

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

Citation for published version (APA):

Oers, van, R. F. M. (2007). *Unifying microdamage- and disuse-targeted resorption: a lack of osteocytic inhibition*. Poster session presented at Mate Poster Award 2007 : 12th Annual Poster Contest.

Document status and date:

Published: 01/01/2007

Document Version:

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.tue.nl/taverne

Take down policy

If you believe that this document breaches copyright please contact us at:

openaccess@tue.nl

providing details and we will investigate your claim.

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

René F.M. van Oers, Ronald Ruimerman, Peter A.J. Hilbers, Rik Huiskes
Biomedical Engineering Dept., Univ. of Technology Eindhoven, The Netherlands

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 mm² 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.

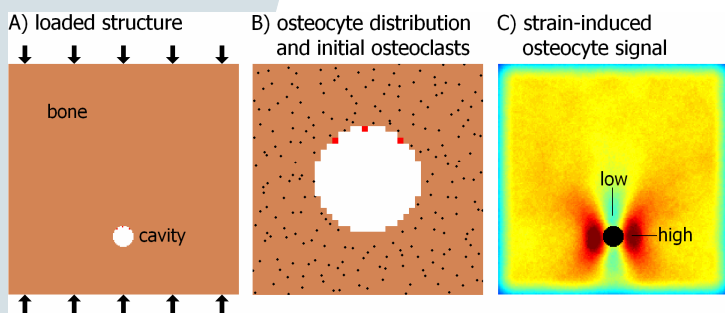


Figure 1: A bone structure with an initial resorption cavity is subjected to external loads (A). Osteocytes in the bone (B) translate strains into a biochemical signal (C).

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).

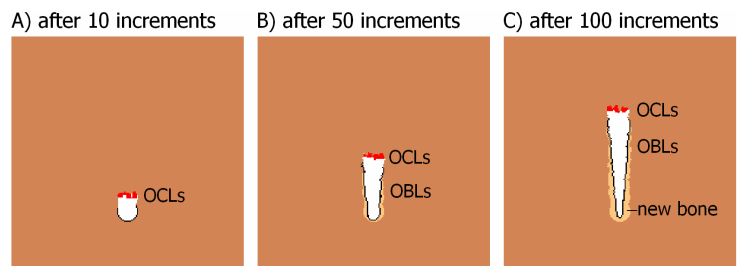


Figure 2: Osteon development after 10, 50 and 100 increments.

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.

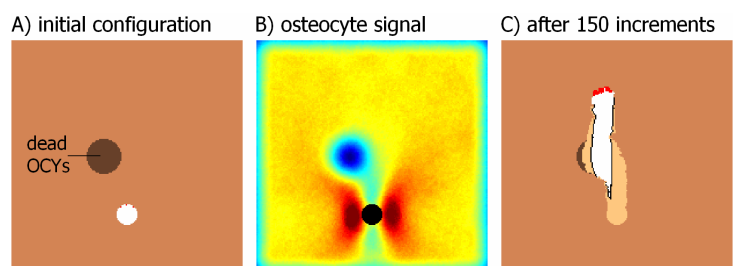


Figure 3: Removal of dead osteocytes

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] Petryl et al. (1996). J. Biomech., 29, 161-169.