Mechano-regulation by deviatoric strain and fluid flow predicts tissue differentiation during distraction osteogenesis

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Mechano-regulation by deviatoric strain and fluid flow predicts tissue differentiation during distraction osteogenesis

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Introduction

Mechano-regulation algorithms have been proposed to explain tissue differentiation of precursor cells during osteogenesis. However, corroboration of these algorithms have shown to be difficult[1-2], partly because repeatable experimental outcomes under controlled mechanical conditions are rarely available. During distraction osteogenesis (DO), a controlled displacement is used to regenerate large volumes of new bone.

The **aim** with the current study was to computationally predict bone regeneration during DO over time and use this model to further validate a mechano-regulation algorithm based on deviatoric strain and fluid flow[3].

Methods

- The model was based on an ovine experimental model[4] which evaluated bone segment transport in tibial shaft defects (20 and 45 mm) over an intramedullary nail (Fig. 1a).
- Distraction started at post op day 3 with rate of 1mm/day until defect was closed. Daily distraction forces, force relaxation, weekly radiographs and undecalcified histology were available for comparison.

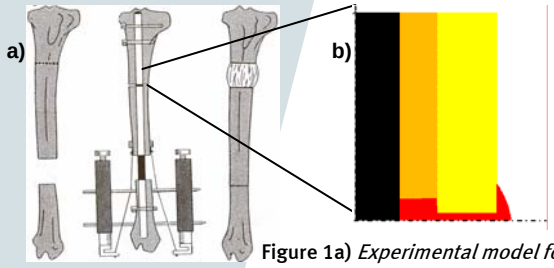

Figure 1a) *Experimental model for bone segment transport*, b) *2D axisymmetric FE model of ovine tibia.*

- Depending on the deviatoric strain and fluid velocity[3] calculated in the FE analysis, cells that migrated into the callus through diffusion, differentiated into fibroblasts, chondrocytes or osteoblasts, and predicted new element material properties. 1 iteration simulated 1 day distraction.
- Due to large geometrical increase, re-meshing and re-mapping of material properties via interpolation were used.
- Matrix production and tissue growth was simulated by allowing tissue relaxation until equilibrium. Tissues were modeled as linear poroelastic.

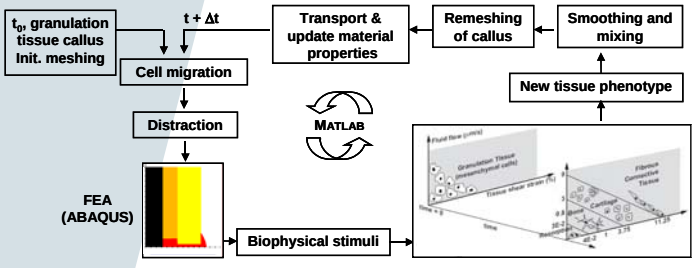

Figure 2 *Distraction osteogenesis simulated adaptively (MATLAB)*

Results

Experimental

- Showed good reproducibility without much variation between defects.
- During week 1, only small slightly radio-opaque areas in distraction gap were seen. From week 2, strips of increased density started from the cortical bone ends and grew towards each other. Throughout transport, an area of soft tissue in the middle of the regenerate were seen.
- Bony bridging was observed after distraction was complete.

Modeling

- The predicted bone formation pattern was overall similar to what was seen experimentally.
- Initially, predicted tissues were mainly fibrous. First bone formation occurred at periosteum (day 6), followed by bone formation in the gap area that grew as distraction proceeded.
- Gap with soft tissue remained until distraction was finalized.
- During consolidation, maturation and final bridging occurred. A steady state situation were observed with similar tissue distributions for both 20 mm and 45 mm distraction.

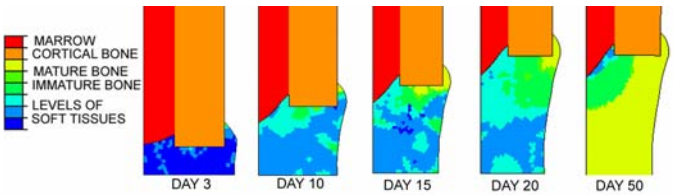

Figure 3 *Predicted bone formation pattern during DO of a 20 mm defect (day 1-20), followed by consolidation and maturation.*

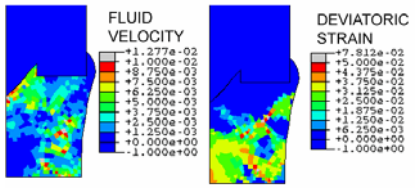

Figure 4 *Magnitudes of a) fluid velocity and b) deviatoric strain after 15 days of distraction*

Discussion

- Mechano-regulation based on deviatoric strain and fluid velocity was able to predict bone formation pattern during DO from initial corticotomy to final consolidation. Comparison of soft tissues (amounts of fibrous tissue vs. cartilaginous tissues) are still pending.
- Relative amounts of endochondral vs. intramembranous bone formation during DO are directly related to distraction rate. Next, this promising model will be used to evaluate variations and optimize & accelerate DO treatment protocols.

References:

1 Isaksson et al, J Biomech, In press; 2 Isaksson et al, J Orthop Res, Accep
3 Lacroix and Prendergast, J Biomech35(9), 2002 4 Brunner et al, CORR 1994