Variation in T2 Values Related to Method of Calculation: Implications for Correlative and Longitudinal Studies

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INTRODUCTION

Articular cartilage (AC) is located on the end of long bones in the human body and acts as a nearly frictionless bearing material between opposing bony surfaces. Osteoarthritis (OA) is a disease of AC and results in degeneration of the tissue with an increase of surface friction and tissue defects. Magnetic resonance imaging (MRI) has been used for in-vivo evaluation of AC, however, basic MR images alone may not be sufficient for an accurate diagnosis of early stage OA [1]. Recently, investigators have examined the MR transverse relaxation time constant, T_2, as a biomarker for OA [2]. An increase of T_2 is related to an increase of local water content and collagen fiber disruption of AC, both events which occur during OA.

T_2 is calculated from a series of MR images since it cannot be measured directly. Limited studies have been performed using musculoskeletal MR data to evaluate how the method of T_2 calculation affects the resulting T_2 values. In addition, it is not understood how differences of T_2 relate to a clinical understanding of T_2 values. Therefore, the purpose of this study was to determine how different methods for calculating T_2 effect the resulting T_2 values of patellar cartilage and how the clinical relationship between T_2 values and clinical factors such as radiographic grading of OA may be altered based on the method of calculation.

METHODS

Subjects: Following local institutional review board (IRB) approval with informed consent, 113 community based volunteers (54.9±11.2 y.o., range 31-82, 28M, 85F) were enrolled in the study. Data Acquisition: Standing lateral radiographs centered on the patella were obtained for each knee. Following the radiological exam, MR images of each subject's patellae were obtained. For T_2 calculations, a series of axial T_2-weighted fast spin-echo (FSE) images were acquired across 10 slices locations spanning the length of the patella. Eight echo images were acquired at each slice location: TR=1000ms, TE=8-76ms, slice thickness=2mm, slice spacing=4mm, FOV=12cm^2, in-plane resolution=0.49mm^2. All images were acquired using a clinical 1.5T scanner with a dedicated transmit-receive knee coil. Data Analysis: Radiographs were graded for patello-femoral OA based on the Kellgren and Lawrence (KL) scale from 0 (no OA) to 4 (end-stage OA). This scale assigns a level of OA based on the evaluation of joint space width and the presence and size of osteophytes. T_2 values of patellar cartilage were calculated on a pixel-by-pixel basis by fitting the echo time (TE) data and the corresponding signal intensity (SI) to a mono-exponential equation: $SI(TE)=S_0 \bullet exp(-TE/T2)$. This equation was fit to the data using three different computational algorithms: linearized least squares [3], weighted linearized least squares [4] and non-linear least squares [5]. Pixels with T_2 values greater than 200 ms were considered outliers and were excluded from statistical analysis [6]. An average bulk T_2 value was generated from all analyzed pixels of each patella. A two factor ANOVA with repeated measures was used to determine the effects of KL OA stage and method of calculation on patellar cartilage T_2 values. A post-hoc Student-Neuman-Keuls test was performed when significance was found. Significance was taken at $p<0.05$.

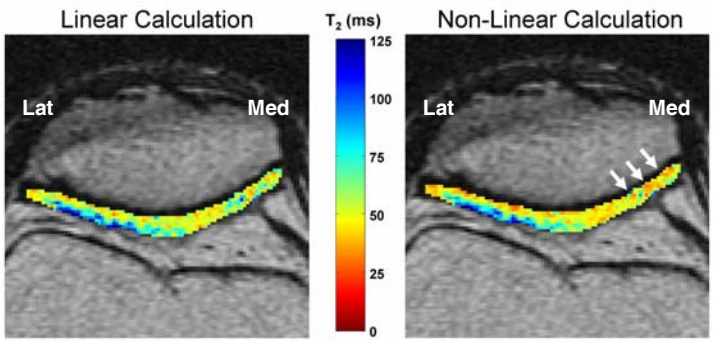

Figure 1. Representative axial T_2 map of patellar cartilage using linear and non-linear calculation methods. Both T_2 maps show an increase in values in the superficial region of cartilage on the lateral side of the image. However, the non-linear T_2 map displays lower local T_2 values on the medial side of the image (white arrows) as compared to the linear T_2 map.

RESULTS

The method of calculation had a significant effect on calculated T_2 value ($p<0.0001$). All methods of calculation resulted in significantly different T_2 values, with linear calculations resulting in the highest T_2 values and non-linear calculation resulting in the lowest T_2 values (Figure 1). Differences of T_2 values by OA stage were insignificant ($p=0.4$). Interaction of OA stage and method of calculation was not significant ($p=0.5$).

DISCUSSION

This study evaluated how different methods of calculating T_2 values may alter the clinical interpretation of the T_2 values. Based on our current analysis, the method of calculation significantly effects the resulting T_2 value. T_2 values calculated using the non-linear method were significantly smaller than T_2 values calculated using the linear or weighted methods. Suprisingly, the relationship of T_2 and radiographic OA stage values remain similar to what we have reported previously [7].

Since recent investigations of T_2 values have used either linear, weighted and non-linear methods to calculate T_2, we evaluated these methods in the current study. Previous investigators have also calculated T_2 time constants using the method of signal ratios at two points [8], with multiple TEs and TRs [9], a bi-component model or a Gaussian distribution model [10]. These methods may increase the accuracy of T_2 calculation, however, the time requirement for a large number of extra image acquisitions at each slice location may not be feasible during a normal clinical exam. Considerable computational time may also be required for some of these methods of calculation. All scanning for the current study was performed during normal operating hours of the clinic and scanning time was limited. Our results indicate it may difficult for direct comparison of T_2 values from one study to another based on the method of T_2 calculation. We believe investigators should clearly indicate which method of T_2 calculation was used in a study. The calculation methods used in this study were straight forward and may be easily implemented in numerous programming languages. Furthermore, the results of this study are important for examining T_2 of cartilage as a biomarker for OA. The different post-processing methods for T_2 calculation may result in different clinical interpretation of OA on a subject-by-subject basis. For example, elevated T_2 values are associated with degeneration of the articular surface. Using a non-linear method to solve for T_2 may underestimate the amount of degeneration. Our future work will continue to focus on examining the applicability and interpretation of T_2 mapping of cartilage in a clinical environment.

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