60min and subsequently at 140mmHg for another 60min. Short- and long-axis retrospectively-gated gradient echo images were obtained with a TR=5.2ms,TE=1.89ms, FOV=20mm, a 128x128 matrix, slice thickness of 2.5mm and a total acquisition time per image of 1.5min. WH and LV contours and average signal intensities of the entire LV were determined with Bruker Paravision software.

Results – Fig 1 shows the PPA signal intensity normalized to heart dry weight at 60 and 140mmHg. Data were significantly ($P<0.03$) different from 50min onwards and the ratio of PPA at 140mmHg/60mmHg at 70min was 1.27 ±0.21. As can be readily seen in the ^{23}Na CSI and the ^{1}H MRI (Fig 2), the cross sectional area (CSA) of the hearts following perfusion at 140mmHg was increased. The Na_e images yield a WH CSA of 1.32±0.11cm at 60mmHg, increasing to 1.89±0.16 at 140mmHg with a 140mmHg/60mmHg ratio of 1.44±0.09, in good agreement with the PPA data. The data from the ^{1}H images were 1.37±0.04, 1.86±0.14 and 1.34±0.09, respectively, demonstrating good agreement between ^{23}Na and ^{1}H data. When analyzing the LV wall, similar data were obtained. In addition to the increase in CSA, we also found an increase in LV Na_e signal intensity, going from 1.04±0.20 (arbitrary units, a.u.) at 60mmHg to 1.37±0.20 at 140mmHg, with a 140/60 ratio of 1.33±0.07. Unexpectedly, we also found an increase in LV Na_i signal intensity, going from 1.57±0.83 (a.u.) at 60mmHg to 1.79±0.97 at 140mmHg, with a 140/60 ratio of 1.15±0.11. With DCE-MRI, LV signal intensity increased from 1.39±0.14 (a.u.) at 60mmHg to 1.50±0.22 at 140 mmHg, with a 140/60 ratio of 1.08±0.08.



< Fig 1: 31P-MRS signal from PPA normalized to heart dry weight as function of perfusion time at 60 and 140mmHg.



> Fig 2: ^{23}Na-CSI of extracellular and intracellular Na and Gd-enhanced ^{1}H MRI at perfusion pressures of 60 and 140mmHg.

Limitations – There are a few limitations to this study that need to be considered. First, the DCE-MRI protocol uses continuous perfusion of contrast agent without nulling of 'remote' myocardium, so direct comparison of the contribution of edema in a clinical protocol is difficult. The separation of intra- and extracellular Na^+ signals is incomplete. Furthermore, the spatial resolution in the ^{1}H images is much higher than in the ^{23}Na images. Finally, both the DCE MRI and Na_e images show spatial heterogeneity, i.e. a mid-myocardial rim of different signal intensity, which is lost in the average signal, but may be related to this edema model and requires further analysis.

Conclusions – Perfusion of hearts with crystalline buffers at high perfusion pressures leads to formation of interstitial edema, as evidenced by a larger distribution volume for PPA, Na_e and Gd. Unexpectedly, images of Na_i also showed an, albeit smaller, increase in signal intensity, which could be explained by altered ion homeostasis, but could also reflect imperfect separation of intra- and extracellular signals. Whether ^{23}Na CSI is better capable than DCE-MRI to distinguish between normal, edematous and infarcted tissue in both acute and chronic myocardial infarction requires further experiments in an infarct model.