Relaxation mechanisms in collagen rich tissues

Greg J Stanisz
Medical Biophysics, University of Toronto, Ontario, Canada

Although, cartilage, tendon and scar tissue have relatively simple bio-structure they exhibit quite complex MRI behaviour. The reason for this complexity is the interaction between collagen molecules and water protons.

Collagen Hydration

Collagen has a high degree of water absorption due to the process of collagen hydration. In tissue such as cartilage and tendon, the water forms a hydrogen-bonded chains running parallel to the axis of long collagen molecule. The overall model of water hydration involves the chain-like inner hydration layer, in which the water molecules are hydrogen-bonded to the collagen and several outer layers which are considerably more mobile (1). In consequence, the magnetic resonance properties of water in collagen-rich structures are highly heterogeneous and complex. In particular, water exhibits multiple resonance frequencies due to different chemical environment of inner and outer shells (2). Since MR signal strongly depends on water mobility and interactions between water protons and collagen hydrogen atoms, collagen-rich structures have very interesting T2 relaxation properties and high degree of magnetization transfer effect.

T2 relaxation

T2 relaxation is the process of the MR signal decay in the transverse plane resulting from time-dependent variations of the effective magnetic field "seen" by an average proton in the measured system. This "classic" T2 characteristic takes into account rotational and diffusional motion of protons in tissue. In the presence of collagen, water protons have different degree of mobility – these associated with the inner shell are less mobile and therefore their T2 relaxation time is relatively short. The water in outer layers has more degree of freedom and longer T2 relaxation. In consequence, collagen-rich structures exhibit multi-component T2 relaxation (3).

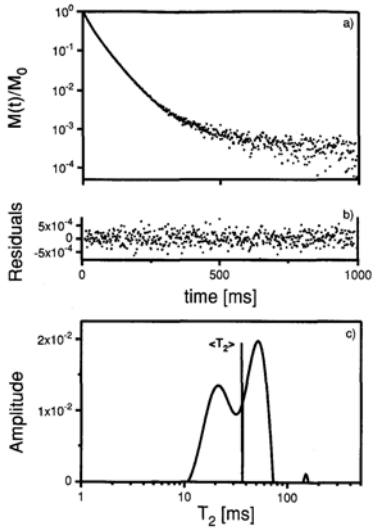

Figure 1. *T2 decay data for cartilage in the direction parallel to collagen long axis -a). Residual deviations of the measured data points from the fitted model of T2 relaxation. The T2 spectra showing the relative number of water protons exhibiting different T2 relaxation times.*

Because of multi-exponential nature of T2 decay, the estimation of T2 relaxation time depends on the experimental parameters. In clinical practise, T2 is typically evaluated using two TE values (two data points in Fig.1a) and may depend on the choice of echo times. Therefore, the quantitative assessment of the T2 relaxation time should be considered with caution.
Moreover, strong orientational dependence of T2 has been observed in collagen-rich tissues (i.e. 1, 4). This T2 anisotropy arises because the dipole-dipole interaction is decoupled when the line between two water spins makes an angle of 55^{o} with the direction of main magnetic field B_0. At this "magic angle", the spins-spin contribution to T2 relaxation is diminished and the T2 relaxation is increased. Interestingly, the strongest anisotropy effect is observed for shortest T2 relaxation times in the T2 spectra (3) (inner shell water). This is to be expected since these protons are associated with water with highly organized hydration layer.

Magnetization Transfer

Very early in the study of cartilage by MRI, it was shown that magnetization transfer (MT) measurements were dependent on the exchange of spins between water and collagen (5). This interaction is also often expressed in terms of magnetization transfer (MT) (6) also known as Nuclear Overhauser Effect (NOE). These spin interactions are mediated by chemical (exchange of protons between water and macromolecule) or physical (dipolar spin) exchange. Figure 2 shows a graphical representation of MT exchange – a two-pool MT model that is simple yet sufficient for quantitative interpretation of MT.

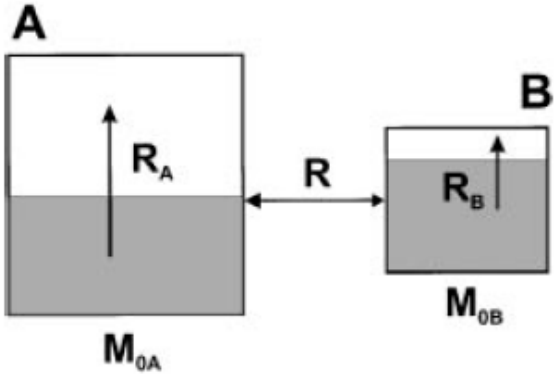

Figure 2. *A two-pool model of magnetization transfer exchange. The shaded region in each pool represents saturated spins. R_A and R_B represent longitudinal relaxation rates ($1/T_1$) in liquid in macromolecular pool. R denotes magnetization transfer exchange.*

Pool A represents the liquid spins (different water layers). The number of spins in this compartment is by convention normalized to unity ($M_{0A} = 1$). Pool B represents the macromolecular spins associated with collagen. In tissues, the number of macromolecular spins is much less than the liquid spins and the relative fraction is given by M_{0B} and is typically in order of few percent. In each pool, and at any instant in time, some of the spins are in the longitudinal orientation represented by the upper un-shaded portion of the compartment and some spins are saturated, represented by the lower shaded portion. The partition into longitudinal

spins and saturated spins depends on the prior irradiation history. In the typical MT experiment the off-resonance saturation pulse is applied. The effect of off-resonance irradiation on this system is different for the two pools. For pool B, the protons in the macromolecules are strongly coupled to each other resulting in a homogeneously broadened absorption lineshape. Thus, off-resonance irradiation results in progressive saturation of the ensemble of spins, with the effective saturation rate being given by the probability of absorption at the corresponding offset frequency times the average radio frequency (RF) power at the offset frequency. In MT experiments, the intent is to manipulate the liquid pool indirectly by saturating the macromolecular pool. However, some direct saturation of the liquid pool is inevitable in this process and must be included in any quantitative analysis of MT effects. The MT data is often presented as a Z-spectrum (6) shown in Fig.3.

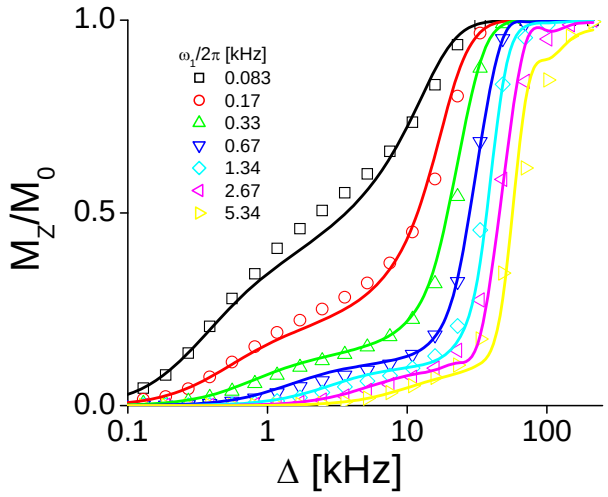

Figure 3. *MT experiment for cartilage. Normalized residual longitudinal magnetization is plotted versus the frequency offset of the RF saturation pulse. Data for seven different RF amplitudes is shown. The solid lines are the fit of two-pool MT model to the experimental data.*

Almost all tissues exhibit MT effects. Interestingly, in collagen-rich tissues the MT effects are the most pronounced. For example, cartilage has the largest macromolecular content, M_{0B} (~17%) and relatively fast MT exchange rate, R = 60 Hz (7). Collagen depleted tissue exhibits significant decrease in macromolecular pool and the rate of MT exchange (8), although these changes are often influenced by the presence of proteoglycans which also contribute to the MT.

Conclusion

In summary, collagen significantly influences MRI water characteristics making it possible to detect changes in collagen structure. However, it is important to realize that MRI sensitivity to collagen structure may be also a source of data misinterpretation in the case of T2 anisotropy and dependence of MRI signal on experimental parameters.

References

1. Berendsen HJC J.Chem.Phys. **36**, 3297 (1962)
2. Chapman GE et al. Proc.R.Soc.Lond. **178**, 465 (1971)
3. Henkelman RM et al. MRM **32**, 592 (1994)
4. Fullerton GD et al Radiology **155**, 433 (1985)

5. Kim DK et al MRM, **29**, 211 (1993)
6. Henkelman RM et al NMR in Biomed **14**, 57 (2001)
7. Stanisz G et al MRM **54**, 507 (2005)
8. Henkelman RM et al MRM **48**, 1081 (2002)