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

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## 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.

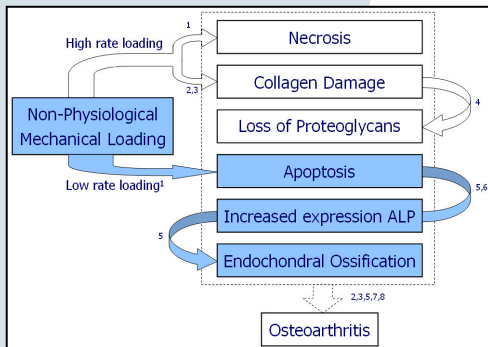


Figure 1: Schematic representation of hypothesis, indicated in blue.

## 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.

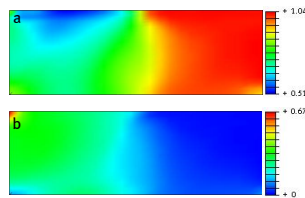


Figure 2: Numerical data. (a) volumetric strain (b) deviatoric strain

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.

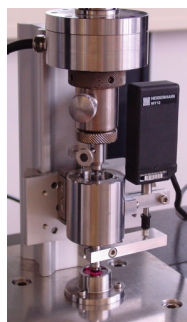


Figure 3: Experimental set-up.

## Results

	Day 0	Day 14
Viability	 22 out of 22	 24 out of 24
Uncleaved	 22 out of 22	 16 out of 24
Cleaved		 8 out of 24
No increase in ALPase	 22 out of 22	 16 out of 24
Increase in ALPase		 8 out of 24

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:

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