### Author's Accepted Manuscript

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 PII:
 S1751-6161(16)30348-4

 DOI:
 http://dx.doi.org/10.1016/j.jmbbm.2016.09.040

 Reference:
 JMBBM2097

To appear in: Journal of the Mechanical Behavior of Biomedical Materials

Received date: 23 May 2016 Revised date: 26 September 2016 Accepted date: 30 September 2016

Cite this article as: Jonathan T. Kaplan, Corey P. Neu, Hicham Drissi, Nancy C. Emery and David M. Pierce, Cyclic Loading of Human Articular Cartilage: The Transition from Compaction to Fatigue, *Journal of the Mechanical Behavior c. Biomedical Materials*, http://dx.doi.org/10.1016/j.jmbbm.2016.09.040

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#### ACCEPTED MANUSCRIPT

## Cyclic Loading of Human Articular Cartilage: The Transition from Compaction to Fatigue

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#### Abstract

Osteoarthritis and articular cartilage injuries are common conditions in human joints and a frequent cause of pain and disability. Unfortunately, cartilage is avascular and has limited capabilities for self-repair. Despite the societal impact, there is little information on the dynamic process of cartilage degeneration. We performed a series of cyclic unconfined compression tests motivated by *in vivo* loading conditions and designed to generate mechanical fatigue. We examined the functional (both stress-stretch and creep) responses of the tissue after recovery from a specified number of loading cycles, as well as histology and second harmonic generation microscopy images. The effect of compaction was complimented by the effect of fatigue in our unconfined compression tests. A three-way, repeated-measures mixed model ANOVA showed significant differences between loading with a physiologically relevant low magnitude, and two more severe loading magnitudes, in terms of the resulting specimen stiffness, time to equilibrium and thickness. There was statistically significant effect of loading frequency on a specimen's time to equilibrium and significant interaction of force and frequency on specimen

Preprint submitted to J. Mech. Behav. Biomed. Mater.

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