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Sensitivity of quantitative UTE MRI to the biomechanical property of the temporomandibular joint disc

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Abstract

Purpose—To quantify MR properties of discs from cadaveric human temporomandibular joints (TMJ) using quantitative conventional and ultrashort time-to-echo magnetic resonance imaging (UTE MRI) techniques and to corroborate regional variation in the MR properties with that of biomechanical indentation stiffness.

Methods—This study was exempt from the institutional review board approval. Cadaveric (four donors, two females, 74 ± 10.7 years) TMJs were sliced ($n=14$ slices total) sagittally and imaged using quantitative techniques of conventional spin echo T2 (SE T2), UTE T2*, and UTE T1rho. The discs were then subjected to biomechanical indentation testing, which is performed by compressing the tissue with the blunt end of a small solid cylinder. Regional variations in MR and indentation stiffness were correlated. TMJ of a healthy volunteer was also imaged to show in vivo feasibility.

Results—Using the ME SE T2 and the UTE T1rho techniques, a significant (each $p < 0.0001$) inverse relation between MR and indentation stiffness properties was observed for the data in the lower range of stiffness. However, the strength of correlation was significantly higher ($p < 0.05$) for UTE T1rho ($R^2 = 0.42$) than SE T2 ($R^2 = 0.19$) or UTE T2* ($R^2 = 0.02$, $p = 0.1$) techniques.

Conclusion—The UTE T1rho technique, applicable in vivo, facilitated quantitative evaluation of TMJ discs and showed a high sensitivity to biomechanical softening of the TMJ discs. With additional work, the technique may become a useful surrogate measure for loss of biomechanical integrity of TMJ discs reflecting degeneration.

Keywords

Jaw; Temporomandibular disorder; Indentation

Introduction

The temporomandibular joint (TMJ) facilitates jaw movement by proper functioning of its articulating components, including the mandibular condyle, articular eminence, and disc. The TMJ disc is a fibrocartilaginous [1] oval structure situated between the mandible and inferior surface of the temporal bone. It serves as a cushion with smooth congruent surfaces for stable mandibular movement. The TMJ disc is composed mainly of fluid (65–80 %) [2–5], with extracellular matrix components including collagen (68–83 %) and proteoglycans (1–10 %) [2–6].

The load-bearing and biomechanical function of TMJ tissues are of great interest [7–13] because of their roles in mastication and speech. While a number of biomechanical testing methods have been introduced, indentation testing, which involves compression of the tissue using the blunt end of a small (~1 mm diameter) cylindrical tip, has been widely used in biomechanical testing of TMJ discs [11, 14]. Indentation is a non-destructive test that can measure stiffness and other biomechanical properties of biologic samples. Indentation measurements are sensitive to changes in the proteoglycan content [15] and structural integrity [16] of cartilaginous tissues in aging and osteoarthritis, during which the stiffness of the tissue usually decreases. The relationship between the biomechanical property of the TMJ tissues and magnetic resonance (MR) properties is also of great interest, but has not yet been assessed.

Temporomandibular disorder (TMD) is a prevalent disease that affects as much as 10–25 % of the population [17, 18]. While TMD pain is multifactorial, when considering pathogenesis [19, 20], TMJ disc degeneration may play a significant role, as evident in discs retrieved from TMJ discectomies [21]. Grossly, degenerated discs exhibit surface fibrillation, thinning, and perforation [22]. Biochemically, degeneration involves the loss of glycosaminoglycan (GAG) content [23]. Such structural and compositional changes likely result in diminished biomechanical properties in discs of TMD patients [24].

Diagnosis of TMD using MR imaging is performed clinically [25–29]. However, the focus of conventional MRI has been on the diagnosis of disc displacement and synovial effusion; in general, their performance in the detection of osteoarthritis of the TMJ has been poor

[19]. While techniques have been introduced to improve visualization of the TMJ anatomy [25, 27], significant challenges remain due to the fibrocartilaginous nature of TMJ soft tissues and their intrinsically short T2 properties as well as susceptibility artifacts due to subjacent mastoid air cells. In many clinical MRIs, TMJ discs exhibit low signals, making their evaluation challenging.

Using ultrashort time-to-echo (UTE) MR pulse sequences, it is possible to detect short T2 relaxation components in tissues before they decay to an undetectable level, unlike the conventional spin echo pulse sequences [30, 31]. In addition, quantitation techniques based on UTE MRI have been introduced for characterization of other musculoskeletal connective tissues [32, 33]. These include T1 and T2* quantification in cortical bone [32] and T1rho in the tendons and the knee meniscus [33] and in articular cartilage [34]. Given the long history of quantitative MRI in musculoskeletal tissue and diseases such as osteoarthritis [35–37], quantitative MRI of TMJ tissues would also likely yield useful results.

The goal of this study was to quantify MR properties of discs from cadaveric TMJ using quantitative conventional and UTE MR techniques and to corroborate regional variation in the MR properties with those of biomechanical indentation stiffness. In addition, in vivo feasibility of the techniques was assessed on a healthy volunteer.

Materials and methods

Tissue preparation

This correlational cadaveric study was exempted by the institutional review board, and informed consent was not required. Skulls were obtained from fresh cadavers ($n=4$, 74 ± 10.7 years; two females, two males) and kept in a closed-mouth intercuspal position based on natural teeth. There was no information available concerning the existence of TMJ disease before death. Bilateral TMJs were harvested en bloc using a band saw with a fine-toothed metal blade (Exact, Apparatebau GmGH, Norderstedt, Germany). Using reference landmarks including the nasal septum, orbital ridge, nasolabial fold, and retroauricular eminence, the TMJ block was sectioned in a true sagittal plane at a ~3-mm slice thickness. A total of 13 TMJ disc samples, grossly intact without perforation, were used for this study. After photography (Fig. 1a), the fresh TMJ slices were stored frozen at -40°C (Bio-Freezer; Forma Scientific, Marietta, OH). Prior to MR imaging, the slices were allowed to thaw for 3 h at room temperature and re-hydrated with saline.

MRI evaluation

MR imaging was performed on a 3-T MR imaging system (Signa HDx; General Electric Healthcare, Milwaukee, WI) with a modified transmit/receive switch and a 3-inch surface coil placed in proximity to the specimen slices.

Conventional quantitative MRI was performed using a clinical spin echo T2 mapping sequence (SE T2): time to repeat (TR)=2,000 ms; time to echo (TE)=10–70 ms (eight echoes); field of view (FOV)=8 cm; slice thickness=2 mm; matrix=320×256; flip angle (FA)=90°; bandwidth (BW)=±42 kHz. Additionally, proton density-weighted fat-suppressed images were acquired for qualitative comparison using the following fast spin echo

sequence: TR=1,800 ms; TE=11.7 ms; FOV=8 cm; matrix=512×512; slice thickness=2 mm; NEX=4.

Several quantitative UTE pulse sequences were performed to determine T2* and T1rho values. For UTE MRI, the basic pulse sequence employs a half radiofrequency excitation followed by radial imaging of the k-space [30, 31]. This was followed by another half radiofrequency excitation with the gradient reversed and repeated radial mapping. The two sets of data are combined to give a single line of k-space (sampled 512 times per line), and the process is repeated through 360° in a certain number of steps (i.e., number of projections). The data are then mapped onto a 512×512 Cartesian grid and reconstructed by 2D Fourier transformation to give a gradient echo-like image. The following specific parameters were used for each sequence.

UTE T2*: TR=300 ms; TE=0.012 to 20 ms (five TEs); FOV=8 cm; number of projections=511; FA=60°; BW= 50 kHz.

UTE T1rho: TR=500 ms; TE=0.012 ms; time to spin lock (TSL)=0.02 to 14 ms (four TSLs); FOV=8 cm; number of projections=511; FA=60°; BW=50 kHz.

Biomechanical testing

Indentation testing, a non-destructive biomechanical test [15, 38], was used on the TMJ disc. A sample slice (Fig. 1a) was placed on a flat stage and secured at the articular fossa and the mandibular condyle, and the TMJ disc was subjected to indentation testing at multiple sites (Fig. 1a and b) using a benchtop apparatus (V500cs, Biomomentum Inc., Quebec, Canada) fitted with a 0.8-mm-diameter plane-ended tip. The stage movement was computer-controlled with ~0.01 mm resolution, which allowed for a high precision position of indentation sites, 0.5 mm apart laterally. Throughout testing, the sample was kept hydrated using phosphate-buffered saline containing proteinase inhibitors [39] to hinder tissue degradation. The indentation protocol consisted of the application of a small tare load (~0.15 g), followed by ramp compression of 100 μm (at 100 μm/s), a hold in position for 1 s, and an unloading at the same rate. Indentation stiffness (a higher value indicates a stiffer sample) was determined from load–displacement data and converted to the units of N/mm [40].

Image analysis

Circular regions of interest (ROIs) (Fig. 1c), equal to the size of the indenter, were selected using a semiautomated MATLAB (R2009a with Image Processing Toolbox, Mathworks, Natick, MA) routine to ensure correct spacing. Signal intensity was averaged within each ROI and fitted to the appropriate monoexponential functions to determine the SE T2, UTE T1, UTE T2*, and UTE T1rho properties. The image analysis was repeated three times, and the MR properties were averaged to reduce the effect of error in ROI selection.

Statistics

Regional variation in indentation stiffness and MR properties was assessed by grouping ROIs into anterior, central, and posterior regions and using repeated measures ANOVA (significance level, $\alpha=0.05$). Linear regression and Pearson correlation were used to assess

the relation between MR properties and indentation stiffness. Correlation coefficients were compared against each other using Fisher's z-transformation [6].

In vivo feasibility

To show the feasibility of performing quantitative UTE MR imaging of human TMJ, the UTE T1rho sequence, adapted for in vivo use, was used to image a 27-year-old male volunteer with no history of TMD. The protocol was as follows: true sagittal plane; TR=300 ms; TE=0.008 ms; TSL=0, 1, 4, and 8 ms; FOV=10 cm; number of projections=311; FA=45°; scan duration of approximately 3 min per TSL.

Results

On visual inspection, TMJ disc tissue appeared low in signal intensity (dark appearance) on the spin echo proton density-weighted image (Fig. 2a) and the first echo image from the SE T2 sequence (Fig. 2b). On UTE MR images (Fig. 2c and d), disc tissue exhibits increased signal intensity (bright appearance), facilitating quantitative analysis.

There were significant regional variations in the conventional SE T2 and UTE T1rho MR properties. Average SE T2 values (Fig. 3a) were lower in the posterior region (~25 ms) compared to the central and anterior regions (~32 ms) ($p<0.01$). In contrast, UTE T1rho values (Fig. 3b) were 10–15 % higher in the posterior region (~23 ms) compared to the central and anterior regions (~20 ms) ($p<0.001$). UTE T2* values (Fig. 3c) did not show regional variations ($p=0.9$).

Indentation stiffness also varied significantly region ($p<0.00001$, Fig. 4). The stiffness in the posterior region (0.59 ± 0.37 N/mm, mean $\pm$ SD) was lower than those of the anterior and central regions (each $p<0.001$; 0.92 ± 0.54 and 1.0 ± 0.48 N/mm, respectively), indicating softer tissue in the region. In addition, the central region had higher stiffness compared to the anterior region ($p<0.001$).

Linear regression between MR values using the entire data initially did not correlate significantly with the indentation stiffness value (Fig. 5a, b and c). Closer observation revealed that for a lower range of indentation stiffness values (<0.8 N/mm), the strength of correlation became statistically significant. The strengths of correlation were the weakest and insignificant for the UTE T2* values (Fig. 5d, $R^2=0.02$, $p=0.1$), stronger for the SE T2 values (Fig. 5e, $R^2=0.19$, $p<0.00001$), and the strongest for the UTE T1rho values (Fig. 5f, $R^2=0.42$, $p<0.000001$). These correlation coefficients were statistically different from each other (each $p<0.05$).

In UTE T1rho images of a healthy volunteer (Fig. 6), a TMJ disc can readily be seen with sufficient resolution and contrast, similar to images obtained on specimens (Fig. 2), which can facilitate quantitative evaluation.

Discussion

This study represents a paradigm shift in the MR evaluation of TMJ soft tissues, from morphologic and qualitative imaging to quantitative measures, and a consideration of other

measures of importance in the tissue such as biomechanical function. While clinical MR imaging such as the proton density-weighted spin echo technique has gained wide acceptance because of its excellent soft tissue contrast, the conventional focus has been on the disc displacement relative to the condyle and articular eminence with an open- and closed-mouth position to determine internal derangement [14, 41–46]. The change in morphology and signal intensity with TMD is less clear. It has been reported that the normal TMJ disc has low signal intensity, and it becomes higher with degeneration [47, 48]. Other reports describe the normal appearance as having intermediate to high signal intensity on T1-weighted MR images with decreasing signal intensity with degeneration [49]. On the contrary, a recent study reported increasing signal intensity with degeneration on T1-weighted images [50]. While novel techniques including 3D visualization [51], dynamic imaging of disc movement [52], and diffusion-weighted imaging [53] have been introduced, these were also not focused on characterizing intrinsic tissue characteristics.

Using quantitative MR techniques, we were able to evaluate topographic variations (Fig. 3) in SE T2, UTE T2*, and UTE T1rho properties of TMJ discs and determined that UTE T1rho properties correlated most strongly to the indentation biomechanical properties. Biomechanical properties of TMJ soft tissues have been of interest [4, 54, 55] because of the load-bearing functional importance of the tissues, which may be altered with diseases [24]. In articular cartilage, osteoarthritis results in markedly diminished biomechanical properties, including indentation stiffness [15, 56]. Indentation testing is also used clinically to evaluate articular cartilage during arthroscopy [57]. Thus, the sensitivity of an MR parameter to the biomechanical property has important clinical implications for noninvasive characterization and detection of functional change in TMJ tissues with degeneration. Quantitative MR parameters are continuous metrics, which could potentially provide more sensitive and precise monitoring of tissue changes through the progression of acute to chronic disease as well as monitoring tissue response to therapy [29].

The inverse relation between the UTE T1rho property and indentation stiffness is consistent with past similar studies on articular cartilage and with the sensitivity of T1rho values to GAG content of soft tissues. In tissues with longer T2 components including articular cartilage, high T1rho values have been associated with low mechanical properties [34]. Additionally, high T1rho values are also found in articular cartilage with low GAG content [34, 58] and osteoarthritic degeneration [35, 36]. Low GAG content, in turn, is related to reduced compressive stiffness [59]. While T2 values have no direct relation with GAG content, T2 also increases with tissue degeneration in cartilage [35, 36], similar to the changes in T1rho values.

There are several shortcomings of this study. Our samples lacked the history regarding TMD, but they were selected based on gross morphology to exclude those exhibiting advanced degeneration such as perforation. Nonetheless, it is difficult to classify our samples as being normal or diseased. Indentation testing was not applied in the physiologic direction (i.e., superior to inferior direction on an intact surface of the disc). This may have resulted in an underestimate of indentation stiffness compared to compressing an intact disc in the physiologic direction, since the superficial collagen fibers of the disc provide resistance to compression. The lack of correlation for the upper range (>0.8 N/mm) of

indentation stiffness may be due to the indentation artifact when tissue is near much stiffer material [16]. This may have happened in thin samples, especially in the narrow central regions of the disc, which was often sandwiched between the condyle and temporal bone. This may have contributed to the highest indentation stiffness in this region (Fig. 4). The lack of correlation involving UTE T2* may be due to susceptibility arising from longer TEs along with inherent limitations of the gradient-echo technique used in the UTE T2* sequence. Some specimens may have had small air bubbles near the TMJ disc, despite efforts to minimize this problem.

In conclusion, our study with UTE MR imaging at 3 T allowed quantitative evaluation of the TMJ disc using high signal made possible through implementation of the UTE technique. Based on a strong correlation against indentation stiffness, UTE T1rho may reflect functional change of the TMJ disc. The use of UTE T1rho measurement may be useful for longitudinal assessment of TMJ disc degeneration involving subtle biomechanical changes in both diseases and after treatments. Although found to be less sensitive, other quantitative UTE MR data are still useful for baseline MR characterization of TMJ tissues, which could be used to calculate the optimal TR, TE, and flip angle for any MR sequences that will optimize signal and contrast [60]. In vivo clinical feasibility was also shown, although additional studies are needed to determine the diagnostic utility of quantitative UTE MR sequences. Quantitative MR techniques may be helpful in the future for grading TMD and may provide a measure or marker of the need for, as well as the outcomes of, surgical interventions.

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Fig. 1.
a Specimen photograph of a sagittal TMJ section overlaid with indentation sites (*yellow dots*). **b** Schematic of indentation testing. **c** Regions of interest (*circles*) overlaid on top of a UTE T1rho MR image

Fig. 2.

a Proton density-weighted fat-suppressed (TR=1,800 ms, TE=11.7 ms), **b** spin echo T2 (TR=2,000 ms, TE=10 ms), **c** UTE T2* (TR= 300 ms, TE=0.012 ms), and **d** UTE T1rho (TR=300 ms, TE=0.012 ms, TSL=0.02 ms) images. Sagittal MR images of the TMJ in a cadaveric specimen showing components of the TMJ disc (*star*) situated between the articular eminence (*triangle*), mandibular fossa (*circle*), and mandibular condyle (*rectangle*) on the PD FS image (**a**). The TMJ disc appears darker in the conventional (**a, b**) compared to UTE MR images (**c, d**)

Fig. 3. Regional variations in quantitative MR values obtained using **a** SE T2, **b** UTE T2*, and **c** UTE T1rho sequences. UTE T1rho data **c** show the highest values in the posterior regions. Mean $\pm$ standard error of the mean, $n=43-96$ sites. Bars represent $p < 0.05$ in pairwise comparison

Fig. 4. Regional variations in indentation stiffness values. The posterior region shows the lowest and the central region shows the highest stiffness values. Mean $\pm$ standard error of the mean, $n=68-73$ sites. Bars represent $p<0.05$ in pairwise comparison

Fig. 5. Linear regression between MR properties and indentation stiffness for **a, d** SE T2, **b, e** UTE T2*, and **c, f** UTE T1rho sequences. *Top row a, b, c* represent the full data set, while the *bottom row d, e, f* shows cropped data with a lower range of indentation stiffness values (< 0.8 N/mm). Moderate correlation was found for the cropped SE T2 data (**d**), while a much stronger correlation was found for the cropped UTE T1rho data (**f**)

Fig. 6. Quantitative UTE T1rho MR images of a healthy volunteer obtained at spin lock time (TSL) of **a** 0 ms, **b** 4 ms, and **c** 8 ms. These images show the feasibility of performing in vivo quantitative UTEMR imaging of human TMJ