Public Abstract

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Title:DEVELOPMENT OF A POST-TRAUMATIC OSTEOARTHRITIS MODEL TO EVALUATE THE EFFECTS OF IMPACT VELOCITY AND MAXIMUM STRAIN ON ARTICULAR CARTILAGE CELL VIABILITY, MATRIX BIOMARKERS, AND MATERIAL PROPERTIES

Post-traumatic osteoarthritis (PTOA) is a painful and debilitating disease that is often associated with mechanical injury to articular cartilage, yet the severity of trauma required to induce the disease process and the steps involved are unknown. Therefore, the objective of this thesis work was to develop a clinically-relevant ex vivo PTOA model with repeatable severity of mechanical injury by delivering a single impact load with controlled combinations of velocity and maximum strain (i.e. severity of trauma categories normalized to cartilage thickness) to a radially-constrained articular cartilage explant to study their effect on articular cartilage's biomarkers: cell viability, extracellular matrix, and material properties. This is part of the broader goal of the Comparative Orthopaedic Laboratory of finding post trauma biomarkers that could clinically be measured to predict the likelihood of the onset of PTOA and its progression for purposes of selecting or determining optimum treatments.

A protocol was developed using a 25 kN actuator servo-hydraulic test machine to measure canine cartilage explant thickness (0.36 to 0.75 mm) and subsequently injure 4 mm diameter radially-constrained ex vivo canine cartilage explants at a constant impact velocity V of 1 or 100 mm/sec to a maximum strain S of 10, 30, or 50%; resulting in six (velocity:strain) test groups, for example high velocity:low strain (100V:10S). (0V:0S) and sham (tissue thickness and material moduli only measured after 12 days in media) test groups were used as controls. Thereafter, explants were cultured in supplemented media for twelve days. Cell viability was analyzed post-injury at day 0 and 12 as was cartilage matrix for collagen (hydroxyproline (HP)) and glycosaminoglycan (GAG) content. Media were changed after day 1, 2, 3, 6, 9, and 12; and tested for GAG content, collagen II synthesis (procollagen II C-propeptide), nitric oxide (NO), and prostaglandin E2 (PGE2). Material testing was performed via stress-relaxation and dynamic testing at day 0 (pre-injury) and days 6 and 12 (post-injury).

Greater cell death (concentrated in the superficial zone) occurred at days 0 and 12 for both high strain (1V:50S, 100V:50S) groups, with greater propagation into the deep zone by day 12 for the higher velocity (100V:50S) group. Both high strain groups released significantly greater GAG and PGE2 into the media at day 1 than the other impacted and non-impacted control groups, indicating that a strain threshold (in the order of 50%) may exist for significant release to occur. Significant differences in PGE2 release continued to be observed 2, 3 and 6 days post impact for the high velocity: high strain (100V:50S) group but not for the low velocity:high strain (1V:50S) group, which implies that higher velocity impact prolongs the release of PGE2. Release of detectable levels of nitric oxide was not observed. There were no significant differences in GAG and HP tissue biomarkers, and CPII media biomarker. Decrease in cartilage explant's radially confined compression elastic modulus and equilibrium modulus were found to correlate to greater GAG release from the explant.

The development of this model will enable further study of biomarkers involved in PTOA that could potentially be clinically measured to evaluate the etiopathogenesis of the disease as well as various treatment strategies to mitigate symptoms of the disease.