Enhancement of MT, CEST and NOE Contrast via Intermolecular Multiple Quantum Coherences

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Introduction

Chemical exchange saturation transfer (CEST) [1] provides a mechanism for MRI contrast originating from tissue constituents that exchange protons with the bulk water molecules. Recently it was shown [2], that magnetization transfer contrast (MTC) can be enhanced by a combination with intermolecular multiple quantum coherences (iMQC) [3-5]. In this approach the ratio S/S_0 (S and S_0 are the water peaks intensities measured with and without off-resonance irradiation), which is equal to M_z/M_0 when measured in the conventional MTC experiment, becomes $(M_z/M_0)^p$ upon combining it with iMQC where *p* is the coherence order used. The basis of this result is the factoring of the expectation value of the tensor the $\langle I_{z1}I_{z2}\rangle$ (the indices 1 and 2 indicate protons on distinct water molecules) into $\langle I_{z1}\rangle\langle I_{z2}\rangle$, where $\langle I_{z1}\rangle$, $\langle I_{z2}\rangle$ are the expectations values of the z-magnetization of these protons as a result of an interaction with the macromolecules. The enhancement effect of the iDQC (*p*=2) was demonstrated [2] also for the Goldman-Shen [6] and the Edzes-Samulski [7] experiments. In the present work we demonstrate that the enhancement by the iDQC applies also for the CEST and NOE effects. Furthermore, this enhancement is not limited to interactions of water with relatively rigid structures but also applies to flexible residues such as glycosaminoglycan (GAG). The GAG residues, which are components of the proteoglycans are of considerable biological interest and play a role in the pathologies of the cartilage and the intervertebral discs (IVDs). Recently, it was shown that CEST can be used to assess GAG in cartilage using MRI [8].

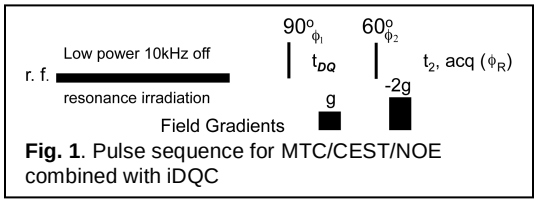

Fig. 1. Pulse sequence for MTC/CEST/NOE combined with iDQC

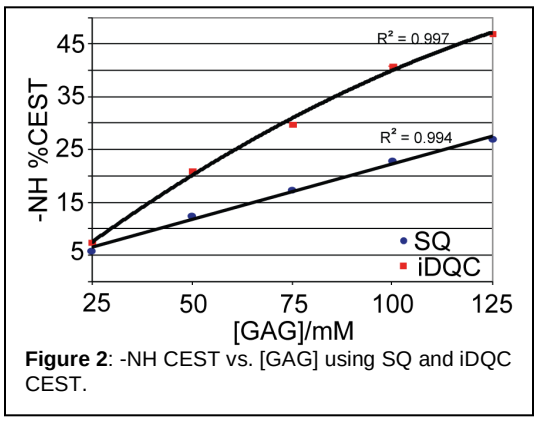

Figure 2: -NH CEST vs. [GAG] using SQ and iDQC CEST.

Materials and methods

NMR measurements: The pulse sequence used in the current study is shown in Fig. 1. A low power pre-saturating pulse is followed by a conventional two pulses iDQC sequence (2-5). Phase cycling was implemented in order to ensure the selection of the desired pathway (coherences: 0 -2 -1). The gradients used were g=18.4 G/cm and 800μs duration. Data are acquired at a 500 MHz Bruker Avance spectrometer equipped with a BBO probe. The temperature of the sample was stabilized at 22°C.

Samples: Two types of samples were examined: (1) glycosaminoglycans (GAG) solution made of chondroitin sulfate in a standard phosphate buffered saline (PBS, pH=7.4) (2) articular cartilage samples cut from bovine tibial plateau obtained from an approved slaughter house within five hours of animal sacrifice (4-6 months old cows). The samples were placed into 5 mm NMR tubes and immersed in flourinated oil (FC-77) in order to prevent void spaces and thus reduce susceptibility artifacts.

Results and Discussion

Figure 2 shows the results of CEST experiments obtained for samples containing GAG with varying concentrations. The conventional CEST method leads to a linear dependence on the concentration. On the other hand in the iDQC experiment the signal depends on the GAG concentration as a second power i.e. $(M_z)^2$ as anticipated for this method. The second power dependence of the iDQC signal on the M_z magnetization was also observed in the measurement of the CEST effect in articular cartilage. A comparison of z-spectra obtained with conventional CEST experiment and by its combination with iDQC is shown in Fig. 3.These results can be well explained using the theory of intermolecular multiple-quantum coherences (iMQCs), as well as, using the classical description based on the dipolar demagnetizing field effects.

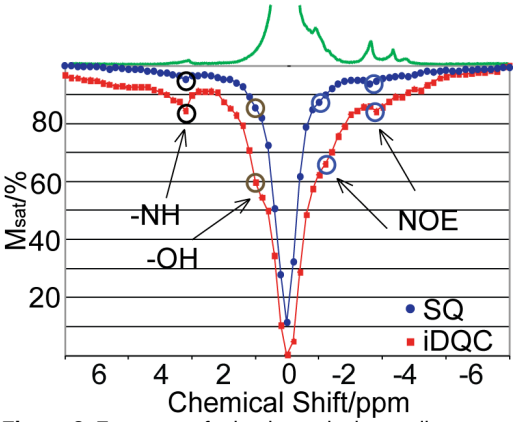

Figure 3. Z-spectra of a bovine articular cartilage sample using conventional and iDQC CEST.

Conclusions

We show here that iMQCs can help enhancing contrast in experiments, which modify the initial magnetization level of spins. Examples are shown for, the CEST, and the NOE effects, as well as, for the MT the Edzes-Samulski, and the Goldman-Shen experiments. Although sacrificing the sensitivity, using iMQCs enhances contrast significantly.

References

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