Spin Echo Amplitude in Biological Tissue with Implications for Vessel Size Imaging

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Introduction:
Transverse relaxation in living tissue can be used as a probe of tissue structure. Vessel size imaging [1-3] is a realization of this potential: The mean size of microvessels can be evaluated by comparison of the gradient echo and spin echo amplitudes. In practical implementation, it is often convenient to use multiple refocusing pulses (CPMG-type measurement) instead of a single spin echo (the corresponding imaging sequences are termed RARE, Turbo Spin Echo or Fast Spin Echo). The problem with these techniques is that the vessel size imaging relies strongly on theoretical interpretation of the signal, which is currently not available for echoes obtained with multiple refocusing pulses. The aim of this study is to provide for such a theory in the static dephasing regime, which is the most relevant for measurements with a contrast enhancement at high fields.

Theory:
The relation between the transverse relaxation rates obtained with a gradient echo and a spin echo is described by the well-known formula, Eq.(1) below in which R_2* is the rate measured with the gradient echo, R_2 is measured with a spin echo and R_2' symbolises the effect of the macroscopically inhomogeneous magnetic field. In other words, R_2 is contributed by irreversible processes while R_2' by those which are fully reversible with refocusing pulses. In this context it does not matter how many refocusing pulses are applied and what is the application timing.

The situation changes radically in biological tissue due to the presence of a mesoscopic scale on which the magnetic field varies, for example, due to a paramagnetic contrast agent in the blood pool [4]. This scale contributes one more term in the relaxation rate, Eqs.(2,3). The relaxation rates are now labeled with the sequence type (GE and SE for the gradient and spin echo, respectively). The mesoscopic contribution depends on the sequence. One has to compare the characteristic time of magnetic field variations experienced by diffusing spins with the refocusing time. The dephasing effect of a given mesoscopic structure (e.g. blood vessels) is reversible with a fast refocusing and irreversible for a slow one. In general, the mesoscopic contribution interpolates between these limiting cases. This transition was observed in blood samples as a dependence of the transverse relaxation on the pulse rate of the CPMG sequence [5].

In structureless media: $R_2^* = R_2 + R_2'$. (1) In biological tissue: $R_{2\,\mathrm{GE}} = R_2 + R_{2\,\mathrm{GE}}^{\mathrm{meso}} + R_2'$, (2) $R_{2\,\mathrm{SE}} = R_2 + R_{2\,\mathrm{SE}}^{\mathrm{meso}}$. (3)

Consider now the mesoscopic contribution of the microvasculature to the transverse relaxation rate in the static dephasing regime. In this regime, the gradient of magnetic field is nearly constant for spin packets that significantly contribute to the signal. The effect of such a gradient is described by the attenuation factor, which is well known from the diffusion measurements. It is

$\exp(-Dg^2T_E/12)$ for the spin echo (4) and $\exp[-Dg^2T_E/(12N^2)]$ for the CPMG sequence with N refocusing pulses. (5)

Here T_E is the echo time at with the signal is recorded. It is considered as constant for all sequences. This gradient is different for different locations. Averaging over all possible locations of spin packets yields the result obtained in Ref.[6] for the spin echo. For the CPMG sequence, this averaging is performed in the same way as in Ref.[6] and thus the final result for the extravascular signal attenuation coincides with the result of Ref.[6] up to the replacement of diffusion coefficient D with D/N^2. In particular, this gives the following results for the long-time relaxation rate [6] and the mean vessel size, $\mathcal{R}$, estimated as described in Ref.[3], but with the CPMG preparation instead of the spin echo:

$$R_{2\,\mathrm{CPMG}}^{\mathrm{meso}} = \frac{1}{N^{2/3}} R_{2\,\mathrm{SE}}^{\mathrm{meso}} , \quad (6) \qquad \mathcal{R} = \frac{0.867}{N} (\zeta D)^{1/2} \frac{R_{2\,\mathrm{GE}}^{\mathrm{meso}}}{(R_{2\,\mathrm{CPMG}}^{\mathrm{meso}})^{3/2}}$$, where ζ is the local blood volume fraction (7)

Discussion:
The presence of paramagnetic structure on the scale of cells or capillaries modifies the well-known formula (1). The additional, mesoscopic term is sensitive to the timing of the pulse sequence. On one hand, this complicates interpretation of experimental data. On the other hand, this enables probing the physiologically relevant structure of living tissue. A promising example is the vessel size imaging. The present result shows that the sequence design should be properly taken into account in the data processing.

The factor $1/N$ in the obtained expression (7) for the mean vessel size compensates for a decrease in the relaxation rate for multiple refocusing (N>1), Eq.[6]. In practical implementations, a large N would decrease the contrast-to-noise ratio and thus should be subjected to a careful optimization.

The present results are valid in the static dephasing regime for long echo times. Practically, this leads to an overestimation of the vessel size at 3 T in measurements with gadolinium chelates as the contrast agent [3]. The overestimation should be smaller at higher field strength or higher magnetic susceptibility effect of the contrast agent. Corrections for deviations from the static dephasing result in a better agreement with the anatomical data [7], but are currently unavailable for the CPMG-type sequences. Development of such corrections and account for more features of real sequences will be performed elsewhere.

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References: [1] Dennie et al, MRM 40(1998)793; [2] Troprès et al, MRM45(2001)397; [3] Kiselev et al. MRM 53(2005)553; [4] Kiselev JMRI 22(2005)693; [5] Gillis et al. MRM 339(1995)93; [6] Kiselev, Posse MRM 41(1999)499; [7] Gall et al. proc. ISMRM 2007, abstracts 1444, 1454.