WORKSHOP

Functional Imaging of Articular Cartilage by MRI

Organizers:
Yang Xia, PhD
Louis E. DeFrate, PhD

Speakers:
Yang Xia, PhD
Louis DeFrate, PhD
Xiaojuan Li, PhD
The deformation of cartilage by microscopic MRI

Yang Xia, PhD
Department of Physics and Center for Biomedical Research, Oakland University,
Rochester, Michigan 48309, USA
Web: http://www.oakland.edu/~xia; Email: xia@oakland.edu

Articular cartilage is the load-bearing tissue in a joint, the weakening of which signals the onset of tissue degradation that would lead to clinical arthritis. In healthy cartilage, molecular properties such as collagen content and GAG concentration increase through tissue depth and give rise to increasing depth-dependent elastic modulus through hydraulic and osmotic pressure, and electronegative repulsion of GAG molecules [1-2].

Magnetic resonance imaging (MRI) is highly sensitive to the molecular environment in soft tissue and also totally non-invasive. The dynamic motions of the water protons and the exchanges among the water protons associated with various molecular constituents in cartilage give rise to a range of rich characteristics in MRI. MRI of articular cartilage while the tissue is being loaded is a functional study of cartilage, where external loading becomes an adjustable tool [3]. By forcing the tissue to reach a new equilibrium with the environment, the ability of the tissue to re-distribute and re-balance its intrinsic properties and structures can be examined by MRI non-invasively.

This presentation focuses on the functional studies of articular cartilage by microscopic MRI (μMRI). At high resolutions, the responses of the tissue to external loading can be resolved across the tissue depth in all histological zones [4-6]. Because of its depth-dependent mechanical properties, the responses of cartilage to external loading are also depth-dependent, different in different zones. The responses of cartilage to loading are also disease-dependent, since a lesioned tissue has a set of totally different mechanical properties. Although MRI at microscopic resolution is currently not possible in whole-body MRI of human, the knowledge gained from these high-resolution studies is essential for the novel design and accurate interpretation of whole-body functional MRI experiments of human [7-8].

REFERENCES:


SPONSOR: R01 grant from National Institutes of Health (AR 052353).
Mechanical loading plays a critical role in maintaining the health and function of articular cartilage. Normal cartilage loading is believed to help maintain cartilage homeostasis, while altered cartilage loading (due to factors such as obesity, joint injury, and malalignment) is believed to play a role in the degradation of cartilage. Thus, understanding the local, in vivo mechanical environment of cartilage in response to normal and pathological conditions could provide critical insights into the mechanisms contributing to osteoarthritis. However, there is limited data characterizing the local mechanical environment of cartilage in vivo. While gait analysis studies provide important information characterizing the total load transferred through the joint, it may be difficult to predict the local tissue response of cartilage from these measurements. In this regard, magnetic resonance (MR) imaging techniques provide the potential to provide additional measurements of the changes in the morphology, deformation, and composition of cartilage in vivo to gain insights into the mechanisms leading to osteoarthritis. To this end, this talk will discuss recent advances in the measurement of in vivo cartilage function using MR imaging techniques. These advances are likely to provide important information that to enhance our understanding of mechanisms predisposing the joint to the development and progression of osteoarthritis. Ultimately, understanding these mechanisms is important to developing new interventions aimed at the prevention of osteoarthritis.
Towards In Vivo Weight-Bearing MRI for Knee OA

Xiaojuan Li, PhD
Department of Radiology and Biomedical Imaging
University of California, San Francisco
Xiaojuan.Li@ucsf.edu

Introduction

Osteoarthritis (OA) is a prevalent disease that is characterized by cartilage degeneration including both morphological and compositional changes of the tissue. OA preferentially affects weight-bearing joints such as the hip and the knee. Therefore to investigate the interrelationship between joint loading and tissue properties and functions are critical to understand the disease mechanism as well as to monitor the disease progression. In particular, cartilage responses to loads may serve as sensitive markers of the disease states. However, in vivo analysis of responses of cartilage to loads remains under-investigated. One technical challenge is oninvasive quantification of the tissue morphology and composition under loading. In this talk, we will introduce the techniques of loaded MRI and the recent studies using the developed techniques in OA and acutely anterior cruciate ligament (ACL)-injured knees. The loaded MRI setup, imaging protocol, image processing and quantification techniques (including morphology and $T_1$ and $T_2$ relaxation times of cartilage, and knee kinematics) and results will be discussed.

Weight Bearing and Loaded MRI

Using modern MRI techniques, human subjects are normally being scanned in a supine or prone position without any loading. Open MRI systems offer the opportunity of scanning subjects in a vertical or more weight bearing position, thus images can be acquired with the joint loaded. Open MRI systems, however, are primarily limited to relatively low field strength (< 1.0 Tesla), which limits the image signal-to-noise (SNR) ratio and image resolution. More recently, loaded MRI techniques have been developed using MR-compatible loading devices. Using a loading device shown in Figure 1 as an example, the axial load to the knee joint is applied through the foot via a plate connected to the weights hanging behind the subject through a pulley system. Although such simple axial and static load does not simulate physiologic loading with normal gait, it provides unique opportunity to investigate the joint tissue responses to loading under a very controlled condition. The high-resolution MR images also allow quantification of these responses, ie, morphological and compositional changes derived from quantitative MRI, with a high accuracy. Below we will discuss a few studies examining the effects of acute loading on cartilage composition and morphology in healthy controls and in subjects with OA, followed by a discussion on studies using loaded MRI to quantify knee kinematics and its application in subjects with ACL-injuries.

Effects of Acute Loading on Tibiofemoral Articular Cartilage

Twenty subjects with radiographic evidence of OA and 10 age-matched controls were studied using a 3T MR scanner. The imaging session consisted of two phases: unloaded imaging, and loaded imaging at 50% body weight. Subjects arrived at the imaging center 45 min prior to their appointment time and were kept in an unloaded position (wheelchair) until their scan time (Figure 1). The study knee was positioned in 10 degrees of external rotation with the knee flexed to 20 degrees. The imaging protocols were identical for the unloaded and loaded sessions including sagittal and coronal fast spin-echo (FSE) images, high-resolution coronal spoiled gradientecho (SPGR) images, and $T_1$ and $T_2$ maps.
Cartilage was segmented into medial and lateral tibial and medial and lateral femoral compartments and subcompartments. Cartilage thickness as well as $T_1$ and $T_2$ relaxation times were quantified. Cartilage lesions were identified using a modified Whole Organ Magnetic Resonance Imaging Score (WORMS) score.

Figure 2. Representative T1rho maps at unloaded (A) and loaded (B) conditions.

Cartilage became significantly thinner during loading in the medial tibia, the weight-bearing medial femur and in the lateral tibia, but not in the lateral femur. The magnitude of deformation in the medial tibia and femur tended to be greater in osteoarthritic knees than in healthy knees. The subregional pattern of cartilage deformation was similar for the different stages of radiographic OA.
A significant decrease in $T_1$ and T2 relaxation times was observed in the medial compartment with loading while no differences were observed in the lateral compartment. This behavior occurred independent of WORMS score. Cartilage compartments with small focal lesions experienced greater $T_1$ changes with loading when compared to cartilage without lesions or cartilage with larger defects. Figure 2 shows representative $T_1$ maps during unloaded and loaded conditions.

In addition, the average area of the contact region in the medial compartment was significantly higher in OA subjects compared with normal subjects in both unloaded and loaded conditions. Changes in area of contact region in subjects with OA were higher when compared to normal subjects.

More recently, the similar loading and imaging set up was applied to a larger cohort ($n=137$), and the $T_1$ and T2 relaxation times were quantified in different layers in subcompartment of femoro-tibial cartilage, Figure 3. In response to loading, significant reductions in $T_1$ and T2 relaxation times were observed, similar to previous studies. Reductions were larger for subjects with OA when compared to healthy controls. Interestingly, however, the superficial layer and deep layer of cartilage showed different responses to loading, and significant increases in $T_1$ and T2 of the deep layer of the femoral cartilage were observed.
These studies showed that OA cartilage tended to display greater deformation and larger changes of relaxation times upon loading than healthy cartilage. These results suggested that the OA cartilage is less capable of retaining water due to damages to collagen/proteoglycan matrix, and consequently has a reduced ability to dissipate loads and damaged mechanical properties. Combining quantitative and loaded MRI, these ‘stress’ responses can be evaluated reliably and non-invasively, and may serve as sensitive markers for OA disease progression.

Quantification of Knee Kinematics after ACL-injury Using Loaded MRI and Its Relationship with Cartilage Degeneration

Abnormal kinematics after acute injuries have been suggested as significant factors contributing to posttraumatic OA development. In particular, a rupture of the ACL of the knee results in high risk for the developing post-traumatic OA, with or without surgical intervention. Abnormal biomechanics even after ACL reconstruction, along with biochemical changes caused by the initial injuries, are hypothesized as the contributing factors to subsequent joint degeneration. Previous studies have reported abnormal knee kinematics following ACL injury and reconstruction using high-speed radiography, fluoroscopic analysis, and motion analysis. In addition, kinematic MRI with static loading or upright MRI has been developed to quantify knee kinematics.

In kinematic MRI, the subjects are scanned with loading (25% body weight or 125N were used) at extended and flexed positions (with flexion angle ranged 15-45 degree). After bone segmentation, coordinate systems are established for the tibia and femur, and kinematics parameters including anterior tibial translation (ATT) and internal tibial rotation (ITR) are calculated after image registered between positions. Lansdown et al. compared the reproducibility of the kinematic parameter quantification using three methods: a tibial based registration system, a combined tibiofemoral-based registration method with manual segmentation, and a combined tibiofemoral-based registration method with automatic definition of condyles and axes. The combined tibiofemoral registration with automatic definition of the posterior femoral condyle and diaphyseal axes allows for improved knee kinematics quantification with excellent in vivo reproducibility. In addition, other kinematics parameters including medial tibial translation, contact areas and meniscus translation as well as patellofemoral kinematics and contact area can be also quantified.

Despite the hypothesis that abnormal biomechanics are associated with OA development in ACL-injured and reconstructed knees, limited studies have provided direct evidence of such link. Using kinematic MRI, Haughom et al. documented a correlation between abnormal knee kinematics and early cartilage degeneration in ACL-reconstructed knees using kinematic MR and T1ρ quantification. Elevated T1ρ in the weight-bearing region of the medial femoral condyle, medial tibia and patellar cartilage were observed in patients with “abnormal” anterior tibial translation (ATT) when compared to a group of patients with “restored” ATT. Similar trends were observed in MFC weight-bearing region in patients with “abnormal” internal rotation (IR) as compared to those with “restored” IR. In a more recent study with 25 patients with acute ACL injury, at one-year following ACL reconstruction, the absolute value of the side-to-side difference (injured vs. contralateral knee) in tibial position during knee extension correlated to the side-to-side difference in cartilage T1ρ values in the MF. This effect was driven by the central subcompartment (cMF) and the posterior subcompartment (pMF). The results from these studies suggest that cartilage degeneration in the medial side may be accelerated due to abnormal joint biomechanics after ACL reconstruction. Loaded MRI provides reliable quantification of knee kinematics; quantitative MRI such as T1ρ can be valuable tools in detecting early cartilage degeneration. Combining kinematic and quantitative MRI provides unique opportunity in exploring the interrelationship between biomechanical abnormalities and tissue degeneration.
Figure 4. Flowchart describing the kinematic MR image processing process. Once subjects are imaged in the two positions (a), the sagittal fast spin echo (FSE) then used to segment the tibia and the femur in both positions (b). The segmentations are then reformatted into a three-dimensional shape (c) and finally the tibae in flexed and extended positions are rigidly registered to one another (d) in order to determine the relative anterior tibial translation (ATT) and tibial rotation (TR) between the two positions.