Measurement of the intra- versus extracellular T_1 and T_2* relaxation times and sodium content in healthy rat myocardium

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Introduction

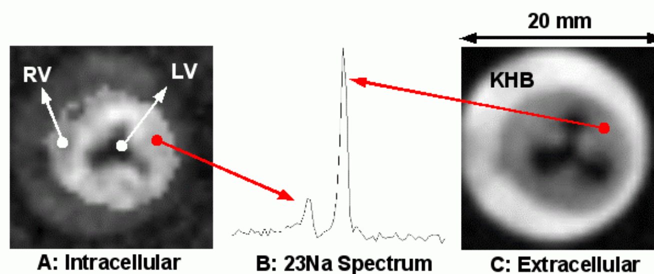
Ischemia of the myocardium is accompanied by substantial changes of the intra- versus extracellular sodium content. However, the ^{23}Na MRI signal intensity is a function of T_1/T_2*-relaxation times and of the sodium content, both of which may be subject to spatio-temporal changes in the time course following myocardial ischemia [1]. Therefore, it is of interest to quantify all these parameters in a localized region [2]. We present a method to perform this task in the isolated rat heart using shift reagent-aided chemical shift imaging.

Methods

Three female wistar rats (290-300g) were sacrificed with an intraperitoneal injection of 0.5ml pentobarbital. The heart was excised, attached to a Langendorff apparatus and perfused with cardioplegic Krebs Henseleit buffer containing 5mM/l of the shift reagent Tm[HDOTP]$^{4-}$ (Macrocyclics, Dallas, TX) and a total concentration of 4 mM/l Calcium. The reagent shifted the extracellular resonance line by 310 Hz with respect to the intracellular resonance line. 1 Liter of the buffer was recirculated.

The experiments were conducted on an 11.75 T Bruker AMX spectrometer (Bruker Biospin, Ettlingen, Germany) using a linearly polarized birdcage resonator. The NMR sequence was: r.f. excitation (angle α) – 3D phase encoding (320us) – data acquisition (512 complex points, sweep width of 14kHz) – spoiling gradient (320µs). The TR was 39.6ms. No long axis angulation was performed. At a given point in k-space, the signal was averaged NS times, with NS being determined by a radially symmetric, discretized Hanning weighting function. The spatial resolution was 1x1x3mm^3, and the duration of one dataset was 18min. Four datasets were acquired, with flip angles α = {68°, 51°, 68°, 85°}. Dataset 1 was acquired directly after placing the heart in the scanner and shimming. Datasets 2 to 4 were divided in 7 segments. The segments were stepped through in an interleaved manner in order to compensate slow fluctuations of the sodium content during the acquisition. The data were Fourier transformed and the spectra were phase corrected. Intra- and extracellular images were reconstructed by integration of the intra- and extracellular peak, respectively. A region of interest (ROI) in the anterior wall of the myocardium (see figure below) was defined, with a volume of 25µl, and the ^{23}Na spectra were averaged over this ROI. The sum of three Lorentzians, two for the fast and slowly decaying component of the intracellular compartment, with an intensity ratio of 3:2, respectively, and one for the extracellular compartment, was fit to the averaged spectra using a Levenberg-Marquard nonlinear fit algorithm. As a result, we obtained compartmentwise $T_{2f}*_{,intra}$, $T_{2s}*_{,intra}$ $T_2*_{,extra}$ and the intensities $M_{0,experiment}(\alpha \mid M_0,T_1)$. In a second step, the model function $M_{0,model}(\alpha \mid M_0,T_1) = M_0 \sin(\alpha)[1 - \exp(-TR/T_1)] / [1 - \cos(\alpha) \exp(-TR/T_1)]$ was fit to the signal course $M_{experiment}(\alpha \mid M_0,T_1)$ of datasets 2 to 4, using again a Levenberg-Marquard algorithm, which yielded a T_1. We used this T_1 to calculate the M_0 of dataset 1. M_0 is proportional to the sodium content. The same procedure was performed for an ROI in the buffer surrounding the heart, the sodium content of which is known (163,5mM/l). Using this reference and the mass density of myocardium tissue (1050 kg/m^3), we calculated the absolute sodium content in the myocardium ROI: $[Na] = (M_0/M_{0,buffer}) \times 23 \times 163.5 / 1050$ g/kg wet weight.

Heart No.	1	2	3	Average
[Na, total] [g/kg wet weigt]	1.81	1.96	2.47	2.08 ± 0.36
[Na,intra] [g/kg wet weight]	0.21	0.32	0.24	0.26 ± 0.06
[Na,extra] [g/kg wet weight]	1.60	1.64	2.13	1.79 ± 0.30
T1,intra [ms]	27.4	52.2	40.1	39.9 ± 12.4
T1,extra [ms]	43.7	44.7	51.0	46.5 ± 4.0
T2f*,intra [ms]	0.95	0.55	0.72	0.74 ± 0.2
T2s*,intra [ms]	6.08	3.89	3.12	4.4 ± 1.5
T2*,extra [ms]	6.86	8.33	9.51	8.23 ± 1.3



Results

The figure shows the intra- (A) versus extracellular (C) sodium images of a slice in the myocardium with nearly short axis angulation. LV and RV denote the left and right ventricular lumen, respectively, KHB indicates the Krebs-Henseleit buffer. The ^{23}Na NMR spectrum averaged over the ROI, as indicated by the circle-shaped end of the red arrows, is shown in (B). The experimentally obtained values of T_1, T_2* and the sodium content [Na] are summarized in the table.

Summary and Discussion

We present a technique to measure the intra- versus extracellular T_1/ T_2*-relaxation times and sodium content localized in a small ROI. The extracellular T_1 and T_2* are similar for all three hearts, while the intracellular relaxation rates show a higher variation. Since the contribution of the extracellular sodium dominates the total sodium content, it is influenced only to a low extent by variation of the intracellular T_1. These results give direction to further evaluation. For example, simulations (not reported here) have shown that the goodness and robustness of the T_1-fit is improved by optimising the set of flip angles α with respect to the relaxation times. In addition, several algorithms to compute the T_1, T_2* and M_0 from the ^{23}Na spectra will now be tested on the experimentally obtained data.

References

[1] Circ Res. 2000 Oct 13;87(8):648-55
[2] Circulation. 1999 Jul 13;100(2):185-92