In Vivo 3D Measurement of Time-dependent Human Knee Joint Compression and Cartilage Strain During Static Weight-Bearing

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INTRODUCTION: The ability to characterize cartilage deformation *in vivo* under physiologically relevant loading conditions would allow more detailed study of joint mechanics and the development of functional indicators of cartilage health relevant to many joint disorders. Cartilage exhibits time-dependent creep deformation in response to sustained compressive loads, and both the rate and extent of deformation increase in degenerated tissue[1]. Magnetic resonance imaging (MRI)-based techniques have been employed to characterize the *in vivo* response of articular cartilage to activity[2]. As much of the typically sub-millimeter cartilage deformation takes places within the first few minutes after loading, however, the relatively long scan times and relatively low spatial resolutions achievable with clinically feasible MRI protocols prohibit accurate measurement of cartilage strain—particularly during the transient response to loading or unloading. Here, we describe an alternate approach to studying knee cartilage compression that employs a C-arm-based cone-beam CT (CBCT) system capable of rapidly acquiring images of standing subjects due to its highly flexible trajectories for the image acquisition[3].

METHODS: Under an IRB-approved protocol and informed consent, three healthy male volunteers (30, 24, 52 years; 81, 70, 68kg) participated in this study. To outline soft tissue structures in the knee, each subject received a 40ml intra-articular injection of a non-ionic, iodinated contrast agent (Omnipaque 300, 647 mg/ml Iohexol) diluted 50% in saline. A CBCT system was first used to acquire a single supine scan (non-weight-bearing, Fig. 1a). Subsequently, standing scans (weight-bearing, shown in Fig. 1b) were acquired at four early time points (5sec, 15sec, 25sec, and 1min) and two late time points (5min and 15min) after the subject began supporting a load of ¾ body weight on the injected limb. For the standing scans, the system employed a weight-bearing scan trajectory parallel to the ground floor with a scan time of 8s. A multi-sweep C-arm CT scan protocol was implemented to obtain the first three standing scans (5sec, 15sec, and 25sec). Visual feedback of readings from a force plate (0.3N resolution) mounted in the standing platform was provided for the patient to better maintain the desired constant load throughout the standing period. Volumetric images at 200μm voxel resolution were reconstructed from the acquired images using filtered back projection. After smoothing, point clouds of the segmented bones and cartilage were fit with triangular mesh surfaces. To track overall joint compression, the pointwise Euclidean distance between the tibial surface and the closest point on the femur (determined by an N-D nearest point search) was defined as Tibial-Femoral separation (Fig. 1c). While qualitatively similar to clinical joint space measurement from projection radiography, this pointwise metric reflects changes due to both translation and rotation of the femur relative to the tibia. To specifically examine time-dependent changes in articular cartilage, the pointwise thickness of the tibial cartilage was similarly calculated at each time point, and the pointwise strain of the tibial cartilage was approximated as the change in thickness divided by the thickness from the supine scan. The regions of interest (ROIs) for the strain analysis were the medial and lateral contact areas between the tibial and femoral cartilage surfaces (not covered by the menisci). Mean strain values in each compartment were analyzed with a multifactor, repeated measures ANOVA with significance at $P<0.05$ and Bonferonni's test for pairwise comparisons.

RESULTS: The weight-bearing C-arm CT protocol captured the transient response of the knee joint to static weight-bearing, including relatively rapid changes during the first minute of loading. Tibial-Femoral separation changes stabilized by 5 minutes (Fig.1d), and demonstrated spatial variation due both to compression of soft tissues and motion of the femur relative to the tibia. Cartilage strain, which specifically indicates relative deformation of the cartilage, progressively increased in both the medial and lateral cartilage-cartilage contact regions (Fig. 2), with rapid increases over the first minute and fairly stable strain after 5 minutes. In subject #2 at 5 minutes of loading, the maximal decrease in Tibial-Femoral separation was 1.64mm, the maximal decrease in tibial cartilage thickness was 0.96mm, and the maximum compressive strain in tibial cartilage over the ROIs was 32%. While there was substantial and significant subject-subject variability in the strain magnitudes, mean values of compressive strain (Fig. 3) in both medial and lateral ROIs stabilized by 5 minutes in all three subjects, and strains at 1, 5 and 15 minutes were significantly greater than strains at 5 and 15s.

DISCUSSION: Leveraging the capabilities of a highly flexible C-arm CT imaging system, time-dependent knee joint compression and cartilage deformation was captured during *in vivo* static weight-bearing at physiologically relevant loads. Cartilage strain patterns in each of these healthy subjects demonstrated progressive, self-consistent strain patterns that exceeded the anticipated artifact due to segmentation error (average of 5.6%). Variation in strain patterns among subjects may be related to differences in joint alignment or other morphological parameters that can be extracted from the CT images, and this issue will be explored as subject numbers increase. Cartilage deformation was captured as early as 5s after the onset of weight-bearing, and stabilized by approximately 5 minutes of loading. Patients with early osteoarthritis (OA) likely have cartilage that is mechanically compromised, and cartilage is expected to exhibit both increased rates and magnitudes of deformation in these patients. Future studies will explore use of weight-bearing C-arm CT as an "orthopaedic stress test" for detecting OA changes and functionally significant lesions.

SIGNIFICANCE: This study measured the *in vivo* time-dependent creep behavior of tibial cartilage during static weight-bearing. This provides a powerful new tool for studying *in vivo* joint mechanics and may provide novel mechanical metrics of cartilage function and health.

REFERENCES: [1] Morton, Am J Occup Ther (1990), [2] Powers et al, J Orthop Sport Phys (2003), [3] Choi et al, Med Phys (2014)

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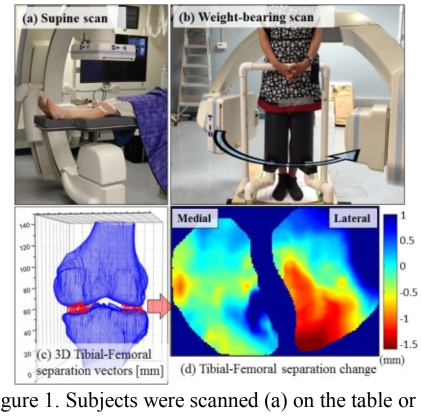

Figure 1. Subjects were scanned (a) on the table or (b) standing in the scanner. (c) Tibial-Femoral separation vectors were drawn for each scan. (d) Representative Tibial-Femoral separation change between the initial scan (supine) and the 5min weight-bearing scan.

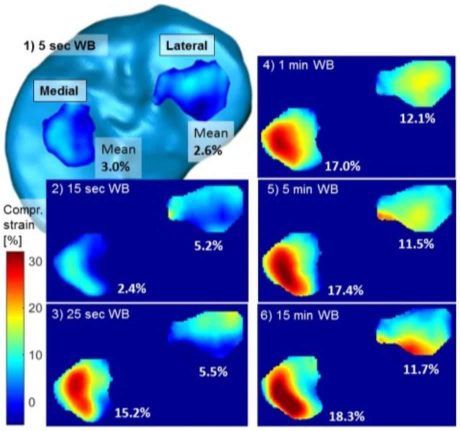

Figure 2. Compressive strain (%) patterns vs. time for cartilage-cartilage contact regions of tibial cartilage in subject #2 at six weight-bearing (WB) time points.

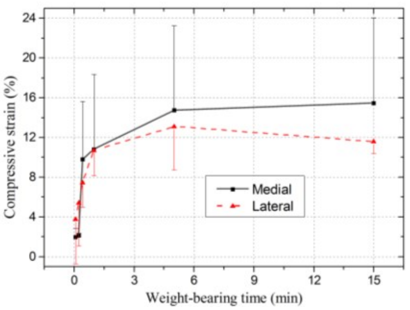

Figure 3. Mean values of the compressive strain (%) in the medial and lateral compartments of three subjects as a function of time.