IN SILICO MODEL FOR BONE ADAPTATION BASED ON IN VIVO MEASURED PARAMETERS

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Introduction

Sophisticated *in silico* simulations of bone remodeling can be used not only for the verification of existing mechanobiological principles; but also, once fully validated, can help transform clinical management of bone diseases. Establishing a direct link between the *in vivo* measured markers of bone adaptation and a mathematical model can further improve the original theories of biological processes in bone and refine the predictive accuracy of the *in silico* simulations. The aim of this project was to revisit the original mechanostat principle [1] by directly linking measured biological markers from the *in vivo* study with the input variables of the *in silico* algorithm. Updated mechanostat curves have been produced for the scenarios of osteoporosis and associated treatments.

Methods

Previously introduced strain-adaptive closed-loop remodeling algorithm [4] was expanded to allow uncoupling of the resorption and formation variables controlling maximum rate of remodeling (u) and sensitivity to the mechanical signal (tau). Strain energy density (SED) values corresponding to resorption, formation, and quiescence were calculated from the *in vivo* study of osteoporosis and associated treatments in mouse vertebrae [2] using high-resolution finite element analysis. These values were used to set the SED thresholds for formation (SED_{upp}) and resorption (SED_{low}) in the model. Maximum formation and resorption rates (u_{max} and u_{min}) for the algorithm were also experimentally-derived from the morphometric assessment. Formation and resorption sensitivity (tau_{upp} and tau_{low}) to the mechanical signal was chosen iteratively for each scenario (Fig.1).

Dynamic and static morphometry, as well as local remodeling sites were compared for the assessment of simulation accuracy.

Results

Dynamic morphometric parameters were targeted as an indication of the simulation accuracy, while static morphometry and visual comparison of local remodeling sites were used to verify the match. Simulations with the expanded algorithm produced improved results across all assessment methods, when compared to the previously used model [3]. Errors in static morphometry remained under 10% for most trabecular parameters, while dynamic morphometric errors decreased by over 50%, and were mostly not significantly different from the *in vivo* results. Better visual local remodeling site matches were observed in all samples (Fig. 1).

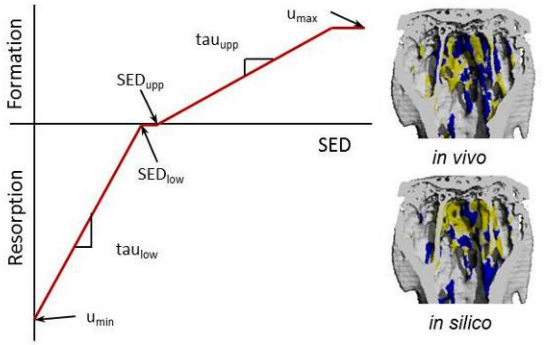

Figure 1: Left: Modified mechanostat curve and in silico model parameters. Right: Local remodeling sites in vivo (top) and in silico (bottom). Blue areas denote resorption; yellow, formation; and grey, quiescent sites.

Discussion

In this study, we established a link between *in vivo* derived morphometric/mechanical parameters and variables of the *in silico* model for bone remodeling. These relationships between biological markers and their mathematical interpretations have allowed us to modify classical mechanostat curves to reflect differences in bone remodeling due to osteoporosis and associated treatments.

References

[1] Frost HM, Anat Rec, 219(1):1-9, 1987.
[2] Kuhn G *et al*, J Bone Min Res, 26:SA0069, 2011.
[3] Levchuk A *et al*, J Biomech, 45:S471, 2012.
[4] Schulte FA *et al*, Bone, 52(1):485-92, 2012.