Creation of a Subchondral Bone Disease Model Ovine Utilizing Impact Loading

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INTRODUCTION: Subchondral bone disease in osteoarthritis is a significant multi-species problem with no "gold standard" animal model. The objective of this study was to develop a focal subchondral bone lesion through single-impact loading to model subchondral bone disease.

METHODS: Utilizing a drop tower and twelve ovine cadaver limbs, ideal height and weight to create focal subchondral bone damage while minimizing cartilage damage were established. A customized impact instrument with a 5 mm diameter sphere tip at the distal aspect of a drop tower was positioned on the radial facet of the third carpal bone through an arthrotomy (Figure 1a). A 2.5 kg weight was dropped at four different heights (n=3): 30, 50, 60, and 70 cm. Six sheep were placed under general anesthesia, and a 2.5 kg weight was dropped from 60 (n=2) or 65 (n=4) cm onto the impact instrument (Figure 1b). Contralateral forelimb was used as control. Peri-impact CT and MRI and post-impact micro-CT were performed. Animals were euthanized following post-impact MRI. Subchondral bone density and bone volume were measured. Measurements were evaluated for normality with Shapiro-Wilk. Paired t-tests and two-factor repeated measure ANOVA were performed. Significance was set at 0.05.

RESULTS SECTION: Bone volume measured on micro-CT did not differ between control and impact third carpal bones (p=0.68). Subchondral bone density did not differ between pre- and post-procedure CT scans or between control and impact third carpal bones (p=0.43; p=0.75). No conclusive subchondral bone changes were apparent on post-impact MRI (performed within one hour of impact). Subchondral bone microdamage was consistently present on all micro-CT following impact from 60 and 70 cm, with no evidence of fissuring following impact from 30 cm. Dropping the 2.5 kg weight from 70 cm resulted in complete fracture of one of the third carpal bones. In vivo impact from 60 cm resulted in mild changes to the subchondral bone. Subsequent impacts from 65 cm resulted in consistent microdamage in the subchondral bone directly below the site of impact (Figure 2). Drop height of 60 or 65 cm did not create osteochondral fragments.

DISCUSSION: A drop tower free-fall impact on ovine third carpal bones in vivo created consistent subchondral bone microdamage without creation of osteochondral fragmentation. Designs for bone-impact models include use of drop-towers positioned over closed joints or spring-loaded impactors applied intra-articular. In vivo drop towers previously investigated in dog and rabbits positioned the drop tower over the stifle, with impact transmitted through the skin and subcutaneous tissue before reaching the cartilage and bone [1,2,3]. The authors reported that transcutaneous transmission of impact onto the articular surface resulted in subchondral bone edema and trabecular microfractures without macroscope changes to the articular cartilage in either dog or rabbit models. Consistent with previous reports, we observed subchondral bone microfractures without osteochondral fragmentation on micro-CT of ovine third carpal bones following free-fall impact. The current study found no bone edema on MRI imaging performed within 1 hour of impact, and previous studies found bone edema on MRI imaging performed 4 hours post loading [1,2,3]. This may indicate an important window for potential treatment of impact loading on subchondral bone.

We observed macroscopic changes to the cartilage at the point of impact consistent with compression. In contrast to the previous drop-tower models, we utilized intra-articular placement of the impact instrument directly on the articular surface of the third carpal bone at the radial facet due to the increased bone density of sheep compared to the dogs and rabbits utilized in previous studies. Intra-articular impacts have previously been performed with spring-loaded impactors positioned through arthroscopic guidance [4,5]. Creation of "clover-leaf" impact on the palmar aspect of metacarpal condyles via arthroscopic guidance resulted in variation of the location, extent, and depth of the lesions with evidence of shear injury rather than perpendicular impact in joints [4]. Malekipour et al. (2013) utilized equine osteochondral explants to determine that the energy absorption per unit volume of cartilage is seven times higher than subchondral bone. The response of cartilage and subchondral bone to impacts is dependent not only on the stress or force over an area delivered, but also on the stress rate and strain of the impact [6,7]. Use of spring-loaded impactors create both cartilage and subchondral bone injury.

SIGNIFICANCE/CLINICAL RELEVANCE: We utilized a drop tower free-fall impact on ovine third carpal bones in vivo to create subchondral bone microfractures without creation of osteochondral fragmentation. This model may be used to evaluate progression and reversal of subchondral bone injury to osteoarthritis.

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ACKNOWLEDGEMENTS: This project was funded by a University of Tennessee Center of Excellence in Livestock Diseases and Human Health Research Award.

IMAGES AND TABLES:

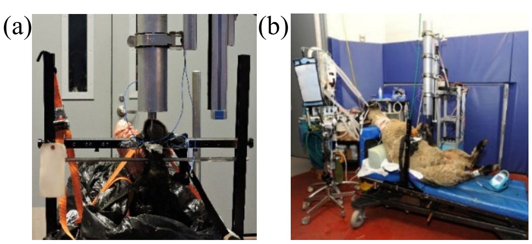

Figure 1. Drop tower positioned over (a) cadaver and (b) live sheep third carpal bones.

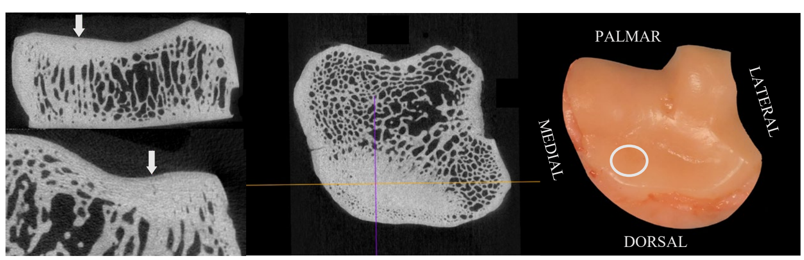

Figure 2. Micro-CT images of ovine third carpal bone and third carpal bone following in vivo impact of 2.5 kg weight from 65 cm.