

Localized NMR spectroscopy on the basis of spin-locking, and $T_{1\rho}$ dispersion imaging

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Introduction

In a previous paper [1] we have shown that spin-lock pulses in combination are suitable for the production of slice-selective signals. The procedure is called SLISE. Assuming a field gradient in x direction, for instance, the slice profile is given by the transverse magnetization component

$$M^{sl}(x) = M_0 \cos^2[\arctan(xG_x/B_1^{sl})] \quad (1)$$

with a half-height slice width of

$$\Delta x_{1/2} = \frac{2 B_1^{sl}}{G_x} \quad (2)$$

(M^{sl} locked magnetization, M_0 magnetization at the beginning of the spin-lock pulse, x coordinate with the origin defined by the resonance condition). Eq. 2 shows that the selected slice thickness is proportional to the amplitude of the spin-lock pulse and inversely proportional to the gradient. Obviously we have the possibility to adjust the thickness by changing B_1^{sl} while the gradient can be kept constant. In particular we do not have to vary the RF pulse shape, and the excitation is independent of the pulse length in contrast to the usual narrow-band pulse techniques. The only condition to be fulfilled is that τ_{sl} is sufficiently long to ensure the complete dephasing of the unlocked magnetization. With the time constant T_2^* with which unlocked coherences decay in the presence of the field gradient, the condition reads

$$T_2^* \ll \tau_{sl} \ll T_{1\rho} \quad (3)$$

The spin-lock procedure can easily be combined with volume-selective spectroscopy methods. As an example, the first slice-selective pulse of the VOSY technique [2] can be replaced by a SLISE pulse. Recently we have proposed another localization technique called LOSY [1]. This method is totally based on the SLISE principle. Localized $T_{1\rho}$ measurements can easily be carried out by the variation of the three spin-lock intervals of the pulse train.

The contrasts of biomedical NMR images are mainly governed by local differences of the relaxation times. Conventional imaging techniques are based on the time constants of spin-lattice relaxation (T_1) of transverse relaxation (T_2). The spin-lattice relaxation rate, T_1^{-1} , is indicative for molecular motions in the regime of the resonance frequency $\omega_0 = \gamma B_0$, where γ is the gyromagnetic ratio and B_0 is external magnetic flux density. The rate of the transverse relaxation, T_2^{-1} , on the other hand reflects molecular fluctuations less than the frequency corresponding to the local fields which arise from the spin interactions.

It has also been suggested [3, 4] to take advantage of the third species of NMR relaxation, the spin-lattice relaxation in the rotating frame with the time constant $T_{1\rho}$. This parameter again is sensitive to slow fluctuation rates. Corresponding pulse sequences (ROSY) have been reported in our previous paper [4]. They permit the determination of local $T_{1\rho}$ values as well as records of $T_{1\rho}$ images.

As a further step towards the definition of more informative image contrasts and measurables for tissue characterization, we now propose the evaluation of the spin-lattice relaxation dispersion, i. e. the frequency dependence

at low frequencies rather than the absolute values of the relaxation times. Clearly the usual method for such investigations, namely field-cycling (e. g. 5) is not feasible in NMR tomography with the exception of special cases [6]. We therefore refer again to the rotating frame. In on-resonance experiments, the relevant frequency corresponds to the amplitude of the spin lock field B_1^{sl} [7] $\omega_1 = \gamma B_1^{sl}$. The range of accessible frequencies can considerably be extended beyond the RF power limit for *in vivo* investigations by the use of the off-resonance technique [8], which will be introduced for tomography purposes in the following section.

Pulse sequences

With the on-resonance technique ROSY [4], the spin-lock pulse serves for the production of the rotating frame conditions and for the preparation of slice signal at the same time. The off-resonance procedure to be described now, consists of a non-volume-selective preparation part followed by a conventional localization technique. The preparation sequence is (fig. 1)

$$(\pi) - \Delta\tau - (\text{spinlock}) - \Delta\tau - \left(\frac{\pi}{2}\right) \quad (4)$$

Basically it is an inversion/recovery sequence. The π pulse inverts the longitudinal magnetization. During the spin-lock interval τ_{sl} spin-lattice relaxation occurs under off-resonance conditions. The $\frac{\pi}{2}$ pulse "reads" the instantaneous z magnetization after the relaxation interval τ_{sl} .

The spin-lock radio frequency ω_{sl} is off-resonance by

$$\Delta\omega = \omega_{sl} - \omega_0 \quad (5)$$

where ω_0 is the resonance frequency. The frequency effective during τ_{sl} therefore is

$$\omega_{eff} = \sqrt{\omega_1^2 + \Delta\omega^2} \quad (6)$$

The effective spin-lattice relaxation rate is [8, 9]

$$\frac{1}{T_{1\rho}(\omega_{eff})} = \frac{\cos^2\phi}{T_1(\omega_0)} + \frac{\sin^2\phi}{T_{1\rho}(0)(1 + \omega_{eff}^2\tau_c^2)} \quad (7)$$

with

$$\phi = \arctan \frac{\omega_1}{\Delta\omega} \quad (8)$$

$T_{1\rho}(0)$ may be approximated by the transverse relaxation time T_2 . The denominator of the last term of eqn. 7 is of particular importance for the envisaged applications.

The locked fraction of the magnetization is proportional to $\cos\phi$. Locking fields with smaller angles ϕ conserve a larger fraction of the magnetization. On the other hand, this angle must not be too low, because otherwise the $T_{1\rho}$ relaxation component becomes negligible. Practically ϕ can be varied between 10° and 45° . This corresponds a variation of ω_{eff} by about one order of magnitude. The dependence of $T_{1\rho}$ on ω_{eff} thus can be evaluated in this range provided that $T_1(\omega_0)$ and $T_{1\rho}(0)$ have been determined or estimated in separate experiments.

For volume selective measurements the reading pulse in fig. 1a is replaced by any volume-selection sequence. In fig. 1b the off-resonance $T_{1\rho}$ technique is supplemented by the VOSY procedure [2], for instance. It is needless to add that the relaxation data in principle can also be recorded for individual spectral lines. In analogy to the on-resonance technique [4] the new procedure is called off-resonance ROSY.

Fig. 2 shows the RF and field gradient pulse sequence for off-resonance $T_{1\rho}$ dispersion imaging as a counterpart to the on-resonance technique [4]. It consists of the off-resonance spin lock sequence fig. 1a with the read pulse replaced by a standard spin echo imaging sequence [10]. The variation of the spin lock interval leads to images weighted according to the different $T_{1\rho}$ decays in this interval. Pure $T_{1\rho}$ images can also be constructed from a whole series of $T_{1\rho}$ weighted images.

On the other hand, variation of the spin lock amplitude and/or the spin lock frequency offset influences $T_{1\rho}$ according to its dependence on ω_{eff} . This dispersion can be transferred into image contrasts by defining an appropriate dispersion parameter. The simplest de-

definition of such a parameter is the mean slope of the dispersion obtained by the aid of the difference of the $T_{1\rho}$ values at two preselected ω_{eff} values

$$p_\rho = \frac{\Delta T_{1\rho}}{\Delta \omega_{eff}} \quad (9)$$

Practically it is however sufficient to record two images merely *weighted* by $T_{1\rho}(\omega_{eff})$ at different frequencies ω_{eff} while keeping the nominal angle ϕ constant. The difference of the pixel intensities, $I(\tau_{sl})$, implies then the information concerning the dispersion of $T_{1\rho}$. In this case the contrast parameter is

$$p'_\rho = I(0) \left\{ \exp\left(-\frac{\tau_{sl}}{T_{1\rho}(\omega_{eff}^{(2)})}\right) - \exp\left(-\frac{\tau_{sl}}{T_{1\rho}(\omega_{eff}^{(1)})}\right) \right\} \quad (10)$$

$I(0)$ is the pixel intensity at time zero. For short spin lock intervals, eqn. 10 can be approximated linearly leading to

$$p'_\rho \approx \frac{I(0)\tau_{sl}}{T_{1\rho}(\omega_{eff}^{(1)})T_{1\rho}(\omega_{eff}^{(2)})} \Delta T_{1\rho} \quad (11)$$

$\Delta T_{1\rho}$ is the difference of the relaxation times at $\omega_{eff}^{(2)}$ and $\omega_{eff}^{(1)}$.

In p_ρ or p'_ρ images, all regions with vanishing $T_{1\rho}$ dispersion are suppressed. The image contrasts thus represent areas where contrast agents are enriched or where the macromolecular composition leads to a sufficient spin-lattice relaxation dispersion in the kHz regime. There may be dispersion parameters other than p_ρ or p'_ρ also suitable for the representation in images, of course. It remains to future studies to find out the quantity most feasible for this purpose.

The applicability in context with the contrast agent MnTPPS4 (manganese porphyrine complex) is demonstrated in figs. 3a and b. $T_{1\rho}$ weighted and p'_ρ images of a mouse with a tumour at the right hind leg are shown. Again no windowing of the grey scale was applied. The detailed description of the mice, of the tumours, and of the contrast agent is reported elsewhere [11]. In this case, the $T_{1\rho}$ dispersion is caused by the scalar or dipolar interactions of protons with the unpaired electrons of manganese. The contrast agent was enriched in the tumour while it was washed out in the intact tissue due to circulation. The

complete disappearance of any intensity outside of the tumour proves that the paramagnetic contrasts can be enhanced by the $T_{1\rho}$ dispersion technique. They exceed those due to enhancement by any of the three relaxation species alone (compare [11]) and are absolutely reliable.

Conclusions and discussion

The spin-lattice relaxation time in the rotating frame, $T_{1\rho}$, is a quantity the dispersion of which potentially provides useful information about molecular motions in macromolecular systems like tissue for instance. Therefore it is of interest to image or to determine volume-selectively a parameter which suitably characterizes this dispersion. Corresponding RF and field-gradient pulse sequences have been presented.

We do not expect dramatic effects with water or normal lipid signals even in the presence of large macromolecular structures, because the mechanisms governing these compounds are known to be relatively fast [12, 13]. Therefore no dispersion of the spin-lattice relaxation at very low frequencies arises. However, signals from the macromolecules themselves are good candidates for dispersion studies.

Spectral resolution normally requires motional narrowing of the resonance lines. This prerequisite does not contradict the expectation of low-frequency $T_{1\rho}$ dispersions: Even in cases where motions are fast enough to fulfill the motional narrowing condition to a high degree, a dispersion can arise if the motions are restricted with respect to reorientations. In the presence of contrast agents with paramagnetic constituents, scalar interaction may be relevant. Under such circumstances, it is the chemical exchange of the interacting molecules rather than reorientations which governs spin-lattice relaxation. The methods are therefore expected to provide the potential of valuable tools for the *in vivo* investigation of tissue with respect to slow motions or chemical exchange processes.