Modeling Mechano-biochemical Couplings in Trabecular and Osteonal Bone Remodeling

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ABSTRACT

Couplings between mechanical and biochemical signalings at cellular level regulates bone remodeling turnover—osteoclastic resorption and osteoblastic formation—on trabecular surface in cancellous bone and osteonal surface in cortical bone, leading to bone functional adaptation. In this process, osteocytes are believed to play key roles as both mechanosensory cells and signal-transducing cells that produce important signaling molecules in bone metabolism, such as sclerostin, RANKL, and OPG. To better understand the mechanism of functional bone adaptation by remodeling, in this study, we propose a mathematical model of bone remodeling at the cellular level that involves the mechano-biochemical couplings, and conduct computational simulation for trabecular and osteonal remodeling.

RANKL/RANK/OPG system known as important regulatory factors of osteoclastgenesis in bone metabolism was introduced in the mechanoregulation model of trabecular and osteonal surface remodeling [1, 2]. RANKL activates osteoclastgenesis and OPG prevents RANKL from binding to its receptor RANK, both of which are produced by osteoblasts on the bone surface and/or osteocytes in the bone matrix. The production of these molecules are coupled, in the proposed model, with mechanical signalings such as stress/strain in the mineralized bone matrix, within which mechanosensory osteocytes are embedded. The RANKL/RANK/OPG system provides complex positive and negative regulations of osteoclast differentiation that initiate the bone remodeling cycles.

Finite element modeling and simulation for trabecular and osteonal remodeling were conducted based on the proposed model under a simple uniaxial compressive loading. As stated in Wolff's Law, the computer simulation predicted that the microscopic trabecular and osteonal structure follows the major axis of the stress (compressive axis) as a result of remodeling. In addition, the effects of the RANKL expression level on the remodeling turnover rate were investigated with a possible extension of the model to further include sclerostin relating to the bone formation. This framwork of the modeling and simulation with complicated coupling mechanism in bone metabolism/remodeling will be a useful tool to predict and discuss the effects of the drugs for metabolic bone diseases, such as osteoporosis, in the near future.

REFERENCES

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