

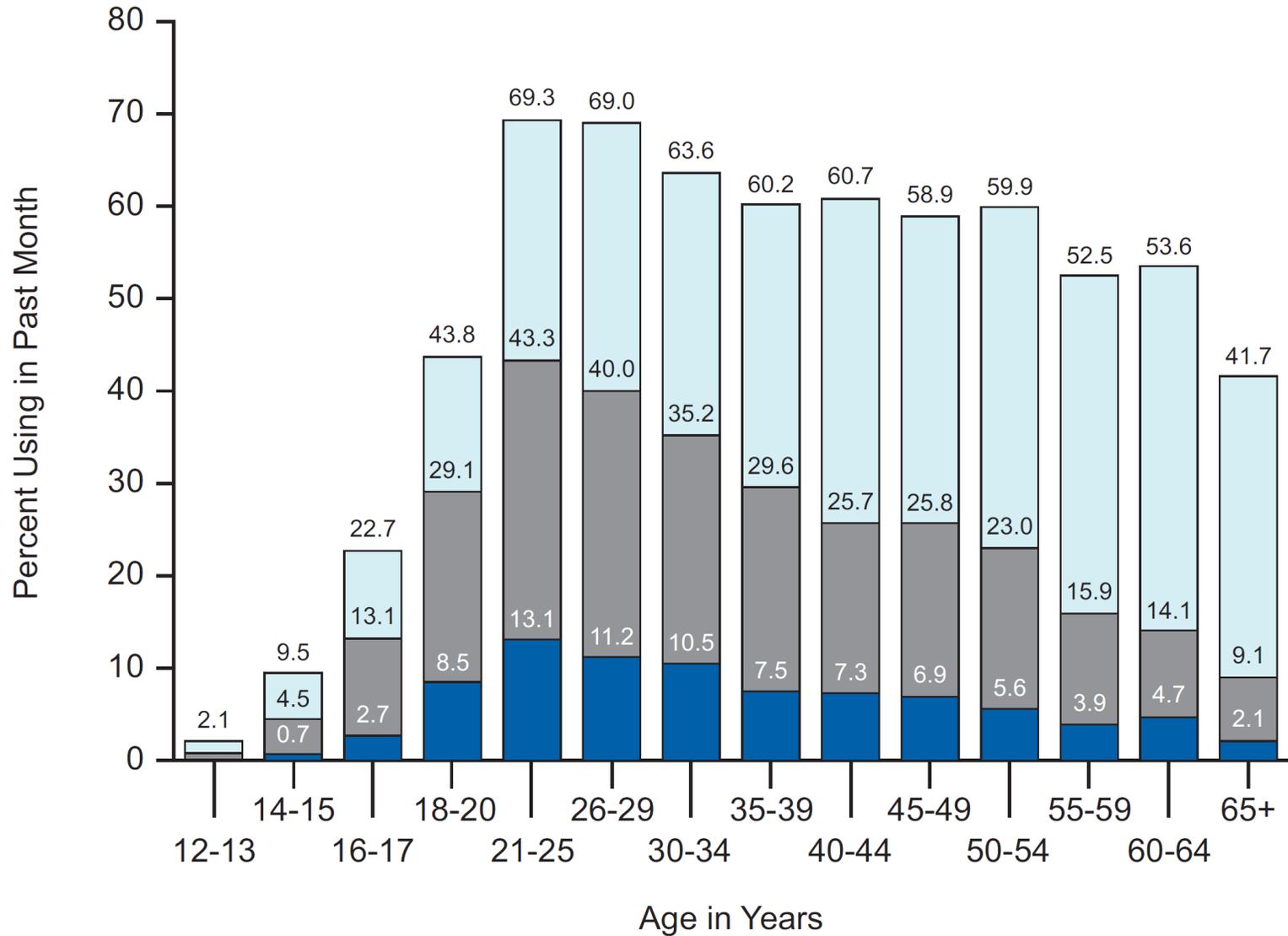
Effects of Ethanol Consumption on Biochemical Markers of Bone Turnover and Intracortical Bone Remodeling in Young Adult Male *Cynomolgus* Macaques

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Why study the skeletal effects of ethanol?



People drink!

Current Use (Not Binge) Binge Use (Not Heavy) Heavy Alcohol Use

Why study the skeletal effects of ethanol?

- Progress in understanding the actions of alcohol on bone metabolism are slowed by
 - Difficulty in performing intervention studies in humans
 - Limitations of commonly used animal models
 - Difficulty in accurately replicating human drinking behavior in animals
- Non-human primates are a highly relevant model for studying the effects of alcohol on the skeleton because
 - Their bones undergo intracortical bone remodeling
 - Once introduced to alcohol as part of their diet exhibit a range of voluntary alcohol consumption (moderate to excessive) observed in humans.

Experiments

Study 1

Effects of graded increases in ethanol consumption on biochemical markers of bone turnover in young adult male cynomolgus macaques (*Macaca fascicularis*)

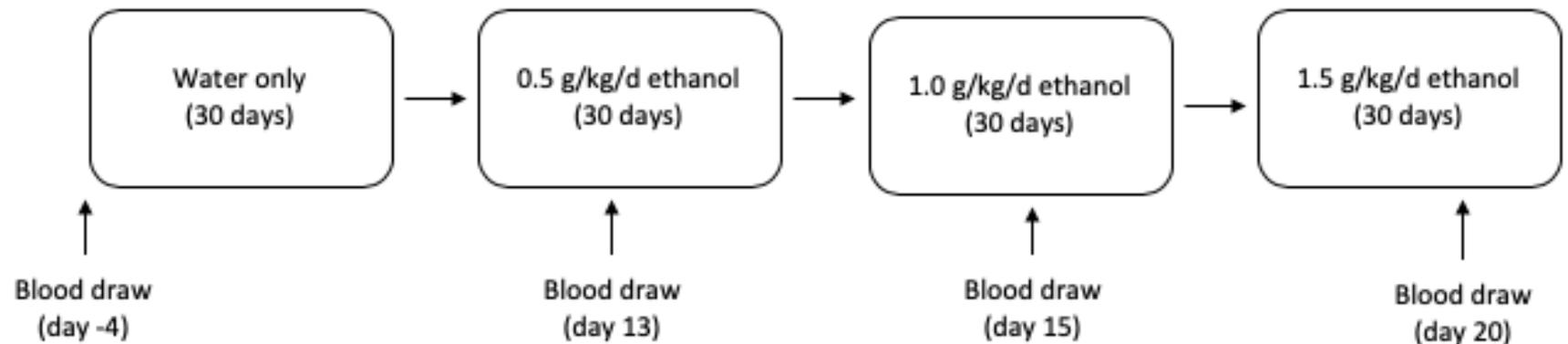
Study 2

Effects of 6 months of voluntary ethanol consumption on intracortical bone remodeling in young adult male cynomolgus macaques

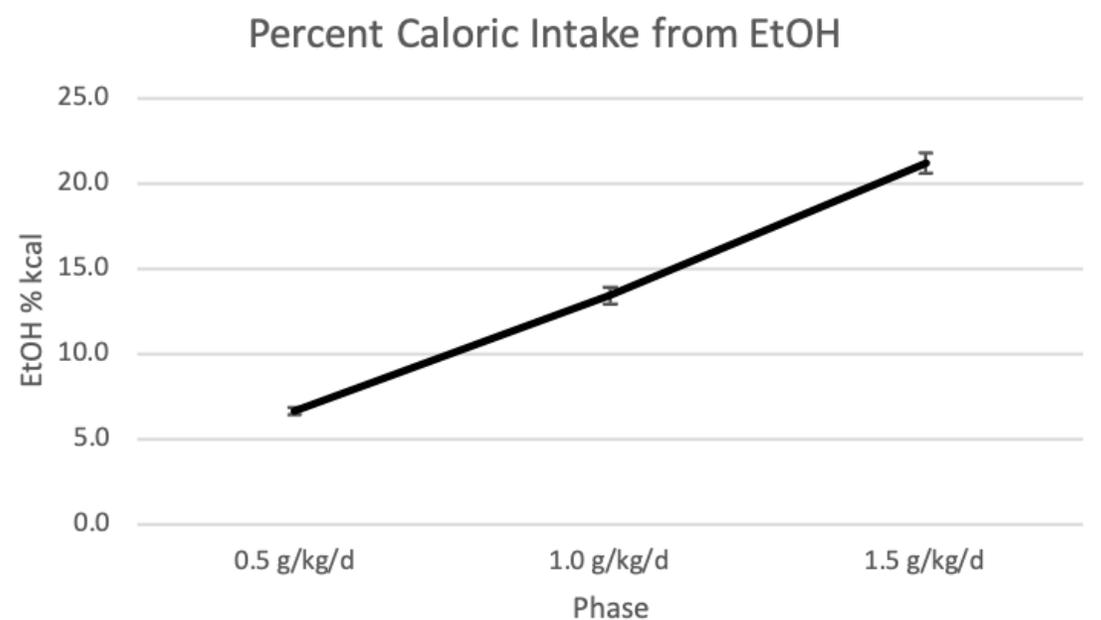
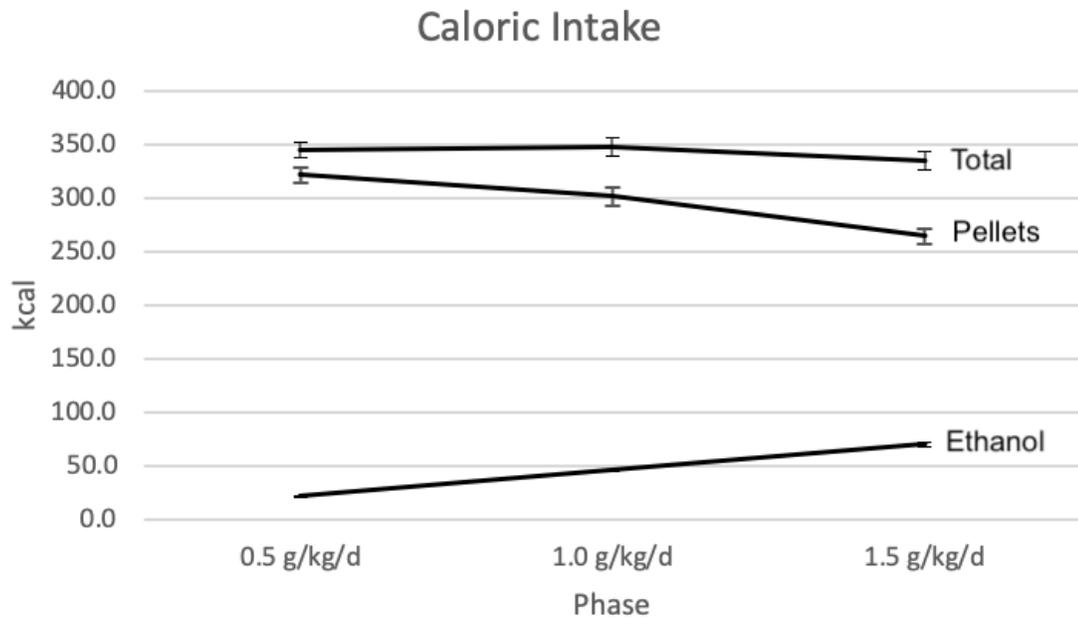
Study #1

Study 1

- Study population:
 - 9 young adult (6.6 ± 0.0 years) male cynomolgus macaques (*Macaca fascicularis*)
- Duration
 - 3 month ethanol induction
- Blood Collection
 - Blood Ethanol Concentrations
 - Osteocalcin
 - CTX

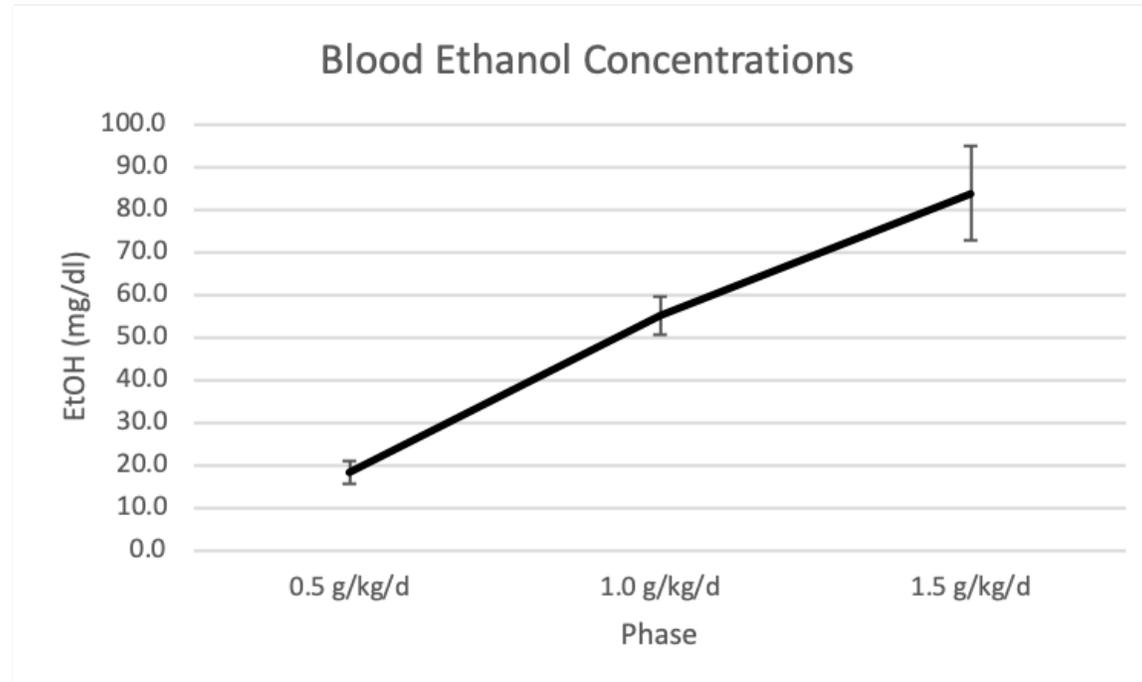


Caloric Intake



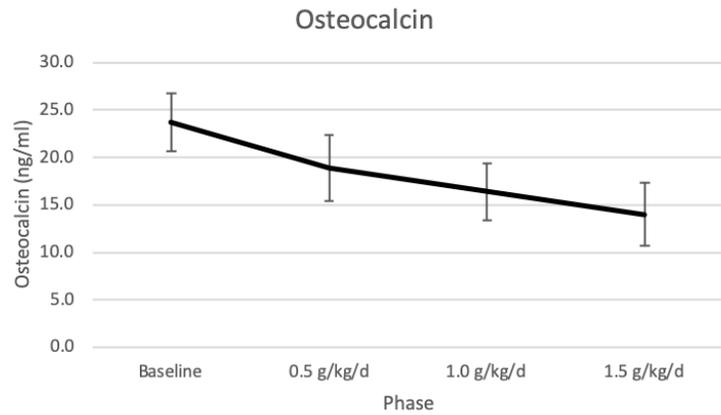
p < 0.0001

Plasma; Blood Ethanol Concentration

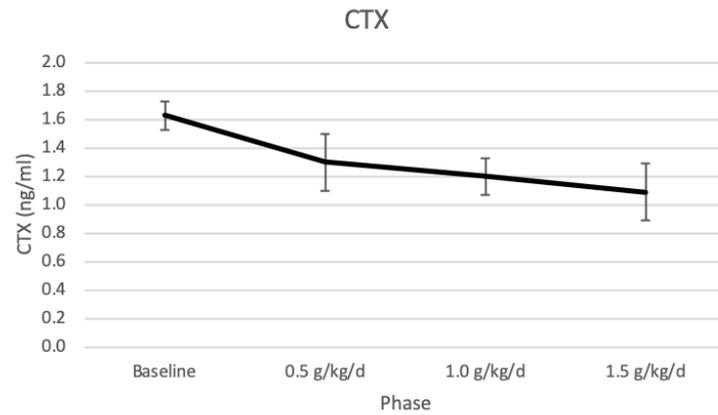


p<0.0001

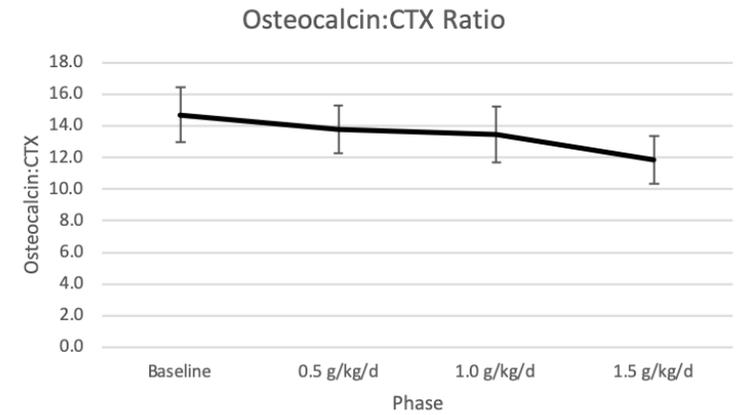
Plasma; Markers of Turnover



p<0.0001



p<0.0001



P=0.0002

Study 1: Conclusion

- In young adult male cynomolgus macaques, ethanol consumption results in lower but unbalanced bone turnover
 - The reduction in bone turnover was dose dependent; no threshold dose was observed
- Over time, the negative remodeling balance could lead to osteopenia and reduced bone quality

- Study population
 - 11 (n = 3 control and 8 ethanol) young adult (control: 7.5 ± 0.0 years; EtOH: 7.0 ± 0.0 years at baseline) male cynomolgus macaques
- Duration
 - 3 month ethanol induction
 - 6 month open access
- Tetracycline label
- Tibia
 - DXA
 - μ CT
 - histomorphometry

Daily ethanol consumption patterns

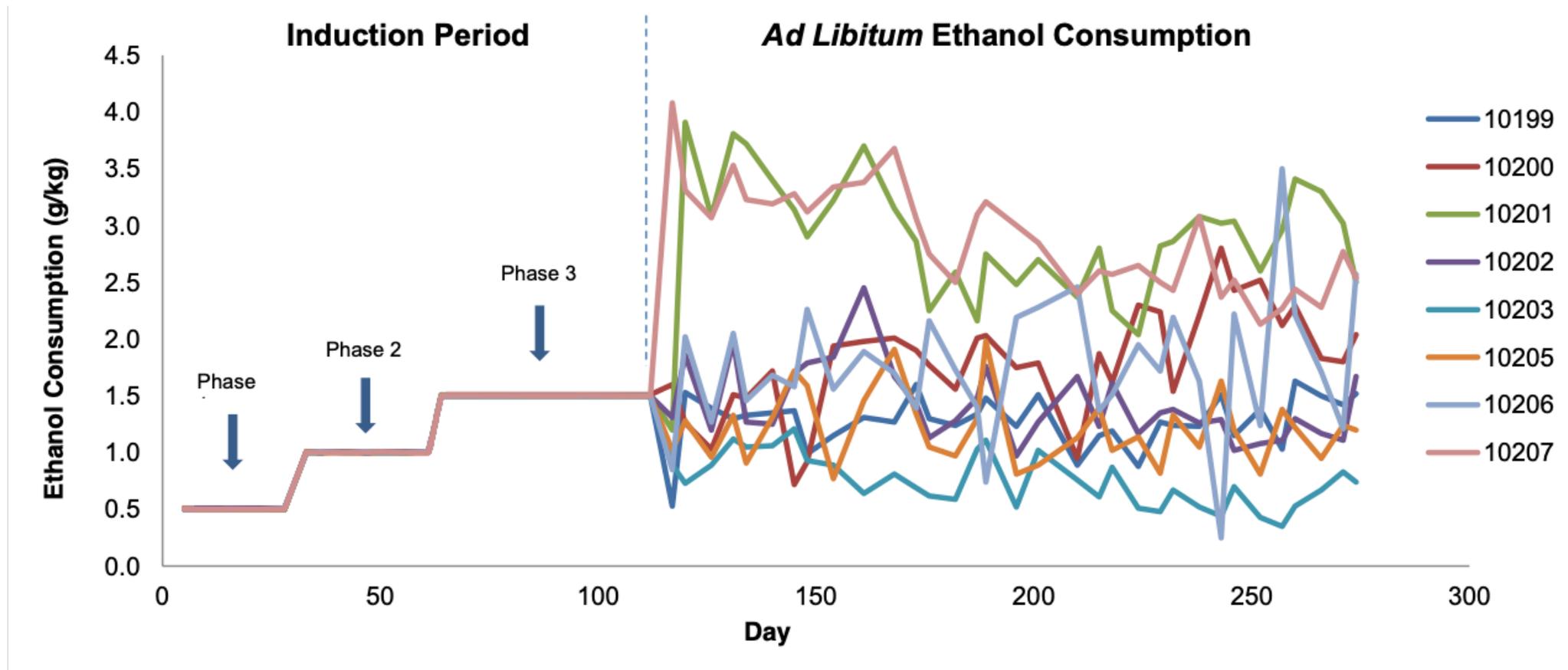


Figure 5. Daily ethanol consumption pattern in ethanol-treated monkeys.

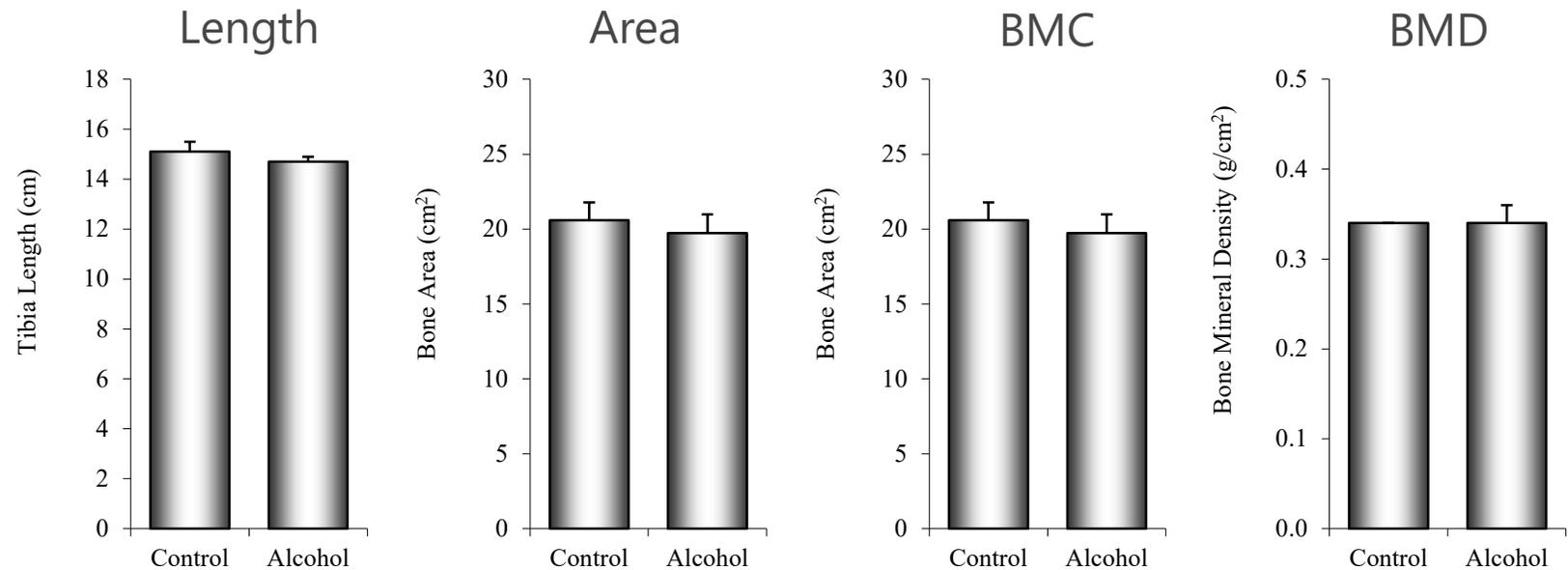
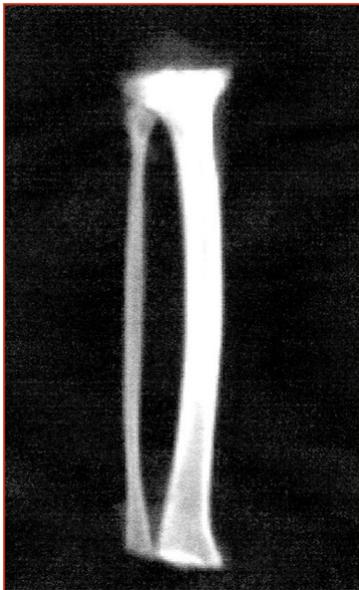
6 months of ethanol consumption had no effect on bone size, BMC and BMD

EtOH consumption (g/kg/d)

1.83 ± 0.3

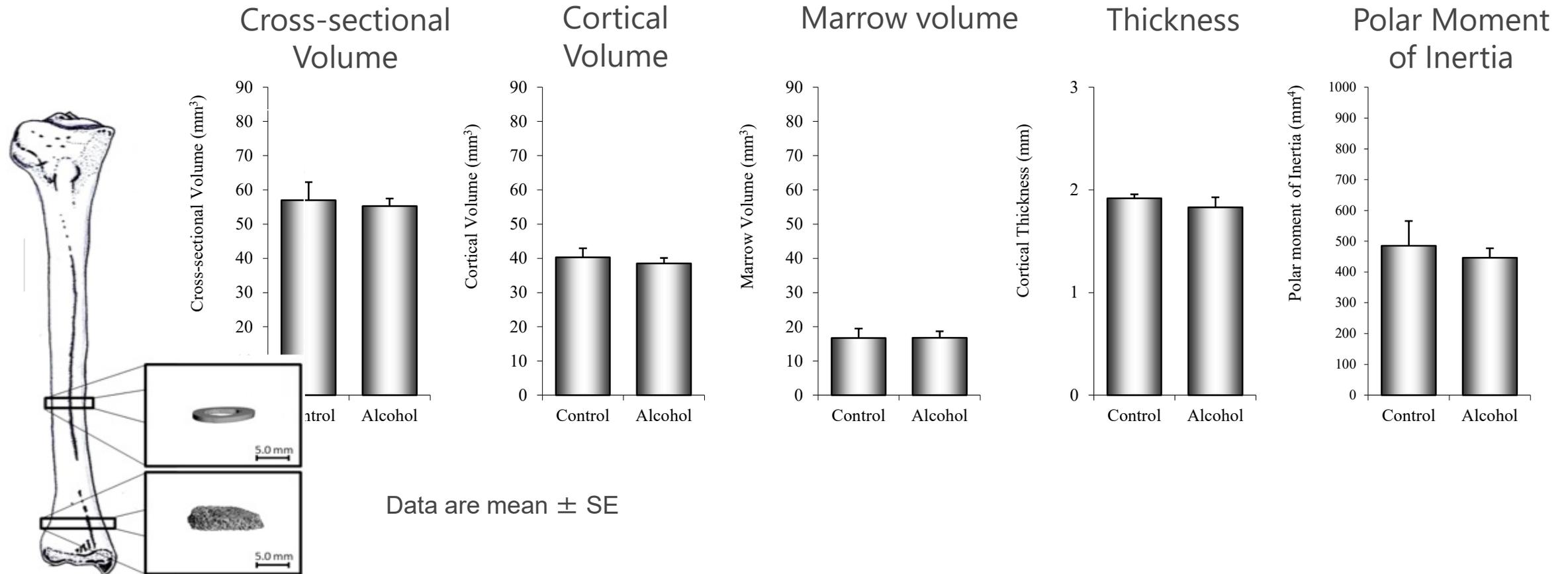
BEC (mg/dL)

50.8 ± 49.8

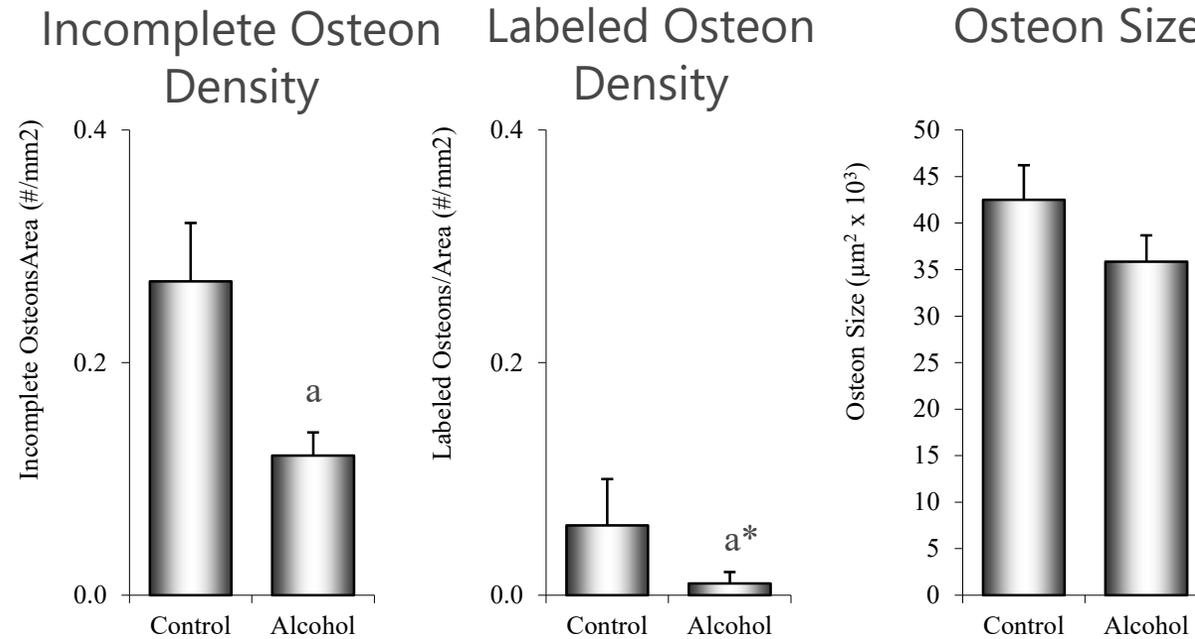


Data are mean ± SE (n=3 control, 8 ethanol)

6 months of ethanol consumption had no effect on cortical bone architecture



Effects of 6 months of ethanol consumption on incomplete and labeled osteons

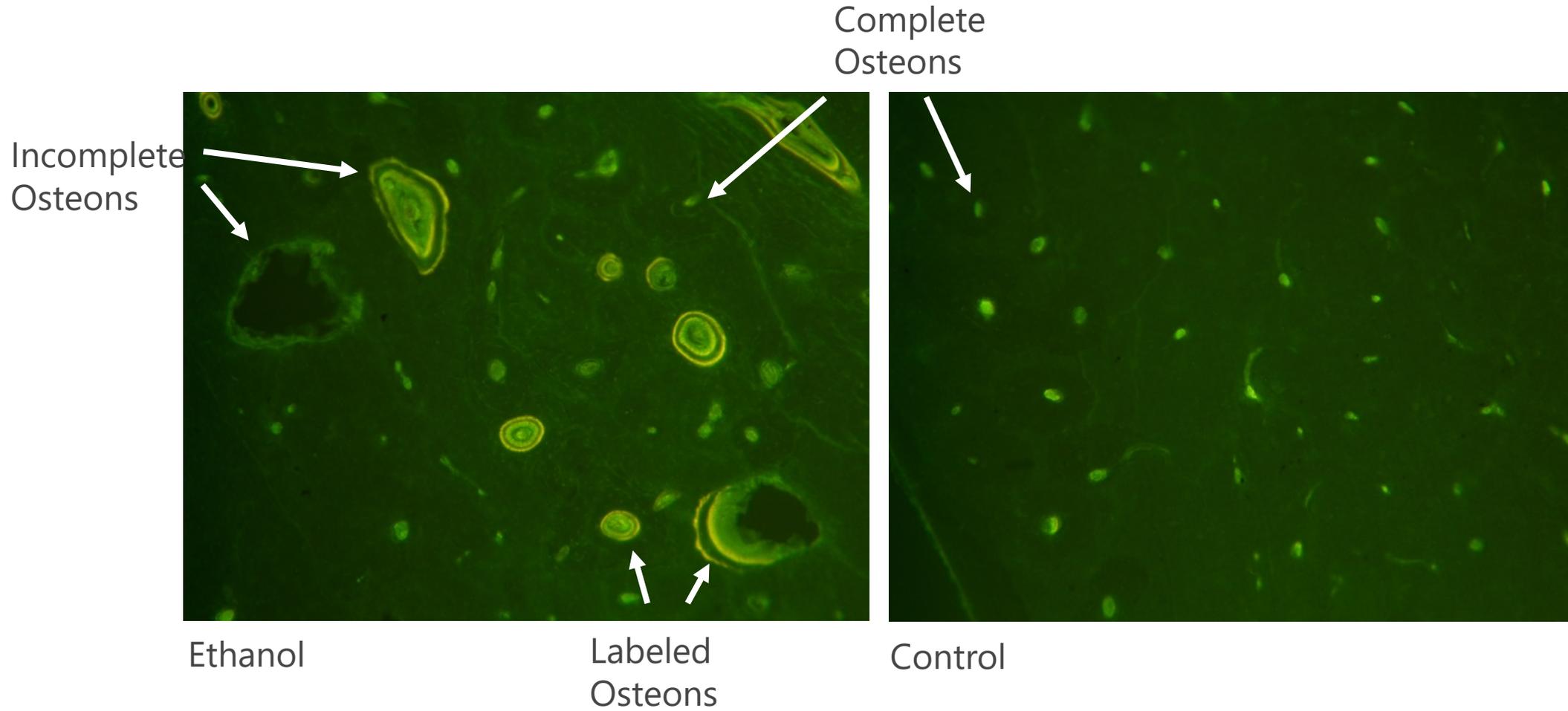


Data are mean ± SE

^aDifferent from Control, P<0.05

^{a*}Different from Control, P<0.1

6 months of chronic ethanol consumption reduced intracortical bone remodeling



Study 2: Conclusion

- Average daily ethanol intake of 1.8 ± 0.3 g/kg/d (BEC, 51 ± 50 mg/dl)
 - had no effect on tibial BMC and BMD or on cortical architecture in tibial diaphysis
 - resulted in reduced intracortical osteon density
- These findings suggest that chronic heavy alcohol consumption may negatively impact bone health, in part, by suppressing intracortical bone remodeling
 - Suppressed bone remodeling, were it to continue indefinitely, could impact bone quality and lead to reduced mechanical properties independent of bone mineral density

Questions?
