The feasibility of inducing endochondral ossification by mechanical loading in osteochondral explants

TU/e technische universiteit eindhoven

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Jasper Foolen[1], René van Donkelaar[1], Wouter Wilson[1] , Pieter Buma[2], Rik Huiskes[1]
[1] Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands,
[2] Orthopaedic Research Laboratory, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Introduction

Non-physiological mechanical loading is believed to be an important contributing factor in the development and progression of osteoarthritis (OA) [9]. Our hypothesis concerning OA aetiology is shown in figure 1.

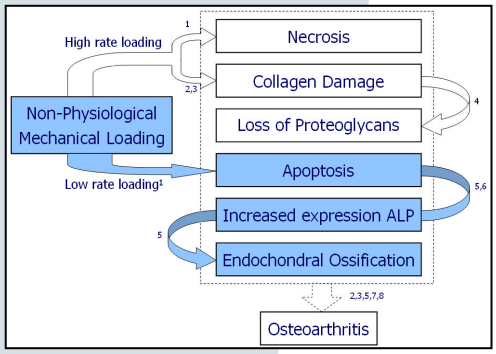

Figure 1: Schematic representation of hypothesis, indicated in blue.

Aim

To test the feasibility of inducing OA in an *in vitro* explant system, by applying an indentation load.

Method: finite element analysis

The loading parameters are determined using finite element analysis (figure 2) to account for two aspects:

1. Optimised tissue deformation in the deep zone, for this zone has been found to be most susceptible to endochondral ossification [8].
2. Effects of indentation had to be unaffected by specimen size.

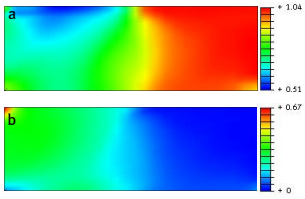

Figure 2: Numerical data. (a) volumetric strain (b) deviatoric strain

The numerical evaluation resulted in a load of 25 N applied at low rate (0.5 N/sec), followed by a dwell period of 300 sec.

Method: experimental set-up

Osteochondral explants, harvested from knee joints of 1 year old pigs, were obtained within 4 hours post-mortem. Explants, loaded (figure 3) as well as controls, were examined at day 0 (n=11) and after 14 days of culturing (n=12). Analysis comprised viability, general histology and ALPase, an early measure for endochondral ossification.

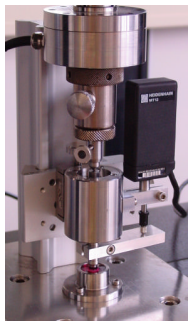

Figure 3: Experimental set-up.

Results

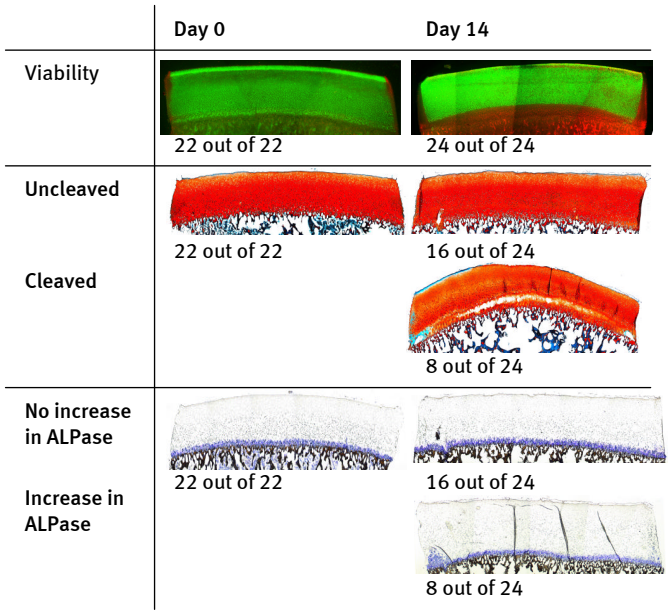

Figure 4: Typical results of viability, proteoglycan and ALPase distribution.

Loading did not increase ALPase expression, nor did it increase cell death.

Culturing resulted in:

- Increased cell death in bone and the calcified/deep cartilage layer.
- Cleft formation in 33% of the explants, loaded as well as controls.
- A slight increase in ALPase at the edges in the deep cartilage layer in 33% of the explants, loaded as well as controls.

Conclusion

- The hypothesis has not been confirmed.
- Osteochondral explants are not suitable for culturing with the current approach.

Discussion

A supplementary hypothesis, to explain these unexpected results, reads: “during culturing, cytokines and growth factors from necrotic subchondral bone diffuse into cartilage, causing matrix degeneration and cell death”.

References:

[1] Lewis, Deloria, Oyen-Tiesma, J Orthop Res, 2003. [2] Maroudas, Nature, 1976. [3] Wilson, Donkelaar, Burken, Buma, Rietbergen, Huiskes, J Orthop Res, 2005. [4] Lin, Chen, Torzilli, Osteoarthritis Cartilage, 2004. [5] Hashimoto, Ochs, Rosen, Proc Natl Acad Sci, 1998. [6] Kirsch, Swoboda, Nah, Osteoarthritis Cartilage, 2000. [7] Guilak, Ratcliffe, Lane, J Orthop Res, 1994. [8] Sugita, Chiba, Kawamata, The Knee, 2000 [9] Repo, Finlay, J Bone Joint Surg Am, 1977.