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An MRI-compatible loading device to assess knee joint cartilage deformation: Effect of preloading and inter-test repeatability

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ABSTRACT

It has been suggested that the extent and location of cartilage deformation within a joint under compressive loading may be predictive of predisposition to further degeneration. To explore this relationship in detail requires the quantification of cartilage deformation under controlled loads on a per-patient basis in a longitudinal manner. Our objectives were (1) to design a device capable of applying controllable axial loads while ensuring repeatable within-patient tibiofemoral positioning during magnetic resonance imaging (MRI) scans and (2) to determine the duration for which load should be maintained prior to the image acquisition, for a reproducible measurement of cartilage deformation, within the restraints of a clinical setting. A displacement control loading device was manufactured from MRI-compatible materials and tested on four volunteers for the following five scans: an unloaded scan, two repeat immediate scans which were started immediately after the application of 50% body weight, and two repeat delayed scans started 12 min after load application. Outcome measures included within-patient changes in tibiofemoral position and cartilage deformation between repeat loaded scans. The differences in tibiofemoral position between repeat loaded scans were <1 mm in translation and $<2^{\circ}$ in rotation. Cartilage deformations were more consistent in the delayed scans compared to the immediate scans. We conclude that our loading device can ensure repeatable tibiofemoral positioning to allow for longitudinal studies, and the delayed scan may enable us to obtain more reproducible measurements of cartilage deformation in a clinical setting.

1. Introduction

Hyaline cartilage is a biphasic, inhomogeneous, anisotropic tissue which plays a fundamental role in the mechanics of the low friction, highly loaded environment of diarthrodial joints. It is well established that chondrocytes, cells in cartilage, are remarkably sensitive to their mechanical environment (Smith et al., 1996; Wong et al., 1997). Aberrant joint loads can influence the metabolism of the cells which may lead to the initiation and progression of osteoarthritis (OA), manifesting as changes in cartilage thickness, matrix components and mechanical properties (Andriacchi et al., 2004, 2009; Cotofana et al., 2011; Griffin and Guilak, 2005). Magnetic resonance imaging (MRI) has been widely used to assess articular cartilage thickness (Burgkart et al., 2001; Coleman et al., 2013; Eckstein et al., 2002), morphology (Cohen et al., 1999; Eckstein et al., 2006; Potter et al., 2012), and the structure and biochemical composition of the tissue (Nieminen et al., 2001; Subburaj et al., 2012). But the relationship between these metrics and cartilage mechanics has not yet been completely defined. It has been suggested that the extent and location of articular cartilage deformation across a joint surface under compressive loading may be predictive of predisposition to further degeneration (Hosseini et al., 2012; Piscoya et al., 2005; Van de Velde et al., 2009). MRI-compatible loading devices offer the opportunity to explore this relationship in patient-based studies by assessing the in vivo cartilage deformation under controlled joint loads, and sequentially over a period of time.

The regional variation in knee joint geometry, articular cartilage thickness and cartilage modulus has been well characterized (Deneweth et al., 2013; Li et al., 2005). Thus, for an applied load, a complex distribution of contact forces across the articulating surfaces results (Guo et al., 2015; Wang et al., 2015, 2014b). To assess

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cartilage deformation within a consistent area of a patient's knee joint in a longitudinal study requires reproducible tibiofemoral positioning across different scans. While a number of devices have been used to apply static loads across the knee joint during MRI scanning (Cotofana et al., 2011; Fellows et al., 2005; Souza et al., 2010; Yao et al., 2008), it is unclear if they allow for reproducible positioning of the knee joint. Another complicating factor is the time-dependent mechanical characteristics of articular cartilage. While in vitro experiments allow articular cartilage deformation to be quantified until equilibrium, which can take >60 min (Mow et al., 1980), such long tests are clinically difficult to implement. Thus, in clinical study there is a need to balance the requirement to load until cartilage deformation is consistent across repeat scans, without subjecting patients to unrealistically long scanning times.

The objectives of this study were (1) to design a device capable of applying known axial loads, while ensuring repeatable within-patient tibiofemoral positioning during MRI scans and (2) to determine the duration for which load should be maintained prior to the acquisition of scans, for a consistent measurement of in vivo knee joint cartilage deformation within the restraints of a clinical setting. Our ultimate goal is to utilize the model to establish if the extent and location of articular cartilage deformation across the knee joint is predictive of predisposition to further cartilage degeneration.

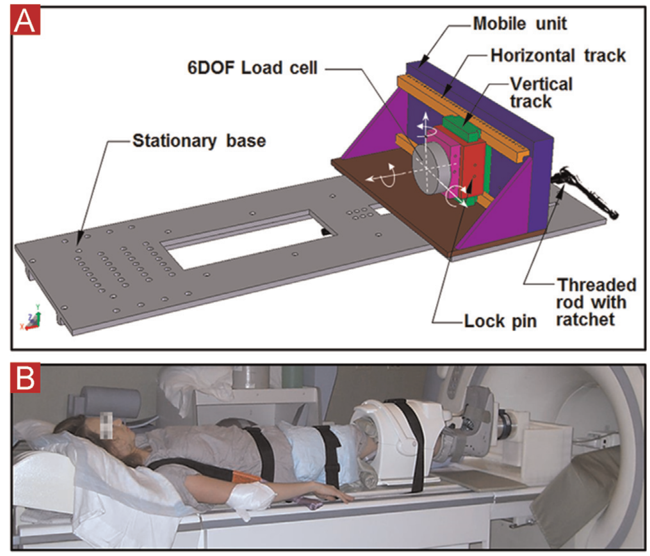

Fig. 1. Custom MRI-compatible loading device: (A) CAD drawing and (B) actual device with patient undergoing axial load (photo was taken after patient pulled out from the scanner).

2. Methods

Four healthy volunteers (3 female, 1 male, age: 35 ± 10 years, height: 1.67 ± 0.10 m, weight: 59.1 ± 11.3 kg) with no diagnosis of knee osteoarthritis or history of lower limb injuries participated in this study. The right knee of each subject was tested. This study was approved by our hospital's Institutional Review Board and informed written consent was obtained prior to participation.

The device was designed as a displacement control apparatus (Koff et al., 2010), manufactured from Delrin, an MRI-compatible synthetic polymer. The assembly consists of a stationary base and a mobile unit (Fig. 1A). The mobile unit was connected to the base by a threaded titanium rod to permit only axial translation. A 6-axis MRI-compatible load cell (model: 45E15A4, JR3 Inc., Woodland, CA) was attached to the mobile unit through a horizontal and vertical track which allows for medial/lateral and anterior/posterior adjustments to accommodate different subjects. An orthotic boot (Eschen Prosthetic & Orthotic Laboratories, New York, NY) was rigidly mounted to the load cell. Compressive load was applied by driving the load cell against the foot via a ratcheting mechanism. A shoulder harness with a waist strap was used to prevent the upper body from moving (Fig. 1B). Additional straps and padding were used to secure to the knee in the coil and the leg to the device. During each scan, forces were collected at 10 Hz (USB 6008 DAQ Cart, National Instruments, Austin, TX) using custom written software (Data Acquisition Toolbox, MathWorks Inc., Natick, MA).

Volunteers arrived at the imaging center 30 min prior to their appointment time and were placed in a wheelchair, to unload the knee. All scanning was performed on a clinical 3 T scanner (GE Healthcare, Waukesha, WI) using an 8 channel phased array knee coil (Invivo, Gainesville, FL). Each subject was positioned supine on the device, with the right knee fully extended and aligned with the load cell. Three-dimensional spoiled gradient recalled echo (3D SPGR) with frequency selective fat suppressive imaging was ;performed using the scanning parameters: echo time = 3.2 ms, ;repetition time = 15.4 ms, field of view = 14 cm, slice thickness = 1.5 mm, acquisition matrix = 512×512, number of excitations = 1, flip angle = 20°, with resulting voxel dimensions = $0.27 \times 0.27 \times 1.5$ mm^3. The scan time was 8 min. A series of five sequential 3D SPGR series were acquired to assess bony geometries and cartilage thickness for the following configurations (Fig. 2):

- *Unloaded*: Baseline images with the knee in an unloaded configuration at 0° flexion.
- *Immediate* (*a*): Following the unloaded scan, the ratcheting system was adjusted to apply an axial force equivalent to 50% BW. After 2 min (Fig. 3A), the force was finely adjusted back to 50% BW, and scanning was started.
- *Delayed* (*a*): The axial force was adjusted back to 50% BW at the end of *immediate* (*a*) and the scan was started. The time from initial load application to initiation of this scan was approximately 12 min.
- The subject was then removed from the scanner and a 15-min rest period was allowed with the imaged knee kept in an unloaded configuration.
- *Immediate* (*b*) *and delayed* (*b*): The subject was repositioned on the device, and two loaded scans were repeated, defined as *immediate* (*b*) and *delayed* (*b*).

Of note, real-time forces were visible only to the investigators. Subjects were asked to remain completely relaxed to avoid any active muscle contraction during scan. The forces were continually recorded throughout the scanning (Fig. 3).

Images were manually segmented (ITK-SNAP) (Yushkevich et al., 2006) to create 3D models of bone and articular cartilage (Fig. 4A). All segmentations were performed by a single investigator. The subchondral bone surface was defined by the sharp contrast of signal intensity between articular cartilage (bright) and bone (dark) commonly seen in standard imaging protocol. The segmentation rules were defined prospectively: image slices which displayed the anatomy of interest were segmented, except in cases of partial volume averaging (Schneider et al., 2012). The repeatability of image segmentation was assessed by performing four repeat segmentation trials on the same knee, and the coefficient of repeatability was determined (Bland and Altman, 1986; Coleman et al., 2013). The 3-dimensional femur models of the loaded configurations were registered to the femur model of the unloaded configuration using an iterative closest point (ICP) shape matching algorithm (Besl and McKay, 1992; Wang et al., 2014a) (Fig. 4B). The changes in tibiofemoral position were calculated as