Multiple Osteochondromas

- Common autosomal dominant heritable disorder
- Inactivating mutations in EXT1 and EXT2
- Multiple osteochondromas, or cartilage-capped bone growths, on the metaphyses of long bones
- Shortened stature and growth deformities are common and challenging to manage

Mouse Model of Osteochondromagenesis

- Settled the controversial mechanism of osteochondromagenesis as dependent on loss of heterozygosity
- Settled the controversy about cell of origin as a proliferating chondrocyte

Remaining Questions

- Is the reduced longitudinal bone growth phenotype recapitulated in mice that form osteochondromas?
- Does bone shortening correlate with number of osteochondromas on that bone?
- Does shortening derive from physeal growth potential steal, such that bone volume is maintained, but length is exchanged for girth?

Data

- 7 mice homozygous for conditional Ext1, but lacking Cre-recombinase to activate disruption
- 21 mice homozygous for conditional Ext1, Cre-recombinase activated in chondrocytes at either P1-3, P7-9, or P15-17
- CT scan at 42micron resolution obtained post-mortem at precisely 13 weeks age

Methods

- Seg3D used to segment relevant bones
- Populations of segmented bones analyzed using ShapeWorks to study group differences and test hypotheses