

Full Field Analyses Of Equine Bone Reveal That Adaptation To Exercise May Be Sensitive To Exercise Mode

Sara G. Moshage¹, Samantha M. Hammack², Annette M. McCoy^{3,4}, Mariana E. Kersh^{1,4,5}

¹Dept. of Mechanical Science and Engineering, ²Dept. of Comparative Biosciences, ³Dept. of Veterinary Clinical Medicine, ⁴Beckman Institute for Advanced Science and Technology, ⁵Carle Illinois College of Medicine, University of Illinois Urbana-Champaign, Urbana, IL
moshage1@illinois.edu

Disclosures: Sara G. Moshage (N), Samantha Hammack (N), Annette M. McCoy (9-Chair-Elect, ORS Preclinical Models), Mariana E. Kersh (N)

INTRODUCTION: Fractures are the leading cause of racehorse fatalities, accounting for 75-80% deaths in North America and Great Britain, and are usually the result of fatigue rather than trauma. More than 60% of fractures in the lower limbs occur in the third metacarpal (MC3) and proximal phalanx (P1) bones, and thus are the focus of this study. Exercise during juvenile growth, when the skeleton is undergoing significant remodeling, may be a means of reducing fracture risk by encouraging bone adaptation. Previous exercise interventions in juvenile horses have reported increased bone area compared to controls, but the analyses were limited to discrete cross-sections. Moreover, it is not clear if the changes in response to exercise resulted in changes in mechanical strength. Therefore, the objectives of this study were to evaluate the effect of an exercise intervention in juvenile horses on (1) MC3 and P1 bone structure and composition along the entire length of the bone and (2) whole bone strength assessed via virtual compression test.

METHODS: This study was approved by IACUC. Six Standardbred foals (3 female, 3 male) took part in an exercise intervention that began at approximately 8 weeks old and lasted for 8 weeks. The study was conducted over two summers with 3 control and 3 exercise foals in each cohort. The exercise protocol consisted of ponying the foal for 1200 m at 3.35 ± 0.36 m/s for 1 week (5 days/week) followed by 1600 m at 3.50 ± 0.27 m/s for 7 weeks. Computed tomography (CT) scans were acquired at 8 weeks of age and 4 weeks after exercise ended. CT scans of six control foals (4 female, 2 male) were acquired at the same ages as the exercise foals. Bone area fraction and mineral density, determined from hydroxyapatite phantoms, were measured along the length of the bone at the total cross-section (all bone tissue), and in the cortical and trabecular compartments. Data were compared using statistical parametric mapping ($\alpha = 0.05$) [1]. The percent difference in bone area fraction and density before and after exercise was also calculated. Finally, subject-specific finite element models of each bone were constructed, using density-modulus relationships specific to juvenile equine MC3 and P1 bone [2], and loaded in a virtual compression test to evaluate whole bone stiffness as a measure of strength.

RESULTS: One exercise and two control foals did not complete the study. Challenges with ponying in cohort 1 required foals to be run in hand. There were no significant differences in area fraction or density (total, cortical, or trabecular) between control and exercise groups prior to exercise. There were also no significant differences in changes of bone area fraction, density, or stiffness at 4 weeks post-exercise between control and exercise groups. However, we did observe a potential cohort effect: bone properties in cohort 2 were on average higher than controls but this was not the case for cohort 1. In the P1, there was an additional ~3.5% increase in density at 20 and 80% length in cohort 2 (Fig 1 blue lines) relative to controls (grey line) (Table 1). In contrast, cohort 1 had smaller increases in density and area fraction (Table 1, Fig 1 pink lines). Similar, but less consistent, changes were observed in the MC3. Average stiffness of the MC3 and P1 in cohort 2 was greater than control horses, while average stiffness of cohort 1 horses was below control values.

DISCUSSION: Our observations of cohort level variability in response to exercise may have several origins. Importantly, there were no significant differences in bone properties between the two cohorts at the beginning of exercise. Limitations of animal availability resulted in an unplanned difference of sex: exercise cohort 1 were all female while cohort 2 were males. However, juvenile Thoroughbred horses do not exhibit differences in osteocalcin level based on sex, indicating similar bone turnover rates [3]. Thus, we suspect that the difference in mode of exercise (running in hand vs ponying) between the two cohorts may have had an effect. Running in hand (cohort 1) resulted in an intermittent mode wherein foals were run for approximately 150 m back and forth along a track. Ponying allowed for a continuous bout of exercise with no pauses. Lower levels of bone adaptation to mechanical loading when rest was included in a murine tibial loading model [4] compared to continuous loading has been reported; however, others have reported no differences or opposite trends. These data highlight the sensitivity of bone adaptation to loading regimes.

SIGNIFICANCE/CLINICAL RELEVANCE: This study was the first to quantitatively evaluate the effect of an exercise intervention when young on the structure and density along the entire length of long bones and subsequent effects on strength. Despite sample size limitations, this work provides an important lower threshold that a future exercise intervention should exceed and underscores the importance of exercise mode when designing studies for improved bone health.

REFERENCES: 1. Pataky+ *J Biomech* 2013. 2. Moshage+ *J Biomech Eng* 2023. 3. Chiappe+ *Arch Phys Biochem* 1999. 4. Yang+ *PLoS ONE* 2017

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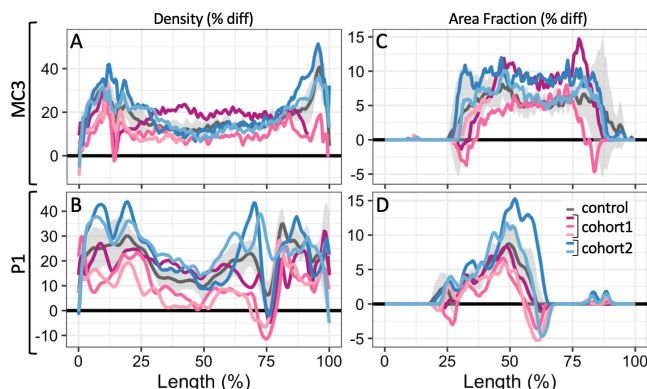


Figure 1. Total cross-sectional density in the (A) MC3 and (B) P1 along the length of the bone (x-axes). Cross-sectional area fraction in the (C) MC3 and (D) P1. Control data are shown in grey (line is group mean). Y-axes = percent difference between pre- and post-exercise CT scans.

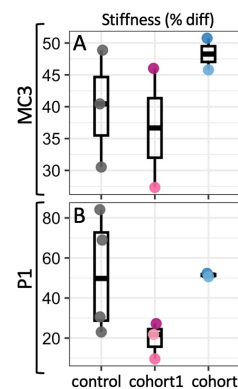


Figure 2. Percent difference in stiffness between scans of the (A) MC3 and (D) P1. See Fig 1 for legend.

| | Length (%) | control cohort 1 cohort 2 | | |
|---------------|------------|---------------------------|------|------|
| | | | | |
| MC3 | Density | 20 | 20.6 | 11.6 |
| | | 50 | 11.6 | 12.8 |
| | | 80 | 15.1 | 17.7 |
| P1 | Density | 20 | 29.9 | 21.5 |
| | | 50 | 9.7 | 6.5 |
| | | 80 | 29.8 | 17.9 |
| Area Fraction | | 50 | 7.4 | 7.8 |
| | | 50 | 8.7 | 5.4 |

Table 1. Percent difference between pre- and post-exercise CT scans at discrete locations along the length of the bone.