DETERMINING CELLULAR MICROSTRUCTURE OF ISOLATED RAT HEARTS USING CORRELATED TIME-DEPENDENT DIFFUSION AND T_2 RELAXATION MEASUREMENTS

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Introduction

The aim of this work is to relate spatial and local mobility of water spins in rat myocardium by correlating time-dependent diffusion coefficient and T_2 relaxation constant ($D(t)$-T_2). From spin mobility we infer compartment specific $D(t)$ in rat myocardium, which enables the determination of cellular microstructure. Due to problems associated with heart motion, such correlation experiments have primarily been performed on other organs and systems [1]. We are able to perform the correlation experiments on viable myocardium by using isolated cardioplegic rat hearts.

Materials and Methods

Three dissected rat hearts were perfused, alternatively, with regular and cardioplegic (20 mM of KCl) Krebs buffer solutions. NMR relaxography was performed *ex vivo* (Maran Ultra, Resonance Instruments Ltd, 23 MHz, 37°C). The flow of buffer solution was stopped during data acquisition. $D(t)$-T_2 correlations were measured using a combined PGSTE-CPMG pulse sequence [2]. The diffusion encoding part of the sequence (PGSTE) employs a set of bipolar gradients (applied along the long-axis of the cardioplegic heart), which reduce the influence of eddy currents on the measured echoes in the CPMG train. The diffusion time varied from 5 ms to 80 ms.

Results

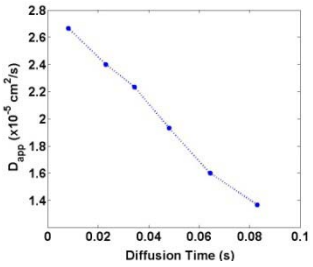

Figure 1 (left). The apparent diffusion coefficient for the tissue at each diffusion time (D_{app}) was estimated from the first echo in the CPMG decay as a function of varying b-values. D_{app} decays with increasing diffusion time, but does not show a characteristic plateau-value. This indicates that the total system does not reach the long-time diffusion limit, but remains in the short-time regime.

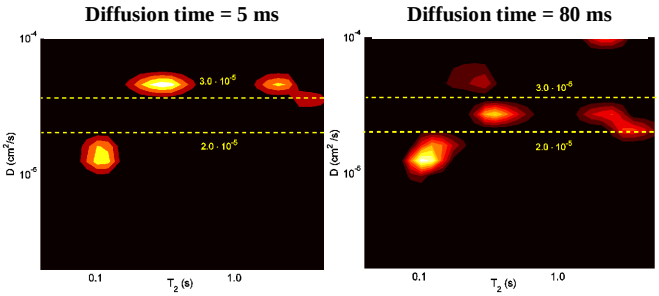

Figure 2 (above right). The D-T_2 data obtained using a two-dimensional inverse Laplace transform (ILT) analysis reveal three T_2 components, with approximate values of 80 ms, 300 ms and 2500 ms, and with different diffusion characteristics, that change when going from shortest to longest diffusion time. The component with longest T_2 is associated with water located on the surface of the heart [3] while the two remaining components most likely represent intra- and extra-cellular water.

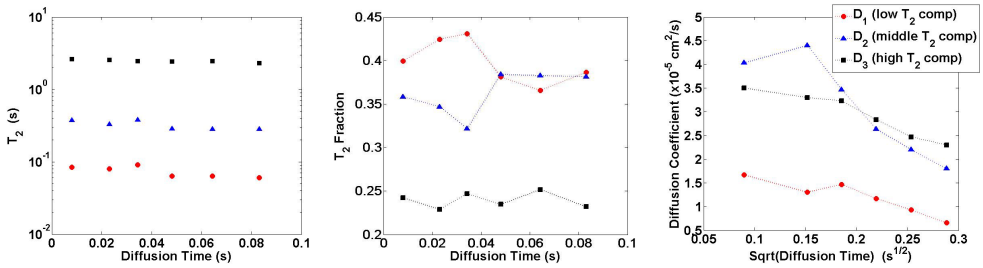

Figure 3. For a quantitative analysis, we used the following procedure: the T_2 values were determined for each b-value using a discrete multi-exponential decay model with three components and seven fit parameters. For each component, the T_2 values obtained at different b-values were averaged. These three averaged T_2 values were then used to perform a three-component, four-parameter forced-fit to the decay curves, resulting in a set of corresponding intensities for each component that decay with increasing b-values. Thus, the diffusion coefficient for each separate T_2 component can be determined. The results obtained at different diffusion times are shown in the three plots above. As expected, the three T_2 values and corresponding intensities do not vary significantly with diffusion time (left and middle figure). As seen in the right figure above (as well as in Figure 2), the two longest T_2 components have similar $D(\sqrt{t})$-behavior, while the shortest one has significantly lower diffusivity. Assuming that the two shortest T_2 components represent intra- and extra-cellular compartments, using the short-time diffusion model [4, 5] and a cylindrical geometry of myocardial cells (length-to-diameter ratio of 5:1) [6], we estimate the diameter of the cells to be 35 µm, and the inter-cell distance to be 20 µm.

Conclusions

We have shown that the correlated data from time-dependent diffusion and T_2 values can be used to study diffusion of individual cell compartments in rat myocardium. Compartmental diffusivity then enabled us to obtain valuable structural information about the intra- and extra-cellular compartments in rat myocardium.

References

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