UTE-T2* relaxation time in Achilles tendinopathy and healthy controls and correlation with clinical score

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Aims and objectives

Achilles tendinopathy, a syndrome with Achilles tendon (AT) pain, tenderness and swelling that limited the tendon function is one of the most common injuries and the prevalence increased in the last decades.\textsuperscript{[1][2]} Nowadays, due to a higher involvement in sports, the prevalence of Achilles tendinopathy is increasing.\textsuperscript{[3]} Although the exact etiology is still uncertain, it is supposed that repetitive overload and overuse are the major causes.\textsuperscript{[4]} They may lead to irreversible degenerative changes of the Achilles tendon (AT), for instance, destruction and decrease of collagen fiber in extracellular matrix, increased vascularity, altered cellularity, et al.\textsuperscript{[5][6][7]} Consequently, a precise way to detect Achilles tendinopathy is highly demanded.

The conventional clinical MRI sequences are useful for visualizing the tissues with relatively long transversal T2 relaxation times.\textsuperscript{[7]} However, AT mainly consists of collagen fibers (mostly type I collagen) which results in extremely short relaxation parameters, a short echo time (TE) must be used to acquire signal from the AT. Three-dimensional ultrashort echo-time (UTE) imaging, with an echo time as short as 0.05-0.5 ms, provided direct visualization and quantitative T2*-mapping of short T2* components such as AT.\textsuperscript{[8][9]} Biochemical changes of early stage Achilles tendinopathy may affect T2* values of AT, thus can be caught and quantified with UTE sequences.\textsuperscript{[10]}

Therefore, the aim of this study was to investigate the capability of quantitative 3D-UTE T2* in evaluating diseased AT and analyze the correlation between T2* value and American Orthopaedic Foot and Ankle Society (AOFAS) score or Achilles tendon Total Rupture Score (ATRS). We hypothesize that the pathologic AT would show increased T2* value while comparing with matched healthy samples and T2* value may be correlated with clinical score.
Methods and materials

Participants

The study was approved by the institutional review board of our hospital and all participants' informed consent were obtained. Ten patients (9 male/1 female, mean age 37.10±8.60 years, BMI 23.00±2.15 kg/m\(^2\)) with pain or abnormalities in the AT and ten healthy volunteers matched for sex, age and BMI(9 male/1 female, mean age 37.40±10.61 years, BMI 23.94±2.32kg/m\(^2\)) participated in the study. Participants were excluded if they had significant tendon rupture or any contraindication for MR.

MRI and clinical evaluation

All the participants were examined on a 3T MR scanner (Discovery 750, GE Healthcare, Waukesha, WI, USA) to get mono-exponential calculation of T2* in the human AT in vivo. As a quantitative 3D-UTE sequence#four echo times (TE = 0.032, 7.5, 20.5, and 28ms) were acquired . The parameters were set as follow: Sagittal orientation, FOV = 140 × 140 mm, slice thickness = 2.0mm, Flip angle = 18, number of excitation (NEX) = 1. Fat-saturated proton-density weighted turbo-spin echo (PD-TSE) sequence was underwent to acquire morphological assessment with the parameters: Sagittal orientation, TR 2843.0ms, FOV 180 × 180 mm, slice thickness 2.0mm, Flip angle 142, number of excitation (NEX) = 2. For clinical evaluation, AOFAS scoring system and ATRS were used to evaluate the patients' clinical outcome. (0-100 points, worst to best)

Imaging analysis

Images from the UTE-T2* sequence were analyzed by a software in the work station of GE. The AT was segmented and divided into three parts equally according to length: insertion (INS), middle (MID) and muscle-tendon junction (MTJ). (Fig. 1) These three ROIs as well as all bulk of AT regions on each echo of UTE-T2* images were drawn to get the mean MR signal. T2* value of each region is calculated by fitting the acquired signal at different echo time to a single exponential decay model. (Fig. 2)

Statistical analysis

All statistical analyses were performed in SPSS 20.0 (SPSS Institute, Chicago, IL, USA). An independent sample t-test was used to compare the differences of T2* values between two groups. Pearson's correlation coefficient was used to analyze correlations between clinical scores and T2* values of patient. The difference would be statistically significant if P value <0.05.
**Fig. 1:** ROIs of Achilles tendon on Sagittal UTE image acquired at TE = 0.032ms. INS = insertion, MID = middle, MTJ = muscle-tendon junction, these three ROIs were equally divided according to the longitudinal length of Achilles tendon. The bulk ROI consisted of all the three ROIs.

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Fig. 2: UTE T2*-mapping on diseased (a) and healthy (b) Achilles tendons of a 36-year-old male acquired at TE = 0.032ms. Color scale represents T2* values. The increase of T2* values was observed in diseased tendon.

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Results

There were no obvious tendon tears on MRI for all patients. The mean T2* value for bulk ROIs was significantly higher in patients than that in volunteers (12.508±0.940 and 11.081±0.297, P=0.001) (Table 1). Separately, MTJ, MID and INS regions of patients had statistically higher T2* value compared with the matched regions of volunteers (MTJ: 11.977±0.831 and 11.005±0.581, P=0.007, MID: 12.474±1.261 and 11.124±0.394, P=0.008, INS: 13.124±0.943 and 11.084±0.522, P=0.000). The difference in INS region is greater than that in MID and MTJ. In patients, the mean AOFAS and ATRS were 70.6±5.58 and 52.8±8.27, respectively. The T2* value for bulk region was negatively correlated with AOFAS as well as ATRS score (r=-0.733, p=0.016 and r=-0.634, p=0.049) (Fig. 3).

In this study, T2* relaxation time in pathologic and healthy AT were measured using UTE-T2* sequence and a significant higher T2* value was observed in all four regions of diseased AT. Besides, T2* value of all bulk of AT in patients was found to be negatively correlated with AOFAS and ATRS score.
**Table 1:** T2* values of patients and volunteers were presented by mean (M) and standard deviation (Sd), and statistical significance of the mean difference between them, and clinical scores of patients.

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
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<th>Volunteers</th>
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<th>P values</th>
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<td>M</td>
<td>Sd</td>
<td>M</td>
<td>Sd</td>
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<td><em><em>T2</em> values</em>*</td>
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<tr>
<td>Bulk</td>
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<td>0.940</td>
<td>11.081</td>
<td>0.297</td>
<td>0.001</td>
</tr>
<tr>
<td>MTJ</td>
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<td>0.831</td>
<td>11.005</td>
<td>0.581</td>
<td>0.007</td>
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<tr>
<td>MID</td>
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<td>11.124</td>
<td>0.394</td>
<td>0.008</td>
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<tr>
<td>INS</td>
<td>13.124</td>
<td>0.943</td>
<td>11.084</td>
<td>0.522</td>
<td>0.000</td>
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<tr>
<td><strong>AOFAS score</strong></td>
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<td>5.58</td>
<td></td>
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<tr>
<td><strong>ATRS score</strong></td>
<td>52.8</td>
<td>8.27</td>
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</tbody>
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Fig. 3: (a) A scatter plot of the bulk T2* and AOFAS of ten patients. The Pearson correlation coefficient was $r=0.733$ ($P=0.016$). (b) A scatter plot of the bulk T2* and ATRS of ten patients. The Pearson correlation coefficient was $r=0.634$ ($P=0.049$).

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Conclusion

UTE-T2* mapping, a novel quantitative technique, could catch the short-T2* relaxations from AT that are not well captured by standard T2 mapping.[10] In the early stages of Achilles tendinopathy, it is usually biochemical but not morphological changes that are found,[11], which consists of destruction of collagen structure, increase of proteoglycan and water content.[12] UTE-T2* mapping is sensitive to these changes, thus it could be a useful tool to detect tendon disease in an early stage.[9] The results of this study suggest that the variability of Achilles tendinopathy can be quantified by UTE-T2*. The increasing of T2* value may due to disorganization of collagen structure and increasing of water content in tendons. What's more, the difference in INS region is greater. The reason could be the enthesis is mostly involved in overuse injuries of AT.[13][14] Gardin et al[15] applied mono-exponential calculation and showed a significant higher T2* relaxation time in symptomatic tendons compared with control tendons. In a study by Juras et al, they compared mono- and bi-exponential T2* analysis using variable-echo-time sequence (vTE) and found that increased T2* in all parts of diseased AT with mono-exponential analysising.[8] Juras et al also reported a similar finding with bi-component quantitative 3D-UTE. They found significant differences between healthy(10.28 ± 2.28 ms )and degenerated AT(12.85 ± 1.87 ms) in the long component of T2*.[7] While estimating the diagnostic value of T1 and T2* relaxation times and off resonance saturation ratio, Grosse et al also observed statistical significant differences between the patients with tendinopathy and controls.[16]

We applied mono-exponential calculation of UTE-T2*. Juras et a[8] found that the short component of T2* reflects the changes of Achilles tendinopathy more accurately than the mono-exponential.[8] However, owing to the longer scanning time and higher sensitivity to movements and the magic angle, bi-exponential calculation is more difficult and. Given the low consistency of monoexponential T2* in this study, biexponential calculation might be even more difficult to be applied to clinical.[15]

To our best knowledge, only a few studies analyzed the correlation between T2* value and clinical score. AOFAS and ATRS score are both widely used in clinical practice and validated in many studies.[17][18] They had general assessment of the AT situation. T2* value of the bulk region in patients was correlated with AOFAS and ATRS score, which suggests the T2* could give a precise guidance to clinical outcome of patients with Achilles tendinopathy. Juras et al got a similar correlation between ATRS score and the mono-exponentially T2*.[8]
There are also some limitations in the study. Firstly, a small number of patients which would lead to increased statistical deviation. The patient cohort would be enlarged in our next study. Secondly, Mono-exponential calculation of T2* reflects the mean value of all the components of relaxation time, which may lead to an underrate of T2*, especially in diseased tendons.\[7\]

In conclusion, the differences between T2* in healthy and pathologic tendons could be observed by UTE-T2*. As the preliminary patient data suggest, UTE T2* is an acute marker to detect AT tendinopathy in the early stage and it gives a precise guidance to clinical outcome. Further investigation in larger cohort of patients, different terms of follow-up after treatments are required to define the exact role of UTE-T2* for monitoring the change of AT.
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References


