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Assessment of bone microarchitecture and mineralisation changes in an animal model of inflammatory bowel disease using high-resolution synchrotron-based microCT

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Background: The Winnie-*muc2* mouse (C57BL/6 background) exhibits pathophysiology of inflammatory bowel disease and other organ system changes, providing an opportunity to study bone loss related to malabsorption and other factors. We hypothesised that both bone microstructure and mineralisation may differ in Winnie-*muc2* mice so performed temporal studies using high-resolution synchrotron-based microCT (HR-S-uCT).

Aim: To characterise cortical and trabecular metrics in Winnie-*muc2* vs C57BL/6 mice including bone volume, bone mineral density (BMD) and other ultrastructural parameters.

Methods: Male and female animals (4-7/group) were euthanised after cardiac perfusion (4% PFA) at 6, 14 and 24 wks and femurs harvested then stored in 10% formol saline. MicroCT images were acquired at the Australian Synchrotron (25keV beam, 1800 projections, 6.82 u3 isotropic volumes, at 2-3 mm below condyls). Volumes were reconstructed using X-TRACT (CSIRO), trimmed using Image-J and processed using the BMA module in Analyze14.0 (Mayo Clinic).

Results:
1. In Winnie-*muc2* males (vs C57BL/6), whole Bone Volume (Ctx+Tb) was 26% lower at 24 wks (0.99 mm3, IQR 0.82-1.155 vs 1.34 mm3, IQR 1.28-1.39 p=0.021) and in Winnie-*muc2* females (vs C57BL/6 females), whole BV was less at 14 and 24wks (21% p=0.011, and 9% p=0.021, respectively) with both female groups decreasing over time.
2. Tb vBMD was sustained over time for all groups but Tb Tissue vBMD (Tb+IntraTb) was lower at 14 and 24wks in Winnie-*muc2* males (vs C57BL/6 males p=0.047 and 0.021) and at 14 wks in females (vs C57BL/6 females; p=0.033).
3. Tb Tissue BMD in Winnie-*muc2* males (vs C57BL/6 males) was 21% less at 14 wks (155 mg/cc, IQR 131-173 vs 203 mg/cc, IQR 175-215 p=0.043) and 32% less at 24wks (116 mg/cc, IQR 105-128 vs 174 mg/cc, IQR 168-175, p=0.021). In females, both C57BL/6 and Winnie-*muc2* showed similar temporal decreases over 6 to 24wks (both p=0.021).
4. Whilst Tb BMD was sustained in Winnie-*muc2* and C57BL/6 males, C57BL/6 females showed an increase from 6 to 24wks (p=0.021), however, the Winnie-*muc2* group did not change over time (p>0.05), indicating compromised mineralisation of trabeculae in female Winnie-*muc2*.

Conclusion: HR-S-uCT analysis reveals microarchitectural and BMD changes in the Winnie-*muc2* that highlight the value of this model to study bone microarchitecture. This model exhibits severe bone loss and altered mineralisation and, through the capabilities of the Australian Synchrotron, will enable the study of mechanisms and potential treatments for diverse bone lytic diseases.

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