TIME-DEPENDENT COMPUTATIONAL MODEL OF CARTILAGE MECHANOBIOLOGY DURING INJURIOUS AND CYCLIC LOADING

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Introduction

Computational models of osteoarthritis have been developed to estimate cartilage damage progression [1,2]. However, the models lack realistic time-dependent insights into the degradation, especially from a mechanobiology-based modeling standpoint. Understanding how rapidly the disease mechanisms act is crucially important for development of interventions.

Methods

Cartilage plugs (n = 75) from young calves (N = 9) were subjected to compressive injurious loading (50%, 100%/s) on day 0, followed by up to 12 days of physiological cyclic loading (15%, 1 Hz, haversine waveform, 40% duty cycle, four 1-h sessions per day). Optical density of Safranin-O-stained sections was measured to estimate aggrecan content [2]. Our time-dependent computational model of cartilage mechanobiology (Fig. 1) included a fibril-reinforced porohyperelastic material model and a lesion in high fibril strain region with the following mechanisms: 1) shear strain-based cell damage (proteolytic enzyme release), 2) fluid velocity-driven aggrecan depletion, and 3) increased aggrecan biosynthesis (function of hydrostatic pressure time derivative) [2,3]. Lesion formation was not explicitly modeled. Experimental and numerical aggrecan contents were compared near (within 50 µm from lesion edges) and away from lesions (absolute, relative near/away fractions; Fig. 2).

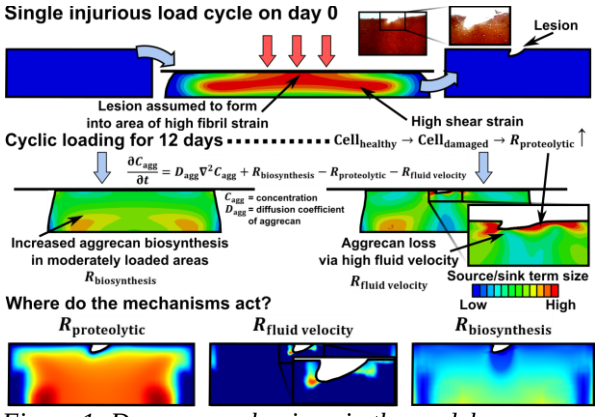

Figure 1: Damage mechanisms in the model.

Results

The simulated injurious loading caused substantial decrease of aggrecan content throughout the plugs by day 12 (Fig. 2A). Injured and cyclically loaded model revealed markedly lower aggrecan content near compared to away from the lesion on day 12, similarly as in the experiments (p < 0.001, linear mixed effects model, Fig. 2B). Simulated cyclic loading resulted in rapid aggrecan depletion near the lesion over the first three days, ultimately reaching 41% of the away-from-lesion aggrecan content by day 12 (87% in the injury-only model; Fig. 2C).

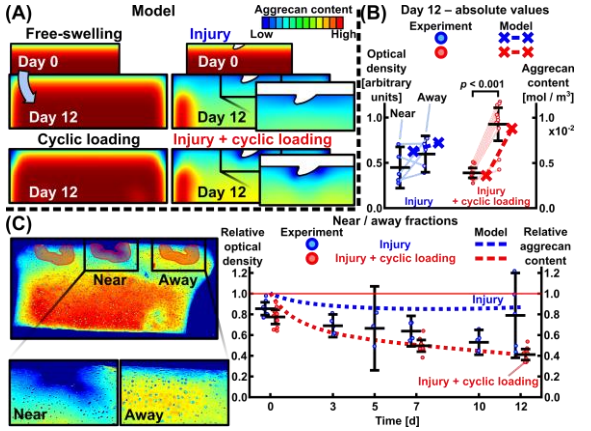

Figure 2: (A) Simulated temporal evolution of aggrecan content. Comparison of experimental and simulated aggrecan contents near vs. away from lesions (B) in absolute values on day 12 and (C) in relative terms over 12 days. Data shows mean ± 95% confidence intervals.

Discussion

In our present state-of-the-art cartilage adaptation model, we combined realistic time, histologically observed lesion, physiological loading, and several mechanobiological mechanisms. The proteolytic enzymes from damaged cells decreased aggrecan content globally and fluid velocity locally near the lesion. Aggrecan biosynthesis was elevated away from the lesion and in the deeper tissues in the model with cyclic loading. The presented cell–tissue-level model improves understanding of time-dependent mechanisms behind cartilage damage progression and could be implemented into joint-level models to estimate how cartilage adapts to different loading scenarios.

References

1. Gardiner et al, Ann Biomed Eng, 44:222-233, 2016.
2. Orozco et al, Sci Rep, 8:15599, 2018.
3. Elder et al, Tissue Eng Part B Rev, 15:43-53, 2009.

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