Contrast-Enhanced Computed Tomography (CECT) Reflects Stiffness of Intact Articular Cartilage

Reza Nickmanesh[1,2]; Rachel Stewart [3,4]; Brian Snyder [4]; Mark Grinstaff [3]; David Wilson[1,2].
1. Departments of Orthopaedics and Mechanical Engineering, University of British Columbia, Vancouver, BC, Canada.
2. Center for Hip Health and Mobility (CHHM), Vancouver, BC, Canada.
3. Departments of Chemistry and Biomedical Engineering, Boston University, Boston, MA.
4. Center for Advanced Orthopaedic Studies, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA.

***Target Audience*:** orthopaedic surgeons, biomechanics researchers, radiologists, cartilage repair researchers

Purpose: Articular cartilage distributes load in joints and provides a low-friction surface for joint movement. Glycosaminoglycan (GAG) in cartilage plays a critical role in its compressive stiffness. Loss of GAG is an early sign of osteoarthritis that leads to lower compressive stiffness and altered viscoelastic behavior [1]. MRI and CT-based imaging techniques have been developed to quantify GAG content in cartilage in an effort to detect osteoarthritic changes early in the disease process. Contrast-Enhanced Computed Tomography (CECT) attenuation using a custom cationic contrast agent[2] (CA4+) correlates with GAG content and equilibrium compressive modulus in bovine osteochondral plug[3,4]. CA4+ demonstrates higher sensitivity to changes in GAGs than commercially available anionic contrast agents[5,6]. Applicability of these results to *in vivo* human studies is not clear because the cartilage is non-human and the plug model affects both diffusion of the contrast agent and cartilage mechanics. Our research question was: Is CECT imaging using CA4+ associated with cartilage stiffness in intact human cartilage?

Methods: Six human femoral condyle compartments (mean age 62±14) with intact healthy cartilage (ICRS grade 0 or 1) were obtained from male cadavers. Cartilage stiffness was measured at x-y locations (number of locations per sample ranged 30-60) across the surface using a Mach 1 testing system (Biomomentum, Montreal) using an indentation test. Cartilage stiffness was defined as the ratio of peak load to the indentation amplitude (0.3 mm). The samples were then immersed in CA4+ solution for 48 hours and then scanned at 41µm resolution in a hr-pQCT scanner (Xtreme CT, Scanco, Zurich). The averages of CECT attenuations at the sites of the indentation tests were computed for both superficial cartilage (600 µm depth from the surface) and for the full thickness of cartilage. Correlations between stiffness and CECT attenuation were assessed with scatter plots and Pearson's correlation coefficient.

Results: Regions with lower stiffness found with the indentation test corresponded with regions with lower CECT attenuations (Fig 1). A significant and positive correlation was observed between stiffness data and mean CECT attenuations in superficial cartilage across all samples, with correlation coefficients ranging from r=0.4 to 0.72, and p<0.01. When data from all testing sites were pooled (n=221), the correlation coefficient was r=0.55 and a regression line fit to the data predicted stiffness from CECT measurements with an estimation error of 20% of the stiffness range (Fig 2). Correlations between stiffness and CECT attenuations in full-depth cartilage were substantially lower and not significant in half of the tested specimens.

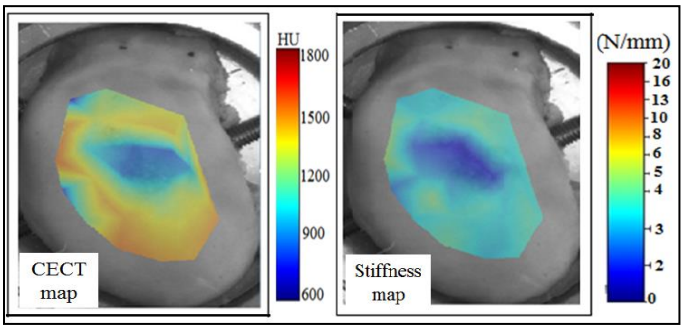

Fig 1: CECT map and stiffness map for an intact surface of human femoral condyle cartilage.

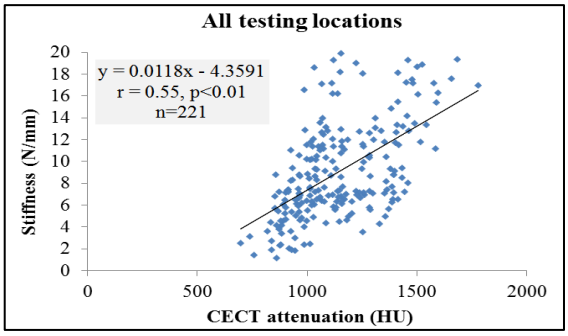

Fig 2: Correlation between the stiffness and measured mean CECT attenuation in superficial cartilage for all testing locations (data from 6 samples).

Discussion: We assessed the correlation between CECT measures of cartilage and mechanical stiffness and found significant correlations in all six tested samples. Our finding that CECT predicts stiffness is consistent with previous studies in bovine cartilage plugs[3,7]. The differences in strength of correlation with mechanics between superficial and full-thickness cartilage emphasize the importance of high resolution in imaging GAG distribution. A number of factors likely explain why CECT measurements do not correlate more strongly with cartilage stiffness. Collagen concentration is not assessed in CECT imaging, and collagen may play a role in both contrast-agent diffusion kinematics and compressive resistance in intact cartilage. Bone properties beneath the region of interest may also play a role, and these were not assessed in our study. A key strength of the study is that both imaging and mechanical testing were performed in intact knee compartments, which more closely simulates the physiological function of the joint than testing in cartilage plugs. A further advantage of our approach is that we assessed instantaneous load response of the tissue, which reflects cartilage stiffness for loading rates comparable to those in physiological activities. One limitation of our study is that only one type of articulating surface was assessed. Further investigation in all articulating surfaces of all joints is warranted.

Conclusion: CECT with CA4+ predicts mechanical stiffness of intact cartilage. This imaging approach may be useful for assessing functional changes in cartilage associated with disease and injury, and monitoring the effect of disease-modifying drugs and other treatments in OA studies.

References: [1] Armstrong, C. G et al. The Journal of bone and joint surgery. American volume 64:88–94. 1982. [2] Joshi N.S et al. Journal of the American Chemical Society 131:13234–35. 2009. [3] Lakin B. et al. Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society 21(1):60–68. 2013. [4] Bansal P.N. et al. Journal of Orthopaedic Research 29:704–9. 2011. [5] Stewart R.C. et al. Radiology 266:141–50. 2013. [6] Bansal P. N. et al. Osteoarthritis and Cartilage 19:970–76. 2011. [7] Bansal P. N et al. Osteoarthritis and Cartilage 18:184–91. 2010.

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