Biomarker Expression in Post-Traumatic Osteoarthritis (PTOA) through the Utilization of a Spring-Loaded Impaction Device

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Introduction

- Post-traumatic osteoarthritis (PTOA) is the most common mechanism of ankle joint osteoarthritis (OA) accounting for 20-78% of ankle OA cases.[1]
- Athletes and Military personnel are the most common demographic.[2]
- Biomarkers associated with ankle PTOA have not been well-established.[3]
- Traumatic impacts on talar articular surface *in vitro* are known to lead to degeneration of the cartilage.
- Purpose: To utilize a spring-loaded impact device to deliver trauma in order to uncover the correlation between no load, physiological load, and traumatic load and the expression of biomarkers in the talus cartilage of these respective groups.
- Hypothesis: If a traumatic load is applied to bovine tali, then there will be a statistically significant up-regulation of the same factors expressed in human ankle OA.

Methods

- Harvest juvenile talar osteochondral plugs and subject them to different loads: no load (0 Mpa – CTRL), walking load (8-10 MPa) and traumatic load (25-27 MPa).
- Sample size (N) = 8 explants per experimental group and the control group as well.
- Impact parameters were correlated with tissue damage, cell viability, and gene expression twenty-four hours post-impact.
- Viability was assessed using Live/Dead™ assay from Life Technologies.
- Gene expression was determined by qRT-PCR.

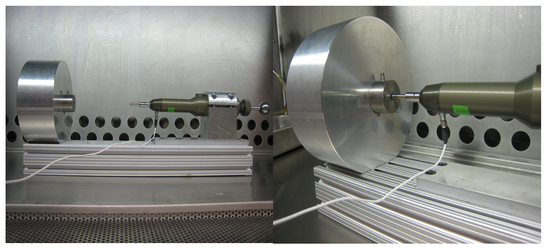

Figure 1: Impactor III device.

Results

Juvenile Bovine Ankle

Figure 2: Dissected bovine talus.

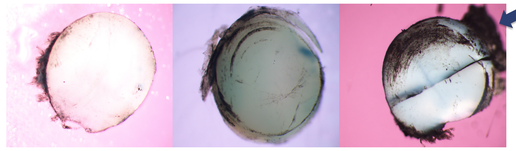

Figure 3: India ink images of no load, physiological load, and traumatic load of juvenile ankle cartilage.

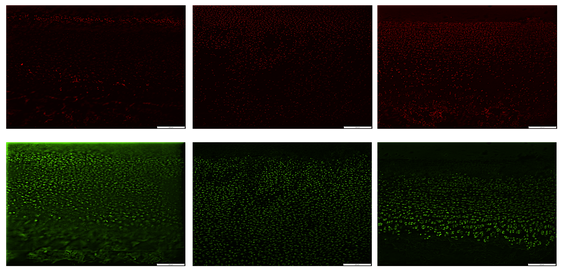

Figure 4: No load (A), walking load (B), and traumatic load (C) Live-Dead assay in juvenile bovine talus cartilage.

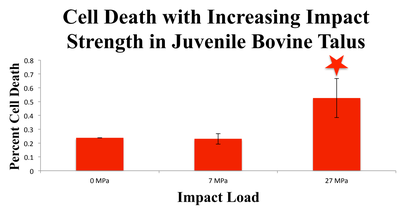

Figure 5: Percent cell death 24 hr after impact in juvenile bovine talus cartilage (P=.0225).

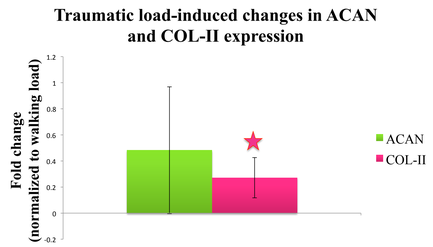

Figure 6: ACAN and COL-II down regulation.

Adult Bovine Knee

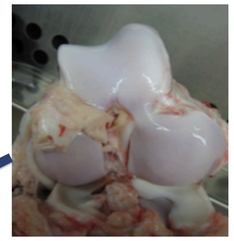

Figure 8: Dissected bovine femoral condyle.[4]

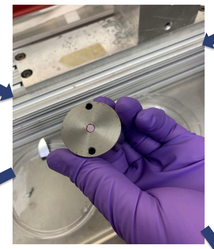

Figure 7: Loaded cartilage explant.

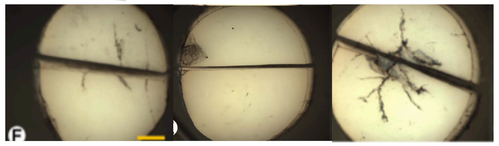

Figure 9: India ink of no load, physiological load, and traumatic load of adult bovine ankle cartilage.[4]

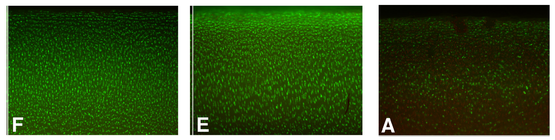

Figure 10: No load (F), physiological (E), and traumatic (A) group Live-Dead assay in adult bovine knee cartilage.[4]

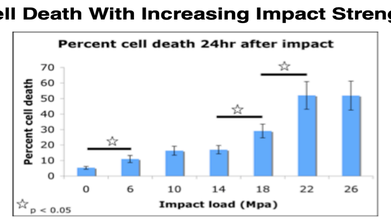

Figure 11: Percent cell death 24 hr after impact in adult bovine knee cartilage.[4]

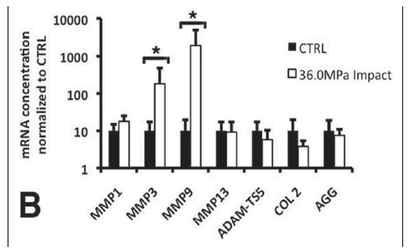

Figure 12: Genetic Up-regulation in bovine knee.[4]

Discussion

- The fracture footprint on juvenile cartilage is a single crack and not a complex fracture pattern.
- Bovine juvenile talus cartilage displays no true up-regulation in cell death between no load and physiological load, but there is a significant up-regulation in the traumatic load group.
- Genes indicative of articular cartilage (COL-II) are down regulated after traumatic load.
- Differences in the fracture patterns and cell death may be due to varying mechanical properties.

Conclusion

- The bovine talus can be used as a comprehensive model to understand PTOA pathophysiology, as well as the origins of OA, which is currently not well understood.

Future Work

- Test the mechanical properties of juvenile bovine ankle cartilage and bone with a comparison to adult bovine ankle cartilage and bone.
- Determine methods to deliver controlled impacts without compromising the subchondral bone.
- A more comprehensive load study with more molecular and biochemical end points.

References

1. Thomas AC, Hubbard-Turner T, Wikstrom EA, Palmieri-Smith RM. Epidemiology of Posttraumatic Osteoarthritis. *J Athl Train*. 2017;52(6): 491–496. doi:10.4085/1062-6050-51.5.08
2. Lübbeke A, Salvo D, Stern R, Hoffmeyer P, Holzer N, Assal M. Risk factors for post-traumatic osteoarthritis of the ankle: An eighteen year follow-up study. IntOrthop. 2012;36(7):1403-1410. doi:10.1007/s00264-011-1472-7
3. Svoboda, S. J., Owens, B. D., Harvey, T. M., Tarwater, P. M., Brechue, W. F., & Cameron, K. L. (2016). The Association Between Serum Biomarkers of Collagen Turnover and Subsequent Anterior Cruciate Ligament Rupture. The American Journal of Sports Medicine, 44(7), 1687–1693. https://doi.org/10.1177/0363546516640515
4. Alexander PG, Song Y, Taboas JM, et al. Development of a Spring-Loaded Impact Device to Deliver Injurious Mechanical Impacts to the Articular Cartilage Surface. *Cartilage*. 2013;4(1):52–62. doi: 10.1177/1947603512455195