Strong collision approximation to predict iron volume fraction in ex vivo atherosclerotic rabbit's aorta

R. P. Joensuu[1], L. M. Anderson[1,2], A. E. Larsson[1], L-M. Gan[1], M. E. Palmér[1], and P. D. Hockings[1]
[1]AstraZeneca R&D Molndal, Mölndal, Sweden, [2]Chalmers University of Technology, Gothenburg, Sweden

Introduction

Intravenously administered ultrasmall superparamagnetic iron oxide (USPIO) particles are known to be internalized in macrophages in atherosclerotic plaques [1]. The purpose of this work was to evaluate the suitability of the strong collision approximation [2] to predict the USPIO volume fraction in atherosclerotic rabbits' vessel wall from the transverse relaxation time, T_2^*.

Methods

In the strong collision model the magnetic particles are assumed to be grouped in impermeable spheres with a radius of R_c situated in the center of spherical NMR signal emitting medium of radius R. The inhomogeneous field around a magnetic core is approximated by that of a magnetic dipole, the diffusion term $D\nabla^2$ in the Bloch-Torrey equation is approximated by a strong collision operator [2], and the transverse relaxation time is approximated by the mean relaxation time [3]. These approximations enable the transverse relaxation time be written as a function of the magnetic material's volume fraction [2]:

$$T_2^* = \mathrm{Re}\left[\frac{\hat{M}_0(\tau^{-1})}{1-\tau^{-1}\hat{M}_0(\tau^{-1})}\right], \qquad (1)$$

where $\hat{M}_0(\tau^{-1}) = \frac{\tau}{1-\eta}\left[G(\eta\delta\omega\tau) - \eta G(\delta\omega\tau)\right]$, $G(x) = \frac{2}{3}\sqrt{\frac{1}{3}\left(1-\frac{1}{x}\right)}(1-2ix)\,arc\coth\left(\sqrt{\frac{1}{3}\left(1-\frac{1}{x}\right)}\right)+\frac{1}{3}$, $\tau = 4R_c^2/9D$ is the correlation time,

$\delta\omega$ is the characteristic equatorial frequency shift, and η is the volume fraction of the magnetic material (assumed to be much smaller than 1). To take into account the tissue's transverse relaxation time it was assumed that the NMR signal can come from two different types of voxels, ones which contain magnetic centers and ones which do not, and the effective signal from multiple voxels is their weighted sum:

$$I(t) = a(\eta)e^{-\frac{t}{T^*_{2,magnetic}(\eta')}} + [1-a(\eta)]e^{-\frac{t}{T^*_{2,tissue}}}, \quad \text{where} \quad a(\eta)\in[0,1] \quad \text{and} \quad \eta' a(\eta) = \eta\,. \qquad (2)$$

For the numerical parameters $D = 0.55\cdot10^{-9}$ m^2/s was used which is in the range of reported diffusion constant of a rabbit's perfused heart [4], $\delta\omega = 2.51\cdot10^7$ Hz which has been rescaled from [5], and $R_c = 6.0$ nm which is the size of a single Sinerem core.

The theoretical curve was compared with the measurements obtained from nine 5 month old NZW rabbits on high fat diet for 11 weeks which were given 500 µmol/kg USPIO i.v. (Sinerem®; Guerbet Research, France). Seven days after the injection the animals were killed and the aorta was dissected out and kept post fixed in neutral buffered formaldehyde. The mean T_2^* value for each aorta was measured at 9.4T, and the mean iron content from the same aortas was determined by using the EPA methods 200.7 (ICP-AES). The details of the imaging and iron analysis procedures have been reported earlier [6].

Results and Discussion

The theoretical relationship between the magnetic particles' volume fraction and the transverse relaxation time together with the measured aorta values are shown in Fig. 1. There is an excellent agreement ($R^2 = 0.98$) between the theory and the measurements for volume fractions larger than 15 ppm. In this region the best correspondence with the measurements was also obtained when the size of the magnetic centers is the same as the size of a single USPIO particle. For lower volume fractions the theory agrees with the measurements poorly, even when attempting to include the tissue relaxation time in the model (red solid line in Fig. 1). A possible explanation can be that the strong collision model predicts correctly the volume fraction from the T_2^* map when every voxel contains a relatively high number of magnetic particles, but the relationship is more complex if the region contains also voxels with few or no particles.

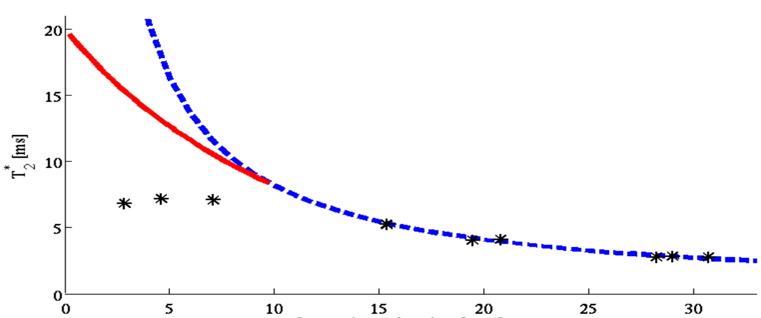

Fig 1. USPIO volume fraction vs. T_2^*. Eq. 1 is drawn as a blue dotted line and the inclusion of Eq. 2 is shown as a red solid line. The measured values are shown as asterisks (*).

References

1. Kresse M et al. Proc Intl Soc Mag Reson Med 1998.
2. Ziener CH et al. Magn Reson Med 2005;54:702-6.
3. Nadler W, Schulten K. J Chem Phys 1985;82:151-60.
4. Forder JR et al. Am J Physiol Heart Circ Physiol 2001;281:H1280-5.
5. Müller RN et al. Magn Reson Med 1991;22:178-82.
6. Joensuu RP et al. Proc Intl Soc Mag Reson Med 2007.