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돼지 슬관절 자기공명영상에서 대퇴  
연골의 지방억제 T2 map 기법:  
기존 T2 map 기법과의 비교

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지도교수 홍 성 환

이 논문을 의학석사 학위논문으로 제출함

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유 영 진

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위 원 장 \_\_\_\_\_ (인)

부 위 원 장 \_\_\_\_\_ (인)

위 원 \_\_\_\_\_ (인)

## Abstract

# Fat-suppressed T2 Mapping of Femoral Cartilage in Porcine Knee Joint at MRI: Comparison with Conventional T2 Mapping

Young Jin Ryu

Department of Radiology, Seoul National University

College of Medicine

The Graduate School

Seoul National University

**Purpose:** To investigate the effect of fat suppression on T2 mapping of the articular cartilage in porcine knee joint at MR imaging.

**Materials and Methods:** Eleven porcine knee joints were harvested *en bloc* with intact capsules and surrounding muscles. We performed T2 mapping of articular cartilage in the medial femoral condyle with (FST2) and without (cT2) fat suppression in sagittal plane with two frequency encoding directions: from superior to inferior (SI) and from inferior to superior (IS). Consequently, four types of T2 map were obtained: FST2-SI, FST2-IS, cT2-SI and cT2-IS. Two observers measured

T2 values of the medial femoral condyle cartilage at four regions including anterior oblique, central horizontal, posterior oblique and posterior vertical portions.

**Results:** There was no significant difference of mean T2 values between FST2-SI and FST2-IS at all regions ( $p = 0.165, 0.873, 0.077, 0.483$ , respectively). Mean T2 values of cT2-SI were, however, significantly lower than those of cT2-IS at three regions ( $p = 0.057, 0.033, <0.001, 0.019$ , respectively). Coefficient of variation (CV) values between two FST2 maps were lower than those between two cT2 maps in all four regions (17.91-25.57 vs. 25.51-78.72). In addition, ICC between two FST2 maps was higher than that between two cT2 maps (0.276-0.800 vs -0.032-0.455) at three regions except the central horizontal region.

**Conclusion:** Frequency encoding direction greatly affects T2 values of the articular cartilage in conventional T2 mapping. In comparison with conventional T2 mapping, fat-suppressed T2 mapping provides more reproducible T2 values of the articular cartilage by eliminating chemical shift artifact.

**Keywords:** Fat suppression, T2 mapping, Articular cartilage, Chemical shift artifact

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## INTRODUCTION

Currently, magnetic resonance imaging (MRI) is the most important imaging modality for evaluation of traumatic or degenerative lesions in the articular cartilage (1-4). Conventional MRI is useful technique to detect morphologic changes of cartilage, but has limitations to assess changes in compositional aspects, including change in collagen content and arrangement and increment of water content and motion, which happen in the earliest stage of osteoarthritis.

Mapping of T2 relaxation time can allow to identify the compositional alterations which precedes the morphologic change in the cartilage degeneration, which it is found that low grade cartilaginous lesions could be observed only as focal increased T2 relaxation time with normal appearing cartilage in the several studies (5-7). In addition, T2 mapping could offer noninvasive and quantitative method for longitudinal monitoring of biochemical change of cartilage and thus, may be a useful technique of assessment of response to surgical or nonsurgical interventions (8-11). Furthermore, interest in physiologic and biochemical change of articular cartilage has increased and there is a great need for research about T2 mapping that can provide information about regional cartilage compressibility and collagen ultrastructures such as zonal variation (12-17). Therefore, optimal T2 mapping to provide more reliable and reproducible T2 values is essential in the clinical practice and research field.

Chemical shift artifact, however, which is one of many artifacts in cartilage T2 mapping would be problematic for measuring accurate T2 relaxation time as well as thickness of articular cartilage because the effect of chemical shift produces artifact at interfaces between subchondral bone and cartilage and between articular surface and

adjacent fat tissue (7, 18, 19). Fat suppression is used to reduce chemical shift artifact in many routine MR imaging, to our knowledge, however, there have been no published reports about T2 mapping with fat suppression in the cartilage MRI. We assumed that T2 mapping with fat suppression would provide more reproducible T2 values than conventional, non-fat-suppressed mapping by minimizing the chemical shift artifact. Thus, the purpose of this study was to investigate the effect of fat suppression on T2 mapping of the articular cartilage in porcine knee joint at MR imaging.

## Materials and Methods

### Preparation of porcine specimens

Eleven fresh porcine knee joints (4-18 month-old) were harvested *en block* with intact capsules and surrounding muscles at a local slaughterhouse in the morning of the day on MRI. Specimens were stored at room temperature and wrapped with plastic wrap before MRI examination.

### Image acquisition

MR examinations were performed using a 3T MR system (TrioTim; Siemens, Erlangen, Germany) with a dedicated 8-channel knee coil. First, sagittal proton-density-weighted image with Spectral Adiabatic Inversion Recovery (SPAIR) fat saturation, sagittal Dual-echo steady-state (DESS) 3D image and sagittal T1-weighted spin echo image were obtained for evaluation for anatomical structure. Next, four sagittal T2 mappings were obtained including conventional T2 mapping with infero-superior and supero-inferior frequency encoding directions (cT2-IS and cT2-SI, respectively) and fat-suppressed T2 mappings with

infero-superior and supero-inferior directions (FST2-IS and FST2-SI, respectively) (**Fig. 1**). T2 maps were generated using a monoexponential fit from multi-slice, multi-echo source images with six different TEs (13.8, 27.6, 41.4, 55.2, 69.0, 82.8 ms). The details of the MR protocol of T2 maps are as follows: TR, 1200ms for conventional T2 maps, 1360ms for fat-suppressed T2 maps; FOV, 140x140mm; Matrix 380x380; slice thickness, 3 mm; flip angle, 180° ; number of signals averaged, 1; bandwidth, 150 Hz/pixel; echo train length, 1; slices, 26. The scan time for each conventional T2 maps and fat-suppressed T2 maps was 12 minute 22seconds and 9minute 20seconds, respectively.

## T2 relaxation time measurement

Four regions of interest (ROI) were manually drawn by one radiologist and one research assistant (4 and 2 years of clinical experience, respectively) on medial femoral condyle as follows: Anterior oblique region (A), central horizontal region (B), posterior oblique region (C), posterior vertical region (D) (**Fig. 2**). The anterior oblique region was defined as the center of medial femoral trochlea. Central horizontal and posterior vertical regions were determined at the most distal and posterior part of medial femoral condyle. Anterior margin of posterior oblique region was the posterior margin of medial meniscus. All ROIs had to be fitted into length of 5mm and encompass as much of full thickness of the articular cartilage.

First, one radiologist (Y.J.R.) selected the source images with highest echo time (TE = 82.8 ms) for each region and each T2 map which show the best appearance of full-thickness articular cartilage and differentiation between cartilage and adjacent structures such as subchondral bone, meniscus and joint capsule. Next, to mark the position of ROI on the images, the radiologist draw and saved 5mm-in-length lines using a ruler at each region on at the picture

archiving and communication system workstation (PACS; Infinitt Co, Ltd, Seoul, Korea). Finally, two observers independently draw ROIs manually in accordance with the lines on the source image and copy and paste the ROIs on corresponding T2 map. T2 values were measured as the mean pixel value of a ROI on a T2 map. T2 value measurement was repeated with three-month intervals by one radiologist (Y.J.R.) to evaluate intra-observer agreement.

### **Averaged depth-normalized line profiles for T2 values**

For further evaluation, depth-normalization and extraction of 10 values from the articular cartilage on T2 maps were done. Our PC-based in-house software was used for obtaining depth-wise T2 value linear profiles of all subjects that was implemented with a dedicated C++ language with MFC (Microsoft Foundation Classes, Microsoft, Redmond, Wash). Overall procedure of this analysis scheme in this study comprised 3 major stages as follows: First, images were interpolated for normalizing density depth of targeted structures using cubic B-spline method. Then three lines manual drawing were conducted at each region on T2 map from subchondral bone to articular surface by one radiologist (Y.J.R.). After finishing above steps, 10 data point comprising internal values from line profiles were computed automatically.

### **Sample size estimation**

The sample size estimation was conducted using a software program (G\*Power 3.1.9.2, Franz Faul, Kiel University, Germany) with 80% power and a 2-tailed alpha error of 0.05 (20, 21). Previous data from our pilot study showed T2 values were  $155 \pm 49$  (mean  $\pm$  SD) for cT2-IS map,  $114 \pm 22$  for cT2-SI map,  $79 \pm 29$  for FST2-IS map and  $86 \pm 17$  for FST2-SI map, and mean difference of T2 values were  $76 \pm 54$  (mean of difference  $\pm$  SD of difference) between cT2-IS and FST2-IS maps,

28 ± 26 between cT2-SI and FST2-SI maps and 40 ± 32 between cT2-IS and cT2-IS maps. Because the minimal number of specimen needed to detect significant differences between T2 mappings were 7 between cT2-IS and FST2-IS mappings, 9 between cT2-SI and FST2-SI mappings and 8 between cT2-IS and cT2-SI mappings, a sample size of 11 piglets was sufficient to obtain statistical significance.

## Statistical analysis

All statistical analyses were performed by IBM SPSS Statistics (version 22; IBM, Armonk, NY) and MedCalc (version 13.3.1; Mariakerke, Belgium). Results with *p*-value less than .05 were considered significant. Paired *t* test was used to compare mean T2 values between four T2 maps. Agreement between each of conventional T2 mappings and FS T2 mappings were evaluated by calculating Intraclass correlation coefficient (ICC; two-way random effects, average measures, absolute agreement) and coefficient of variation (CV). Averaged T2 values obtained by the two observers were used for statistics. Pixels with T2 values higher than 400 were excluded from our analysis. Interobserver and intraobserver agreements were also assessed by use of intraclass correlation coefficient (ICC; two-way random effects, single measure, absolute agreement). An ICC less than 0.40 was considered to signify poor agreement; an ICC of 0.40-0.75, fair to good (moderate) agreement; and an ICC greater than 0.75, excellent agreement (22, 23).

## Results

### Comparison of mean T2 relaxation times of four T2 mappings

Four outliers with T2 values higher than 400 were observed only on

cT2-IS mapping (1 at region B, 2 at region C and 1 at region D) and were excluded in the following analysis. **Figure 3** demonstrates the mean T2 values of the four T2 maps at each region. There was no significant difference of mean T2 values between FST2-SI and FST2-IS at all four regions. Mean T2 value of cT2-SI was, however, significantly lower than that of cT2-IS except the anterior oblique region. In comparison between cT2 and FST2 maps, the mean T2 values on FS T2 maps were significantly lower than those on cT2 maps with the same frequency encoding directions at the central horizontal and posterior vertical regions. In the anterior oblique region, mean T2 value obtained with FST2-IS map was significantly lower than that with cT2-IS map. On the other hand, no significant difference of the mean T2 values was observed between cT2 map and FST2 map using the same frequency encoding directions at the posterior oblique region.

### **Reproducibility of conventional T2 map and fat-suppressed T2 map**

In **Table 1**, CV values between two FST2 maps were lower than those between two conventional maps in all four regions. In addition, ICC between FST2-IS and FST2-SI maps were higher than that between cT2-IS and cT2-SI maps at all regions except central horizontal region. ICC of FST2 maps showed excellent agreement at the anterior oblique region and fair to good agreement at posterior oblique and vertical regions. In contrary, ICC of cT2 maps showed poor agreement at those three regions. **Figure 4** shows the representative case which demonstrates the chemical shift artifact is more prominent on cT2 maps compared with FST2 maps.

### **Averaged depth-normalized line profiles for T2 values**

**Figure 5** illustrates the averaged depth-normalized line profiles for T2 values of four maps at each region. All linear profiles had peak value at the superficial layer of the cartilage. In addition, the similar spatial variation between FST2- IS map and FST2-SI map were observed at all regions. There is a trend toward higher T2 values obtained with conventional maps than those obtained with FS T2 maps. At the posterior oblique region, however, the lowest T2 value on conventional T2 map with supero-inferior direction was observed among four T2 map, which was more prominent at the superficial layer of the cartilage.

### **Interobserver and intraobserver agreement**

The interobserver agreements in the measurement of T2 value were excellent regardless of cartilage region or type of T2 map (ICC = 0.904 - 0.999) (**Table 2**). The intraobserver agreements were also excellent in all measurements (ICC = 0.832 - 0.998) (**Table 3**).

## **Discussion**

The results of our study demonstrated that fat-suppressed T2 mapping of femoral articular cartilage revealed higher reproducibility than conventional T2 mapping. To our knowledge, this is the first study that elucidates the effect of fat suppression on T2 value of the articular cartilage. This study was initiated by the concerns about potential errors in MR-based measurements of T2 values of the articular cartilage with the presence of chemical shift artifact. Our results indicate that chemical shift artifacts most likely affect T2 values of the articular cartilage in conventional T2 mapping. This means that we may have inconsistent cartilage T2 values according to types of MRI

machine and examination protocol. And it would be problematic to use those T2 values in longitudinal follow-up studies, particularly in multicenter clinical research.

By comparing the T2 values of the images acquired with the diametrically opposite frequency encoding directions, we intentionally magnified the chemical shift effect in the conventional T2 mappings. There were no significant difference of mean T2 values between the paired fat-suppressed T2 mappings, whereas mean T2 values of the paired conventional T2 mappings differed significantly. In addition, the T2 values from the paired fat-suppressed T2 mappings demonstrated the higher ICC and smaller CV than those from the paired conventional T2 mappings. This implies that the fat-suppressed T2 mapping of femoral articular cartilage has higher reproducibility by minimizing the chemical shift artifact as compared to the conventional T2 mapping.

Some outliers with extremely high ( $> 400$ ) T2 values were observed on the conventional T2 mapping method, whereas no outlying T2 value was observed on the fat-suppression method. It is highly suspected that the chemical shift artifact at the cartilage interfaces resulted in quantitative error in conventional T2 mapping, and this can be another explanation for the advantage of fat-suppressed method over the conventional T2 mapping, on the issue of accuracy.

The degree of chemical shift artifacts varied among the cartilage regions. The chemical shift artifact was the severest at the posterior oblique region and the weakest at the central horizontal and posterior vertical regions. It is a reasonable explanation that insufficient fat deposition of young porcine bone marrow was not able to generate sufficient chemical shift artifact at the bone-articular interface at the central horizontal region where the artifact is most prominent on adult



human knee MR imaging. Interestingly, the chemical shift artifact was the most prominent at the anterior and posterior oblique regions. This might be due to the interfaces between articular surface and adjacent fatty tissues, which is a porcine specific anatomical structure but absent in human.

The T2 values measured on fat-suppressed T2 mapping was lower than those on conventional T2 mapping. We assume that both chemical shift artifact and fat suppression can influence T2 values of the articular cartilage. In particular, T2 values obtained with fat-suppressed T2 mapping were significantly lower than those with conventional T2 mapping at the central horizontal and posterior vertical regions in this study. Because the chemical shift artifact was minimal at these two regions, fat suppression per se, seems to be the major factor to reduce T2 values on fat-suppressed T2 mapping. Interestingly, there was an unexpected lower T2 value of the articular cartilage on cT2-SI than on fat-suppressed T2 mappings at the posterior oblique region (Fig. 4F). This exceptional low T2 value on conventional T2 mapping can be explained with chemical shift artifact. We observed lower T2 value of the periarticular fat tissue in comparison with the articular cartilage, and chemical shift-induced fat overlapping on the articular cartilage resulted in such a low T2 value on cT2-SI.

By the advantage over the conventional T2 mapping on the reproducibility in T2 relaxation time evaluation, fat-suppressed T2 mapping of cartilage imaging can be useful as a routine practice, in the following occasions. First, given that the fat-suppressed method allows accurate detection of early cartilage degeneration, it can be a sensitive tool for the longitudinal screening of people in risks for osteoarthritis, which enables timely intervention and subsequent

improvement of the clinical outcome. Second, it can be more reliable than conventional T2 mapping for the evaluation of treatment response by measuring the difference of T2 values between pre- and post-treatment MRI. Finally, it can precisely assess the magnitude and regional distribution of the physiologic loading applied in the articular cartilage without influence of regional variability of chemical shift artifact.

There are some limitations in this study. First, magic angle effect could influence T2 values, particularly at the anterior and posterior oblique regions (24, 25). Albeit with the greatest effect, the magic angle effect would affect four different T2 mapping equally and have minimal implication for comparison of four T2 values at the same region. Second, our results may not be valid in human, due to the variations of the collagen network architecture, thickness of cartilage, and amount of fatty bone marrow among the different ages and species (26-28). A further human study is needed to investigate the effect of fat suppressed on T2 mapping of the articular cartilage. Third, partial volume averaging artifact might have occurred inevitably, because T2 mapping was originally designed as two-dimensional image (1, 2). Finally, we could not assess the accuracy of fat-suppressed T2 mapping because the standard reference method of T2 value measurement has not been established yet.

Our results showed that chemical shift artifact significantly changes T2 values of the articular cartilage in conventional T2 mapping. Fat suppression technique reduces T2 variability of the articular cartilage by minimizing chemical shaft artifacts. We conclude that fat-suppressed T2 mapping of the articular cartilage can provide more reproducible T2 values than conventional T2 mapping.

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Table 1. Reproducibility between two frequency encoding directions on conventional T2 maps and fat-suppressed maps in each region

Region*	Conventional T2 mappings		Fat-suppressed T2 mappings	
	CV (%)	ICC	CV (%)	ICC
A	25.51	-0.032 (-1.296, 0.661)	21.34	0.800 (0.316, 0.945)
B	28.46	0.455 (-0.428, 0.844)	17.91	0.276 (-2.323, 0.815)
C	78.72	0.382 (-0.159, 0.818)	25.57	0.582 (-0.254, 0.880)
D	54.89	0.216 (-0.560, 0.739)	21.81	0.569 (-0.640, 0.885)

Note.—Data in parentheses are 95% confidence intervals. CV = coefficient of variation, ICC = intraclass correlation coefficient

\* Regions of A, B, C, and D mean anterior oblique, central horizontal, posterior oblique, and posterior vertical regions, respectively.

Table 2. Interobserver agreement of T2 maps

Region*	cT2-IS		cT2-SI		FST2-IS		FST2-SI	
A	0.976	(0.800, 0.995)	0.919	(0.742, 0.977)	0.999	(0.997, 1.000)	0.994	(0.968, 0.998)
B	0.908	(0.680, 0.976)	0.904	(0.691, 0.973)	0.984	(0.943, 0.996)	0.988	(0.957, 0.997)
C	0.993	(0.936, 0.999)	0.996	(0.986, 0.999)	0.998	(0.993, 0.999)	0.985	(0.945, 0.996)
D	0.934	(0.662, 0.985)	0.953	(0.771, 0.989)	0.933	(0.823, 0.987)	0.963	(0.721, 0.992)

Note.—Data in parentheses are 95% confidence intervals.

\* Regions of A, B, C, and D mean anterior oblique, central horizontal, posterior oblique, and posterior vertical regions, respectively.



Table 3. Intraobserver agreement of T2 maps

Region*	cT2-IS		cT2-SI		FST2-IS		FST2-SI	
A	0.996	(0.985, 0.999)	0.929	(0.769, 0.980)	0.998	(0.994, 1.000)	0.963	(0.871, 0.990)
B	0.832	(0.486, 0.955)	0.904	(0.683, 0.973)	0.945	(0.811, 0.895)	0.914	(0.701, 0.977)
C	0.970	(0.842, 0.993)	0.992	(0.961, 0.998)	0.989	(0.908, 0.998)	0.985	(0.920, 0.996)
D	0.980	(0.921, 0.995)	0.977	(0.920, 0.994)	0.967	(0.887, 0.991)	0.978	(0.925, 0.994)

Note.—Data in parentheses are 95% confidence intervals.

\* Regions of A, B, C, and D mean anterior oblique, central horizontal, posterior oblique, and posterior vertical regions, respectively.



Figure 1. Sagittal first echo time (13.8ms) source images of the porcine femoral cartilage for T2 mapping: conventional T2 map with inferosuperior frequency encoding direction (A), conventional T2 map with superoinferior direction (B), fat-suppressed T2 map with inferosuperior direction (C) and fat-suppressed T2 map with superoinferior direction (D).

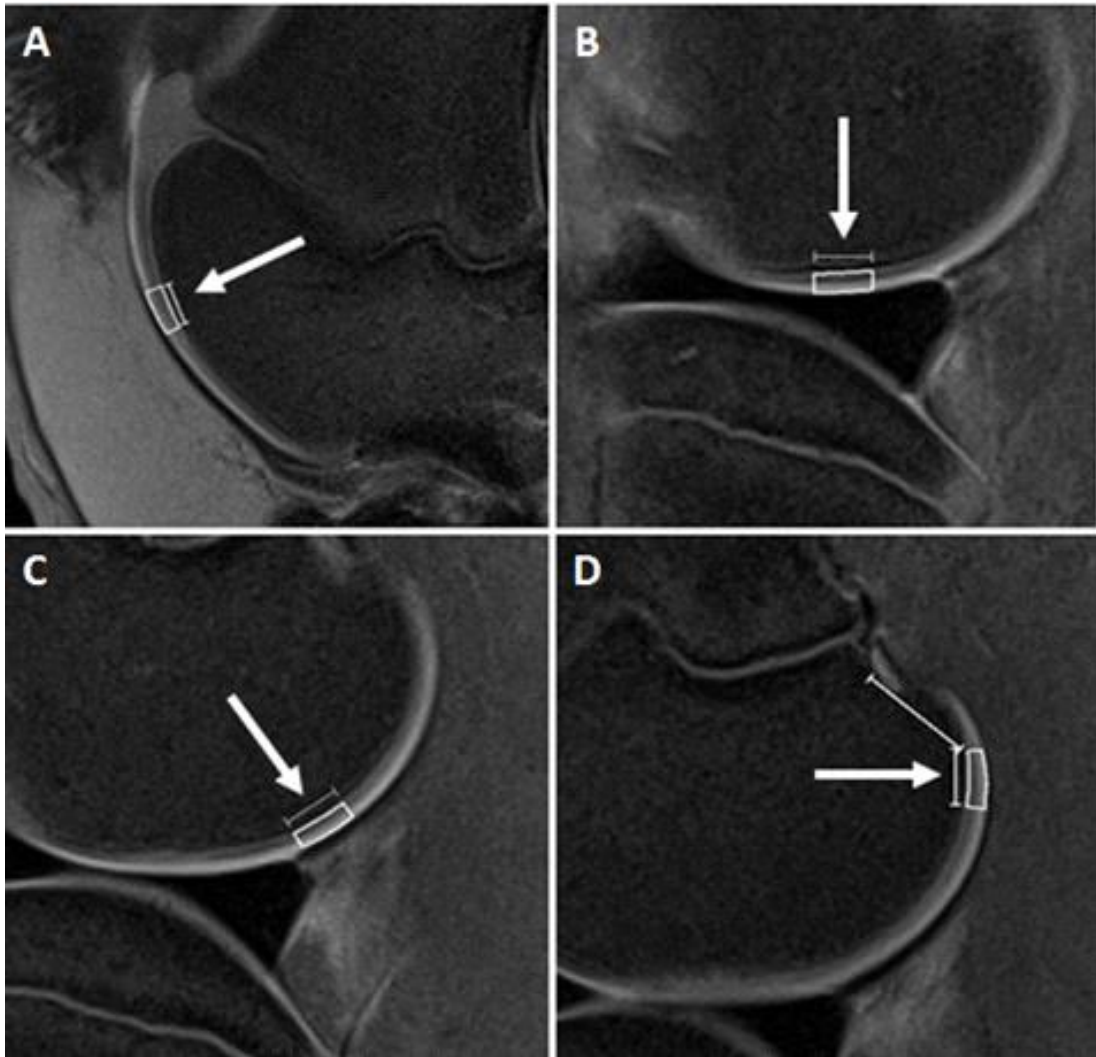


Figure 2. Four regions of interest in the porcine femoral cartilage: anterior oblique region (A), central horizontal region (B), posterior oblique region (C), and posterior vertical region (D).

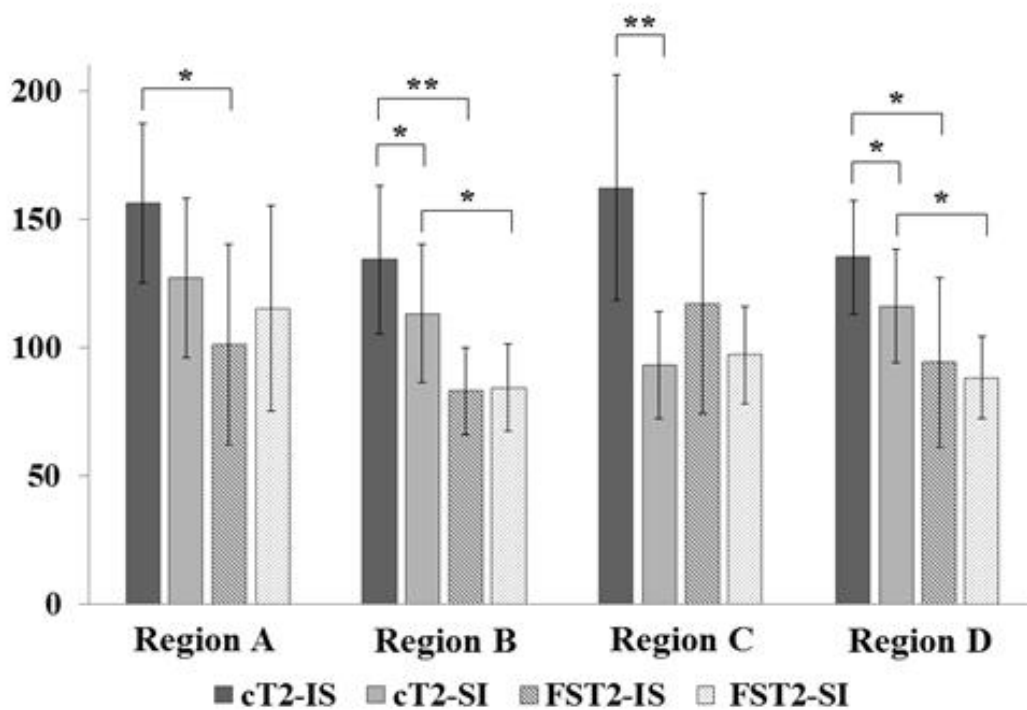


Figure 3. Mean T2 values of four T2 maps in each region (N=11)

Note. — An asterisk (\*) denotes significant differences with  $p$ -value  $<0.05$  and two asterisks (\*\*) signify significant differences with  $p$ -value  $<0.001$  between two groups.  $P$ -values were calculated using paired  $t$ -test. Error bars represent 1 SD above and below mean.

cT2-IS, cT2-SI, FST2-IS and FST2-SI indicate conventional T2 mapping with infero-superior frequency encoding direction and supero-inferior frequency encoding directions, fat-suppressed T2 mappings with infero-superior and supero-inferior directions, respectively.

Regions of A, B, C, and D mean anterior oblique, central horizontal, posterior oblique, and posterior vertical regions, respectively

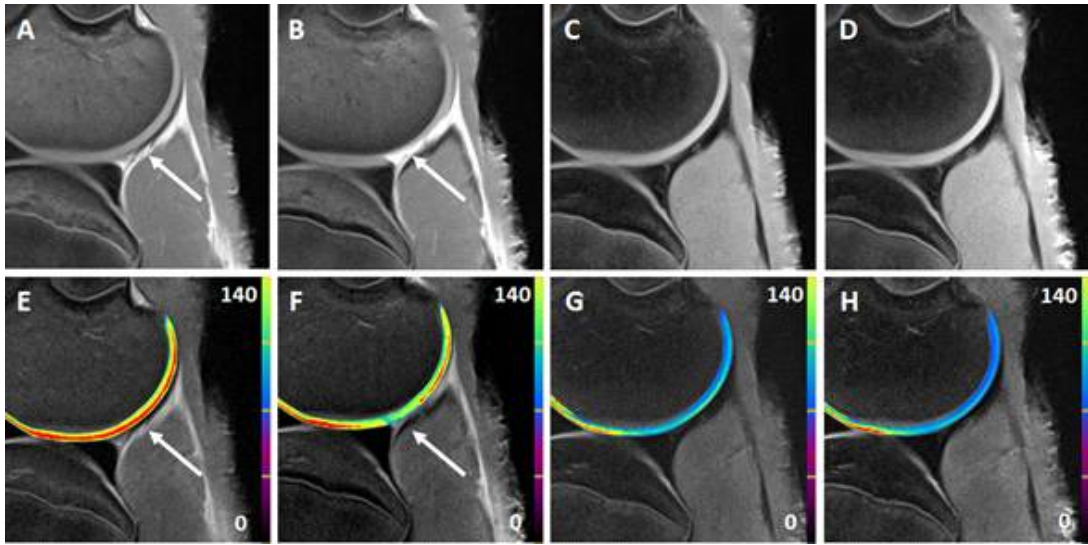


Figure 4. Representative sagittal MR images of the porcine femoral cartilage: first echo time (13.8ms) source images of conventional T2 map with inferosuperior direction (A), conventional T2 map with superoinferior direction (B), fat-suppressed T2 map with inferosuperior direction (C), and fat-suppressed T2 map with superoinferior direction (D). The lower column figures are the corresponding T2 maps (E-H). Chemical shift artifact is shown as a dark line on a source image of cT2-IS map (A, arrow) and a bright line on a source image of cT2-SI map (B, arrow) at the border between the articular surface and adjacent fatty tissue at the posterior oblique region. The artifact at the border disappears with fat suppression (C and D). The cT2-IS map reveals increase of T2 value (E, arrow) and the cT2-SI map shows decrease of T2 value at the corresponding area where the artifact occurred, in the superficial layer of the articular cartilage (F, arrow). T2 values are 153, 88, 69 and 63 on the T2 maps (E-H), respectively.

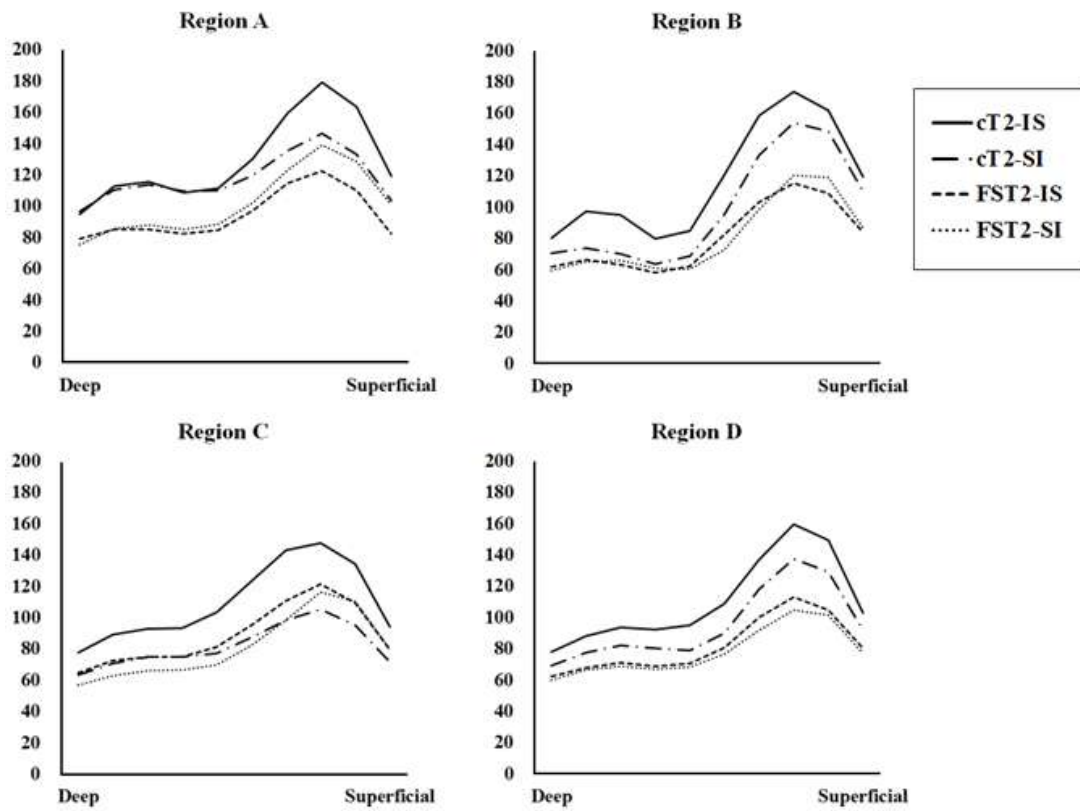


Figure 5. Averaged depth-normalized line profiles for T2 values of four maps at each region

## 국문초록

**목적:** 돼지 슬관절 자기공명영상을 이용한 대퇴 연골의 T2 매핑(mapping)에서 지방억제가 T2 값에 미치는 영향을 알아 보고자 하였다.

**재료 및 방법:** 총 11개의 돼지 슬관절을 주변 관절막과 근육조직이 손상되지 않도록 채취하여 대퇴 연골에 대한 자기공명영상 T2 매핑 검사를 시행하였다. 시상면에서 두 가지 주파수 부호화 방향(상하, 하상 방향)을 적용하여 검사하였고, 이를 지방억제를 적용한 것과 적용하지 않은 상태에서 각각 시행하였다. 결과적으로, 지방억제 T2 매핑-상하 방향, 지방억제 T2 매핑-하상 방향, 기존 T2 매핑-상하 방향, 기존 T2 매핑-하상 방향의 총 4가지 T2 매핑 영상을 얻었다. 두 명의 관찰자가 내측 대퇴골과 관절연골의 네 군데 영역 - 전사위 영역, 중심 수평 영역, 후사위 영역, 후수직 영역 - 에서 T2 값을 측정하였다.

**결과:** 네 가지 모든 영역에서 지방억제 T2 매핑-상하 방향, 지방억제 T2 매핑-하상 방향 간에 T2 값은 의미 있는 차이가 없었다 ( $p = 0.165, 0.873, 0.077, 0.483$ ). 반면에 기존 T2 매핑-상하 방향의 T2 값은 세 영역(중심 수평, 후사위, 후수직)에서 기존 T2 매핑-하상 방향의 T2 값보다 의미 있게 낮았다 ( $p = 0.059, 0.033, <0.001, 0.019$ ). 지방억제 T2 매핑-상하 방향, 지방억제 T2 매핑-하상 방향 간의 변동계수는 기존 T2 매핑-상하 방향, 기존 T2 매핑-하상 방향 간의 변동계수보다 낮았다 (17.91-25.57; 5.51-78.72). 급내 상관 계수는 지방 억제 T2 매핑이 중심 수평 영역을 제외한 세가지 영역에서 기존 T2 매핑보다 높게 나왔다 (0.276-0.800; 0.032-0.455).

**결론:** 기존 방식의 T2 매핑에서 주파수부호화 방향에 따라 연골의 T2 값은 유의한 차이를 보였다. 지방억제를 시행한 T2 매핑에서는 화학변위 인공물이 제거되어 주파수 부호화 방향에 따른 T2 값의 변동폭은 감소하였다.

주요어: 지방억제, T2 기법, 관절 연골, 화학 변위 인공물

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