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Altered Internal Strain Distributions in Adult Ovine Cartilage Before and After Full-Thickness Cartilage Defect

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INTRODUCTION

Articular cartilage and surrounding soft tissues in the knee are important to normal joint function. However, disease, trauma, and progressive degeneration can alter the function of the joint, often changing the distributions of tissue deformation through the tissues of the knee [1], and lead to advanced osteoarthritis [2]. Knowledge of the mechanical properties of the soft tissues in the knee is important to characterize both normal and damaged joints. Additionally, the ability to restore the strain distribution of damaged regions to accepted normal values could be used as a measure of success of a tissue engineering solution. Noninvasive imaging technologies, such as magnetic resonance imaging (MRI), can be used to study normal tissue, detect tissue damage, and monitor both degeneration and the progress of repair treatments.

MRI has shown promise in the study of soft tissue biomechanics, including various quantitative MRI techniques [3]. In particular, displacement-encoded MRI can directly measure mechanical behavior [4, 5]. Because displacement-encoded MRI is noninvasive and nondestructive, it may be applied to longitudinal studies of cartilage treatments, which are typically performed in animal models, including sheep. Therefore, the aim of this study was to visualize the change in cartilage deformation and strains at the tibiofemoral interface as a result of a full-thickness cartilage defect. Additionally, this *in situ* study can be used as test of feasibility and precursor to future *in vivo* studies of defect models.

METHODS

An ovine stifle knee specimen was obtained from a local abattoir and frozen immediately after slaughter. Prior to the experiment, the joint was thawed and excess tissue was excised from the stifle without compromising the joint capsule. The joint was flexed at 50° to replicate the stance phase of gait [6], and the tibia and femur were potted with polymethylmethacyrate to allow for attachment to a custom MRI-compatiable loading device, which was secured inside a 9.4T Biospec MRI scanner (Bruker Medical GMBH, Ettlington, Germany). Gauze wet with phosphate-buffered saline (PBS) and plastic wrap was used to prevent desiccation of the joint.

The stifle was cyclically loaded to 445 N (one-times body weight, 45.4 kg) for 2.0 seconds every 5 seconds, with loads transferred through the tibia to the femur in the distal-to-proximal direction. Once steady state cartilage displacement in response to cyclic loading was confirmed via standard MRI scans taken before and during the load plateau, MRI acquisitions were synchronized with cyclic compression of the joint.

For displacement-encoded imaging, displacement encoding with stimulated echoes (DENSE, [7]) with a TrueFISP acquisition (DENSE-FISP) was implemented using an encoding gradient moment of 0.65 π/mm and a mixing time of 600 ms [8]. Encoding gradients were applied in the loading (y) and transverse (x) directions, as previously described [4, 8], to measure in-plane displacements in the sagittal imaging plane, which was selected to cut through the most distal aspect of the medial condyle. Other DENSE-FISP parameters were as follows: flip angle=25°, echo/repetition time=1.65/3.30 ms, field of view=64.0×64.0 mm^2, spatial resolution=250×250 μm^2, slice thickness=1.5 mm, and 8 averages for each scan, with three complementary scans with phase advances of 60°, 180°, or 300° between each radiofrequency pulse [8]. In-plane displacements and strains were computed within the cartilage regions of interest, using software (MATLAB, MathWorks, Natick, MA) as previously described [4, 8].

Upon completion of the first set of scans, the stifle was removed for surgery. A 8-mm diameter full-thickness (i.e. 5-mm deep) defect was created at the most distal aspect of the medial condyle. The joint was flushed with PBS both before and after suturing, and a PBS+protease inhibitor cocktail was introduced into the joint capsule. The defect joint was again wrapped in PBS-soaked gauze and plastic before imaging with DENSE-FISP.

Changes to strains in the articular cartilage with the defect were quantified and compared in cartilage-cartilage contact regions not removed by the surgery.

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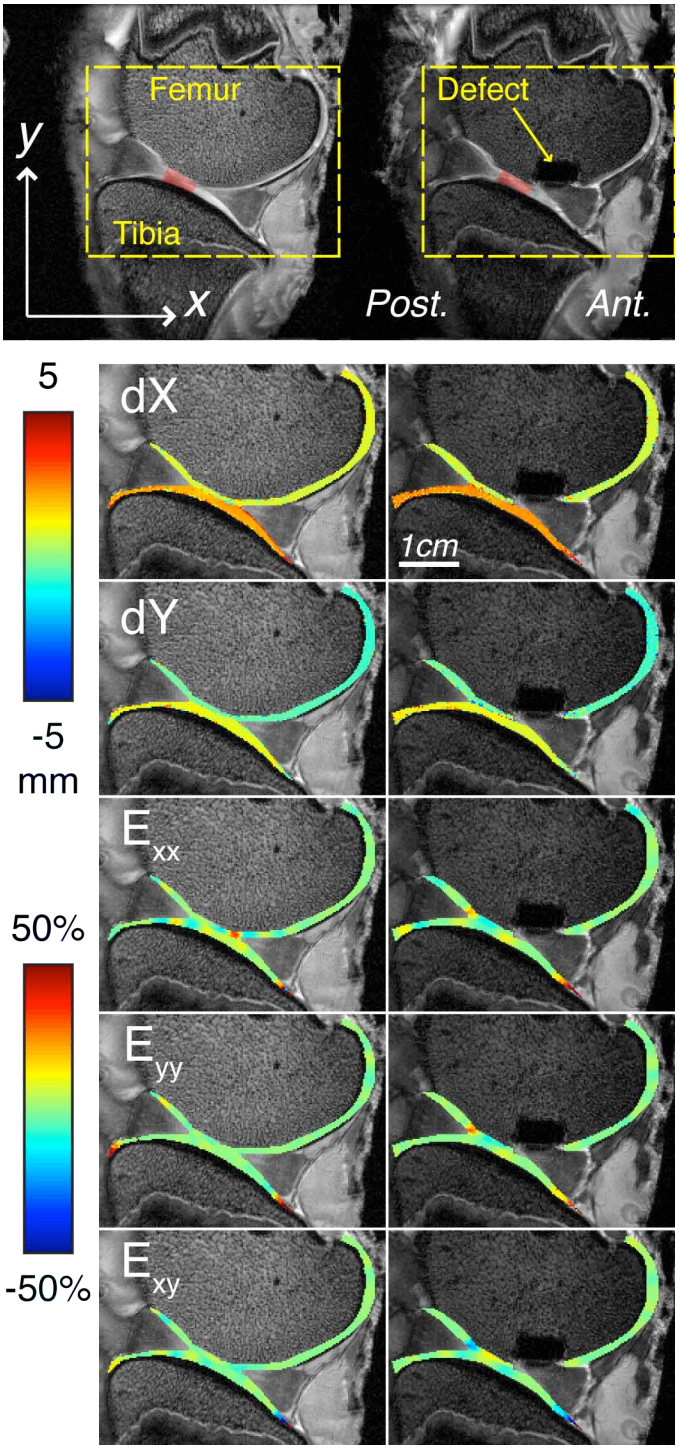

Figure 1. Strain distributions shifted with creation of a full-thickness cartilage defect. Red overlay (top) indicates the cartilage-cartilage contact area selected for comparison (Table 1). Displacements and strains were measured in a sheep stifle before (left) and after (right) creation of the defect.

RESULTS

Displacements in the loading and transverse directions were computed in the femoral and tibial articular cartilage of the joint before and after surgery (Figure 1). Rigid body displacement dominated displacements in the x and y directions. Strain maps were heterogeneous and showed a shift in strain patterns after the defect. In the intact cartilage-cartilage contact regions, average strains in the femoral cartilage increased (Table 1). E_{yy} and E_{xy} increased but E_{xx} decreased in the tibial cartilage.

Table 1. Average strains (%, mean ± S.E.M.), as measured within the cartilage-cartilage contact area, changed with the defect.

	Femoral Cartilage		Tibial Cartilage	
	Normal	Defect	Normal	Defect
E_{xx}	-1.64 ± 0.53	-6.53 ± 0.51	0.32 ± 0.56	0.03 ± 0.51
E_{yy}	-1.19 ± 0.26	-5.63 ± 0.56	0.99 ± 0.18	1.05 ± 0.38
E_{xy}	1.05 ± 0.27	6.34 ± 0.62	-0.92 ± 0.34	-1.15 ± 0.46

DISCUSSION

The purpose of this study was to examine the changes in cartilage displacements and strains with the introduction of a full-thickness defect. Previous studies with displacement-encoded MRI have used adult explants [4] and intact juvenile joints [5]. However, intact adult joints present the challenge that the imaging volume must be large, pushing the limits of decreased spatial resolution with relatively thin cartilage. Additionally, internal deformations are expected be lower in adult joints, due to decreased cartilage thickness and increased modulus in weight-bearing areas with maturation [9].

In this study, the overall displacements measured using DENSE-FISP indicated that rigid body motions dominated the displacements (Figure 1). The heterogeneous strain fields better represent the internal deformation and the changes that occur after the creation of the defect. In particular, localized areas of high tensile strain were observed in the transition areas between the cartilage-cartilage and cartilage-meniscus contact areas. With the creation of a defect, strains increased in the femoral cartilage, with increased variation in E_{yy} and E_{xy} (Table 1). The observation that tibial cartilage was not as affected by the defect may indicate that the integrity of the tibial cartilage was not immediately affected by introducing the defect.

Although differences are seen in the strain fields after the defect occurs, it is important to note some limitations of this *ex vivo* study. The defect resulted in lower signal-to-noise in surrounding areas due to banding artifacts typical of TrueFISP sequences. Although using the same joint allows for repeatable positioning, protease inhibition is necessary to prevent biochemical degradation and preserve cartilage integrity. Additionally, the defect treatment is imaged immediately after surgery, so no time effects or healing can be observed in this study. Nonetheless, these results indicate the mechanical conditions that exist after surgery at the most immediate time point.

Future studies could examine the changes to displacements and strains with defects in multiple joints, in addition to the introduction of a tissue engineered construct or other treatment. Translation of this technique to a clinical (3.0T) MRI system would permit *in vivo* studies. Successful implementation of an *in vivo* technique to evaluate and monitor mechanical changes after tissue damage and repair could significantly reduce the number of animals needed to test a particular treatment regimen. This study represents progress towards that goal by showing that changes to mechanical behavior with a full-thickness cartilage defect can be detected with displacement-encoded MRI.

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