Published in final edited form as:

Curr Cardiovasc Imaging Rep. 2014 February 1; 7(2): 9248–. doi:10.1007/s12410-013-9248-7.

Assessing Myocardial Disease Using $T_{1\rho}$ MRI

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Abstract

There is great interest to use magnetic resonance imaging (MRI) for non-invasive assessment of myocardial disease in ischemic and non-ischemic cardiomyopathies. Recently, there has been a renewed interest to use a magnetic resonance imaging (MRI) technique utilizing spin locking radiofrequency (RF) pulses, called $T_{1\rho}$ MRI. The spin locking RF pulse creates sensitivity to some mechanisms of nuclear relaxation such as ^1H exchange between water and amide, amine and hydroxyl functional groups in molecules; consequently, there is the potential to non-invasively, and without exogenous contrast agents, obtain important molecular information from diseased myocardial tissue. The purpose of this article is to review and critically examine the recent published literature in the field related to $T_{1\rho}$ MRI of myocardial disease.

Keywords

Ischemic; Non-ischemic; Heart disease; Magnetic resonance imaging; $T_{1\rho}$ relaxation; Spin lock radiofrequency pulse

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This article is part of the Topical Collection on *Molecular Imaging*

Conflict of Interest Yuchi Han, Timo Liimatainen, Robert C Gorman, Walter RT Witschey declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Introduction

The purpose of this article is to critically examine and discuss recent developments in spin lock or $T_{1\rho}$ (“T1-rho”) MRI for assessing myocardial disease. While a considerable amount of published work on spin locking exists in medical research related to osteoarthritis [1, 2], acute cerebral ischemia [3], cancer [4], and liver fibrosis [5], there are very few studies reporting the use of spin locking in diseases of the myocardium. This is somewhat surprising since, in particular, osteoarthritis is partially a disease affecting the normal molecular structure of cartilage, a tissue containing few chondrocytes supporting a dense extracellular matrix of collagen and proteoglycan; likewise, ischemic heart disease post-myocardial infarction (MI) is characterized by cardiomyocyte replacement with fibrotic tissue abundant in collagen. Yet despite this similarity, there remains little research - but nevertheless a strong expectation - that the nanoscopic magnetic environment of ^1H nuclei is sufficient to generate endogeneous MRI contrast in diseases of the myocardium. From this perspective, it seems logical that $T_{1\rho}$ MRI would be useful for imaging of fibrotic scar tissue in the heart. Although non-ischemic myocardial diseases such as left ventricular hypertrophy are also sometimes characterized by increased tissue fibrosis, at this time, there is currently no published research of $T_{1\rho}$ MRI in this area and therefore we will focus this report exclusively on recent work involving $T_{1\rho}$ MRI of acute and chronic ischemic heart disease.

An Overview of Spin Locking and $T_{1\rho}$ MRI

Spin locking is used primarily as a contrast-generating mechanism in cardiovascular MRI. We use spin locking to non-invasively study molecular changes in diseased myocardial tissue, differentiate normal and diseased myocardial tissue and potentially determine myocardial area-at-risk. Unlike contrast agents, like gadolinium chelates in MRI or radioactive tracers in positron emission tomography (PET), the contrast in $T_{1\rho}$ MRI arises from the interaction between tissue water ^1H nuclear intrinsic angular momentum (spin), an applied radiofrequency (RF) field called the spin lock field and the local (nanoscopic) magnetic environment of the nucleus. Since contrast is generated through a RF field, spin locking can be used safely in humans without concern for contrast agent toxicity or radioactivity, as long as the RF fields do not cause excess tissue heating.

Although this report describes MRI methods, spin locking has historical roots in nuclear magnetic resonance (NMR) spectroscopy [6]. In the NMR literature, spin locking is most commonly used for the determination of low frequency (Hz-kHz) chemical exchange rates in small molecules and proteins [7]. While spin-lattice (T_1) relaxation is sensitive to intermediate (kHz-MHz) exchange rates, low frequency exchange rates are not easily analyzed by T_1 relaxation because of the low polarizability of the nuclear spin system at requisite low magnetic field strengths. Spin locking avoids this restriction using a radiofrequency (RF) field instead of the static field to probe the effect of exchange rate on nuclear relaxation. In these experiments, the spin lock amplitude is varied and the exchange rate is indirectly measured through its effect on the rotating frame relaxation time $T_{1\rho}$; this is called a rotating frame NMR dispersion experiment.

The term “spin locking” provides a helpful visual description of the dynamics of the nuclear spin system. A simple spin lock experiment is shown in Fig. 1, as seen from a frame of reference rotating at the Larmor frequency ($\omega_0 = \gamma B_0$). The net magnetization is excited from equilibrium using a 90° pulse and nutated into the transverse plane. A continuous RF pulse is then applied with a phase and frequency so that the effective magnetic field remains nearly parallel to the net nuclear spin magnetization for a suitably long duration (several tens to hundreds of milliseconds). In the absence of this continuous RF pulse, the nuclear spin magnetization would ordinarily dephase (contributing to T_2^* relaxation) and undergo both

T_2 and T_1 relaxation. However, the RF pulse locks the magnetization so that dephasing is hindered. This can be seen by direct inspection of the equations of motion for the nuclear spin system, the Bloch equations

$$\frac{d\mathbf{M}}{dt} = \gamma \mathbf{M} \times \mathbf{B}_e.$$

In the rotating frame, the time dependence of the magnetization is related to the cross-product between the effective magnetic field $\mathbf{B}_e$, the net magnetization $\mathbf{M}$, and gyromagnetic ratio γ . The effective magnetic field is the sum of the RF field amplitude and the residual component of the static field

$$\mathbf{B}_e = \omega_1 \hat{x} + \Delta\omega \hat{z}.$$

When the two vectors $\mathbf{M}$ and $\mathbf{B}_e$ are closely aligned, the overall motion of $\mathbf{M}$ is constrained to a narrow cone around $\mathbf{B}_e$. Furthermore, although T_1 and T_2 nuclear relaxation still occur, if the RF field is sufficiently strong, magnetization is continuously disturbed by the RF field and will not return to the initial equilibrium condition, but instead reach a steady-state in a time on the order of $T_{1\rho}$ and not the usual spin-lattice relaxation time T_1 . With RF fields appropriate for *in vivo* imaging, $T_{1\rho}$ is always longer than T_2 , but not as long as T_1 . As a point of terminology, $T_{1\rho}$ MRI refers to imaging methods as a whole that exhibit $T_{1\rho}$ relaxation-time contrast, whereas spin locking refers directly to the locking RF field itself.

Cardiac $T_{1\rho}$ MRI Contrast

$T_{1\rho}$ Image Contrast and Tissue Fibrosis

Post-infarction cardiomyocytes undergo cell necrosis and are partially replaced by inflammatory cells, neutrophils and macrophages within the first 24 hours. Within 6–8 weeks, infarcted tissue is almost entirely composed of a vast network of type I and III collagen, supported by myofibroblasts and neovasculature.

We initially explored the relationship between $T_{1\rho}$ MRI contrast and the tissue composition of fibrosis and myocardium in *ex vivo* experiments on heart tissue dissected from pigs 8 weeks post-infarction. In these experiments, segmental, transmural tissue sections containing visible scar and adjacent myocardium were prepared for high resolution $T_{1\rho}$ MRI. The scarred tissue was found to have greater signal intensity than remote and adjacent normally perfused borderzone myocardium (Fig. 2a). We also observed that there was heterogeneity in the scar appearance in $T_{1\rho}$ images, which may result from heterogeneous collagen fiber orientation in scar.

To further validate that the difference in $T_{1\rho}$ MRI signal was a result of differences in tissue composition between scar and cardiomyocytes, we correlated $T_{1\rho}$ images with histology [8•]. Heart sections containing both scar and cardiomyocytes were dissected into 80 mm (circumferential) $\times$ 20 mm (radial) $\times$ 10 mm (longitudinal) sections. The tissue was further divided along the longitudinal axis and contiguous 5 mm sections were separated for *ex vivo* MRI and histology; these sections were thin enough to preserve the overall scar geometry and size. We then obtained $T_{1\rho}$ images (spin lock time, TSL = 50 ms) and $T_{1\rho}$ maps and correlated these images with Masson's trichrome stain of the adjacent tissue section (Fig. 3). There was wall thinning in the infarcted region and subendocardial scar can be seen, although we also observed areas with normal appearing myocytes. The overall shape and size of the fibrotic area resembled the adjacent trichrome-stained histological section (compare Fig. 3a, b, and c).

Origins of $T_{1\rho}$ Contrast in Cardiac Muscle

From the previously described *ex vivo* experiments, we established that $T_{1\rho}$ contrast was sensitive to tissue composition, but we did not yet know what specific tissue components of cardiac muscle structure contributed to ^1H $T_{1\rho}$ nuclear relaxation and how they would ultimately affect the $T_{1\rho}$ signal. There are several potential mechanisms for this effect, such as water molecular motion, ^1H chemical exchange, molecular diffusion, magnetization transfer, residual dipolar interactions, and nuclear Overhauser effects. The relative size of these contributions is not known for cardiac muscle.

The usual way to untangle the various exchange contributions to $T_{1\rho}$ in solutions is to measure the $T_{1\rho}$ dependence on the spin lock amplitude or dispersion. The spin locking pulse will effectively quench low frequency contributions to $T_{1\rho}$ when the spin lock amplitude ω_1 greatly exceeds their rate k ($\omega_1 = \gamma B_1 \gg k$), reducing the relaxation rate $R_{1\rho} = 1/T_{1\rho}$. For diffusion, this occurs when the spin lock amplitude exceeds any magnetic field gradients through which water molecules travel. For ^1H chemical exchange, this occurs when the spin lock amplitude exceeds the exchange rate k_{ex} . A suitable model for the observed $T_{1\rho}$ dispersion is used to determine the contribution of individual relaxation mechanisms.

Without determining yet what the specific mechanisms of $T_{1\rho}$ dispersion were, we hypothesized there would nonetheless be significant nuclear relaxation dispersion in cardiac muscle. Figure 2b and c show the results of a $T_{1\rho}$ dispersion experiment performed over RF amplitudes 0–2.5 kHz in *ex vivo* heart tissue dissected from pigs 6–8 weeks following direct ligation of the left anterior descending coronary artery ($n = 5$). We quantified relaxation rates in the infarct, borderzone and remote myocardium distant to the infarcted area and observed significant relaxation dispersion in all three types of tissue (Fig. 2c). Overall, there was good correspondence between the infarcted area on MRI and the fibrosis on histology.

We fit the $T_{1\rho}$ dispersion data to a model with two mechanisms for $T_{1\rho}$ relaxation: one contribution from all sources of ^1H chemical exchange and another contribution from molecular tumbling. In this experiment, we found it was not possible to isolate individual ^1H exchange contributions to $T_{1\rho}$ in cardiac muscle because there were many contributions and the dispersion curve itself had few features. Despite these challenges, there is a strong dispersion with clinical implications regardless of their origins.

One important clinical implication of this experiment is that compared to T_2 MRI (single spin echo, compare Fig. 2b with spin lock amplitude $B_1 = 0$ Hz and 500 Hz), there was an almost two-fold increase in the ^1H relaxation times at spin lock amplitudes appropriate for clinical use ($B_1 = 500$ Hz). This significantly increases contrast between fibrotic tissue and myocardium. Although it has long been known that T_2 increases with myocardial fibrosis, mixed reports *in vivo* are likely related to inadequate contrast-to-noise ratio (CNR) in routine clinical MRI, especially when compared to late gadolinium enhanced (LGE) MRI.

Potential Contributions of ^1H Chemical Exchange to $T_{1\rho}$ Relaxation Dispersion

For chemical exchange in which there is ^1H transfer between water and another molecule, there are a large number of potential candidates that might contribute to $T_{1\rho}$ dispersion in myocardium. The main candidates are organic acids, such as amino acids or their derivatives, with amine, amide and hydroxyl functional groups including the main backbone of proteins and the side chains of charged amino acid residues. The important properties that determine whether there will be chemical exchange contrast are the exchange rate and contributions to the exchange rate, such as pH and temperature, and overall abundance of the exchanging site. To generate a $T_{1\rho}$ dispersion, the exchange mechanism must be in the

intermediate exchange regime on the rotating frame timescale ($1/\omega_I$). If the exchange is too slow, then there is no observable exchange on the rotating frame timescale. On the other hand, if the exchange is too fast (kHz-MHz), then two resonances with distinct chemical shift will coalesce to a single chemical shift, a consequence of motional averaging on the rotating frame timescale. It is not clear if it is possible to distinguish between the multiple chemical exchange mechanisms using an on-resonance spin lock pulse *in vivo* since water saturation involves magnetization exchange with all potential exchange pathways. However, it can be shown that combinations of exchanging pools of protons can give rise to a similar overall shape and defined by an apparent exchange rate rather than a definite single exchange rate.

Using a slightly different method called chemical exchange saturation transfer (CEST) [9, 10], it is possible to improve exchange specificity if the RF pulse is delivered away from the ^1H water resonance, instead targeting the Larmor frequency of a ^1H nucleus on the same molecules listed above. In this case, continuous saturation and exchange of ^1H nuclei between the selected metabolite and water can result in observable reduction in the image signal intensity. Although this method has been used to target molecules such as creatine [11•] and glucose [12], there are also potential contributions of ^1H transverse relaxation and nuclear Overhauser effects to the detected signal.

$T_{1\rho}$ MRI of Ischemic Heart Disease

There are a few studies reporting the use of $T_{1\rho}$ MRI to visualize acute myocardial infarction. Like T_2 MRI, the main reason for signal enhancement in $T_{1\rho}$ MRI appears to be edema in the myocardial area-at-risk in the acute setting, associated increased tissue water mobility and reduction of the rotational correlation time. Figure 4 shows an example of a $T_{1\rho}$ MR image in a patient four days post-infarction. The infarcted area has greater signal intensity than myocardium remote from the infarction and this area closely correlates with the injury appearing on a late gadolinium enhancement (LGE) MRI scan. Overall the injury appears larger with $T_{1\rho}$ MRI than with LGE MRI, presumably because of differences in the size of the area-at-risk and the area of irreversible injury, as depicted on LGE MRI. In a $T_{1\rho}$ MRI study of 21 patients performed within the first week after reperfusion for myocardial infarction, Muthupillai et al. observed a $66 \pm 39\%$ enhancement in the infarcted area compared to the remote myocardium [13]. In one patient, however, reduction of $T_{1\rho}$ MRI signal intensity was found and closely correlated with microvascular obstruction on LGE MRI. We have also observed the persistence of reduction of $T_{1\rho}$ signal intensity in a patient one year after MI who had microvascular obstruction on his MRI three days after infarction (Fig. 5). In this patient, we observed hypointense MR signal on the LGE MR image with a narrow perimeter of region of enhanced signal intensity. Likely this area was associated with subendocardial microvascular obstruction. One year later, we repeated LGE MRI and also performed $T_{1\rho}$ MRI. We observed signal enhancement on LGE in the previously hypointense region, but also hypointense signal intensity on $T_{1\rho}$, which could possibly be associated with subendocardial hemorrhage.

We performed a $T_{1\rho}$ MRI study at 8 weeks post-infarction in pigs *in vivo* and found similar overall scar size on $T_{1\rho}$ and LGE MRI and after dissecting the left ventricle for *ex vivo* planimetry [14•]. Figure 6 shows $T_{1\rho}$ MR images in a pig with an LAD artery ligation and another with circumflex artery ligation. Similar $T_{1\rho}$ signal intensity enhancement was observed at the infarct in both MRI scans.

As was mentioned earlier, the pathology of tissue molecular changes from acute ischemic injury to fibrosis is a process that evolves over several weeks after infarction. Mustafa et al. reported a serial $T_{1\rho}$ MRI study in mice following permanent ligation of the LAD coronary

artery, studying $T_{1\rho}$ relaxation times at baseline, 1, 3, 7, and 20 days post-infarction ($B_1 = 1,250$ Hz, TSL = 0–54 ms) [15••]. Significant changes in $T_{1\rho}$ were observed after 7 and 20 days infarction, but only moderate, non-significant relaxation time enhancement at earlier times post-injury (Fig. 7).

Contrast Agents

There is very little research exploring the effect of contrast agents on $T_{1\rho}$ contrast. Gadolinium contrast agents are frequently used for myocardial perfusion and LGEMRI to detect ischemia and fibrosis. In poorly perfused or infarcted tissue, gadolinium has very different tracer kinetics and extracellular concentration than in normal myocardium, so it is possible to exploit these differences using an inversion recovery- or saturation-prepared pulse sequence to generate T_1 contrast. Gadolinium contrast agents also are expected to have an effect on $T_{1\rho}$ relaxation, but there is no evidence to suggest that $T_{1\rho}$ relaxation rate enhancement after contrast administration would be superior to T_1 . Huber et al. performed a study to determine the effect of contrast dose and time of imaging after contrast administration $T_{1\rho}$ MRI in patients within a few days post-myocardial infarction and reperfusion [16]. Performing a $T_{1\rho}$ scan at 40 minutes post-contrast resulted in significant contrast between injured and normal myocardium, however, because of the cine pulse sequence timing, the relative contribution of post-gadolinium T_1 relaxation to image contrast is uncertain. Two recent studies have shown the potential for $T_{1\rho}$ sensitivity to albumin-binding gadofosveset [22] and iron oxide [23].

Pulse Sequences for Cardiac $T_{1\rho}$ MRI

In vivo cardiac $T_{1\rho}$ images can be obtained using software to control a sequence of RF pulses and magnetic field gradients and without any additional hardware modifications to a clinical MRI scanner. Usually it is possible to separate the sequence timing into two parts: a first part in which $T_{1\rho}$ contrast is generated using the spin lock RF pulse and a second part in which this contrast is spatially encoded with magnetic field gradients. The encoded data may then be reconstructed into an image with a suitable reconstruction algorithm. For cardiac imaging, this type of sequence is generally referred to as “magnetization-prepared” or, specifically, “ $T_{1\rho}$ -prepared”, because the spin lock pulse prepares the magnetization with contrast for spatial encoding. In cardiac MRI, we have found it best to employ multishot balanced gradient echo or spoiled gradient echo sequences for spatial encoding [17]. This seems to be the most time efficient and robust method to acquire cardiac $T_{1\rho}$ images in humans, when it is important to constrain the scan to a single breath-hold to reduce motion artifacts.

An example of a $T_{1\rho}$ MRI sequence used in humans is shown in Fig. 8. This pulse sequence consists of the spin lock composite pulse cluster and readout sequence. This sequence uses a rotary echo pulse cluster, although dual rotary echospin echo or adiabatic half-passage excitation pulses are commonly used to further reduce sensitivity to field heterogeneity. We deliver the spin lock pulse with moderate duration (TSL < 50 ms) and amplitudes ($B_1 < 600$ Hz) to maximize contrast and limit RF power deposition. A different way to form $T_{1\rho}$ contrast is to repeatedly deliver the spin lock pulse interleaved with cine MRI [18]. This technique also provides myocardial motion information, but in our experience also requires lower spin lock amplitude, limiting contrast, and does not allow for quantification of $T_{1\rho}$ relaxation times.

There is interest to devise faster cardiac $T_{1\rho}$ sequences by incorporating parallel imaging and compressed sensing, obtain multislice or 3D $T_{1\rho}$ data using respiratory gated methods. Using state-of-art acceleration methods, it is possible to obtain 4 $T_{1\rho}$ images and create a $T_{1\rho}$ map within 16 heartbeats (4 beats per $T_{1\rho}$ image), using odd heartbeats to acquire data and

even heartbeats to allow for T_1 recovery. In a patient at rest (60 bpm), this is sufficient time to acquire a $T_{1\rho}$ map from one slice within a single breathhold. When a parametric map is synthesized from multiple images, image registration can be used to minimize motion artifacts in the final $T_{1\rho}$ map.

Challenges for $T_{1\rho}$ MRI in Humans

The sensitivity to field heterogeneity at low spin-lock amplitudes and excess tissue power deposition at higher spin lock fields are problems for $T_{1\rho}$ MRI. These problems are compounded in human cardiovascular MRI, where significant magnetic susceptibility differences can exist between lung parenchyma, myocardial tissue and inflowing blood. In our experience, there is only a very narrow range of spin lock amplitudes available for use *in vivo* that result in safe and artifact free images. Consequently, there remains considerable interest to develop spin lock pulse sequences that are less sensitive to the field heterogeneity. Incorporating composite excitation and inversion pulses and using amplitude and frequency modulated RF pulses, we have developed spin lock pulses that reduce these artifacts [19, 20]. At this time there has been little or no effort to safely increase the spin lock amplitude through the development of innovative transmit coil hardware or to justify less conservative SAR limits using electromagnetic simulations and experiments for cardiovascular spin lock MRI. If the *ex vivo* $T_{1\rho}$ dispersion experiments discussed earlier were any indication, amplitudes as high at 1 kHz would be very beneficial for contrast while simultaneously minimizing $T_{1\rho}$ image artifacts. One adaptable solution is the use of methods that lower spin lock efficiency – those that acquire spin lock amplitudes for only a subset of k-space lines [21]. Still these methods only reduce time-averaged RF power and not peak power, which is subject to a different, higher set of restrictions over a short window.

Future Work

There is much work to be done in cardiac $T_{1\rho}$ MRI. Continued development of $T_{1\rho}$ MRI in both ischemic and non-ischemic disease will lead to multi-parametric analysis of the myocardium along with T_1 and T_2 mapping methods. Pulse sequence improvements are needed such as correction for field heterogeneity to allow consistent measurements of signal intensity across the myocardium and enable comparisons between patients. Faster cardiac $T_{1\rho}$ sequences are needed by incorporating parallel imaging and compressed sensing methods to obtain multi-slice or 3D $T_{1\rho}$ data and combine respiratory-gated methods. Finally, serial studies of $T_{1\rho}$ MRI in both acute and chronic ischemic and non-ischemic heart disease are needed in humans and require validation and correlation with histology in animal models.

Conclusions

$T_{1\rho}$ MRI is a promising non-contrast method for tissue characterization in the myocardium. Recent experiments have demonstrated that $T_{1\rho}$ is sensitive to edema in the acute setting and scar in chronic myocardial infarction. In chronic MI, $T_{1\rho}$ was found to have improved contrast compared to T_2 MRI between scar and myocardial tissue because of suppression of low frequency contributions to the relaxation rate. $T_{1\rho}$ MRI can also be used in patients who are unable to receive contrast agents because of impaired renal function. Further research is needed to improve $T_{1\rho}$ methods in the clinic and to understand the molecular basis for $T_{1\rho}$ contrast in diseases of the heart.

Acknowledgments

The authors thank Dr. Ravinder Reddy for reviewing this work and providing valuable insight and expertise.

Sources of Funding

The authors gratefully acknowledge support from the National Institutes of Health, National Heart Lung and Blood Institute grants K99-HL108157, R01-HL063954, Cardiovascular Medical Research and Education Fund, the Academy of Finland and the Sigrid Juselius Foundation.

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Fig. 1.

The dynamics of the nuclear spin magnetization with and without a spin locking pulse in a frame of reference rotating at the Larmor frequency. The figure insert is the pulse sequence for each situation. **(a)** Dynamics of the net magnetization M without a spin locking pulse. The magnetization is nutated into transverse plane with an initial 90°_x RF pulse. The magnetization then proceeds to rotate around the effective magnetic field B_e . For a large number of isochromats, it can be shown that this process results in dephasing of the net magnetization and T_2^* relaxation. **(b)** Dynamics of the net magnetization with a spin locking pulse. The magnetization is again nutated into the transverse plane with an initial 90°_x RF pulse. However, now the spin locking pulse constrains the motion of the net magnetization around the effective field in a cone. Dephasing is limited and $T_{1\rho}$ relaxation occurs

Fig. 2.

High resolution $T_{1\rho}$ MRI of *ex vivo* heart tissue from a pig 8 weeks post-infarction. The resolution is $50\ \mu\text{m} \times 50\ \mu\text{m} \times 1\ \text{mm}$. (a) Myocardium has lower $T_{1\rho}$ signal intensity (dark gray) compared to fibrotic tissue (light gray). * indicates a possible residual blood clot from dissection and may appear black because of strong magnetic susceptibility gradients from iron and hemoglobin, greatly reducing $T_{1\rho}$ signal intensity. (b) $T_{1\rho}$ parametric maps at five different spin lock amplitudes $B_1 = 0, 500\ \text{Hz}, 1, 1.5,$ and $2.5\ \text{kHz}$. Note that $B_1 = 0$ is a T_2 map obtained using a spin echo sequence with a single refocusing RF pulse. (c) $T_{1\rho}$ relaxation times in infarcted, borderzone and remote myocardial tissue ($n = 5$). The variation in $T_{1\rho}$ relaxation times at different spin lock amplitudes is the $T_{1\rho}$ dispersion. Improved contrast-to-noise ratio at higher spin lock amplitudes is a consequence of increased $\Delta T_{1\rho}$ between infarcted and normal myocardium

Fig. 3.

Correlation between $T_{1\rho}$ MR images and histology. **(a)** A single $T_{1\rho}$ image (TSL = 48 ms). **(b)** $T_{1\rho}$ relaxation time parametric map for the same slice as **(a)**. **(c)** Masson's trichrome stain of an adjacent tissue section. Notice that the relaxation time enhancement in **(b)** corresponds with fibrotic tissue. **(d)** photograph of the same region immediately after left ventricular dissection. The left ventricle has been sliced along the vertical long axis, unwrapped, and sliced again along the short axis (narrow thin strip of tissue on the left). The interface between infarct and borderzone tissue identified for *ex vivo* imaging is outlined (black rectangle)

Fig. 4.

$T_{1\rho}$ (left) and late gadolinium enhanced (LGE) MR images (right) in a patient four days post-myocardial infarction (MI). The enhanced signal intensity in the $T_{1\rho}$ image likely corresponds to edema in the area-at-risk. This area appears larger than the poorly perfused area in the LGE MR image. Images were obtained on a 1.5 T clinical MRI scanner (Avanto, Siemens Healthcare, Erlangen, Germany). $T_{1\rho}$ images were obtained in systole with a TSL = 50 ms spin lock pulse at $B_1 = 500$ Hz and a balanced gradient echo sequence with TE = 1.5 ms, TR = 3 ms, slice thickness = 7 mm, image resolution = 1.4 mm $\times$ 1.4 mm, bandwidth = 558 Hz/pixel, flip angle = 70°, segments = 16 and parallel imaging = 2

Fig. 5.

LGEMR images in a patient four days (left) and one year (middle) post-myocardial infarction and correlation with $T_{1\rho}$ MRI at one year (right). There was hypointense signal intensity on LGE MRI and a hyperintense signal perimeter, which we associated microvascular obstruction at four days post-infarction and reperfusion (left). At one year, the same region appears hyperintense on the LGE MRI image, but appears hypointense on $T_{1\rho}$. Images were obtained on the same 1.5 T clinical MRI scanner (Avanto, Siemens Healthcare, Erlangen, Germany). $T_{1\rho}$ images were obtained in diastole with a TSL = 50 ms spin lock pulse at $B_1 = 500$ Hz and a balanced gradient echo sequence with TE = 1.5 ms, TR = 3 ms, slice thickness = 7 mm, image resolution = 1.4 mm $\times$ 1.4 mm, bandwidth = 558 Hz/pixel, flip angle = 70°, segments = 16 and parallel imaging = 2. LGE images were obtained at approximately 15 minutes post-Gadolinium injection with a phase-sensitive inversion-recovery prepared spoiled gradient echo sequence, TE = 3.2 ms, TR = 6 ms, TI = 300 ms, image resolution = 1.5 mm $\times$ 1.5 mm, slice thickness = 8, segments = 16 and parallel imaging = 2

Fig. 6.
T_{1ρ} MRI images in two pigs at 8 weeks post-myocardial infarction. The first image (left) was from a pig with LAD artery ligation and depicts hyperintense T_{1ρ} signal at the area of infarction. The second image (right) was from another pig with circumflex artery ligation and shows both wall thinning associated with chronic infarction as well as hyperintense T_{1ρ} signal at the area of infarction

Fig. 7.

$T_{1\rho}$ relaxation time measurements from infarct and remote myocardium from a longitudinal study in mice after ligation of the LAD artery. Data points are mean $\pm$ SEM ($n = 4$ [days -1 and 20], $n = 6$ [day 3] and $n = 7$ [days 1 and 7]). (* $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$, two-way ANOVA with Bonferroni's post hoc test)

Fig. 8.

AT_{1ρ} pulse sequence designed for use in humans using a breath-hold and electrocardiogram (ECG)-triggering. The pulse sequence is synchronized to the *R*-wave using a MRI-compatible vector ECG. A delay T is used to capture images in either cardiac diastole or systole; T is the time between the *R*-wave and the start of the first excitation pulse in the spin lock pulse cluster. The spin lock pulse cluster shown here is a rotary echo-type spin lock, consisting of a pair of continuous RF spin locking pulses with opposite phase ($\pm y$) to refocus magnetization in a heterogeneous B_1 magnetic field. TSL is total spin lock time. After the T_{1ρ} pulse cluster, a magnetic field gradient is delivered to crush remaining transverse signal and then an acquisition sequence (readout) is performed. Usually the readout sequence employed is a multi-shot spoiled gradient echo or balanced gradient echo acquisition sequence. Additional pulse sequence modules may be used for fat suppression or to reduce transient modulations of the magnetization during spatial encoding