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Investigation of Regional Influence of Magic-Angle Effect on T_2 in Human Articular Cartilage with Osteoarthritis at 3 T

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Abstract

Rationale and Objectives—The objectives of this research study were to determine the magic-angle effect on different subregions of in vivo human femoral cartilage through the quantitative assessment of the effect of static magnetic field orientation (B_0) on transverse (T_2) relaxation time at 3.0 T.

Materials and Methods—Healthy volunteers (n = 5l; mean age, 36.4 years) and clinical patients (n = 5; mean age, 64 years) with early osteoarthritis (OA) were scanned at 3.0-T magnetic resonance using an 8-channel phased-array knee coil (transmit-receive).

Results—The T_2 maps revealed significantly greater values in ventral than in dorsal regions. When the cartilage regions were oriented at 55° to B_0 (magic angle), the longest T_2 values were detected in comparison with the neighboring regions oriented 90° and 180° (0°) to B_0. The subregions oriented 180° (0°) to B_0 showed the lowest T_2 values.

Conclusions—The differences in T_2 values of different subregions suggest that magic-angle effect needs to be considered when interpreting cartilage abnormalities in OA patients.

Keywords

Osteoarthritis; T_2 mapping; cartilage imaging; magic-angle effect; transverse relaxation time

The primary macromolecules in human cartilage are collagen type II and proteoglycans. Proteoglycan is responsible for much of the compressive stiffness through electrostatic repulsion, whereas collagen provides the tensile and shear strength (1). The earliest biochemical changes in osteoarthritis (OA) are the modifications at the molecular level of cartilage matrix, which occur without obvious morphologic changes. The loss of

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glycosaminoglycan and the collagen breakdown are the typical characteristics of early OA (2–4).

Human articular cartilage is a highly ordered and depth-dependent ultrastructure and is essentially defined by the organization of the collagen fibrils (5). Collagen fibers in histology have three predominant organizational zones across the depth of the cartilage tissue. In the superficial (tangential) zone, the collagen fabrils are parallel to the cartilage surface, whereas in the radial (deep) zone, the fabrils are oriented perpendicular to the surface. However, in the transitional (middle/intermediate) zone, the arrangement of collagen fibers is almost random. The characteristic arrangement of collagen fibers results in the "magic-angle effect" and exhibits anisotropic properties when measured at different tissue depths and from different physical orientations in the proton magnetic resonance (MR) images (5–7).

T_2 mapping is a promising approach for assessing the underlying collagen microstructure in the extracellular matrix of articular cartilage. Damages to the extracellular matrix of articular cartilage and the increase of water content in degenerated cartilage give rise to increases in the T_2 relaxation times (8–10).

Previous studies (5–7,11–14) have revealed that the T_2 values will be elevated when the articular cartilage surface is placed at approximately 55° with respect to the external static magnetic field B_0. The signal changes that occur at angles approximating 54.7° are known as the magic-angle phenomenon because the dipolar interaction between two nuclei scales is $3\cos^2\theta - 1$, where θ is the angle between the internuclear vectors joining the nuclei and B_0. The dipolar interaction that tends to reduce signal intensity will vanish when $(3\cos^2\theta - 1) = 0$, which is satisfied when θ equals 54.7°.

One manifestation of this magic-angle phenomenon is that the T_2 decay of cartilage tissue is greatly retarded, and the signal intensity is maximal when the collagen fiber is oriented at this angle in relation to B_0 (5,11). Other investigators (7,10,13,15–19) reported that T_2 relaxation reflects the ability of free water proton molecules to move and to exchange energy inside the cartilaginous matrix. The T_2 variation may be due to the regional differences in cartilage compression. The weight-bearing portion of the femoral–tibial joint is subject to compressive force that may lower the water content of the cartilage.

The aim of this work was to perform a quantitative assessment of the effect of B_0 orientation on T_2 relaxation times to determine the magic-angle effect on different subregions of in vivo human femoral cartilage at 3.0 T. We measured and compared the global and regional changes of femoral cartilages in T_2 relaxation times for healthy controls and OA patients using quantitative T_2 relaxation method at 3.0 T.

MATERIALS AND METHODS

Human Subjects

Five healthy volunteers (n = 4 men and n = 1 woman, ranging in age from 24 to 45 years, with an average age of 35.6 years) and five patients (n = 3 men and n = 2 women, ranging in

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age from 53 to 82 years, with an average age of 65 years) with clinically documented early knee OA by radiography (Kellgren–Lawrence [K–L] grading scale 1 and 2) (20) were recruited. All healthy volunteers and OA patients were scanned for T_2 mapping. To limit the patient motion between acquisitions, the knee was fixed with foam padding, which is very important because the subject's positioning is extremely critical for subsequent orientation studies of regional cartilage T_2 values. All the human subjects provided informed consent to participate in the research, which was approved by our institutional review board.

Imaging Hardware

All MRI experiments were performed on a 3.0-T clinical MR scanner (MAGNETOM Tim Trio; Siemens Medical Solutions, Erlangen, Germany). An 18-cm diameter, 8-channel, transmit–receive, phased-array (PA) knee coil was used for all the imaging measurements.

Imaging Protocol

The protocol included the following sequence: 2D sagittal T_2-weighted spin-echo (SE) imaging with the following imaging parameters: time of repetition (TR)/time of echo (TE) = 4000/16.5, 33, 49.5, 66, 82.5 milliseconds; field of view = 15 cm; matrix = 256 × 256; bandwidth = 130 Hz; slice thickness = 1.5 mm.

MR Images Analysis and Processing

All the MR images were analyzed based on global and regional compartments. Three subregions (55°, 90°, and 180° [0°] with respect to B_0) were defined in the femoral cartilages of each subject. The in-house developed routines in MATLAB (version 7.1; The MathWorks, Natick, MA) and C++ were used for offline processing of the acquired MR images.

T_2-weighted images with the shortest TE (16.5 milliseconds) were used for the segmentation of femoral cartilages. Regions of interest (ROIs) were segmented manually for each slice for all the subjects. These segmentations were used to draw ROIs for each MR image with different TE values. T_2 maps were computed with custom-built MATLAB routines using the corresponding expression (10,12,13,15).

The intersubject variability of the T_2 maps was quantified using root mean square coefficients of variation percentage (RMS-CV%), and the Student *t* test was used to determine whether there were any statistically significant differences in the T_2 values among the local/global regions of femoral cartilages for asymptomatic and OA subjects.

RESULTS

Figure 1a displays the three subregions oriented 55°, 90°, and 180° (0°) related to the external static magnetic field B^0 in the ventral and dorsal regions with the corresponding magnified details showing the highly organized collagen structure of the human cartilage, respectively. Figure 1b is the plot showing the $(3\cos^2\theta - 1)$ factor as a function of angle with respect to B_0 for nuclear dipolar interaction. In the two positions with two arrows identifying the discrete sampling points where $(3\cos^2\theta - 1) = 0$, the θ equals approximately

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55° and 125°, respectively, and the magic-angle effect may emerge in these two sampling positions. Other arrows show the sampling points where the $(3\cos^2\theta - 1)$ factor has the maximal and minimal values, respectively.

Two representative T_2 (top row) slices obtained from an OA patient overlaid onto the shortest TE (16.5 milliseconds) were displayed in Figure 2a and b, respectively. Figure 2c and d correspondingly showed a series of subregions on the femoral cartilage segmented at every 20° with respect to B_0. Figure 2e is the T_2 profiles of the corresponding subregions segmented in Figure 2c or d. As shown in Figure 2e, the T_2 values of OA generally were greater than those of healthy controls. In the sections oriented 55° relative to B_0 (magic angle, 120°–140° and 240°–260° as shown in Fig 2c or d), the longest T_2 values were detected in comparison with the neighboring sections oriented 90° (100° and 280° as shown in Fig 2c or d) and 180° with respect to B_0. The subregions oriented 180° relative to B_0 showed the lowest T_2 values. Furthermore, the T_2 values displayed obviously greater values in the ventral than in the dorsal regions.

Figure 3 displayed the bar charts of the average ventral and dorsal T_2 values in the subregions oriented 55°, 90°, and 180° relative to B_0 for healthy controls, respectively. The T_2 values showed obviously greater values in the ventral than in the dorsal regions. The subregions oriented 55°, 90°, and 180° with respect to B_0 showed the greatest, the intermediate, and the lowest T_2 values for ventral and dorsal regions, respectively (for ventral: 48 ± 6 milliseconds [mean ± standard deviation] vs. 43 ± 4 milliseconds vs. 37 ± 3 milliseconds; for dorsal: 47 ± 4 milliseconds vs. 41 ± 2 milliseconds vs. 37 ± 3 milliseconds). The *P* values of subregions oriented 55° versus 90°, 90° versus 180°, and 55° versus 180° relative to B_0 for ventral were .0048, .0285, and .0112, respectively, whereas the *P* values of subregions oriented 55° versus 90°, 90° versus 180°, and 55° versus 180° relative to B_0 for dorsal were .0019, .1128, and .0153, respectively. The root mean square coefficients of variation percentage (RMS-CV%) were 11.96, 10.25, and 7.22 for ventral subregions oriented 55°, 90°, and 180° relative to B_0 among healthy subjects, respectively. The RMS-CV% were 8.33, 5.46, and 7.22 for dorsal subregions oriented 55°, 90°, and 180° relative to B_0 across healthy subjects, respectively.

Figure 4 was the bar charts of the average ventral and dorsal T_2 values in subregions oriented 55°, 90°, and 180° relative to B_0 for OA subjects, respectively. Similarly, the T_2 values were obviously greater in the ventral than in the dorsal regions. The subregions oriented 55°, 90°, and 180° with respect to B_0 showed the greatest, the intermediate, and the lowest T_2 values for ventral and dorsal regions (for ventral: 56 ± 5 milliseconds vs. 51 ± 2 milliseconds vs. 47 ± 3 milliseconds; for dorsal: 54 ± 5 milliseconds vs. 48 ± 3 milliseconds vs. 47 ± 3 milliseconds). The *P* values of subregions oriented 55° versus 90°, 90° versus 180°, and 55° versus 180° with respect to B_0 for ventral were .0478, .0327, and .0234, respectively. And, the *P* values of subregions oriented 55° versus 90°, 90° versus 180°, and 55° versus 180° relative to B_0 for dorsal were .0031, .1778, and .0018, respectively. The RMS-CV% were 9.7, 4.26, and 5.92 for ventral subregions oriented 55°, 90°, and 180° relative to B_0 in OA subjects, respectively. The RMS-CV% were 8.46, 7.06, and 5.92 for dorsal subregions oriented 55°, 90°, and 180° relative to B_0 in OA subjects, respectively.

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Figure 5 displayed the combined bar charts of the average ventral and dorsal T_2 values in subregions oriented 55°, 90°, and 180° relative to B_0 for healthy and OA subjects, respectively. Generally, the T_2 values were obviously greater in OA subjects than in healthy controls except that the T_2 values were obviously greater in the ventral than in the dorsal regions. The subregions oriented 55°, 90°, and 180° with respect to B_0 showed the greatest, the intermediate, and the lowest T_2 values for ventral and dorsal regions. All these T_2 variation trends were consistent with those shown in Figure 2e. In subregion oriented 55° relative to B_0, the *P* values of control versus OA subjects for ventral and dorsal were .0217 and .0011, respectively. In subregion oriented 90° relative to B_0, the *P* values of control versus OA subjects for ventral and dorsal were .0019 and .003, respectively. Similarly, in subregion oriented 180° relative to B_0, the *P* values of control versus OA subjects for ventral and dorsal were .0039 and .0039, respectively.

DISCUSSION

In this work, we compared the effect of static magnetic field orientation on the global and local T_2 relaxation time of in vivo human femoral cartilage to determine the magic-angle effect on different subregions of in vivo human femoral cartilage at 3.0 T.

It is generally accepted that the free water is responsible for the elevation of T_2 values in cartilage (8,10). OA is related to the damage to or the loss of the collagen component of the cartilage matrix, which results in the decrease of the cartilage tensile strength (18). T_2 relaxation time mapping is one of the more promising methods for evaluating the underlying collagen structure in the extracellular matrix of articular cartilage. T_2 mapping studies of articular cartilage have demonstrated a strong relationship between water T_2 in cartilage and the underlying collagen structure (10,12). It is likely that early degenerative change in the cartilage matrix will alter the mobility, and thus, the T_2 of cartilage water (7). As shown in Figure 2e, our T_2 relaxation time measurements in both ventral and dorsal regions of human cartilage for OA subjects were generally greater than those for the healthy controls, which is in agreement with prior work (7–10).

The angular anisotropy of T_2 in human cartilage implies that T_2 is strongly influenced by the structure of the collagen extracellular matrix. As shown in Figure 1a, the highly organized structure in cartilage collagen is capable of restricting the motion of water molecules such that the spin–spin coupling becomes to some degree orientation dependent. On the other hand, because human femoral cartilage has a higher curvature than tibial or patella cartilage, the angle between its collagen fibers and the external static magnetic field orientation throughout the femoral cartilage tissue attains a wide range of values (14).

Our results further validated this magic-angle effect of maximal T_2 values at approximately 55° with respect to B_0 orientation. As shown in Figure 1b, Figure 2e, Figure 3, and Figure 4, the T_2 values of subregions oriented approximately 55° relative to B_0 orientation were obviously greater than the neighboring subregions oriented approximately 90° and 180° relative to B_0 orientation for healthy and OA subjects with the minimal increase of about 4.5% in T_2 values across all the sampling subregions along the femoral cartilage. The femoral/tibial joint is a weight-bearing joint and is subject to different biomechanical

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stresses than patella cartilage (13). Generally, the femoral and tibial cartilages bear more weight than patella cartilage. This is another reason that we chose human femoral cartilage of healthy and OA subjects for T_2 quantitative assessment except that the femoral cartilage has a higher degree of flexion, which is more sensitive to the magic-angle effect.

The overall T_2 values in ventral femoral cartilage are greater than those in dorsal femoral cartilage for healthy and OA subjects, which corresponds to the weight-bearing and non–weight-bearing femoral cartilage regions (Fig 2e, Fig 3, and Fig 4). This is most likely due to the known exudation of water from cartilage under compression. Because T_2 relaxation time varies linearly with water content, cartilage under biomechanical load should show lower values (7). On the other hand, the magic-angle effect seems to show the same trend along the measured subregions of human femoral cartilage with the maximal increase of ~17% in ventral region and ~14% in dorsal region of T_2 values between OA and healthy subjects (Fig 2e). The positions of the maximal increase in T_2 values between OA and healthy subjects in both ventral and dorsal regions are all close to the magic angle (120°–140° and 240°–260°). Therefore, it is hypothesized that the magic-angle effect may need to be considered in the interpretation of T_2 data.

As was shown in Fig 2e, the average T_2 values were 48 and 39 milliseconds near the subregions oriented 55° and 180° relative to B_0 orientation in ventral regions for healthy controls, respectively. However, the average T_2 values were 56 and 45 milliseconds near the subregions oriented 55° and 180° relative to B_0 orientation in ventral regions for OA subjects, respectively. The percentage increase in T_2 values for the subregions oriented 55° and 180° relative to B_0 orientation in ventral regions between healthy controls and OA subjects were ~17% and ~15%, respectively. On the other hand, the percentage increase in T_2 values between the subregions oriented 55° and 180° relative to B_0 orientation in ventral regions for healthy controls was ~23%, whereas the percentage increase in T_2 values between the subregions oriented 55° and 180° relative to B_0 orientation in ventral regions for OA subjects was ~24%. It seems that the magic-angle effect is relatively more obvious based on the percentage change between the subregions oriented 55° and 180° relative to B_0 orientation in ventral regions for OA subjects.

As were shown in Figure 3, Figure 4, and Figure 5, there exists significant difference in T_2 values between subregions oriented 55° relative to B_0 and those of the neighboring subregions oriented 90° and 180° relative to B_0 in ventral and dorsal femoral cartilages for healthy and OA subjects ($P < .05$). Although the longest T_2 values were detected in sections oriented 55° to B_0 (magic angle) in comparison with the neighboring sections oriented 90° and 180° to B_0, the subregions oriented 90° to B_0 showed the intermediate T_2 values, and the subregions oriented 180° to B_0 showed the lowest T_2 values, there is no significant difference in T_2 values between subregions oriented 90° relative to B_0 and those of subregions oriented 180° relative to B_0 in ventral and dorsal femoral cartilages for healthy and OA subjects (for healthy controls: ventral, $P = .0285$; dorsal, $P = .1128$, as shown in Fig 3; for OA subjects: ventral, $P = .0327$; dorsal, $P = .1778$, as shown in Fig 4). This may be because of the relatively lower insensitivity of magic-angle effect on subregions oriented 90° and 180° relative to B_0 in comparison with the sections oriented 55° to B_0 and the more biologic load in subregions oriented 180° than subregions oriented 90° with respect to B_0

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may lead to the lowest T_2 values for the former which may exude more water from the cartilage collagen matrix and thus give rise to the decrease of T_2 values (2,7–10).

The T_2 relaxation time is sensitive to slow molecular motions of water protons and anisotropy of the human cartilage and has been shown to demonstrate modifications in anatomically intact tissue in vivo (10). The inherent T_2 relaxation time of cartilage is derived from the interactions of cartilage water with the cartilage macromolecules (predominantly from collagen integrity), which are modulated by their chemical and structural states.

Previous in vitro studies (5,6) have reported that T_2 relaxation time variations showed the obvious orientation dependence on the static magnetic field. The present preliminary study is the first to ever report that a quantitative assessment of the effect of static magnetic field orientation on T_2 relaxation time was performed to determine the magic-angle effect on different subregions of in vivo human femoral cartilage at 3.0 T for healthy and OA subjects. Although it was unlikely that the magic-angle effect for T_2 map accounted for regional differences in cartilage signal intensity in the case of the small orientation effect (12) and the angular dependence on the external B_0 magnetic field for T_2 values has made it difficult in acquiring a correct appearance of T_2 maps, previous in vivo (10) and our own results showed obvious increase in T_2 values in OA patients when compared to the healthy subjects ($P < .5$, Fig 5); therefore, it is of great significance to measure and compare the T_2 mapping of different subregions of human cartilage because of the magic-angle effect, which may provide a consistent information for the in vivo evaluation of cartilage physiology and pathology. Although previous studies (5,6,10) have shown the T_2 dependence of oriented water in the ordered collagen matrix in cartilage, the present work extends these experiments to both in vivo and regional cartilage experiments. The results of this study are likely to impact future research studies on T_2 relaxation in cartilage.

There are several limitations to this work. First, we evaluated this phenomenon exclusively at 3 T, extrapolation to 1.5 T, or 7 T should be done with care. Second was the relatively small number of both volunteers and patients studied. Future study may include the investigation of the effect of static magnetic field orientation on T_2 relaxation time and the determination of the magic-angle effect on in vivo human tibial and patella cartilages at different field strengths with larger numbers of individuals evaluated.

CONCLUSIONS

The preliminary results indicate that magic-angle effect may play an important role in cartilage T_2 mapping and needs to be considered when interpreting the cartilage abnormalities in OA patients.

Acknowledgments

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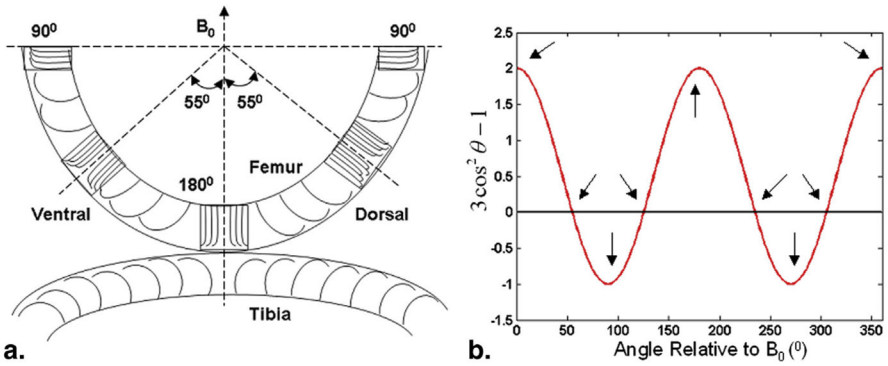

Figure 1.

(a) The schematic diagram of the arrangement of collagen fibers across different layers of human cartilage. Three magnified details of the local regions of human femoral cartilage display the corresponding subregions oriented 90°, 55° (magic angle), and 180° with respect to the external static magnetic field B_0, respectively. **(b)** The plot showing the $(3\cos^2\theta-1)$ factor as a function of angle with respect to B_0 for nuclear dipolar interaction. Two *arrows* identify the discrete sampling points where $(3\cos^2\theta-1)$, the θ equals approximately 55° and 125°, respectively, and the magic-angle effect may emerge in these two sampling positions. Other *arrows* show the sampling positions where the $(3\cos^2\theta-1)$ factor has the maximal and minimal values, respectively.

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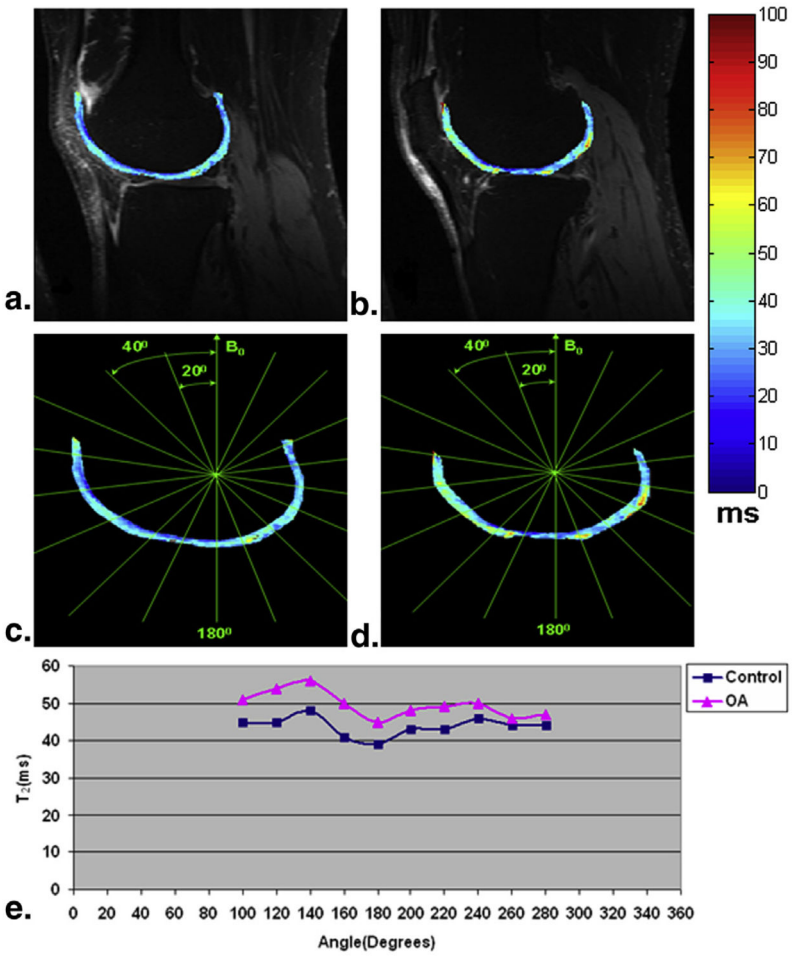

Figure 2.

Two representative T_2 (*top row*) slices obtained from an osteoarthritis (OA) patient were displayed **(a** and **b)**. A series of subregions on the femoral cartilage segmented at every 20° with respect to B_0 **(c** and **d)**. The T_2 profiles **(e)** of the corresponding subregions segmented in **c** and **d**.

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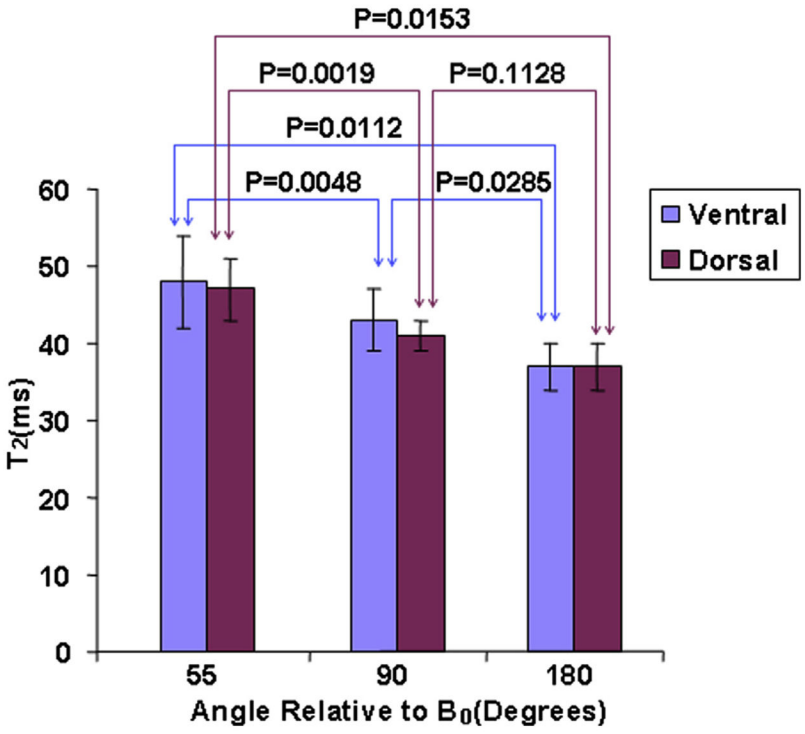

Figure 3.

The bar charts of the average ventral and dorsal T_2 values in subregions oriented 55°, 90°, and 180° relative to B_0 for healthy controls, respectively.

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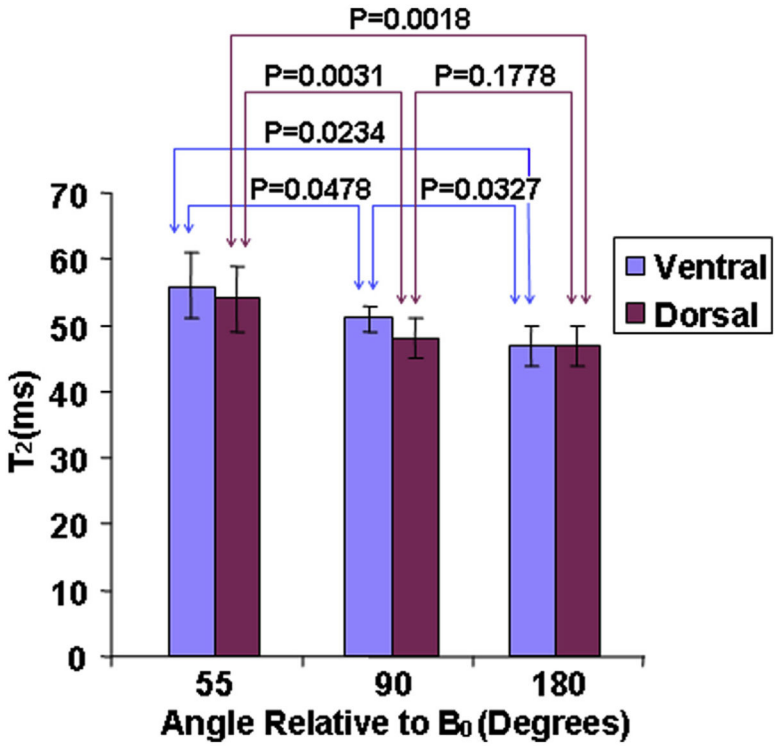

Figure 4.

The bar charts of the average ventral and dorsal T_2 values in subregions oriented 55°, 90°, and 180° relative to B_0 for osteoarthritis subjects, respectively.

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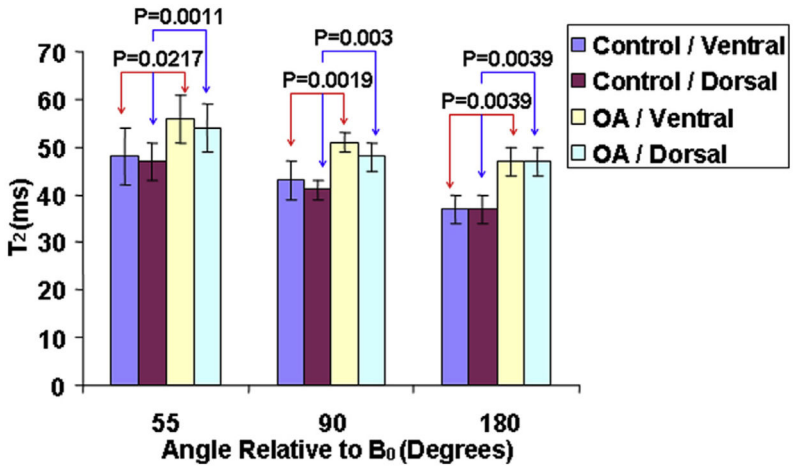

Figure 5.

The combined bar charts of the average ventral and dorsal T_2 values in subregions oriented 55°, 90°, and 180° relative to B_0 for healthy and osteoarthritis (OA) subjects, respectively.