INFLUENCE OF THE PERICELLULAR MICROENVIRONMENT ON CHONDROCYTE MODELLING

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INTRODUCTION

Chondrocytes, the living cells in articular cartilage, synthesize and maintain the extracellular matrix. The mechanical environment of chondrocytes is known to influence the health of joints. Previous experimental studies have shown that the magnitude of cell deformation is less than what would be expected based on the large differences in material properties between cell and extracellular matrix [1]. This means that cells may have a mechanism to protect themselves from high deformation in the surrounding extracellular matrix. A possible protective mechanism may be the presence of the pericellular matrix and the capsule, which, together with the chondrocyte itself, constitute the chondron. The function of the chondron is not fully understood. It has been speculated that it functions to protect chondrocytes during cartilage loading [2]. This hypothesis is supported by theoretical models of cell-matrix interactions in cartilage [3]. However, previous theoretical cell-matrix models did not entirely explain the cell deformations observed in experiments. Therefore, we hypothesised that the pericellular microenvironment, represented by the material gradient in pericellular matrix and capsule, may be responsible for the observed cell deformations.

METHODS

In order to model cell deformation, we used a multi-scale step method [3] [4]. Cartilage was assumed to be biphasic, and the elastic solid phase was modelled as a transversely isotropic, transversely homogeneous composite material [5] comprised of a proteoglycan matrix, cell inclusions, and a depth-dependent, statistically oriented collagen fibre inclusion phase. The fluid phase was assumed to be inviscid, incompressible, and associated with a deformation-dependent permeability. The cartilage specimen was assumed to be cylindrical, 1.0*mm* thick, and with a diameter of 6.0 *mm*. A spherical cell (5 μm radius) from the middle zone was modelled as a biphasic inclusion embedded in the extracellular matrix (ECM). In order to model the pericellular microenvironment, we assumed that the pericellular matrix (PCM) is 2.5 μm thick, and the pericellular capsule (PC) is 0.5 μm thick with a high volume fraction of collagen fibres, which has been observed by scanning electron microscopy [2]. All material properties for the cartilage, cell model were taken from the literature [6] [7]. Numerical simulations were performed by means of the commercially available software ABAQUS v6.3. The cartilage specimen was subjected to a 15% unconfined compression test, at a constant rate during a ramp period of 300 *s*, and the deformation was then kept constant until 1200 *s*.

RESULTS

The study of the axial displacement fields shows that the presence of the pericellular capsule influenced the discontinuity of the normal strain in the axial direction at the interface between the chondron and the surrounding matrix (Fig 1). The prediction of the ratio between cell height decrease (H_c) and local tissue strain (E_t) is more accurate when considering the capsule (Figure 2) compared to the case when the capsule is neglected, which causes an overestimation of, the predicted cell height decrease and the ratio H_c/E_t observed in experiments (Fig 2).

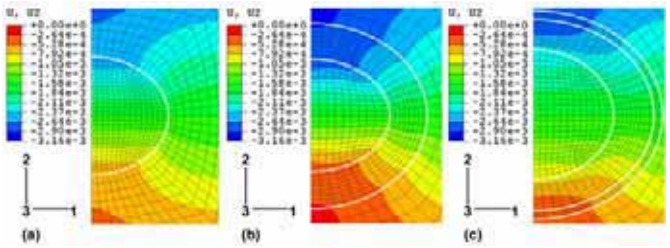

Figure 1. Comparison of the axial displacement around cell inclusions; (a) cell and ECM model (b) cell, PCM and ECM model (c) cell, PCM, PC, and ECM model.

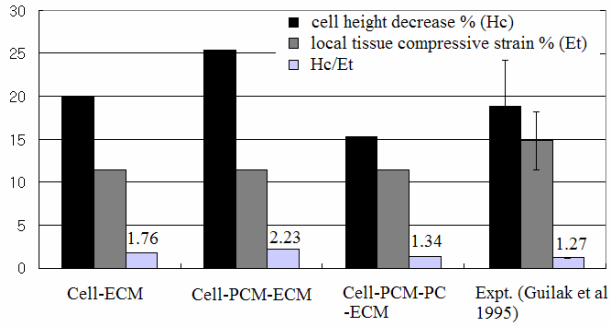

Figure 2. Comparison of cell height decrease, local tissue compressive strain, and the ratio between the two for different cell inclusion configurations.

DISCUSSION

The present analysis demonstrated that the pericellular microenvironment might explain why cells deform much less than expected during articular cartilage loading. In further studies, cell modelling should be extended to the superficial and the deep zones, where cells are no longer spherical (i.e., they are flattened and elongated, respectively). Another improvement of the current model might be achieved by incorporating the osmotic and biochemical environments.

REFERENCES

[1] Guilak, F. et al., 1995. *J. Orthop. Res. 13, 410-421*. [2] Poole, C.A. et al 1987 *J. Orthop. Res* 5, 509-522. [3] Guilak, F., Mow, V.C. 2000 *J. Biomech.* 33, 1663-1673. [4] Wu, J.Z., Herzog, W. 2000 *Ann. Biomed. Eng.* 28, 318-330. [5] Federico, S. et al. 2005 *J. Biomech.,* in press. [6] Shin, D., Athanasiou. K. A. 1997 *Trans. Orthop. Res. Soc*. 22:1: 352. [7] Alexopoulos et al. 2003 *J. Biomech. Eng*, 125, 323-333.

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