Intra-articular hyaluronic acid treatment of knee osteoarthritis in rats investigated by quantitative T2 measurements

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Introduction

Knee osteoarthritis (OA) is a popular disease characterized by the degradation of cartilage, pain, and inflammation, which may lead to increased disability [1]. Intra-articular injection of hyaluronic acid (HA) has become a common treatment for knee OA [2]. HA is part of the substance of the synovial fluid and cartilage, and is associated with the viscoelastic properties of synovial fluid. Although the mechanism of intra-articular injection of HA for the treatment of pain with knee OA is currently unknown, several studies demonstrate the potential of HA treatment to reduce the pain from OA [3, 4]. On the other hand, the measurement of T2 relaxation time has gradually become a useful quantitative method to evaluate the degradation of knee cartilage. As a result, the purpose of this study is to investigate the relationship between the HA treatment and articular cartilage T2 in a rat model of OA by MR quantitative measurements.

Method

Twelve Sprague Dawley rats (aged 8-week-old, weighed around 300g) were enrolled in this study and randomly separated into two groups (n=6 for each group). Both groups were performed with right anterior cruciate ligament (ACL) transection for induction of cartilage degeneration at 8 weeks of age. Group 1 was the control group. Group 2 was the experimental group whose right knee was injected of HA four times from 5th to 8th weeks after ACL transection. At 0, 4th and 13th week after ACL transection, all the right knees of the rats were imaged in a supine position in a 4.7T MR system (Bruker, Ettlingen, Germany) after being anesthetized with a halothane/oxygen mixture. The proceeding of this study is illustrated in Figure 1. The images were acquired with a quadrature surface coil using a multi-slice multi-echo spin echo sequence with TR = 4500 ms, TE = 10/20/30/40/50/60/70/80 ms, slice thickness = 500μm, matrix size = 256 x 256, in-plane resolution = 117 x 100μm^2, NEX = 4, acquisition time = 1h16m48s. The T2 maps were calculated on a pixel-by-pixel basis by fitting the echo time data and the corresponding signal intensity to a single exponential relaxation model. Regions of interest (ROI) were manually placed on the femorotibial cartilage by referencing to the first-echo image to calculate the mean and standard deviation of the T2 relaxation time (Figure 2). Student t-test was performed to investigate the difference between control and experimental groups on the T2 values.

Results

The statistical results of the right knee cartilage T2 values are shown in Figure 3. At 0 week (i.e., 8 weeks of age before ACL transection), the cartilage T2 value was 26.18±1.00 ms and 26.79±0.64 ms in the group 1 (i.e. the control group without HA treatment) and group 2 (i.e. the experimental group with HA treatment), respectively. There was no significant difference between them ($P > 0.05$). At 4th week after ACL transection, the cartilage T2 value increased to 28.66±1.24 ms in the group 1, and to 29.81±1.19 ms in the group 2. At 13th week after ACL transection, the cartilage T2 value increased to 32.48±1.65 ms and to 30.72±2.24 ms in the group 1 and group 2, respectively. Except the time points of 4th and 13th week in the group 2, it shows significant difference between the T2 values of any two time points in any one of the two groups. The tendency of increasing T2 value slows down in the group 2 ($P < 0.05$).

Discussion

The present study indicated the feasibility of quantitative MR T2 measurement of rat knee cartilage to investigate the treatment effects of intra-articular injection of HA after ACL transection. Previous reporters demonstrated the progressing of OA manifested as significant increase of T2 value, which is possibly related to the disruption of cartilage architecture and consequent increasing of water content [5]. Our finding reveals consistent results in the group 1. On the other hand, the T2 value of HA-treated knees in the group 2 became lower than that in the group 1 at the 13th week, which is likely related to the enhancement of proteoglycan synthesis and preventing its release from the cell matrix. Although the change of T2 value in the knee cartilage is associated with many factors, our preliminary findings suggest that HA treatment may prevent the degradation of knee cartilage and has a potential to promote the regeneration on the OA knee, which is observable by longitudinal quantitative MR T2 measurements as shown in the slowdown of the tendency of increasing T2 value.

Reference

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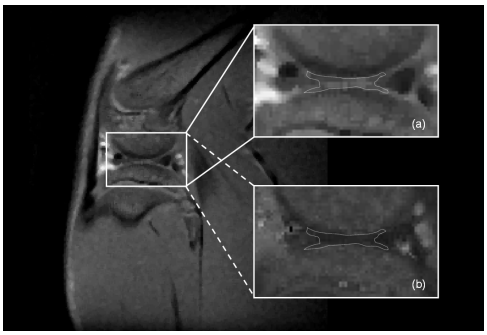

Figure 2 Example of an ROI selection based on the enlarged first-echo image (a), and the corresponding T2 map (b)

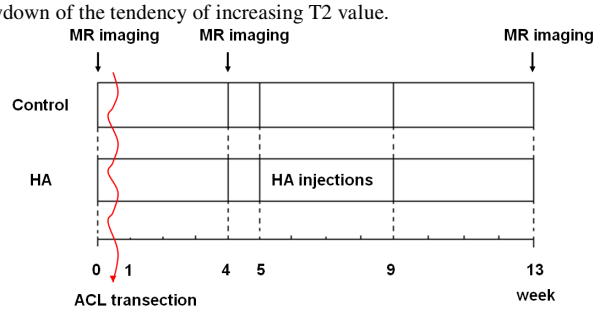

Figure 1 A diagram to represent the proceeding of this study.

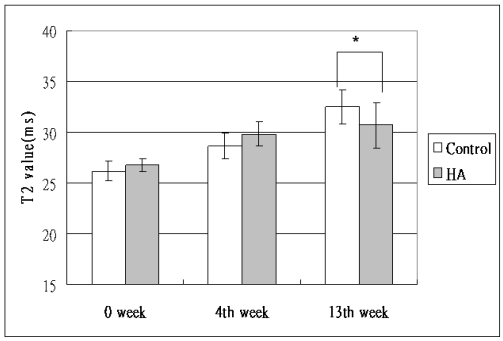

Figure 3 A plot of cartilage T2 (mean ± SD) measured at 0, 4th and 13th week in the groups of control and HA.