

The role of IGFBP-2 in bone loss after vertical sleeve gastrectomy

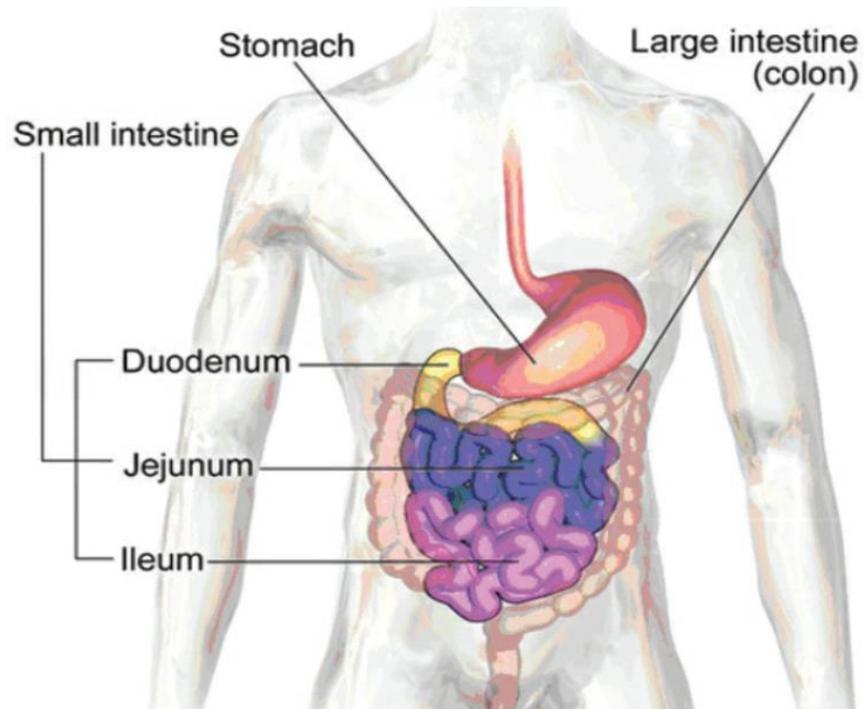
Alison Pletch, PGY4

August 1, 2020

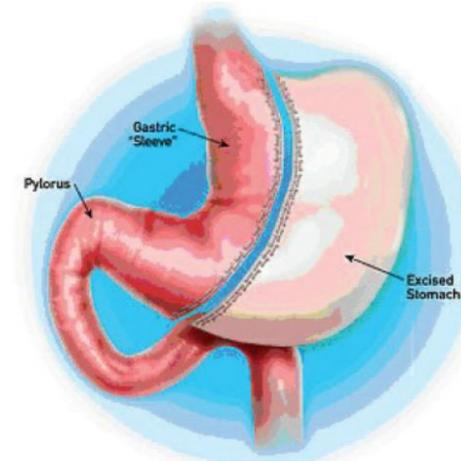


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Normal anatomy



**Roux-en-Y
Gastric Bypass**



**Vertical
Sleeve
Gastrectomy**



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BONE LOSS AFTER BARIATRIC SURGERY

Muschitz C, et al. Sclerostin levels and changes in bone metabolism after bariatric surgery. *J Clin Endocrinol Metab.* 2015;100(3):891-901.

- Gastric bypass surgeries (RYGB and SG) cause significant ongoing bone loss
- Overall loss in total-body BMD 18%
- Bone turnover markers persistently elevated

Yu EW, et al. Two-year changes in bone density after RYGB surgery. *J Clin Endocrinol Metab.* 2015;100(4):1452-1459.

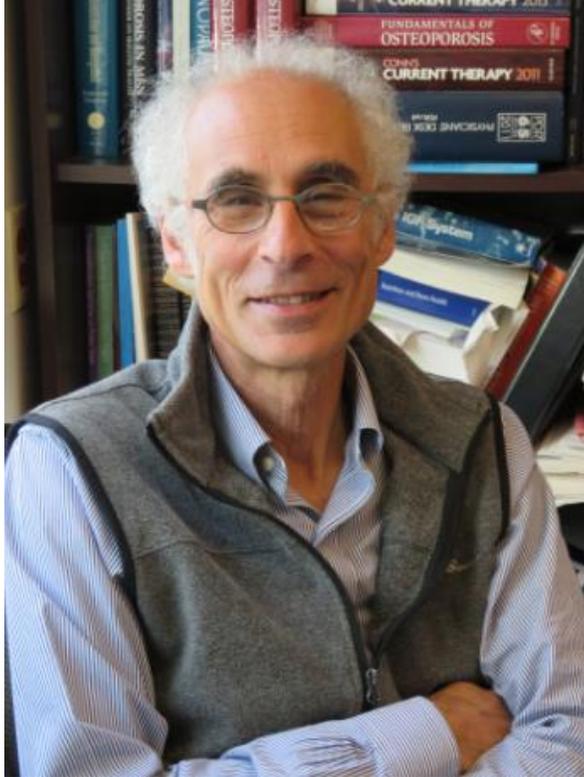
- BMD at 2 years was 5-7% lower in the spines and 6-10% lower in the hips of surgery patients vs controls
- Bone turnover markers persistently elevated

Nakamura KM, et al. Fracture risk following bariatric surgery: a population-based study. *Osteoporos Int.* 2014;25(1):151-158.

- At 7.7 years: 3x increase in spinal fracture and 5x increase in hip fracture after bariatric surgery.

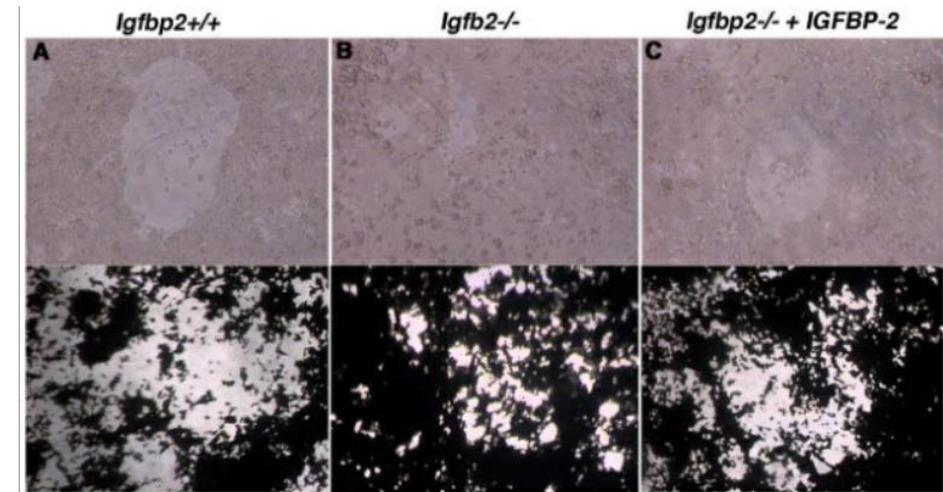
Scibora LM, et al. Examining the link between bariatric surgery, bone loss, and osteoporosis: a review of bone density studies. *Obes Surg.* 2012;22(4):654-667

- Review of 15 prospective studies
- After first year: BMD dropped 9.2% - 10.9% (femoral neck) and 8% - 10.5% in total hip. In some individuals, declines in BMD were as large as 15% at 1 year.



Dr. Clifford Rosen
Faculty Scientist
Director, Center for Clinical and
Translational Research

Insulin-like Growth Factor Binding Protein 2



› [Endocrine](#). 2019 Jul;65(1):86-93. doi: 10.1007/s12020-019-01915-y. Epub 2019 Apr 3.

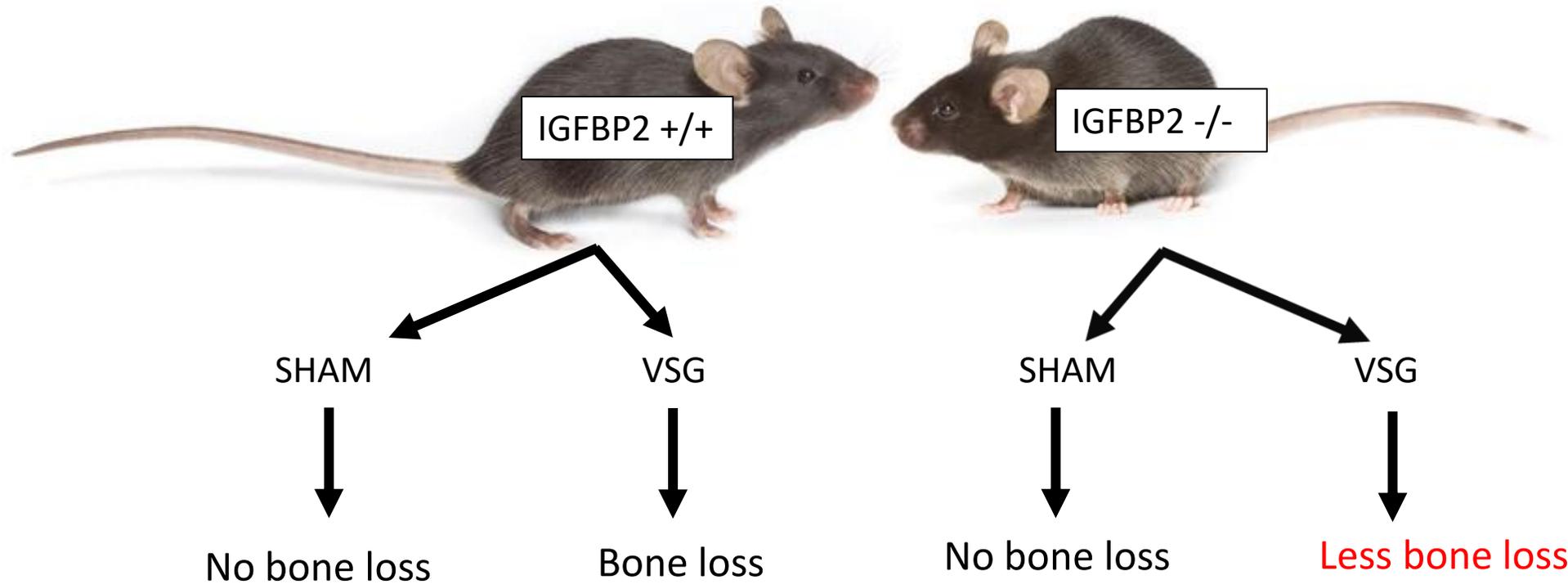
Serum IGF-binding protein 2 (IGFBP-2) concentrations change early after gastric bypass bariatric surgery revealing a possible marker of leptin sensitivity in obese subjects

Giovanni Ceccarini ¹, Caterina Pelosini ², Federica Ferrari ², Silvia Magno ², Jacopo Vitti ², Guido Salvetti ², Carlo Moretto ³, Antonio Marioni ⁴, Piero Bucciatti ⁴, Paolo Piaggi ^{2 5}, Margherita Maffei ^{2 6}, Ferruccio Santini ²



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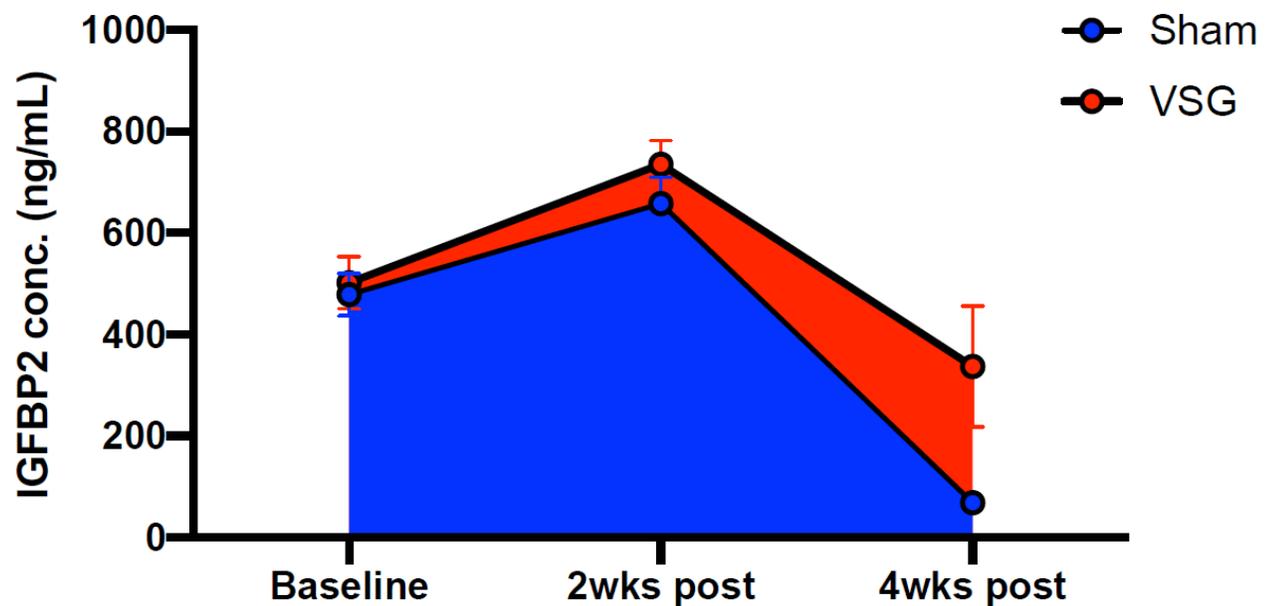
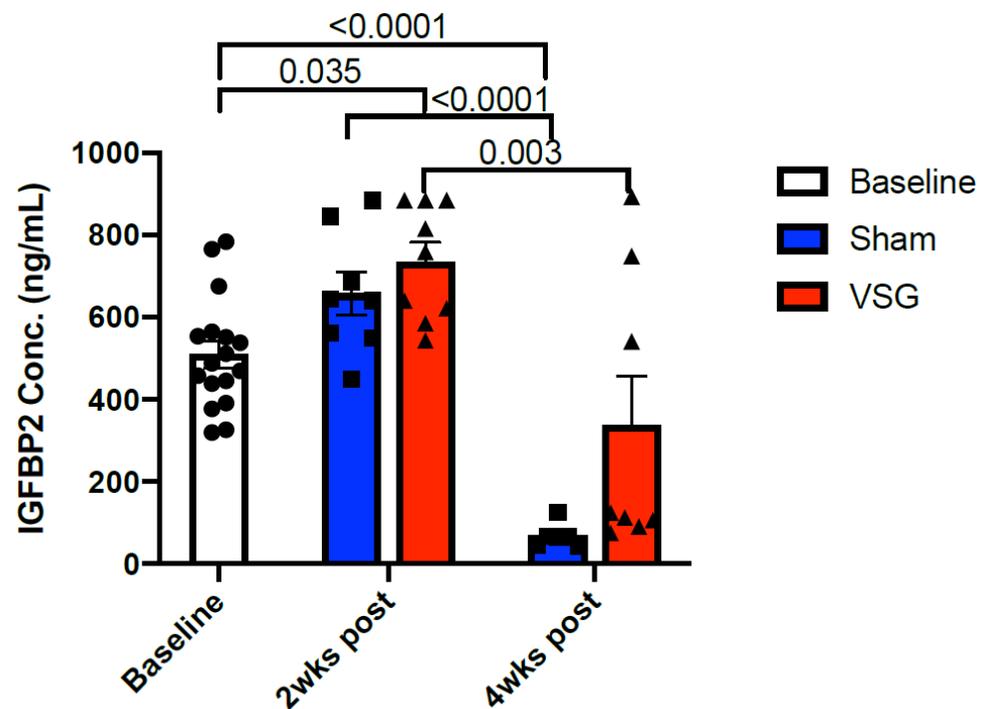
Experimental design



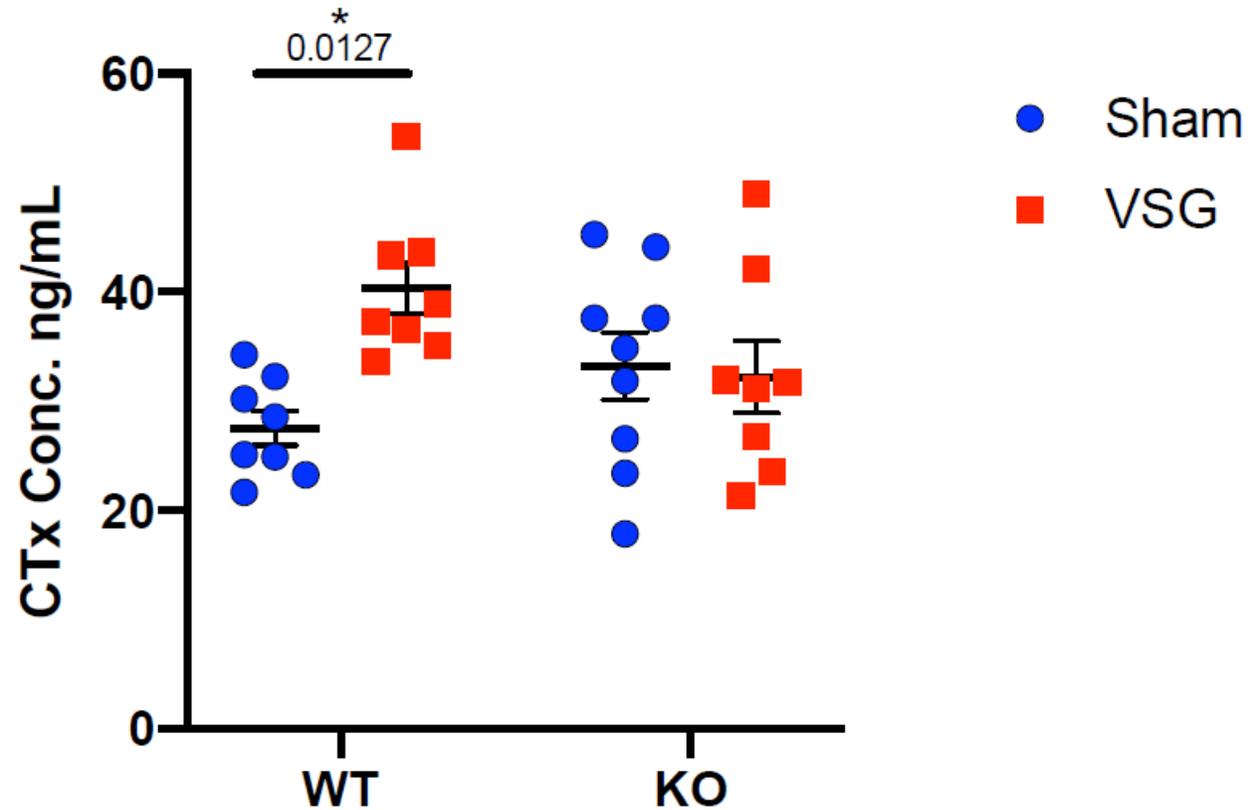
Serum analysis	What it is	Why do we care?
IGFBP2	Protein that modulates IGF-mediated signaling	Does IGFBP2 significantly change in these mice after VSG?
CTx	Marker of bone resorption	May help characterize what is driving any observed changes to bone
P1NP	Marker of bone formation	

Tissue analysis	Why do we care?
DEXA scan	Body composition, bone mineral density and content
MicroCT	Cortical and trabecular microarchitecture of femur
Histology	To assess inguinal fat pads and bone marrow adipose tissues using H&E staining
Histomorphometry	To assess bone structural parameters and cellular activities in addition to the dynamic parameters of bones
qPCR	To determine the RNA expression levels of bone formation and resorption markers extracted from tibial whole bones

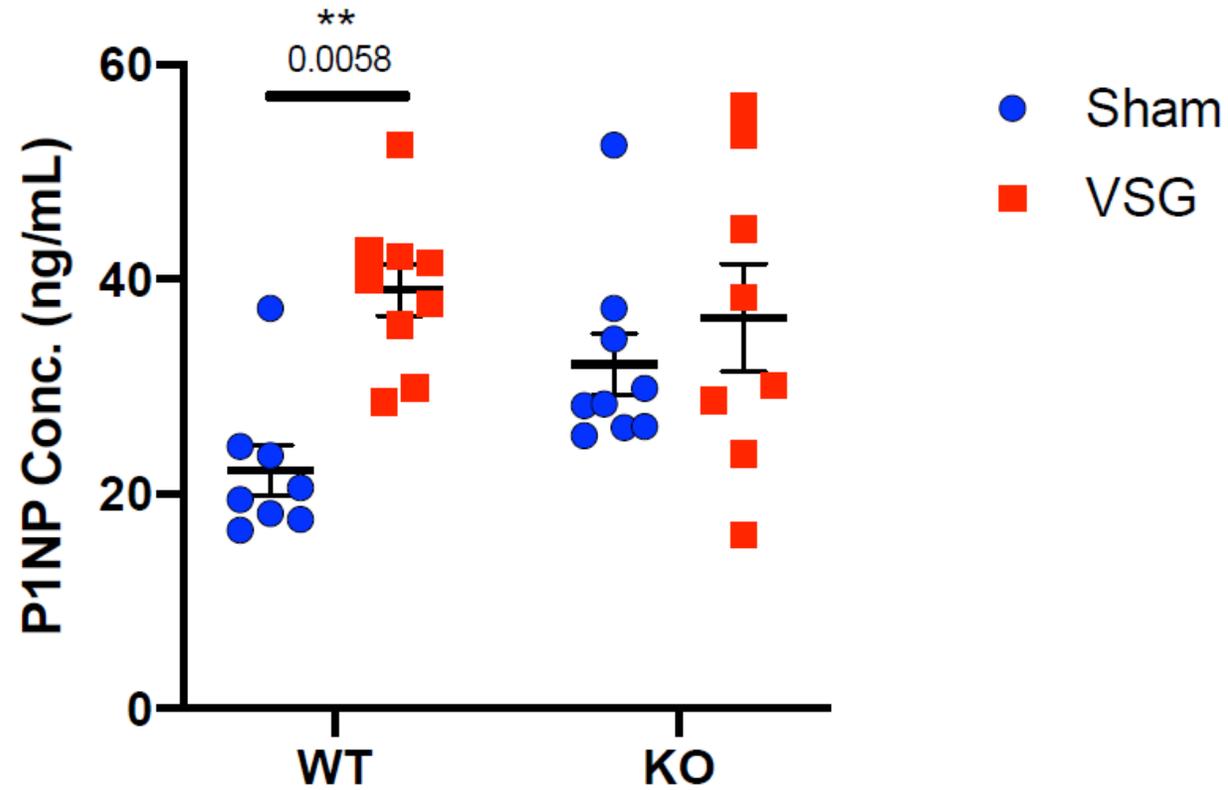
Results – Serum Assays – IGFBP2 in the wildtype mice



Results – Serum Assays – CTX in the wildtype mice at 4 weeks after surgery

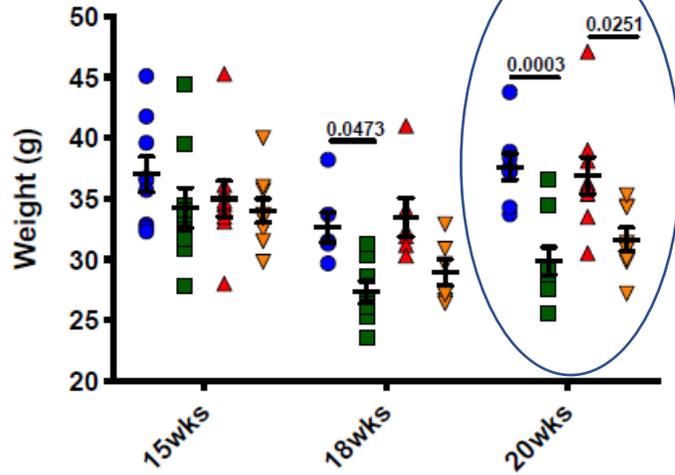


Results – Serum Assays – P1NP in the wildtype mice at 4 weeks after surgery



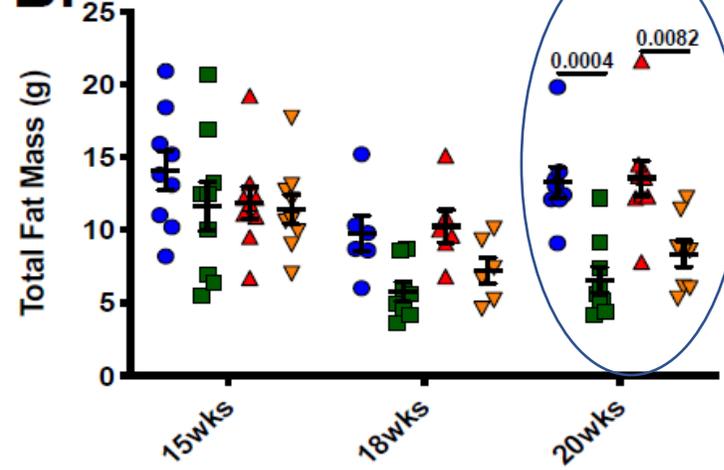
Results - DEXA

A.



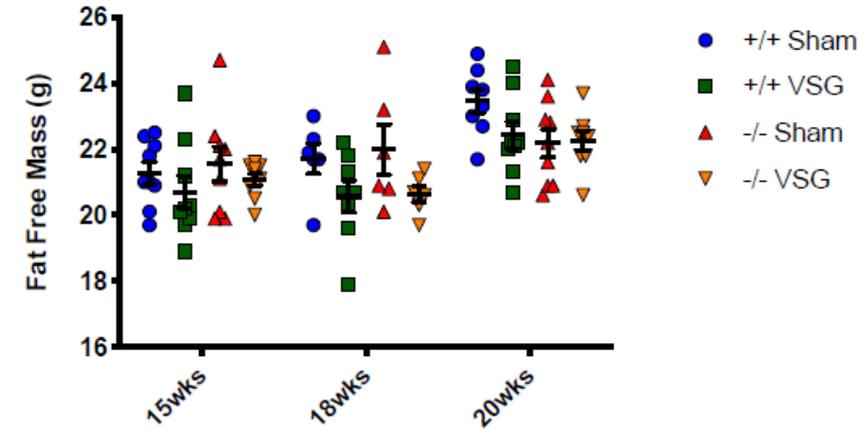
- VSG lost significantly more weight.

B.



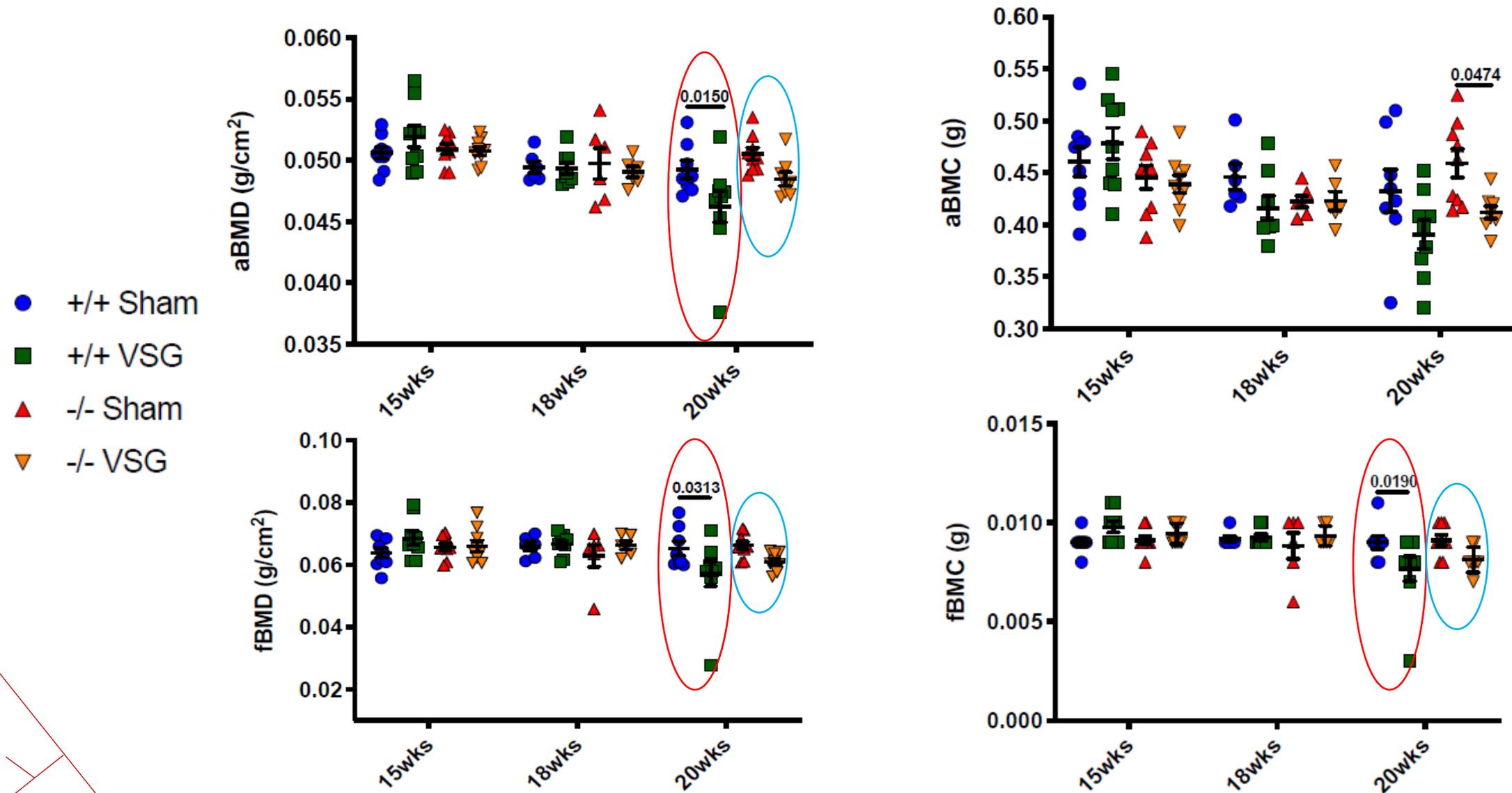
- Weight loss primarily due to fat loss.

C.

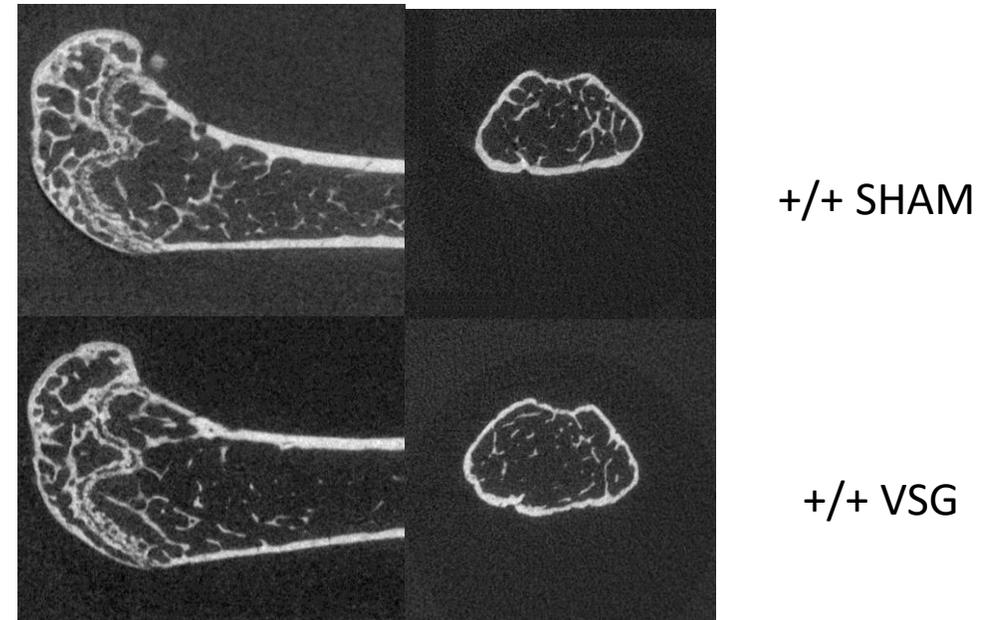
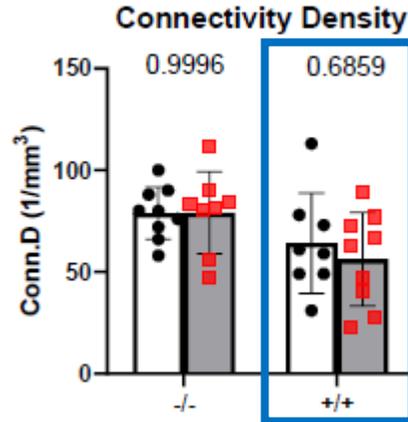
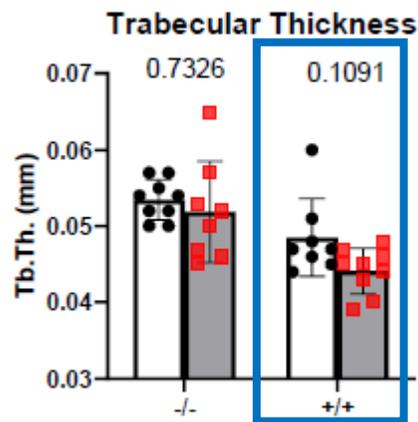
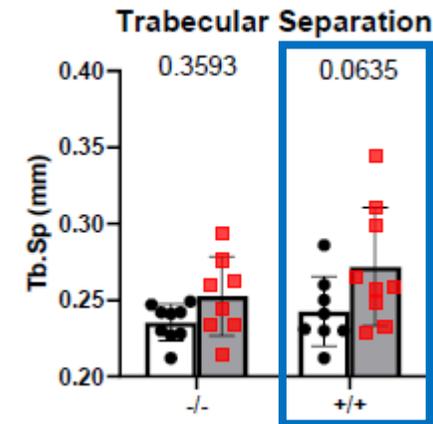
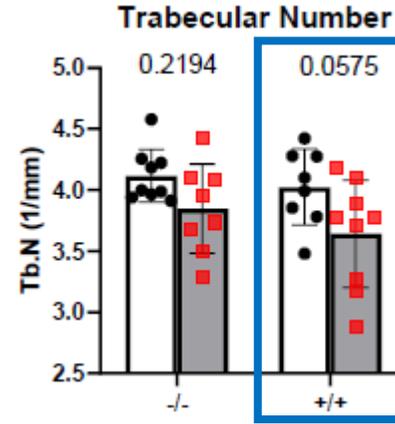
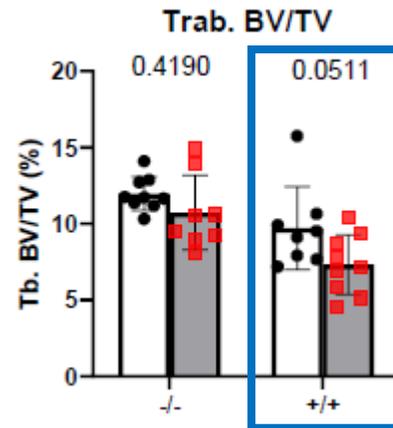
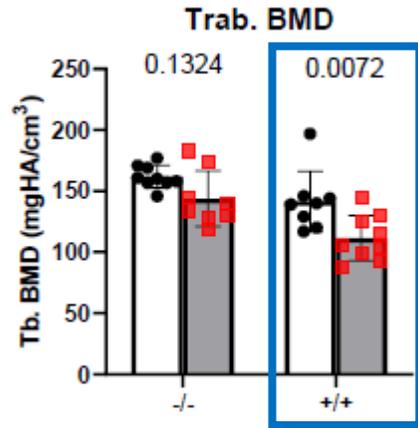


- No changes observed in fat free mass.

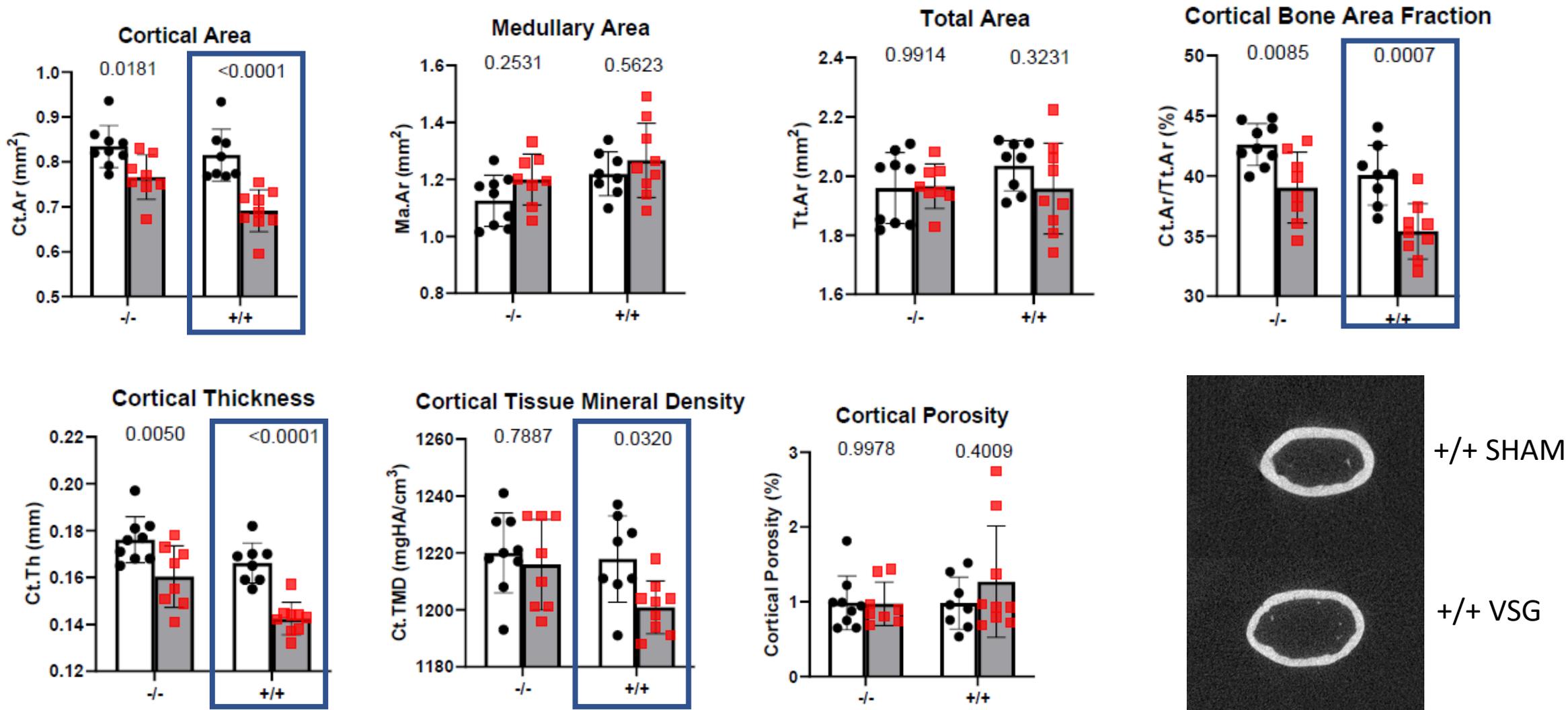
Results - DEXA



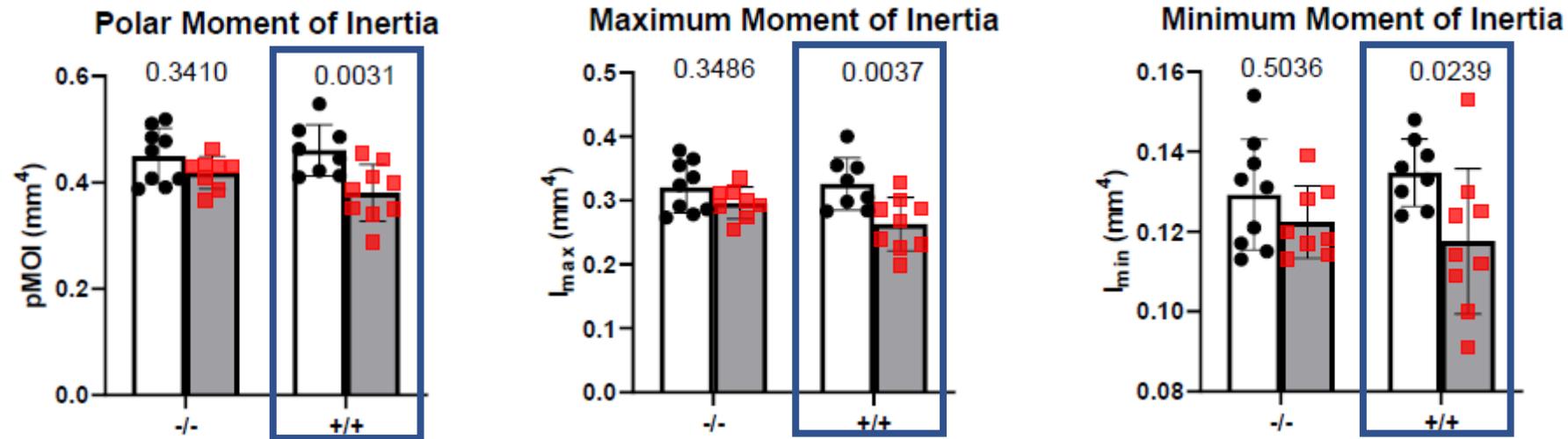
Results – microCT – Trabecular bone architecture



Results – microCT – Mid-diaphysis cortical bone architecture



Wildtype mice lose bone, knock out mice are protected from bone loss. Why should I care? Will it be clinically relevant?



Conclusions

- Significant bone loss is observed after VSG
- Wildtype mice who undergo VSG lose more bone than BP2 null mice who undergo VSG, suggesting that IGFBP2 plays a role in bone resorption

Next steps

- Histomorphometry
- Histology
- Medical Student to work on inflammatory changes in bone marrow after VSG

Many thanks!

- IACUC
- Seeley/Sandoval lab, University of Michigan
- MacDougald lab, University of Michigan
- Physiology core
- Rosen Lab family
- Lab techs
- Ben Harris
- NIH funding