Repetitive Stress Cycle Numbers Greater Than Physiologic Decrease Femoral Epiphyseal Bone Volume and Density In Growing Knees

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Introduction: Osteochondral lesions have been reported to occur with increasing frequency and severity in children and adolescents. One type, juvenile osteochondritis dessicans (JOCD), is most often diagnosed in patients involved in high-level athletics. Proposed etiologies include genetic factors, vascular injury, and mechanical overuse. One hypothesis is that JOCD involves injury to the secondary physis. The secondary physis lies between the articular cartilage and epiphyseal bone. Because the secondary physis produces the trabecular bone of the epiphysis, injuries might be expected to alter the growth of new epiphyseal bone. The present study employed a previously reported juvenile animal overuse model that produced osteochondral lesions evident on qualitative histology and micro-CT. The purpose of this study was to test the hypothesis that skeletally immature joints subjected to excessive repetitive stress cycles exhibit decreased epiphyseal bone volume and density in the femoral epiphyses in this overuse model.

Methods: Skeletally immature New Zealand White rabbits (n=6, age: 29-36 days) were subjected to periodic mechanical loading over a five week protocol (approved by IACUC). The subjects were anesthetized and placed on a table in the prone position with the right hind limb projecting through a hole. The limb was loaded, with the knee in 20 degrees of flexion, at 1 Hz for 45 minutes a day, five days per week, for 5 consecutive weeks. Peak loads were 125% body weight. The unloaded left hind leg was used as a paired control. Except during testing, rabbits were kept with the mother and were allowed free mobility within the cage. Following euthanasia, the hind limbs were dissected and skin and muscle were removed with careful attention to joint preservation. The limbs were immediately placed in ice, then imaged with microCT (MicroCAT II®, ImTek, Knoxville, TN). The knees were scanned in the transaxial plane at a voxel resolution of 36 μm/voxel. Scan parameters were: potential 80 kVp, anode current 500 μA, and field size 1280 by 1280 voxels. Matrix images were reformatted for interpretation into standard sagittal and coronal planes with three dimensional reconstructions (Amira, Visage Imaging (VSG), Andover MA). Scans were analyzed using visualization software (Amira 5.4, VSG).

Lesion location and volume were found using the isosurface, the visualized bone boundary of the 3D reconstruction, after applying a threshold of 950 HU based on published guidelines. Lesions were classified as being on the medial or lateral condyle. Lesion size was determined by multiplying the length, width, and depth. An orthogonal slice at the intersection of the axis of the length and width was used to find lesion depth. Femoral epiphyses were extracted from the full scan, then bone volume and density were determined for both full and thresholded (> 950 HU) image sets to derive, respectively, total bone volume and density and the mineralized bone volume and density. Measured outcome variables were total epiphyseal volume (V_t), mineralized bone volume (V_b), bone volume fraction (BVF = 100*[V_b/V_t]), total epiphyseal density (p_t), and mineralized bone density (p_b). To test for statistical differences, two tailed, paired t-tests were used followed by the Bonferroni post-hoc correction (α=0.05/4).

Results: Four rabbits completed 5 weeks of testing and 2 rabbits completed 4 weeks. All rabbits grew at rates within published norms. Although all rabbits demonstrated mild limb avoidance beginning week 1 of testing they appeared to tolerate testing well, and remained active in their cages. One rabbit developed a displaced physeal fracture in week 5. At least one osteochondral lesion was observed in every loaded limb, while none were noted in any contralateral limb. Lesion volumes in the medial condyle were >2x lesion volumes in the lateral condyle. Mineralized bone volume in experimental knees was 23% less than paired controls (p<0.01), whereas total epiphyseal volume was not different between control and experimental joints (p>0.8). Bone volume fraction of the experimental side was 24% less than control (p<0.01). Total epiphyseal bone density was 12% lower in experimental knees than in paired controls (p<0.005). Mineralized bone density in experimental knees was 3.5% lower than control (p< 0.005).

Discussion: Excessive repetitive stresses significantly decreased both bone volume and bone density in the epiphyses of skeletally immature knees. The translational applicability of this overuse protocol to repetitive loading of juvenile rabbit knees is currently limited by analysis of a single time point and loading parameter set. Correlation with clinical parameters is not yet known. However, a model of osteochondral lesions in a young animal is needed to test different treatment approaches, and for better understanding of the etiology for prevention of these difficult and increasingly frequent injuries in children. This model supports the concept that excessive numbers of loading cycles on juvenile joints may compromise the structural integrity of the subchondral bone.
Significance: In young children, daily repetitive activities that greatly exceed physiological levels in number and duration, even at physiologically normal load magnitudes, may be a cause of osteochondral injuries that result in reduced formation of trabecular and subchondral bone that support the articular cartilage.

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