

## ABSTRACT

Osteoarthritis is one of the most common, debilitating, musculoskeletal diseases in the world. Currently, there is no cure. It is well-known that a traumatic, joint injury increases the risk of developing post-traumatic osteoarthritis (PTOA). Therefore, in order to improve clinical treatment and prevention strategies for post-traumatic osteoarthritis (PTOA), a series of translational studies were conducted to develop research models to evaluate the effects of impact injury.

The first section of this dissertation (Ch. 1-2) provides a comprehensive introduction and literature review related to both clinical PTOA as well as previous research investigations of PTOA. The second section of this dissertation (Ch. 3-6) describes the methodology of optimizing a servo-hydraulic test machine to deliver a controlled impact injury (Ch. 3) as well as subsequent studies using this device to injure articular cartilage (Ch. 4) and cartilage-bone explants (Ch. 5-6). Further, the effects of dynamic, compressive loading to mimic walking after impact injury of cartilage-bone explants was investigated (Ch. 6). The third section of this dissertation (Ch. 7-8) details the development of an impactor device that may be used for pre-clinical, animal models.

Many significant findings were discovered through this dissertation work. Specifically, by using the proportional-integral-derivative (40, 0, 0) values, a large (25kN) servo-hydraulic test machine may be used to deliver a controlled impact injury to explants (Ch. 3). Biomarkers glycosaminoglycan (GAG) and prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) were elevated after cartilage impact injury with PGE<sub>2</sub> having the highest mechanosensitivity than any other biomarker (Ch. 4). Energy absorbed during cartilage-

bone injury is dependent upon trauma severity; PGE<sub>2</sub> and monocyte attractant protein (MCP-1) were elevated following cartilage-bone injury (Ch. 5). Dynamic, compressive loading retained cell viability in non-impacted cartilage-bone explants and mitigated GAG release in impacted explants; GAG and PGE<sub>2</sub> were elevated due to cartilage-bone injury whereas matrix metalloproteinase-2 (MMP-2) and interleukin-8 (IL-8) were elevated due to injury plus dynamic, compressive loading (Ch. 6). The development of a 8mm diameter impactor does create articular cartilage damage (Ch. 7), albeit a smaller, 2mm diameter impactor creates higher impact stresses and may be used arthroscopically for pre-clinical animal models (Ch. 8).