Z-spectroscopy with phase alternating irradiation (ZAPI) in articular cartilage

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INTRODUCTION

Magnetization transfer (MT) experiments have been used earlier for characterization of articular cartilage [1,2]. Due to the large MT exchange between collagen and bulk water, the method could be useful for assessment of cartilage status. In the present study, a recently introduced MT method, alternating phase (AP) Z-spectroscopy (ZAPI) [3] was applied to bovine cartilage samples. In ZAPI, the long irradiation pulse is chopped and the phases of subpulses are alternated between 0 and 180, resulting in an MT pulse saturating only short T_2 spins, such as in macromolecules. Furthermore, ZAPI provides a unique possibility for T_2 filtering; the subpulse duration τ determines the T_2 threshold for spin pools avoiding the saturation. Here on-resonance MT by ZAPI was used for cartilage samples and the MT at different T_2 thresholds was studied in different parts of the tissue.

MATERIALS AND METHODS

Full thickness cartilage samples with underlying bone were prepared from bovine patellae (n = 4, dia. = 8.5 mm) using a core drill and a saw. Two of the plugs were degraded 150 minutes in 1 mg/ml trypsin at 37°C while the other two, the control samples, were immersed in phosphate buffered saline (PBS) containing enzyme inhibitors. Eventually all samples were frozen in PBS at -20°C. Prior to imaging the samples were thawed and immersed in fomblin. The data was collected at room temperature using a 9.4 T vertical magnet with a Varian DirectDrive console and a 19 mm volume coil (Rapid Biomed). Three different MT experiments were conducted: (1) Conventional Z-spectroscopy experiment with constant phase (CP) RF irradiation at 68 Hz RF amplitude, probing offset frequencies from -100 kHz to +100 kHz (43 steps); (2) ZAPI experiment with an AP irradiation at the same RF amplitude, using sinusoidal pulse shape and a fixed τ of 50 µs, frequency range from -100 kHZ to +100 kHz (37 steps) and (3) ZAPI experiment with on-resonance saturation at the same power, but using different τ lengths from 10 to 100 µs. In all the experiments, preparation pulse length of 7 seconds was used, followed by a fast spin echo imaging sequence (TR=12s, TE_{eff}=5ms , ETL=8, 256x64 matrix, 19.2x19.2 mm FOV, 2 averages). Saturation at -100 kHz served as non-saturated control to which all presented values have been normalized. Three ROIs were defined by dividing the cartilage into three approximately equally sized portions: superficial, intermediate and deep cartilage (Fig. 1).

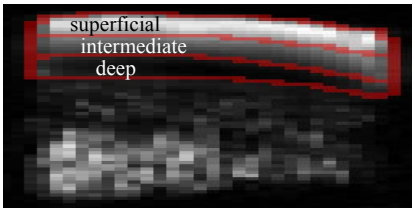

Figure 1. Non-saturated control image of one sample with the cartilage ROIs indicated.

RESULTS

Both AP and CP Z-spectra from different control group ROIs indicated an increase in MT from superficial to deep cartilage (Fig. 2). Both experiments showed a decrease in the superficial MT after trypsin treatment. Interestingly, an increase in MT was seen in the intermediate zone after the trypsin treatment (Fig. 2). Direct saturation sidebands were seen in the AP Z-spectra at ±25 ppm. As expected, the shorter the subpulse duration τ, the fewer macromolecular spin pools are saturated and the less MT is observed (Fig. 3). In superficial cartilage, τ of 10 µs caused very little saturation, and after degradation the MT was lost. In deeper parts of cartilage MT was also present at the shortest τ, indicating more short T_2 spin pools contributing to the signal. Most of the change in MT as function of τ occurred at shorter τ values (Fig. 3). The change in MT induced by trypsin treatment varied depending on the τ in deep cartilage (Fig. 3). The T_2-filtering effect of τ is illustrated in Fig. 4: with long subpulse duration (τ = 100 µs), spins throughout cartilage are saturated, whereas with τ = 20 µs, saturation is seen only in the deepest part of cartilage.

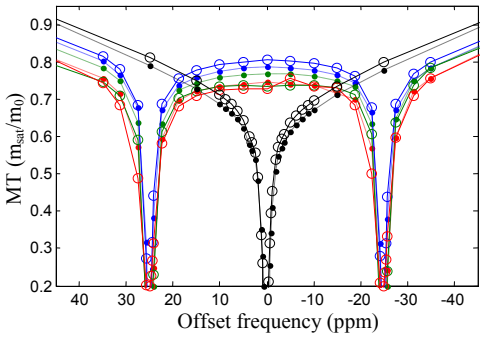

Figure 2. CP irradiation Z-spectra (dashed black control, solid black trypsin treated. Only superficial cartilage ROI shown) and AP (τ = 50µs) irradiation Z-spectra in three cartilage ROIs at different offset frequencies (for legend see Fig. 3), RF amplitude 68 Hz in both. The superficial layer showed the least MT and the contrast was further increased by trypsin treatment.

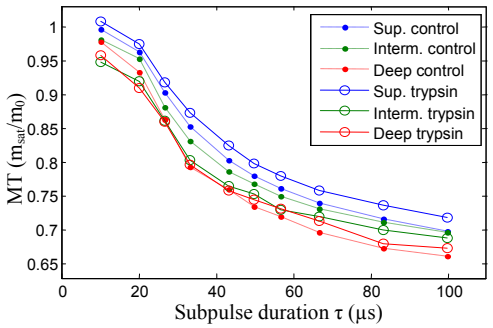

Figure 3. Effect of the subpulse duration τ of AP irradiation at 68 Hz RF amplitude in three cartilage ROIs. Least magnetization transfer was seen in the superficial tissue at all τ (different T_2 filters). MT decreased with shorter τ, but in the deep tissue, MT was seen also with the shortest τ of 10 µs.

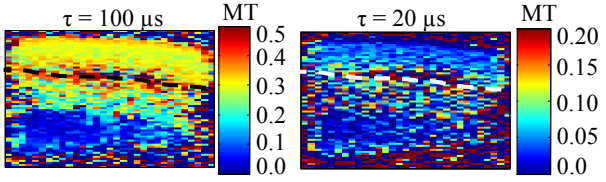

Figure 4. T_2-filtering effect of the subpulse duration τ on-resonance. With τ = 20 µs, only deepest parts of cartilage exhibited MT. Here the image signal is $1\text{-}m_{sat}/m_0$. Dashed lines indicate the cartilage-bone boundary. Please note different MT scales.

DISCUSSION

In the present study, MT in articular cartilage was investigated using a recently introduced ZAPI method. The selective saturation of the macromolecular spin pool and the ability to adjust the T_2 selection criteria provides two exciting possibilities: (i) true on-resonance MT experiments and (ii) a handle to the T_2 distribution in the sample. The difference between control and trypsin-treated samples was seen both in ZAPI experiment as well as in conventional Z-spectroscopy: MT decreased in the superficial and increased in the intermediate cartilage. This suggests that the changes observed are related to the MT between the free water pool and spins associated with hydrophilic proteoglycans. A marked change in MT was seen as a function of the subpulse duration, likely opening possibilities for further analysis of biochemical properties of cartilage: at all τ, a constant decrease in superficial and a constant increase in intermediate cartilage MT was seen after degradation. In the deep tissue, however, after degradation an increase in MT at short τ gradually changed to a decrease at longer τ values, an observation warranting further investigation. Furthermore, it appeared that the T_2 filter could pick up structural and/or biochemical differences along the cartilage depth, likely associated with the depth-wise variation in macromolecular constituents. It is worthwhile to note that ZAPI uses low RF amplitudes, a necessary feature for clinical implementation. Moreover, the preparation pulse is fairly straightforward to implement to typical imaging sequences.

REFERENCES

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