Unifying microdamage- and disuse-targeted resorption: a lack of osteocytic inhibition

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Unifying microdamage- and disuse-targeted resorption: a lack of osteocytic inhibition

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Introduction

Osteoclast activity is enhanced by disuse [1] and by microdamage [2]. These targets appear contradictory, as microcracks occur in high strain conditions. Can one mechanism explain both disuse- and microdamage-targeted resorption?

Microdamage and subsequent resorption have been associated with osteocyte apoptosis [3, 4]. This suggests that osteoclasts target apoptotic osteocytes rather than the microdamage itself. Osteocyte-osteoclast communication is also key in our bone adaptation model, where **strain-induced osteocyte signals** [5, 6] **inhibit osteoclasts** [7]. We found that this mechanism guides resorbing osteoclasts along the principal load direction [8], thus providing an explanation for osteon-load alignment [9]. In the present study **we investigate whether the mechanism guides resorbing osteoclasts to regions of osteocyte death**.

Methods

Osteonal remodeling is simulated in a 2x2 mm^2 piece of compact bone tissue, subjected to compressive loads in the vertical direction (Fig.1A). Osteocytes are distributed in the bone tissue. Osteoclasts start from an initial resorption cavity (Fig.1B) . Load transfer through the structure is calculated by finite element method. Depending on local strains osteocytes send signals to the bone surface (Fig.1C). A high signal inhibits resorption and activates formation.

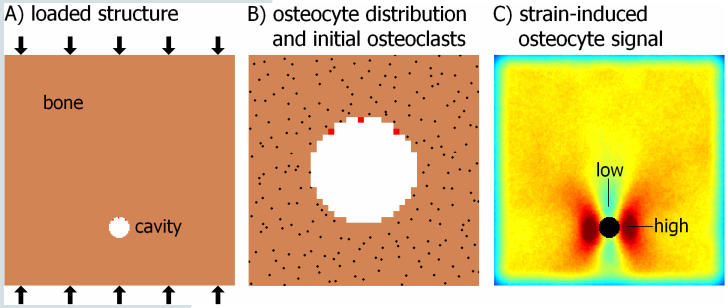

Figure 1: A bone structure with an initial resorption cavity is subjected to external loads (A). Osteocytes in the bone (B) translate strains into a biochemical signal (C).

To investigate whether apoptotic osteocytes are targeted, we artificially 'kill' the osteocytes in a tissue region near the expected path of the cutting cone (Fig. 3A).

Results

Around the cavity, strains are low in loading direction and high in transverse directions. The osteocyte signal reflects this pattern (Fig.1C). Guided by the signal osteoclasts resorb a tunnel along the loading axis and osteoblastic bone formation is initiated on the tunnel walls (Fig.2).

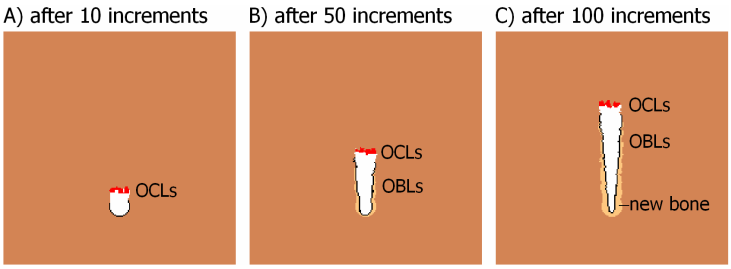

Figure 2: Osteon development after 10, 50 and 100 increments.

In the simulation with the dead osteocyte region (Fig.3A), the strain distribution remains unaffected, but there is no osteoclast-inhibiting signal from the apoptotic region (Fig.3B). Hence, the cutting cone alters its course to remove this region (Fig. 3C). After resorbing the apoptotic region, the cutting cone resumes its load-directed course.

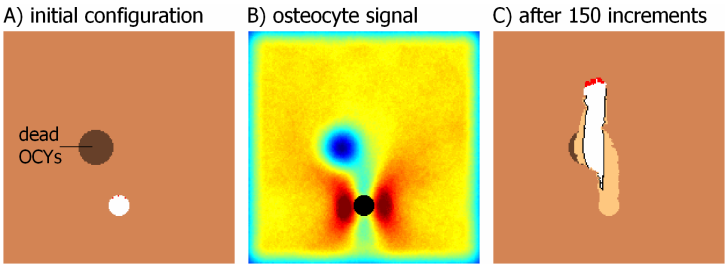

Figure 3: Removal of dead osteocytes

Conclusions

Our simulations show that the proposed mechanism guides resorbing osteoclasts to nearby regions of osteocyte death. If microdamage causes osteocyte death [3, 4], then a lack of osteocytic inhibition to osteoclasts could explain microdamage-targeted resorption. And if these osteocyte signals are strain-induced [5, 6], the same mechanism might explain osteon orientation and disuse-targeted resorption.

References

[1] Young et al. Bone 1986;7;109-17. [2] Burr et al. J Biomech 1985;18;189-200. [3] Bentolila et al. Bone 1998;23;275-81. [4] Verborgt et al. J Bone Miner Res 2000;15;60-7. [5] Burger et al. FASEB J 1999;13;S101-12. [6] Huiskes et al. Nature 2000;405;704-6. [7] Heino et al. J Cell Biochem 2002;85;185-97. [8] Ruimerman et al. Trans. 51th ORS 2006;poster 1642. [9] Petrtyl et al. (1996). J. Biomech., 29, 161-169.