# Mechanically induced muscle damage

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## Introduction

Within the research of the aetiology of decubitus, the present study will focus on mechanically induced damage in muscle tissue. To study the development of damage, a tissue engineered muscle model will be developed. As the damage is initiated on a cellular level, markers for the evolution of cell damage will be applied to establish threshold values for damage development. The markers may be used as biosensors in decubitus prevention. To achieve this, tissue damage will have to be defined in terms of reversible as well as irreversible damage and also cell death.

### Objective

To investigate the relationship between sustained compressive loading and the development of tissue damage, with the ultimate aim to:

- provide threshold levels for damage development induced by compression
- establish guidelines for decubitus prevention

## Material and methods

### Tissue engineered muscle

The method for self-assembly of a tissue engineered muscle, by Dennis et al. [1], will be adapted to create tissue engineered muscles from cell lines without the use of a scaffold material (figure 1).

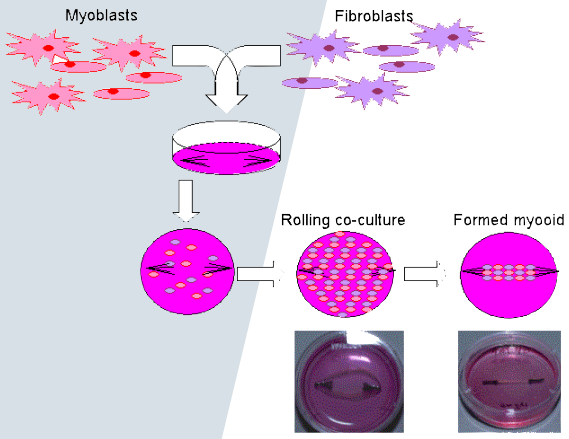


**Figure 1** *Myoblasts and fibroblasts were co-cultured in a petri dish. After spontaneous detachment (2-3 weeks) the layer rolled up and the myooid was formed. Photos from [1].*

In short, fibroblasts and myoblasts were co-cultured on a modified culture dish surface. After a culture time of 2 to 3 weeks, the cell layer detached. However, the layer stayed attached to a pair of suture anchors and thus rolled up to form a cylindrical, so-called myooid (figure 2).

### Markers of cell damage

The tissue engineered muscles will be compressed in a loading device. The degree of cell damage will be evaluated with markers, which should be measurable. Some biochemical candidate markers for reversible as well as irreversible cell damage (and possibly biosensors) are shown in figure 3. Furthermore, a suitable marker for cell death has to be found; for example nuclear staining with propidium iodide.

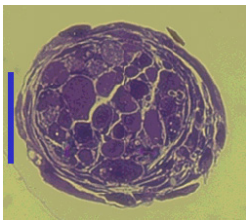

**Figure 2** *Microscopic cross-section of a myooid, stained with 1% toluidine blue. An annulus of fibroblasts is surrounding the myotubes. The scale bar denotes 100 $\mu$m. [1]*

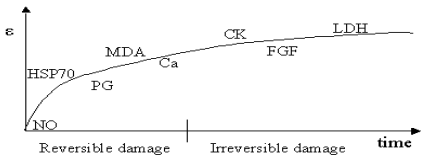


**Figure 3** *Estimation of marker response on muscle damage in time. NO = nitric oxide, HSP70 = a heat shock protein, PG = prostaglandin, MDA = malondialdehyde, Ca = calcium, CK = creatine kinase, FGF = fibroblastic growth factor and LDH = lactate dehydrogenase.*

## Future

**Short term goals:**

- application of protocol for myooid formation
- finding suitable markers for cell damage and cell death

**Long term goals:**

- optimization of protocol for engineering myooids
- design of a compression device
- compression studies on the myooids
- damage definition and assessment with markers
- effects of electrical stimulation of myooids on tissue development and damage evolution
- implementation of established damage thresholds in numerical model

*References:*

[1] Dennis R.G., Kosnik P.E. 2nd, Gilbert M.E., Faulkner J.A.: *Excitability and contractility of skeletal muscle engineered from primary cultures and cell lines, Am J Physiol Cell Physiol., 2001, 280(2): C288-95.*



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