Contributions of ischaemia and cellular deformation to the aetiology of deep pressure ulcers

Contributions of ischaemia and cellular deformation to the aetiology of deep pressure ulcers

K.K. Ceelen, C.W.J. Oomens, F.P.T. Baaijens
Biomechanics and Tissue Engineering, Mechanical Engineering

Introduction

Sustained mechanical loading can lead to deep pressure ulcers (PUs), involving skeletal muscle tissue. These wounds constitute a serious health care problem. Incomplete understanding of the aetiology makes it difficult to identify sensitive people to take the right precautions.

Objective

The aim is to understand the major damage producing processes inside muscle tissue when it is compressed for a long time.

Pressure ulcer aetiology

Ischaemia is generally believed to be an important factor in PU aetiology, but it cannot be the only one. Reperfusion injury and impaired lymphatic drainage might also be involved, but our current hypothesis is that cellular deformation somehow exacerbates the ischaemic injury, leading to accelerated damage development.

Critical cell parameters are the energy status (ATP), and cell membrane integrity. The latter could be changed by deformation, changing permeability. Especially elevated Ca^{2+} is harmful since it interferes a.o. with ATP-generation and membrane integrity:

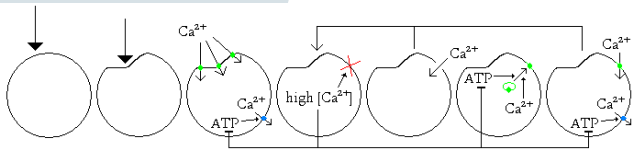

Figure 1 *A deformation-induced permeability change leads to more Ca^{2+} entering the cell than can be pumped out. High [Ca^{2+}] damages the membrane and interferes with repair.*

Future plans

To separate and couple the ischaemic and deformation damage pathways, a numerical FE model will be developed using results of experiments on single cells, TE muscle samples, and rat muscles:

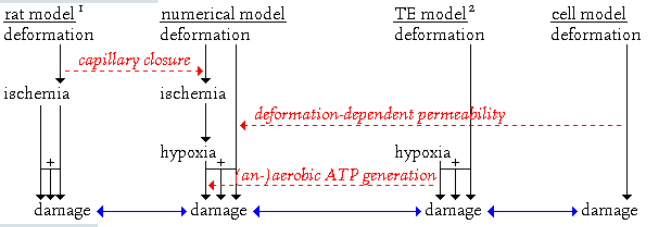

Figure 2 *Connections between experiments and numerical model. (1: A. Stekelenburg; 2: D.Gawlitta)*

Ischaemia

Deformation is thought to compress capillaries, diminishing the oxygen supply. Modelling O_2 diffusion and damage due to lack of O_2, the distribution of O_2 consumption appeared to be important (fig.3). This will be extended with (an-)aerobic ATP-generation on specific subcellular sites, and a damage law based on ATP, which will be validated with anoxia experiments on TE muscle models.

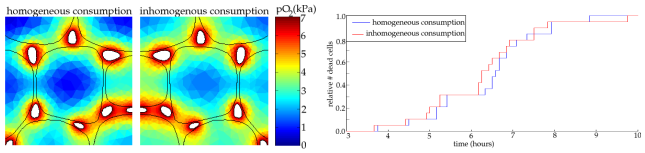

Figure 3 *Left: Oxygen pressures in the cells in a mesh with homogeneous (left) and inhomogeneous O_2 consumption, and white capillaries. Right: The amount of dead cells in time for both meshes.*

Deformation

Our current hypothesis is that cell deformation changes membrane integrity and permeability, hence deformation-dependent membrane transport has to be described. Compressing single cells while monitoring permeability or Ca^{2+} can provide support for deformation-induced permeability changes or a Ca^{2+}-related damage law.

Ischaemia and deformation

ATP provides a link between deformation and ischaemia, since many membrane ion pumps are fuelled by ATP, and membrane repair is also ATP-dependent. Intracellular Ca^{2+} accumulation in turn, disturbs metabolism. The result of the numerical coupling between these 2 damage pathways can be compared with combined anoxia and deformation TE experiments.

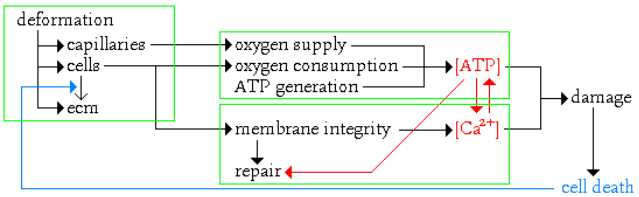

Figure 3 *Overview of numerical model.*

Finally, it would be interesting to make the step from cell-level to muscle-level via a multi-level model to see the distribution of damage in the muscle and compare it with rat experiments. In this model, the effect of narrowing lumina of larger blood vessels on the O_2 supply to the cells can also be studied.