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Quantitative T2 mapping of glenohumeral joint osteoarthritis: a case-control study

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Abstract

Background: T2 relaxometry is a highly sensitive technique used to assess morphological changes in the cartilage prior to anatomical changes; it provides the quantification of the disparate components of cartilage such as water, proteoglycans, and collagen. This study aims to assess T2 values of glenohumeral joint cartilage using 1.5 T magnetic resonance imaging (MRI) and comparing T2 relaxation time values between two groups—the control group and the group of patients with osteoarthritis (OA). The study was conducted among 35 OA patients (27 females and eight males; median age, 60 years; age range, 43–69 years). This group was divided into primary OA (n = 15) and secondary OA (n = 20). The control group had 30 patients (25 females and five males; median age, 46 years; age range, 30–56 years). All patients were assessed using plain radiography to determine the grade of osteoarthritis followed by a multi-echo spin pulse sequence (T2 mapping) of the coronal plane. Three areas were considered to evaluate the cartilage-humeral zone, glenoid zone, and central zones by manually drawing the region of interest (ROI). The values were compared statistically by using Mann-Whitney U tests.

Results: Median T2 values differed significantly between the control group (43.4 ms [interquartile ranges, 41.54-45.33 ms]) and the OA patients for grades I (59.2 ms [interquartile ranges, 57.54-63.33 ms]), II (64.7 ms [interquartile ranges, 62.54-67.39 ms]), and III (61.9 ms, [interquartile ranges, 57.54-64.53 ms]). Mean T2 values were significantly higher in the different zones when comparing the OA patients whatever the cause primary or secondary (p value < 0.05) with the control group; no significant difference was noticed between the primary and secondary OA (p value > 0.05).

Conclusion: T2 relaxometry is a reliable, quantitative method for the assessment of the glenohumeral cartilage for significant differences in T2 values between the control group and the OA patients.

Keywords: Glenohumeral cartilage, Osteoarthritis; Quantitative method, T2 mapping, Relaxometry

Background

Shoulder osteoarthritis (OA), described as damage to the articular surface covering the ball and socket of the joint, can be due to many factors including disease, tear and wear, and injury [1]. Shoulder OA may be primary or secondary; indeed, in this instance, the primary one occurred without predisposing factors, while the secondary one occurred mainly because of the rotators cuff tear, trauma, and operation [2, 3].

The glenohumeral joint was not a weight-bearing joint so the primary OA was more common, and its degeneration occurred through a cell-mediated mechanism rather than a mechanical stress; in turn, the degeneration affected the cartilage diffusely. On the other hand, the secondary (OA) occurred mainly because of the rotator cuff tear that elevated the humeral head; the cartilage affection then differed according to the anatomical site [4]. A conventional MRI of the shoulder joint had been used for assessing the anatomical changes such as cartilage thickness, erosion and edema. However, the morphological changes, as early degenerative and irreversible cartilage damage, could not be assessed and they are in

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need for a more quantitative method. The cartilage mainly comprised a mixed matrix of type II collagen, proteoglycans, and water. It is worth nothing than proteoglycan size and glycosaminoglycan have been found to decrease with aging and disease [5].

Newly developed quantitative MRI methods for the evaluation of the articular cartilage and assessment of matrix composition are available including T2 mapping, T1 relaxation time in a rotating frame (T1rho), and diffusion tensor tractography (DTI); and here, T2 relaxation times were correlated with collagen matrix and water changes [5, 6].

T1rho mapping was sensitive to the macromolecule content of tissue, and therefore it was highly effective in visualizing the early changes in OA. However, it needed field strengths greater than 3.0 T and an enormous RF power applied in the preparation. The spin-lock pulse might cause heating of tissues and problems with a specific absorption rate. In addition, the limited accessibility of this sequence of commercial MRI systems is responsible for its nonuse in clinical applications [7].

DTI offered a unique insight into cartilage structure and orientation; however, it could be difficult in vivo, as it maximized cartilage signal at short TEs and diffusion-sensitizing gradients increased TE and motion sensitivity. Low SNR and spatial resolution limited single-shot techniques [8].

Few studies have tried to assess the role of T2 mapping in the shoulder joint [4, 9], as it is a non-invasive means for assessing the water content of cartilage and the interaction of water with the extracellular cartilage matrix at a molecular level [10].

Our study aimed to quantitatively assess both normal and OA glenohumeral joints and tried to evaluate the T2 values of the control group, as well as the primary and secondary OA patients.

Methods

It is a case-control study, conducted between October 2018 to October 2019, and included 35 OA patients (27 females and eight males; median age, 60 years; age range, 43–69 years). The study group had primary OA (n = 15) and secondary OA (n = 20) in the glenohumeral joint; and we used 30 patients as a control group (25 females and five males; median age, 46 years; age range, 30–56 years).

The ethical committee of our institution approved the study. Inclusion criteria included any patient with osteoarthritis detected by X-ray and graded by the same two musculoskeletal radiologists who later evaluate MRI. The Samilson Prieto method used for the X-ray grading [11, 12]: grade 0, normal; grade I, inferior humeral and/or glenoid exostosis, both measuring < 3 mm in size; grade II, inferior humeral and/or glenoid exostosis, > 3 and < 7 mm in height, with slight glenohumeral joint irregularity; grade III, an inferior humeral and/or glenoid < 7 mm in height, with narrowing the glenohumeral joint and sclerosis. The inclusion criteria of the control group were normal X-ray findings of the shoulder joint; they conducted MRI for many reasons, as 20 individuals had distal soft tissue swelling because of minor trauma and 10 had bone tumors. The exclusion criteria of both the control group and the OA patients were fracture, acute arthritis, history of previous shoulder joint operation, and any contraindication for MRI.

MRI technique

We made an MRI using a 1.5 T MR scanner (Signa; 16channel, Excite, GE Healthcare, Milwaukee, WI, USA). Conventional MR sequences included coronal oblique T2-weighted (T2W) images (repetition time/echo time, 3220/70 ms), coronal oblique T2W images with fat suppression (3230–3245/70 ms), coronal oblique T1-weighted images (630/10 ms), sagittal oblique T2W images (3360/80 ms), axial proton density-weighted images (3500/20 ms), and axial T2W images with fat suppression (3130/60 ms) with a shoulder coil. Field of view (FOV) 22 × 18 mm; matrix, 310 × 620; slice thickness, 4 mm and slice gap, 0.4 mm. Three coronal oblique data sets were evaluated through the shoulder to get T2 mapping by using multi-echo spin-echo with a TR of 2630 and seven TEs (13 ms, 26 ms, 39 ms, 52 ms, 65 ms, 88 ms, and 10 ms) [4]. FOV 22 × 18 mm; matrix, 159 × 318; slice thickness, 3 mm; slice gap, 1 mm. The total acquisition time for T2 mapping was 5 min. We preprocessed the images with an automatic motion correction to remove any motion artifact. Our MR technologist created a colored T2 map using the default functions and software setting. The T2 maps contained 16–22 color coronal oblique images with basic parameters of the T2 intensity with default parameters of 25–75 ms. The color scale ranged from red to blue. To standardize segmentation, we identified the central slice of coronal oblique where the total volume of the cartilage was observed and the partial volume effect markedly decreased. We extracted T2 values from a mono-exponential fit to the signal decay curve for each voxel using commercially available software (PRIDE; Philips Medical Systems). The slice position was the same as that of the conventional MRI. We chose three areas to evaluate the glenohumeral cartilage: humeral zone (the most superior-lateral portion), glenoid zone (the most inferior portion of the glenoid cavity), and central zone (the central part of cartilage) by manually drawn region of interest (ROI) visually inspected on the

sequences. ROIs were drawn keeping a margin between 0.5 and 1.1 mm from the bone surface to avoid the inclusion of a nearby subchondral bone. T2 map and a corresponding standard MRI were placed side by side, and a multi-planar localization key used on the picture archiving and communication system (PACS). The total time of segmentation ranged from 20 to 25 min.

Statistical analysis

We assessed T2 values by two independent musculoskeletal radiologists (one with 4 years of experience and the

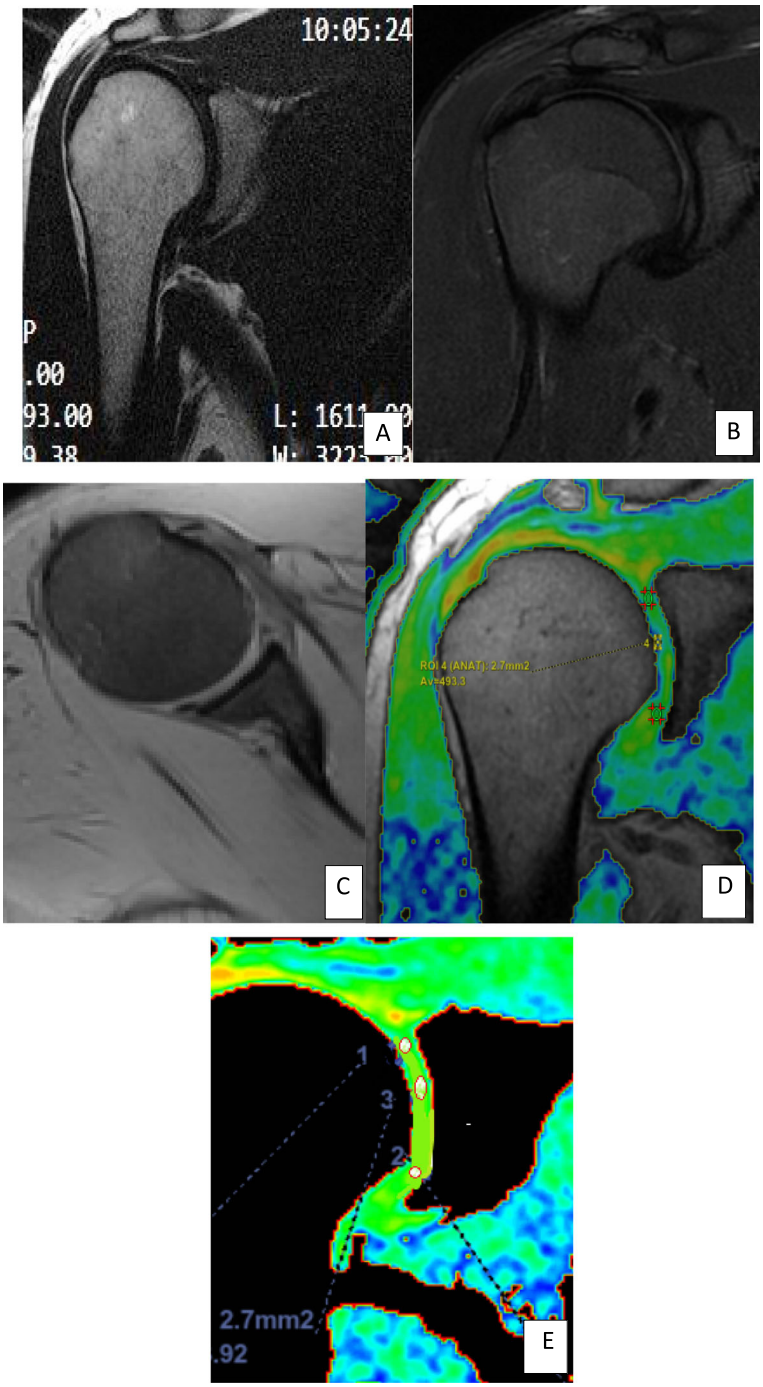

Fig. 1 **a** Coronal T1 WI. **b** Coronal proton density (PD) WI. **c** An axial T2WI in control individual with no detectable osteoarthritic changes. **d** T2 colored mapping. **e** Processed image showed average T2 values of 36.4 ms, 40.83 ms and 41.56 ms ,glenoid zone (2), mid zone (3), and humeral zone (1) respectively (red arrows)

other with 2 years of experience in reading T2 mapping of the knee joint). We collected and compared individually all the readings of both the control group and the OA patients (primary and secondary) in the three zones (humeral, mid, and glenoid zone) were collected and compared individually; we compared a control group with both primary and secondary OA patients, and primary OA with secondary OA. Also, different zones were compared together. We made the comparisons by using Mann-Whitney *U* tests as the got T2 values deviated

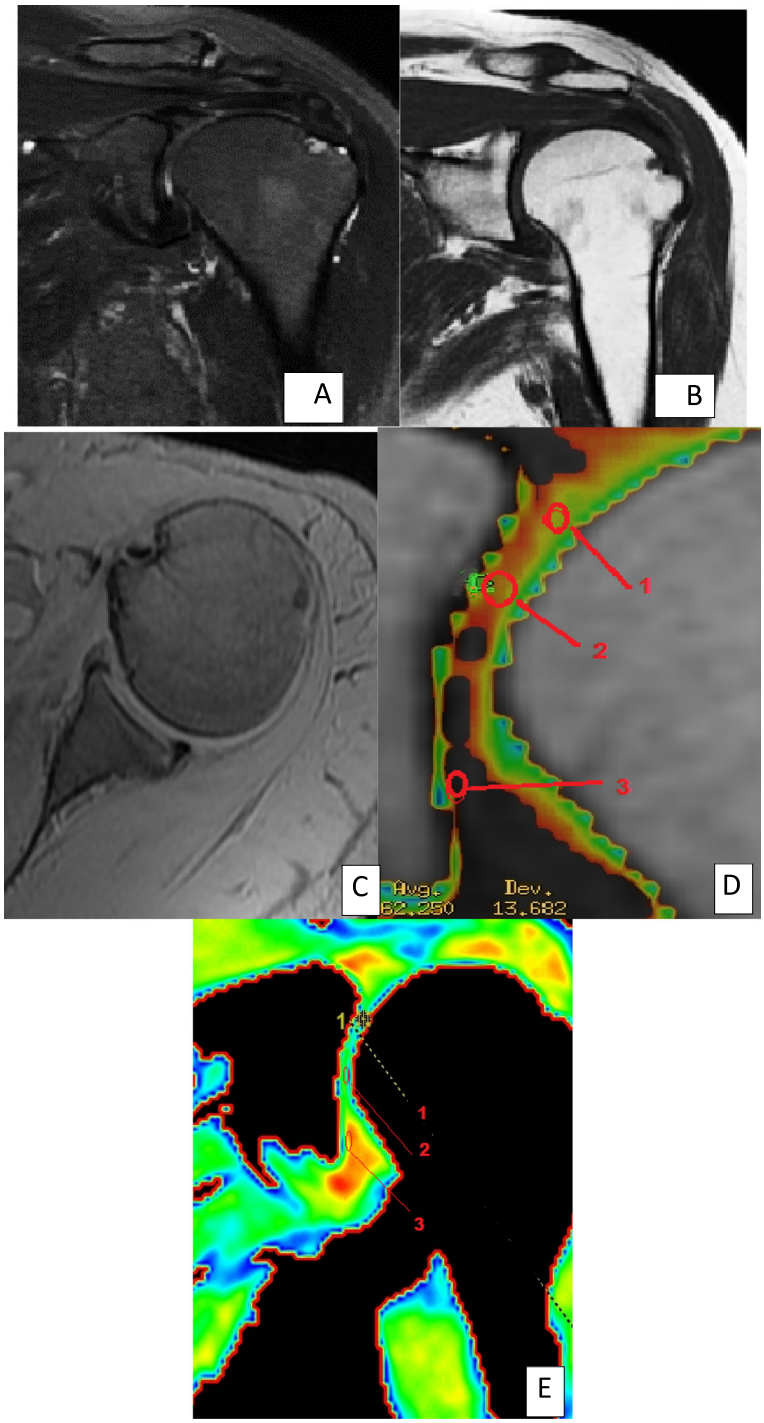

Fig. 2 **a** Coronal T1 WI. **b** Coronal proton density (PD) WI. **c** An axial T2 gradient echo WI revealed osteoarthritic changes in form of osteophytes, irregular articular surface and abnormal sub articular bone marrow SI (grade II). **d** T2 colored mapping. **e** A processed image showed T2 values of 62.4 ms, 63.83 ms and 59.56 ms, glenoid zone (3), midzone (2), and humeral zone (1) respectively (red arrows)

Table 1 Mean T2 mapping values at three original sites with a comparison of the values

Zone	Control group (A) (n = 20)	Primary OA (B) (n = 15)	Secondary OA (C) (n = 20)			A versus B	A versus C	B versus C
		Grade I	Grade I (n = 7)	Grade II (n = 9)	Grade III (n = 4)			
Humeral surface	44.75 ± 6.5	60 ± 7.0	65 ± 1.2			0.004	0.001	0.12
Mid zonal	46.47 ± 4.5	59.81 ± 3.7	65 ± 8			0.001	0.001	0.17
Glenoid surface	46.9 ± 5.1	57 ± 5.2	63 ± 1.0			0.006	0.003	0.23

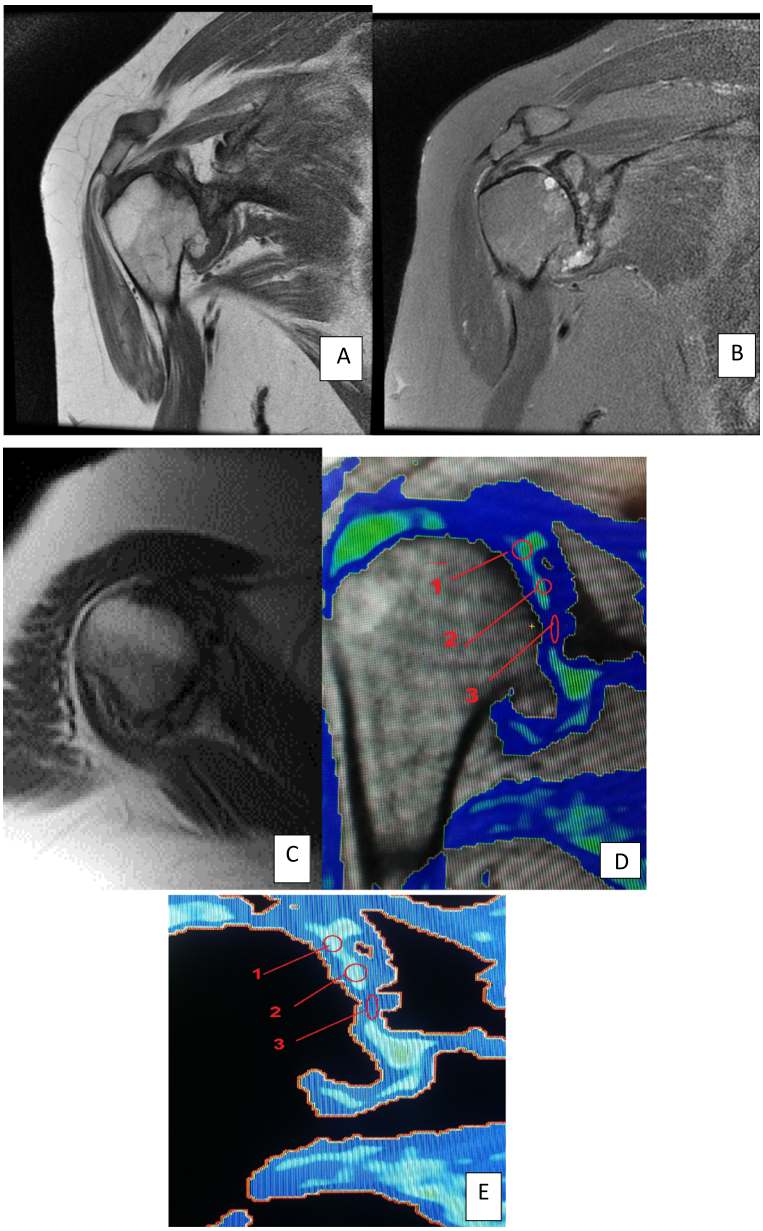

Fig. 3 **a** Coronal T1 WI. **b** Coronal proton density (PD) WI **c** An axial T2 WI revealed advanced secondary osteoarthritic changes in form of narrowed joint space, marked osteophytosis, and irregular articular surface (grade III). **d** T2 colored mapping. **e** A processed image showed T2 values were 75 ms, 70 ms, and 69 ms for the glenoid zone (3), mid zone (2), and humeral surface (1) respectively (red arrows)

from a normal distribution. We statistically described T2 values in terms of mean ± standard deviation (±SD). The inter-observer reliability of the T2 value measurements was assessed using intra-class correlation coefficients (ICC), with ICC values of < 0.40, 040–0.75, and > 0.75 showing poor, good, and excellent agreement, respectively [13]. We performed All statistical analysis using the commercial software (SPSS, version 25, SPSS Inc., Chicago, IL, USA). *P* values < 0.05 were considered statistically significant.

Results

Our study included 65 individuals (30 in the control group and 35 in the OA group). OA patients included 27 females and 8 males with a median age of 60 years (age range from 43 to 69 years). The OA group divided into primary OA (n = 15) and secondary OA (n = 20). The control group involved 25 females and 5 males with a median age of 46 years (age range from 30 to 56 years). Median T2 values of the control group were lower than that of the patients with different grades of osteoarthritis: 43.4 ms [41.54-

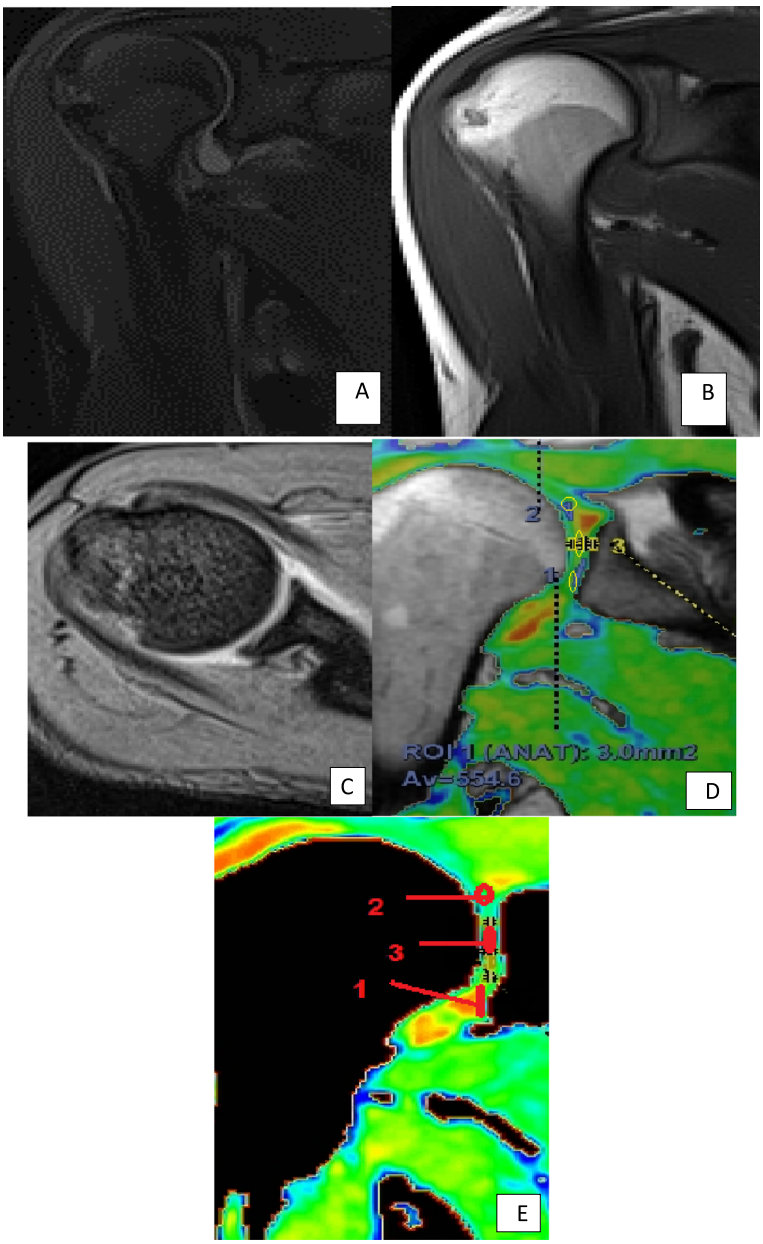

Fig. 4 **a** Coronal T1 WI. **b** Coronal proton density (PD)WI. **c** An axial T2WI showed a very mild osteoarthritic change in the form of minimal osteophytes (grade I). **c** T2 mapping. **d** Processed image showed T2 values, 55.52 ms, 53.9 ms, and 65 ms for glenoid zone (1), mid zone (3), and humeral zone (2) respectively(red arrows)

45.33 ms IQR], 59.2 ms [7.54-63.33 ms IQR], 64.7 ms [62.54-67.39 ms IQR], 61.9 ms [57.54-64.53 ms IQR]. The mean T2 value of the control group was 45.8 ± 8 ms, 45.2 ± 65 ms, and 43.9 ± 7.1 ms in humeral cartilage, mid-zone, and glenoid cartilage, respectively.

The mean T2 values tended to be higher in patients with OA than in the control group as seen in Figs. 1 and 2 with significant p value < 0.05 (Table 1).

In our study, OA patients were grouped into 15 patients with primary OA and 20 patients with secondary OA. All the primary OA patients were graded as grade I OA while the secondary OA patients were graded as 7 grade I, 9 grade II, and 4 grade III. The mean T2 values of the primary OA patients were 60 ± 82 ms, 60 ± 57 ms, and 59 ± 65 ms in humeral cartilage, mid-zone and glenoid cartilage, respectively while the mean T2 values of the secondary OA patients were 65 ± 12 ms, 56 ± 8 ms, and 63 ± 10 ms in humeral cartilage, mid-zone and glenoid cartilage, respectively.

In a comparison of mean T2 values between the different groups that were included, we found no statistically significant difference between the primary and secondary OA in different zones (Table 1) with p value > 0.05. In a comparison of the different zonal compartments of T2 values, we found a statistically significant difference between the humeral and glenoid zones in all studied groups (control, primary OA, and secondary OA groups) with p value < 0.001 and a significant difference between the mid-zone and glenoid zone in all studied groups with p values < 0.001 (Figs. 3, 4 and 5), while no statistically significant difference was observed between the mid-zone and humeral zone in control and primary OA groups with p values > 0.05 (Table 2).

Discussion

T2 mapping is a form of functional imaging that is used primarily in the evaluation of the knee joint. It assesses the water content of the cartilage in the knee joint. When the knee joint degenerates, the water content and the proteoglycan content of the joint decreases, leading to an increase in the T2 values in the degenerated cartilage compared to those found in healthy joint [14].

In our study, we assessed the feasibility of using quantitative T2 mapping for assessment of shoulder osteoarthritis (OA). This study compared the median T2 values between a control group and a study group comprising patients with different grades of OA. It also compared the mean T2 values of the OA patients from three specific articular surface zones at the coronal plane: the humeral zone, the central zone, and the glenoid zone. The T2 measurements obtained in this study were within the range of the mean and the median T2 values of 3 T MRI reported in the existing literature produced by So-Yeon Lee et al. [4], Yusuhn Kang et al. [15], and Kramer EJ et al. [16]. Significantly different T2 measurements (p value < 0.05) were found in comparing the OA patients with the control group, with no significant difference found among the different grades of OA. This matches with the results obtained by So-Yeon Lee et al. [4], who claim that the degeneration of cartilage causes a reduction of water content. Our study also proved a significantly higher T2 value (p values< 0.05) in all measured zones when comparing the control group to the OA group. So-Yeon Lee et al. [4] obtained nearly the same results, which they attribute to the difference in the histological component with regard to water and collagen content as well as to the magic angle due to the spherical shape of the humeral head. For the OA patients in our study, the T2 values of the humeral and the glenoid zones were higher than those of the mid-zone because of the friction force. Contrary to our study, the mean and the median T2 values reported by Nardo et al. [17] and Y. Kang and Choi [15] varied widely. These differences might be due to the different segmentation and regions of interest (ROIs) used in the selection protocols of the two studies. The difference in the T2

Table 2 Mean T2 mapping zonal variations in different cartilage compartments among the healthy subject and patients with primary and secondary osteoarthritis

Comparison between different cartilage zones	Control group	Primary OA	Secondary OA
Humeral zone	45.8 ± 84	60 ± 82	65 ± 12
Glenoid zone	43.9 ± 71	57 ± 65	63 ± 10
P value	< 0.001*	< 0.001*	< 0.001*
Mid zone	45.2 ± 65	60 ± 57	65 ± 8
Humeral zone	45.8 ± 84	60 ± 82	63 ± 10
P value	> 0.05	> 0.05	< 0.001*
Mid zone	45.2 ± 65	60 ± 57	65 ± 8
Glenoid zone	43.9 ± 71	57 ± 65	63 ± 10
P value	< 0.001*	< 0.001*	< 0.001*

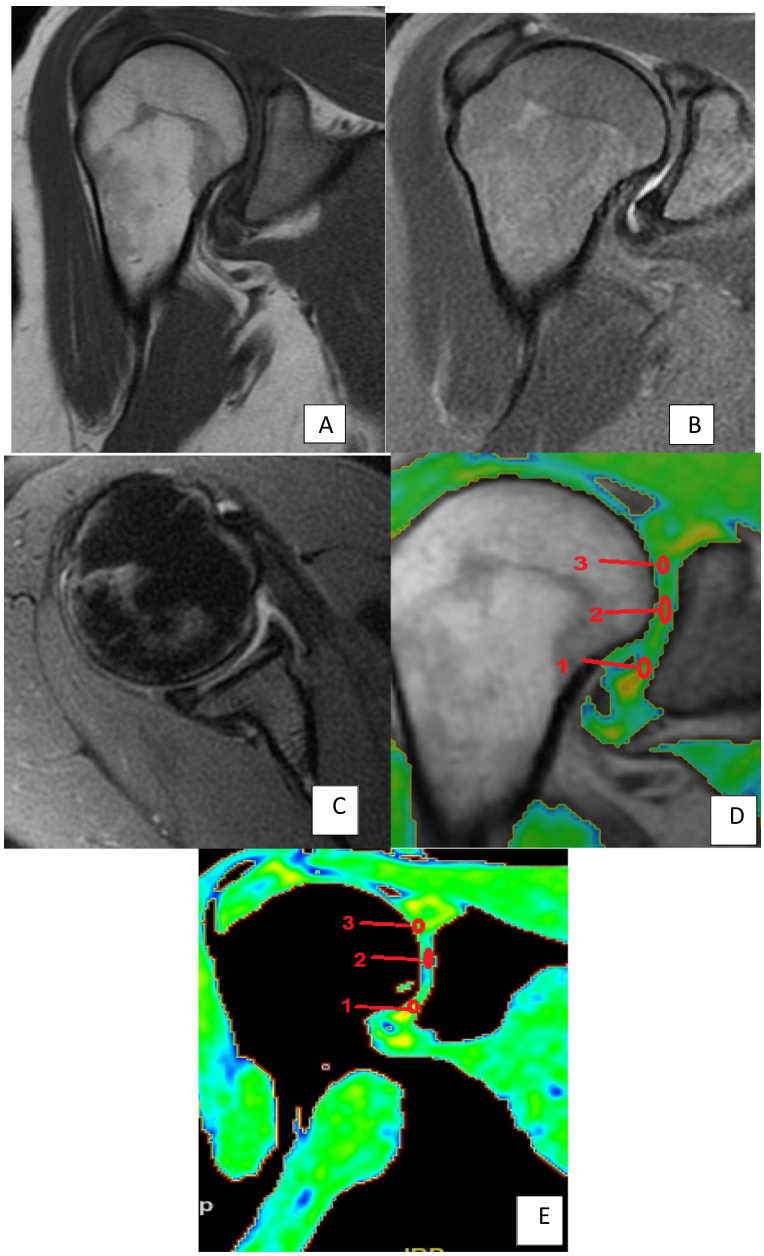

Fig. 5 a Coronal T1WI. **b** Coronal proton density (PD) WI. **c** An axial PD WI MRI showed osteoarthritic changes in the form of an irregular articular surface of glenoid, narrowed joint space, and minimal osteophytes(grade II). (C)T2 mapping and (D) processed image showed average T2 values 57.7 ms, 65.8 ms, and 72 ms at glenoid zone (1), mid zone (2), and humeral zone (3) respectively(red arrows)

mapping values of the glenohumeral joint reported by other studies and our study might be for several causes, including the potential variation between ROIs. As there were regional differences even in the asymptomatic shoulders, each mapping plane captured a different region of cartilage with partial overlap between the regions captured in each plane. Furthermore, a specific region on the articular surface might be prone to degeneration more than other regions, as in the case of chronic trauma with a rotator cuff tears; cartilage damage typically occurrs in posterior and inferior portions of the glenoid, whereas degeneration of central and superior portions is more common in patients without a rotator cuff tear [18].

Our study faced a major challenge in determining the anatomical landmarks in the glenohumeral joint for creating ROI segmentations. The identification of landmarks for the needed borders of the ROI and the subdivision of the cartilage into sub-regions might improve the reproducibility of the study; it might also have

allowed for more focused cartilage evaluation, as a single T2 mapping plane could not capture the entire expanse of the cartilage, and there was a risk of missing part of cartilage when assessing the glenohumeral joint. Further studies of the shoulder joint and small joints, like the wrist and sacroiliac joints, using three-dimensional (3D) quantitative mapping are needed to avoid the joint-curvature and partial-volume-overlapping difficulties, and to clarify the differences in the regional T2 mean values without the additional variable of the different mapping planes.

Another challenge faced with T2 mapping in this study was the very thin layer of cartilage in the small joint spaces; and to avoid the inclusion of subchondral bone, a margin between 0.5 and 1.1 mm from the bone surface was kept when drawing a ROI [19, 20]. We excluded post-operative patients from our study. Although many studies have tried to implant postoperative quantitative T2 mapping in assessing the articular surface, zonal T2 mapping is highly promising in the postoperative assessment of cartilage. These studies [21, 22] have hypothesized that the repaired tissue might reduce the level of collagen fiber anisotropy that is responsible for zonal T2 relaxation in native cartilage and that water content might play an important role. This hypothesis will play an important role in the future of postoperative quantitative T2 zonal measurement, especially in patients with chronic rotator cuff tears, improving understanding of the many complications that might be encountered with postoperative rotator cuff tear patients. Accurate knowledge of normal postoperative findings and postoperative complications is highly important in providing an accurate diagnosis to direct the surgeons in the right direction and in improving the clinical outcomes of patients subjected to rotator cuff repairs [23].

Several studies have tried to use combined quantitative T2 mapping and magnetic resonance arthrography (MRA) in the joint's evaluation as MRA is associated with high diagnostic performance, especially in some areas, such as the shoulder, the wrist and the hip, in which evaluation of the joint space might be suboptimal because of the anatomic configuration of the joint itself. To overcome these limitations, diluted Gadolinium-based contrast agents might be injected into the joint space for better distention of the joint capsule and to mak the intraarticular structures more visible [24]. A study was conducted by V. Zeev et al. in 2009 [25] to quantitatively compare the T2 mapping of five glenohumeral joints before and after an MRA; it showed that the joint distention created an interface between the articular surfaces, which allowed better visualization of the cartilage; however, this was considered an invasive technique.

Our study had many limitations, the first and the most important of which was the lack of the gold standard of pathological correlations among the different grades of OA. The second limitation was the difficulty in measuring the actual T2 value of the articular cartilage while excluding the surrounding tissues, such as the joint effusion or subchondral bone; this difficulty might be due to the poor contrast between the cartilage and the surrounding tissue, but might also be due to the partial-volume effect or the chemical-shift artifact. To reduce the error of T2 mapping analysis and to implant it in a manner that is practical and reproducible within normal clinical workflows in the future, automated segmentation should be used. The third limitation of this study was the inadequate distention of the small joint spaces, which might be corrected through the use of complementary MRA. We believe that further developing techniques that may reduce these limitations and enable high-resolution imaging will be possible in future subsequent studies. We highly recommended the correlation of the measured T2 values from this study with arthroscopic findings pertaining to the different grades of OA.

Conclusion

Comparing quantitative T2 mapping of the glenohumeral joint in both control and OA patients showed a significant difference in assessing the degenerative change of the articular cartilage. T2 values are more significant in the mid-zone. We highly recommended further work for evaluating the potential clinical usefulness of these measurements.

Abbreviations

MRI: Magnetic resonant imaging; SI: Signal intensity; ROI: Region of interest; OA: Osteoarthritis; T1rho: T1 relaxation time in rotating frame; DTI: Diffusion tensor tractography; PACS: Picture archiving and communication system

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Authors' contributions

R.A correlated the study concept and design and had the major role in analysis, collected data in all stage of manuscript, performed data for analysis, supervised the study with significant contribution to design the methodology, MR.A revised the manuscript and finalized revision, drafted the manuscript, and designed the figures. All authors discussed the results and contributed to the final manuscript. All authors had read and approved the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Informed written consents taken from the patients and healthy volunteers, the study approved from the ethical committee of the Faculty of Medicine, Tanta University number 2265-2019.

Consent for publication
All patients included in this research gave written informed consent to publish the data contained within this study. If the patient was less than 16 years old, deceased, or unconscious when consent for publication was requested, written informed consent for the publication of this data was given by their parent or legal guardian. I and all authors accept to publish the paper.

Competing interests
The authors declare that they have no competing interests.

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