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SHORTER MORE REGULAR ACTIVITY IMPROVES CARTILAGE FUNCTION COMPARED TO LONGER LESS REGULAR ACTIVITY

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INTRODUCTION

Our sedentary lifestyle has been associated with increased risk of cardiovascular disease, metabolic disorders, cancers, and all-cause mortality.[1,2] On this basis, the CDC has recommended a minimum of 30 minutes of daily exercise in order to maintain health.[1] Nonetheless, a pervasive impression exists among the lay public, and among many practitioners, that osteoarthroses result from 'wear and tear'; leading to concerns that even moderate activity can promote cartilage wear. However, innumerous studies refute this relationship, instead, epidemiological studies indicate that moderate physical activity can decrease risk of joint disease.[3,4]

The link between exercise and cartilage health is at least partially understood. Static loading (during sitting and standing) pressures the interstitial fluid of cartilage, which preferentially supports loads, minimizes tissue strains and shear, and reduces frictions.[5,6] However, because cartilage is porous, load-driven exudation drives fluid losses and defeats this interstitial lubrication.[6] Consequently, loss of interstitial fluid due to compressive loading represents a serious impediment to cartilage's mechanical, tribological, and biological function. However, during articulation, cartilage recovers interstitial fluid and pressure, as evidenced by *in vivo* observations of activity-induced joint-space (cartilage) thickening.[7,8]

Links between joint movement and cartilage hydration, hydration and mechanical function, and mechanical function and chondrocyte function suggest that activity promotes cartilage health by preventing the detrimental mechanical, tribological, and biological effects of cartilage dehydration. However, direct insight into practical matters such as how activity should be prescribed to support and optimize joint health outcomes (how much and how often) has been sorely lacking. This is in part due to the fact that the gold standard platform for conducting 'controlled' studies of cartilage tribology and mechanobiology, the stationary contact area, induces rapid fluid exudation without providing any mechanism for competitive recovery, leading to functional compromise of the tissue and an inability to realistically study the link between cartilage tribology and health.

Recently, we have shown that by enlarging cartilage explant samples to allow for the creation of a convergent wedge at the leading edge of the stationary contact area (cSCA), one can drive sliding-induced fluid and deformation recoveries (which we term 'tribological rehydration') similar to that observed *in vivo*.[9] Follow-up studies have suggested that sliding-induced hydrodynamic pressures restore cartilage hydration by competing directly against the load-induced exudation process, and this restoration of hydration and interstitial pressurization facilitates both surface lubrication and solute transport.[10,11] Here, we leverage the cSCA testing configuration to determine if and how one distributes of a fixed volume of activity (i..e 30 min. of sliding) affects cartilage strain, which we use as a real-time predictor of cartilage health, within a simulated day of joint activity.

METHODS

19 mm diameter osteochondral cylinders (n = 5) were harvested from the femoral condyles of mature bovine stifles and tested on a uni-directional pin-on-disc materials tester (a.k.a. tribometer). When compressed against the glass disc, the curvature of the cartilage explants creates a convergence zone at the contact periphery that permits hydrodynamic effects during siding that are necessary for tribological rehydration.[9] Since the contact area is kept stationary relative to the cartilage, this geometry is referred to as a convergent stationary contact area (cSCA).[9] Explants were subject to a 150-min 'equivalent day' (based on area-exudation scaling of time); which consisted of 90-min 'awake' period in which a constant 5N load (~0.25MPa) was applied, and a 60-min 'sleep' periods in which the load was reduced to 0.1N load

and held (**Figure 1A**). The awake period was further divided into a 30 min 'active' (100mm/s sliding) and 60 min inactive 'sedentary' period. Each specimen (n = 5 explants) was subjected to five different equivalent daily activity regimens in a random order, consisting of 1 (1x30-min), 3 (3x10), 6 (6x5), 15 (15x2), or 30 (30x1) equally spaced bouts (see **Figure 1B**). Direct measurements of normal force, friction force, compression, and thickness were used to quantify a number of biomechanical outcomes including compressive strain, friction coefficient, contact radius, contact pressure, shear stress, effective modulus, interstitial pressure, and fluid load fraction (**Figure 1C**).

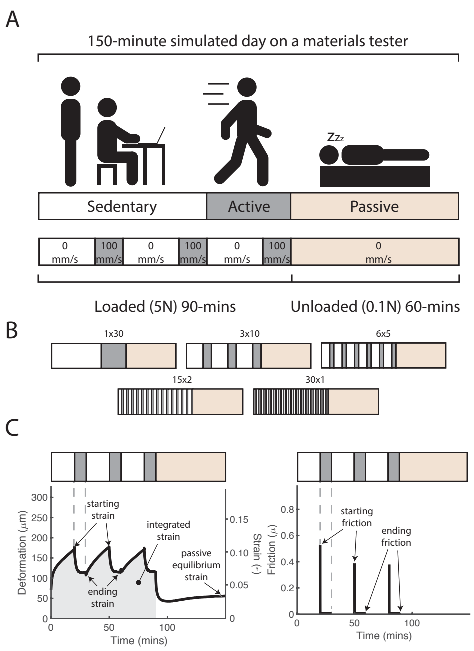

Figure 1: Figure caption centered below the graphic.

RESULTS

The data in **Figure 1C** illustrates the effects of loading, sliding, and resting on the deformation and strain recovery responses, and friction response of cSCA articular cartilage (data for 3x10-min activity paradigm shown). When loaded statically, the deformation jumps more or less immediately to 100 um, which represents the elastic response of cartilage. Over time under static load, deformations increase due to load-induced fluid exudation. Subsequent high-speed sliding restores thickness via tribological rehydration to nearly the original 'elastic' limit of 100 um; this rehydration process also restores interstitial pressure (not shown) and lubrication (friction coefficient).

Increasing the regularity of activity bouts (decreasing sedentary interval length) within our fixed 30-min of 'daily' activity substantially reduced the total loss of interstitial fluid as illustrated by **Figure 2A**. Increasing the number of bouts from 1 ('daily') to 30 ('half-hourly') decreased max strain accumulation and the loss of interstitial fluid by 80%, while also decreasing the extent of sliding friction at the start-of-sliding (**Figure 2B**). However, for a fixed volume of 'daily' sliding activity (30-min), strain at the end of each sliding bout, at the end of the loaded portion of the day, and at the end of the overnight unloading period were insensitive to the regularity of activity (or the length of contiguous time spent sedentary).

DISCUSSION

Our results demonstrate that the tribomechanical functions of cartilage are significantly affected by the length of sedentary bouts they are exposed to when controlling for total sedentary (60-min) and active (30-min) time in the cSCA. The results provide new insights into both cartilage biomechanics and cartilage function. The application of static load causes cartilage to lose interstitial fluid and pressure, and lubricity when sliding/activity is initiated.[6,9] Without any change in load, sliding-induced tribological rehydration reverses this exudation, restoring numerous biomechanical functions.[9] Because exudation increased over time, the detrimental biomechanical effects of inactivity increased with sedentary bout length. From a cartilage biomechanics standpoint, the results demonstrate that shorter and more regular bouts of intermittent activity are preferred to longer and less regular bouts.

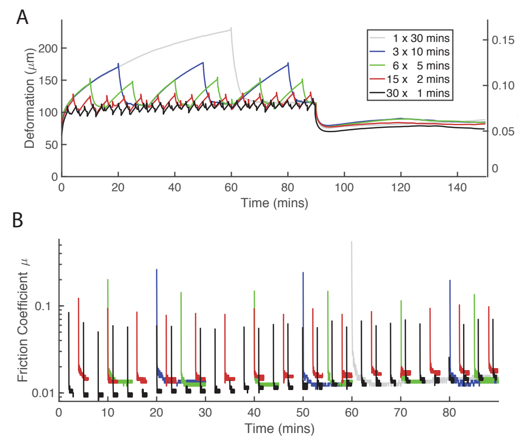

Figure 2: A) Deformation/strain and B) Friction traces for a representative sample subjected to the 5 different activity regimens tested in the present study.

The cSCA, and the discovery of tribological rehydration, offers us an opportunity to speculate about mechanistic connections between exercise, inactivity, joint health, and cartilage degradation. While it is intuitive that exercise might promote physical 'wear and tear' of joints, which are bearings after all, our results suggest the counterintuitive possibility that activity-induced mechanical damage is actually least likely to occur under conditions of sliding and joint activity that co-opt tribological rehydration to prevent the excessive loss of interstitial hydration and lubrication.

In conclusion, the result of this work demonstrates that the regularity of the ex vivo activity regimen, specifically the duration of each sedentary bout, has a significant effect on the biomechanical functions of cartilage. In more practical terms, the results suggest that brief but regular movement patterns (*e.g.* every hour) may be biomechanically preferred to long and infrequent movement patterns (*e.g.* a long walk after a sedentary work day) when controlling for daily activity volume (*e.g.* 30 minutes).

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