High resolution fully quantitative sodium mapping in the acutely infarcted mouse heart

Mahon L Maguire[1], Kiterie M Faller[1], Debra Medway[1], Victoria Thornton[1], Craig A Lygate[1], Andrew M Blamire[2], Stefan Neubauer[1], and Jurgen E Schneider[1]
[1]*Dept. Cardiovascular Medicine, University of Oxford, Oxford, United Kingdom,* [2]*Newcastle Magnetic Resonance Centre, Newcastle University, Newcastle upon Tyne, United Kingdom*

Introduction: Measurement of myocardial sodium levels can provide insight into electrophysiological disruption and tissue injury. Tissue sodium concentration can serve as a marker for disruption of ion homeostasis and for oedema with both energy depletion and swelling increasing tissue sodium [1]. Myocardial sodium concentration increases rapidly after acute ischaemia [2]. The high spatial resolution required for accurate imaging *in vivo* in the mouse, the fast heart rate (~400-600 bpm), extremely short T2, and the complexity of the flip angle and receive sensitivity corrections required to absolutely quantify the metabolite concentrations *in vivo* make such measurements technically challenging. Here we present accurate tissue sodium concentration maps *in vivo* in control and acutely infarcted mouse hearts. This is a necessary first step in the quantification of myocardial energetics and electrophysiology during ischaemic injury.

Methods: Experiments were carried out on a 9.4 T/210 mm bore Magnex magnet with Varian direct drive console (Agilent, US). ^{1}H imaging and shimming was performed using a 39 mm quadrature birdcage resonator (Rapid Biomedical, Germany). ^{23}Na Chemical Shift Images (CSI) were acquired using an actively decoupled 39 mm quadrature birdcage transmit resonator and a 14 mm curved square actively decoupled surface receive coil (Rapid Biomedical, Germany). C57Bl/6 mice (n=5, "baseline") were subjected to MR examination twice with ~7 days between examinations. Mice (n=4, "infarct") with permanent occlusion of the left coronary artery were subjected to MR examination 24 h post surgery. ^{1}H short axis scout images (128 x 128, 10 slices, 1 mm thick, 25 x 25 mm FOV) were acquired covering the left ventricle. Corresponding acquisition (Hanning) weighted, cardiac gated, ^{23}Na chemical shift images (CSI) were acquired to assess ^{23}Na concentration (68 x 68 PE steps, 25 x 25 mm FOV, 2 slices, 2.0 mm thick, 0.625 x 0.625 mm nominal resolution, TR ~250 ms, 25528 averages, ~50 min acquisition time, nominal voxel volume 0.79 µl). A Late Gadolinium Enhanced (LGE) T1 weighted short axis GE3D image was acquired to assess infarct volume and location (30 x 30 x 16 mm FOV, 6144 scans, 20 min acquisition time) [3]. CSI data were fitted using in house software. High resolution 3D B1 maps were acquired for ^{23}Na transmit and receive coils to allow correction for flip angle and receive profile. A 1 mol/L NaCl sample was included in the animal cradle as an external concentration reference. A 4 mm point sphere filled with saturated NaCl solution with Tm[DOTP]$^{5-}$ was used to allow rapid pulse calibration over a defined volume using an unlocalized pulse-acquire experiment.

Results: ^{23}Na signal from the "baseline" myocardium was homogeneous (32.6±4.1 mmol/L) and lower than that of the blood (72.3±9.3 mmol/L) (Fig 1a,b). Heart anatomy was well defined in the ^{23}Na images with papillary muscles clearly visible. $B1_{Rx}$ correction accurately compensates for the drop in signal with increasing distance from the coil arising from the use of a surface coil. Ligation of the left coronary artery resulted in an infarct in the left ventricular free wall and was visible in the ^{23}Na images (69.1±5.6 mmol/L) (Fig 1c,d). 'Baseline" myocardium and remote myocardium (43.9±9.7 mmol/L) exhibited a similar tissue sodium concentration. Receive coil loading effects were compensated.

Conclusion: High resolution ^{23}Na CSI can be used to image detailed anatomy in the beating mouse heart. Use of B1 and concentration reference correction with correction for receive coil loading effects allowed accurate measurement of *in vivo* regional total tissue sodium concentration. This methodology can be applied to *in vivo* mouse models of cardiac disease to quantify dysfunction of ion homeostasis.

Acknowledgements: This work was funded by a MRC/EPSERC research grant (G0600829).

References: Weidensteiner et al., Magn Reson Med, **48**, 89-96 (2002), Ouwerkerk *et al.*, Radiology, 2008, **248**, 88-96, Bohl *et al.*, Am J Physiol Heart Circ Physiol, 2009, **296**, H1200-1208

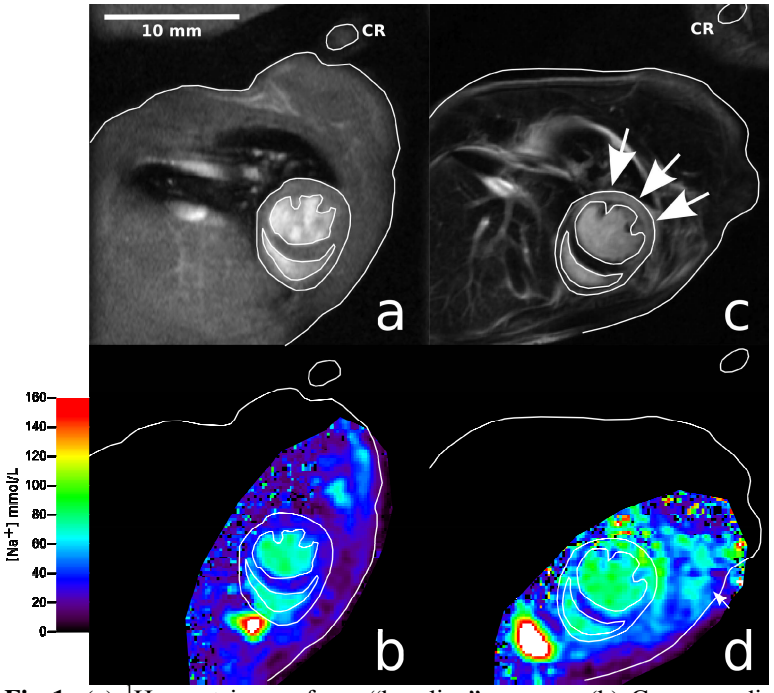

Fig 1: (a) ^{1}H scout image for a "baseline" mouse. (b) Corresponding ^{23}Na CSI showing uniform myocardial ^{23}Na concentration. (c) ^{1}H LGE image from an "infarct" mouse. Arrowheads indicate the infarct. (d) Corresponding ^{23}Na CSI showing elevated ^{23}Na concentration in the region of the infarct. CR indicates concentration reference phantom.