# How the Morphologies of Progenitor and Mature Osteocytes Contribute to their Mechanotransduction

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## ABSTRACT

With increasing life expectancy in the US and in Europe, bone pathologies related to massive bone loss occurring later in life carry $5-$10 billion financial burden on the healthcare system. Human Haversian cortical bone is a complex hierarchical heterogeneous tissue resulting from continuous remodeling. Microdamages are resorbed by osteoclasts followed by osteoblasts that form tubular lamellar structures called osteons. Osteoblasts derive from mesenchymal stem cells (progenitor osteocytes) that produce bone mineralized collagen fibrils ECM. Trapped, osteoblasts further differentiate into mechano-sensitive mature osteocytes that detect stimulations from microdamage. Osteocytes bear 40 to 60 cytoplasmic processes extending into canaliculi to create a syncytial network with the neighboring cells. Because osteocytes regulate healthy bone turnover, it is essential to quantify the relationship between *in situ* mechanical stimulation and the cell biological response in order to improve allograft bone treatments.

Hybrid experimental and numerical top-down approach applied to micro tests conducted in human femoral fresh samples made it posible to image the growth of controlled nascent sub-microscopic damage near live osteocytes. The multi-scale local constitutive fracture mechanisms has been identified scale by scale after the balance of the energies at the global scale to evaluate the *in situ* stress field near bone cells. The finite element model is based on explicit morphology. Multi-modal imaging techniques using SEM, UV and fluorescent microscopy coupled to a hierarchical multi-level numerical simulations contributed to enhance the measurements of yield strengths of the diffuse damage within osteon lamellae appear prior to visible microcracks [1] confirming the known brittle/ductile fracture behavior of bone. An *in vitro* model presents a Live Allograft Bone System (LABS) where a patient progenitor (bm hMSCs) or mature (MLOY4) osteocytes were reseeded into fresh human donor cortical bone tissues under mechanical loading. Progenitor and mature osteocytes rearranged as in vivo and exhibited a differentiation process that could adapt the calcium membrane exchange rate, labelled by CFSE, that adapts to the expected amount of mechanical loading in the *in situ* natural tissue environment seen *in vitro* in the presented Live Allograft Bone Systems(LABS) [2].

## REFERENCES

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