

Understanding osteopenia in the context of interstitial fluid flow

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Decades of studies on bone adaptation have helped to clarify the critical role of interstitial fluid flows in mediating growth and resorption responses in bone tissue. Surprisingly, little of this knowledge base has been translated to clinical medicine, which would permit improvements to be made in the prevention and treatment of bone adaptation problems such as osteopenia and osteoporosis. Consequently, these clinical conditions are primarily treated through the use of drugs such as bisphosphonates which block bone resorption, but which can produce significant long term complications.

To advance such translational efforts, our work over the past five years has been focused on clinical studies of bone adaptation, with an emphasis on relating changes in fluid flow through bone to changes in bone density. Fluid flow in bone is driven, in part, by mechanical strain induced pressure gradients. However, for the majority of the day and night, bone fluid flows are driven predominantly by blood pressure and hydrostatic pressure gradients.

A series of recent clinical studies from our lab, which have addressed the role of these chronic interstitial flows in mediating bone adaptation, will be reviewed. This review will include investigations on the effect of upright posture on bone density; the effect of postural sway on bone density; age related changes in postural muscle dynamics; the role of skeletal muscle pump activity on lower limb fluid flows; the role of blood pressure; the role of muscle stimulation; and the differential effects of blood flow and interstitial flow in mediating bone growth.

These studies demonstrate that consideration of fluid flow rates and patterns in bone provides a more clear and mechanistic understanding of bone adaptation than possible through the traditional focus on mechanical stress and strain distributions. Moreover, such a perspective has set the stage for the development of non-pharmacologic clinical interventions which could be utilized to prevent bone loss or even enhance bone formation in the elderly, those in extended bed rest, and as well, those with a distinctly sedentary lifestyle.