Analysis of T_1, T_2 and $T_{1\rho}$ spin lock field dependency in myocardial infarction tissue using HRMAS spectroscopy at 11.7 T

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Introduction

After myocardial infarction (MI) scarring fibrosis is formed[1]. For prediction of clinical outcome and to study the effects of therapy, it is important to accurately determine the scar tissue location. Gold standard for imaging myocardial fibrosis is MRI with late gadolinium enhancement (LGE)[1]. A direct measurement based on endogenous characteristics MR would be beneficial for accurate detection and follow-up of the infarction area. High Resolution Magic Angle Spinning (HR-MAS) NMR spectroscopy provides information of biochemical changes in tissue. Identification of alterations in MR relaxation parameters after MI could provide information to develop a MRI sequence with endogenous contrast. Studies in cartilage show that an increase in collagen can be identified with the presence of a short T_2 component (2.3 ms)[2] and an increase in the $T_{1\rho}$ relaxation time[3]. The strength of the spin lock field has shown to be sensitive to macromolecular changes in cartilage[4]. Although some studies showed the first evidence for the ability to detect myocardial fibrosis with these methods[5,6], no study was performed on the change in these relaxation times after MI over time, and for the dispersion of $T_{1\rho}$ with increasing spin lock field.

The goal of this study is to quantify the effect of biochemical changes after MI on T_1, $T_{1\rho}$ and T_2 relaxation times with HRMAS spectroscopy.

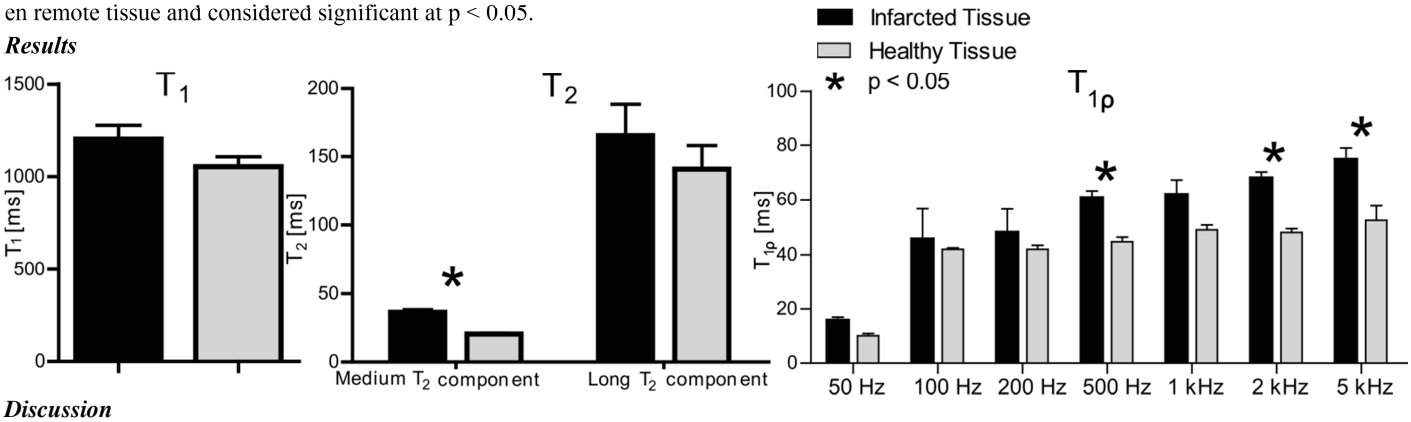
Materials and Methods

The proximal left circumflex coronary artery of one landrace pig (76 kg) was occluded under anesthesia. Two weeks after myocardial infarction, the heart was explanted. Two tissue samples from infarcted and healthy heart muscle tissue were extracted, and flash-frozen at -80º C for storage. The experiment was approved by the animal welfare committee of the University of Utrecht and conform the Guide for the Care and Use of Laboratory Animals.

Two infarcted and two healthy tissue samples were scanned in a 500 MHz Bruker Biospin spectrometer in a 3.2 mm rotor. The sample was spun at 4 kHz, at a temperature of 4º C to limit tissue degeneration. A FWHM of 12 Hz for the water peak was obtained after shimming. ^{1}H NMR spectra were acquired with a spectral bandwidth of 30 kHz and an acquisition time of 200 ms. T_1 measurements were performed with an inversion recovery experiment, with 15 different recovery delays ranging from 1 to 10000 ms (8 av). T_2 was measured using a rotor-synchronized CPMG sequence (0.5 ms echo spacing) with 70 TEs ranging from 0.5 to 320 ms, with stepsize increasing from 0.5 to 16 ms (8 av.). $T_{1\rho}$ was measured with 7 different frequencies for the spin lock pulse; 50, 100, 200, 500, 1000, 2000, 5000 Hz and the spin lock duration was varied from 2 to 200 ms (8 av.) for each frequency.

The spectra were analyzed using jMRUI and a mono-exponential was fit to the amplitudes of the water peak to obtain T_1 and $T_{1\rho}$. A bi-exponential was fit to the T_2 data to identify the different T_2 components. A two-tailed t-test was used to compare the differences between infarct en remote tissue and considered significant at $p < 0.05$.

Results



Discussion

No significant different T_1 was observed in the myocardial infarction tissue. This is in agreement with clinical studies in which no or little increase in T_1 is observed after myocardial infarction[7]. For both the remote and the infarcted tissue, two T_2 components could be identified. The medium T_2 component was significantly higher in infarcted tissue (37±3 vs. 21±1), where no significant difference for the long component was observed. It other studies the medium and long T_2 components are associated with intra- and extracellular water[8]. The increase of the short T_2 component could be explained by the cell death after MI. We hypothesized the presence of a short T_2 component (2.3 ms) in the infarction tissue, because of the increased collagen content. However, this short T_2 component could not be observed. Future measurement with older infarction tissue (increased fibrosis formation) and increased SNR should be performed to study the presence of the short T_2 component in infarcted tissue. $T_{1\rho}$ of infarction tissue was found to be significantly higher for higher spin lock fields of 500 Hz, 2 kHz and 5 kHz. In literature it was shown that $T_{1\rho}$ is sensitive to macromolecule-water interaction[9]. The increase of intracellular proteins due to apoptosis and the formation of collagen could explain the increase in $T_{1\rho}$ after MI. Compared to T_1 and T_2, $T_{1\rho}$ is less sensitive to the strength of the static B_0 and more to the spin–lock field, and therefore translation from these high field $T_{1\rho}$ results to a clinical method is more straightforward.

Conclusion

The results indicate that the medium T_2 component and $T_{1\rho}$ are most promising for endogenous detection of myocardial fibrosis. The $T_{1\rho}$ weighted sequence needs a high spin lock field (500 Hz or higher) which is particularly important because clinical *in vivo* $T_{1\rho}$ sequences are limited by SAR.

References: [1]Mewton N jACC 2011 [2]Reiter DA MRM 2009 [3]Mlynárik V jMR 2004 [4]Akella SV MRM 2004 [5]Witschey W jCMR 2012 [6]de Jong S jMCC 2011 [7]Dulce M AJR 1993 [8]Saab G MRM 1999 [9]Rommel E MRM 1989