# Dynamic MR Elastography of Cartilage Degradation

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Introduction:

The unique functional state of normal articular cartilage is primarily attributed to the structural integrity of its extracellular matrix, where a collagen fiber network, proteoglycans (PGs) and water are main contributors to its mechanical capacity. During Osteoarthritis (OA), a common and severe musculoskeletal disease, degenerative structural changes in the cartilage matrix are known to characterize the disease, whereby early degeneration has been associated with decreased PG concentration and disruption of the collagen network thus causing cartilage softening and, in time, irreversible damage [1-3].

Therefore, it is desirable to have a sensitive method of detecting cartilage degeneration at its early stages in order to minimize structural changes to the matrix with timely intervention. The aim of this work was then to develop a laboratory tool based on Magnetic Resonance Elastography (MRE) technology that overcomes limitations of current *in vitro* methods for direct and noninvasive quantification of the dynamic mechanical properties of articular cartilage through its depth. MRE of cartilage promises to significantly aid in analysis that better relates local mechanical properties to corresponding cartilage structure.

As proof of concept, MRE of bovine articular cartilage plug samples of 1 cm in diameter was performed using control and enzyme digested cartilage groups, with collagenase and trypsin to digest collagen and PGs matrix components, respectively.

Methods:

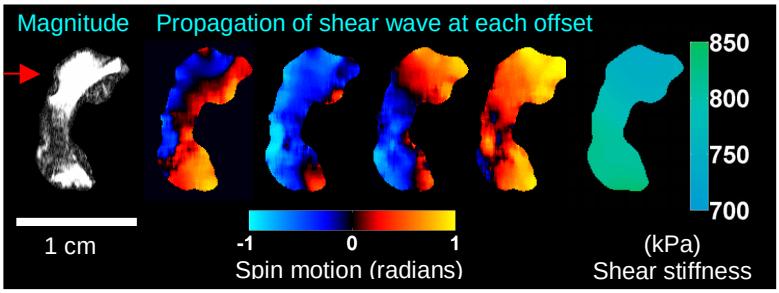
MRE of cartilage requires a customized system to adequately generate and detect high frequency (>1 kHz) propagating shear waves in small-stiff material samples [4]. The system consists of an RF coil for imaging small samples, a mechanical transducer with high frequency response, and a strong local gradient coil to enhance motion encoding of high frequency propagating waves, all to accommodate a 1cm diameter cartilage sample. Important design considerations for the local gradient coil were aimed at minimizing its impedance response at high frequencies to achieve gradient strengths > 5 times that of the whole body coil (i.e. 2.2 G/cm). Performance of the system was tested using phantoms of cartilage mimicking media.

Cartilage plug samples of 1cm in diameter were extracted from a femoral condyle of a 9 month bovine fetus. The samples were divided into three groups: a control group (n=3), collagenase-digested group (n=3) and a trypsin-digested group (n=3). All samples were incubated for 6h at 37°C in phosphate buffer solution (PBS). Enzyme induced degradation was performed by adding 30U/ml collagenase type VII for collagen type II degradation, and 200ug/mL trypsin for PG disruption. No enzymes were added to the control samples. After 6h, the cartilage samples were rinsed and placed in PBS solution for equilibration prior to MRE testing. MRE of the cartilage samples was performed at 1 kHz of mechanical shear excitation. Stiffness estimates were made using current inversion algorithms available in our Lab.

Results:

MRE of a cartilage sample extracted from a femoral condyle of a 9 month bovine fetus at a mechanical excitation of 2 kHz is shown in Figure 1. Fig. 1 shows the gradient echo image of the specimen, given in sagittal view using a FOV of 2x2 cm and TR/TE = 250 / 17 ms. The center panel shows four phase offsets of the shear wave as it propagates through the thickness of the cartilage from the articular surface (red arrow) to the bone. The elastogram given at the right was derived from these wave images. The estimated distribution of shear stiffness within the thickness of the cartilage appears to fall within ranges specified in the literature [1-3]. MRE of the cartilage samples from the control group and enzyme digested groups produced estimates of stiffness indicative of a trend in decreased stiffness with enzyme degradation. Figure 2 shows a box plot of stiffness estimates from all three sample groups: controls, trypsin-digested and collagenase-digested samples. The mean shear stiffness values of the digested samples were significantly different than the untreated cartilage samples.

**Figure 1. MRE of a fetal bovine cartilage plug at 2 kHz of mechanical excitation.**




Discussion:

This work has demonstrated the use of MRE in the study of articular cartilage mechanics by enabling direct and noninvasive quantification of its dynamic mechanical properties. Also important is the sensitivity of the technique to detect minor structural changes, as induced by our enzymatic degradations. Although these are initial results, our stiffness estimates seem to agree with the literature. In particular, our results agree with other cartilage degradation studies that have reported more significant changes in mechanical function of cartilage due to collagenase-digestion than trypsin-digestion. Overall, MRE promises to be a valuable investigative tool for *in vitro*, and eventual *in vivo*, cartilage research.

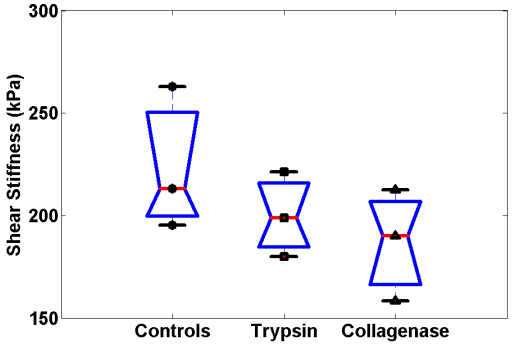



**Figure 2. Shear stiffness estimates for control and enzyme digested cartilage samples obtained from MRE at 1kHz of mechanical excitation. Each box gives lines at the lower quartile, median, and upper quartile of shear stiffness estimates. Individual stiffness estimates from each sample are shown in black markers.**

References:

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