Measurement of Cartilage Water Content Using T1 and T2 Relaxation Time Measurements

J. E. Kurkijärvi[1], M. Nissi[1], J. S. Jurvelin[1,2], and M. T. Nieminen[3,4]

[1]Department of Physics, University of Kuopio, Kuopio, Finland, [2]Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland, [3]Department of Diagnostic Radiology, Oulu University Hospital, Oulu, Finland, [4]Department of Radiology, University of Oulu, Oulu, Finland

INTRODUCTION

Articular cartilage is comprised of the collagen network (15-22% by wet weight), proteoglycans (PGs) (4-7%) and water (60-80%) [1]. In degenerative joint diseases such as osteoarthritis (OA), the extracellular matrix of cartilage is disrupted. This leads to an increase in cartilage water content as the collagenous network poorly resists the swelling pressure caused by the PGs. Thus, the measurement of water content can serve as a surrogate marker for cartilage degeneration. In this study, we determined the ability of T_1 and T_2 mapping to estimate the bulk water content of cartilage. The dependence of the MRI parameters on water content and proteoglycan content was studied.

METHODS

Full-thickness cartilage disks (dia.=4mm, n=20) without subchondral bone were prepared from bovine patellae (PAT, n=8), lateral patellar groove (LPG, n=4), medial tibial plateau (MTP, n=4) and the femoral medial condyle (FMC, n=4). The samples were immersed in phosphate buffered saline (PBS) containing enzyme inhibitors and frozen prior to measurements. After thawing, the samples were equilibrated for one hour in PBS. T_1 relaxation time was determined at 9.4T and 25°C using a high-resolution spectroscopic volume coil and a saturation recovery sequence (TE=14 ms, 6 TRs between 200 and 5000 ms, 1-mm slice thickness, depth-wise in-plane resolution of 39µm). This was followed by T_2 relaxation mapping with a single echo spin echo sequence (TR=2500ms, six TEs between 14 and 84 ms). Depth-wise full-thickness relaxation time profiles were determined and bulk values were calculated by averaging the profiles.

A small piece from the edge of each cartilage disk was cut and processed into 3-µm thick sections that were stained with Safranin-O, and the optical density (OD) was determined to represent cartilage PG content. The water content of the remaining tissue was determined by weighing the samples with a high-resolution digital scale before and after 72-hour freeze-drying.

The interrelationship between the parameters was studied using the Pearson linear correlation analysis. First order partial correlation analysis was used to assess the dependence between T_1 (or T_2) and water content or PG content (i.e. OD measurements) while controlling for the other constituent. Topographical variations between the samples were analyzed using the Friedman post hoc-test.

RESULTS

Strong correlations were observed between water content and T_1, T_2 or OD (Table 1, Figure 1). A significant correlation was also found between OD and T_1 or T_2. The first order partial correlation showed significant dependencies between water content and T_1, T_2 or OD (Table 1).

Significant topographical variation ($p<0.01$) was revealed for water content, bulk T_1 and T_2 between the samples from the patella (PAT) and the medial tibial plateau (MTP). OD showed a significant difference between the samples from the LPG (lateral patellar groove) and MTP (Figure 2).

DISCUSSION

Previously, the dependence of T_1 relaxation time of cartilage constituents has been unclear. The present results demonstrate a strong linear relationship between T_1 and water content in articular cartilage. Also, T_2 relaxation time correlated with the cartilage water content, which is in line with a previous study [2]. Both T_1 and T_2 were able to reveal the topographical differences in water content between different joint surfaces. Significant dependencies were observed between various MR and compositional parameters, suggesting complex interactions between different constituents, which are also reflected in the relaxation time properties.

Previously, water content of cartilage has been estimated through proton density using a calibration phantom [3] and T_2 relaxation time measurements [2]. T_2 relaxation is, however, dependent also on the orientation of the collagen network through interactions between water bound to collagen fibrils, i.e. the "magic angle effect" [4]. The shape of a typical T_2 relaxation profile is not in agreement with the known depth-wise variation in water content, whereas the monotonically decreasing depth-wise T_1 profile (data not shown) resembles the characteristic water content profile [5]. Given the limitations of the proton density and T_2 –based techniques, more robust methods, such as T_1 relaxation time mapping, are required for determining the cartilage water content. As native T_1 relaxation time measurements may be required for a reliable dGEMRIC experiment [6], the assessment of T_1 alone can provide further aspect into such an experiment as a surrogate marker for water content. The former findings on the negative correlation between T_1 and mechanical properties of articular [7,8] and tissue-engineered cartilage [9] are likely explained by the observed dependence of T_1 on cartilage water content.

Table 1. Linear correlations between different test sites in bovine knee joint (n=20). First order partial correlation coefficient are presented in **bold**.

	T_1(ms)	T_2(ms)	OD	H_2O(%)
T_1(ms)	-	0.74**	-0.78**	0.82**
T_2(ms)	**0.25**	-	-0.67**	0.81**
OD	**-0.22**	**0.08**	-	-0.86**
H_2O(%)	**0.50***	**0.61****	**-0.62*****	-

*p<0.05, **p<0.01, ***p<0.005

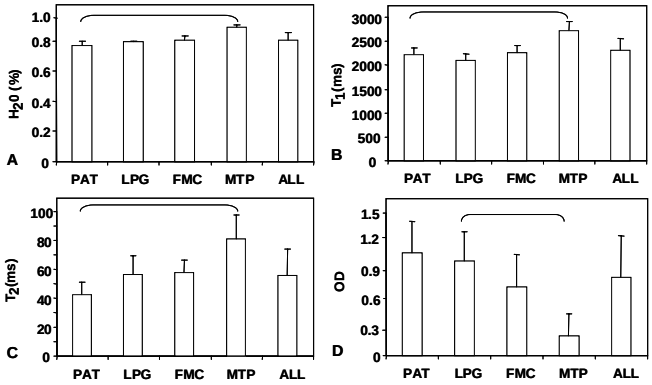

Figure 2. Topographical variations of MRI and compositional parameters in intact bovine articular cartilage. Significant differences between different sites are indicated (Friedman post hoc test, $p<0.01$).

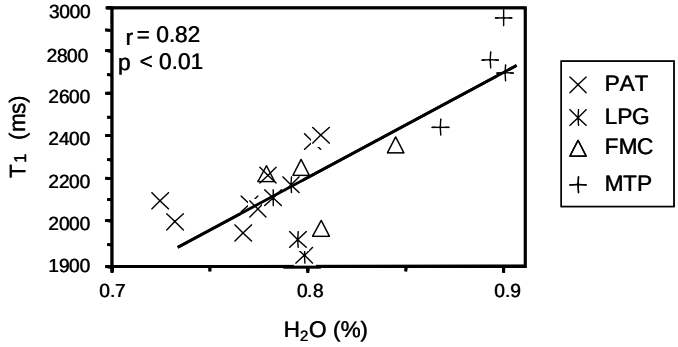

Figure 1. Linear correlation between T_1 relaxation time and water content in bovine articular cartilage (n=20).

REFERENCES [1] Mow C et al. Biomaterials 1992;13:67-97. [2] Lüsse S et al. Magn Reson Imaging 2000;18:423-430. [3] Shapiro E et al. Osteoarthritis Cartilage 2001;9:533-538. [4] Nieminen MT et al. Magn Reson Med 2000;43:676-681. [5] Rieppo J et al. Transact Orthop Res Soc 2004; 29:1021. [6] Watanabe et al., Radiology 2006;239:201-208. [7] Nieminen MT et al. J Biomech 2004;37:321-328. [8] Kurkijärvi JE et al. Magn Reson Med 2004;52:41-46. [9] Miyata S, et al. J Biomech 2007;40:2990-2998.