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IMPORTANCE OF SPLIT-LINES OF CARTILAGE AND COLLAGEN FIBRILS IN THE PERICELLULAR MATRIX ON CELL DEFORMATIONS IN A KNEE JOINT

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INTRODUCTION

Collagen fibrils have been shown to control articular cartilage response under impact loading of a joint [1]. The superficial collagen fibril (*i.e.* split-line) patterns of intact cartilage directly alter tissue strains [2]. Thus, split-lines should also have a direct influence on chondrocyte deformation within the tissue [3]. The pericellular matrix (PCM) surrounding the chondrocyte is thought to protect cells under impact loading of cartilage [4]. Moreover, the collagen fibrils in the PCM have been suggested to modulate cell strains [3]. Recently, a knee joint model with depth-dependent collagen fibril orientations and split-lines was presented [2]. However, to date, coupling of the joint level loading, depth-dependent mechanical properties of the extracellular matrix (ECM) and PCM, and consequent strains and stresses at the tissue and cell level has remained largely elusive.

The objectives of the study were to investigate the importance of the split-line patterns of the ECM and the collagen fibrils in the PCM on cell morphology, strains and stresses in a human knee joint. For this purpose, a fibril reinforced poroviscoelastic material incorporating depth-dependent fibril orientations and split-line patterns was first implemented in a three-dimensional geometry of cartilage. More detailed tissue and cell level submodels were then run by the joint level model, and chondrocyte and PCM strains and stresses were analyzed in the models with and without the collagen fibrils in the PCM. The presented model can show how the collagen fibrils in the ECM and PCM modulate the mechanical signals sensed by chondrocytes, which are important for cartilage mechanotransduction.

METHODS

A knee joint of a healthy male was imaged with magnetic resonance imaging (MRI). Cartilage and meniscus tissues were segmented and meshed for the finite element analysis (Figure 1). Fibril reinforced poroviscoelastic material properties were implemented for cartilage, while menisci were considered as transversely isotropic [2]. The knee joint was loaded by an axial force of 1 kN, simulating impact loading.

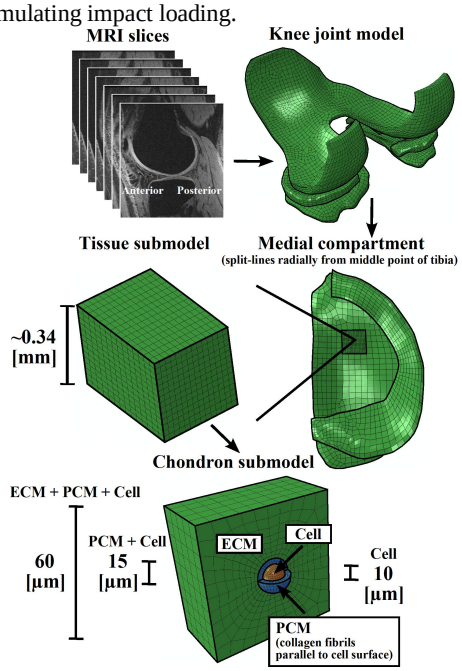

Figure 1: A knee joint model was created from MR images. A tissue submodel was implemented in the region of interest and it was driven by the joint model output. A chondron submodel was further created and its boundary conditions were obtained from the tissue submodel.

A tissue level submodel was created in the contact area in medial tibial cartilage (Figure 1). The model was driven by the boundary conditions (displacements, pore pressures) obtained from the global joint model. A chondron submodel was further created including a cell and PCM (Figure 1). In the tissue and chondron submodels, the properties of the ECM were captured directly from the global joint model in that region. The cell material properties were assumed to be isotropic and poroelastic, while the PCM was modeled as a fibril reinforced poroviscoelastic material with fibrils oriented parallel to the cell surface [3]. The PCM was also modeled without fibrils. The material parameters for the cell and PCM were obtained from the literature [3]. Cell and PCM strains, stresses and pore pressures were analyzed in the models with and without the collagen fibrils in the PCM, and the importance of the split-lines on cell morphology was analyzed. The values of the parameters were analyzed from the node points of the mid-PCM in x-, y- and z-directions, as well as from the adjacent nodes in the cell.

RESULTS

Cell morphology was dependent on the direction of the split-lines, and strains and stresses of cells were greater perpendicular than parallel to the split-line directions (Figure 2, middle; Table 1). The cell elongated substantially more, particularly perpendicular to the split-line direction, than it compressed in the axial direction (Table 1). This trend was also observed in the direction-dependent stress values. The pore pressure distribution in the cell was inhomogeneous, but in contrast to strains and stresses, the highest pore pressure values were seen along the split-line direction (Figure 2, bottom; Table 1).

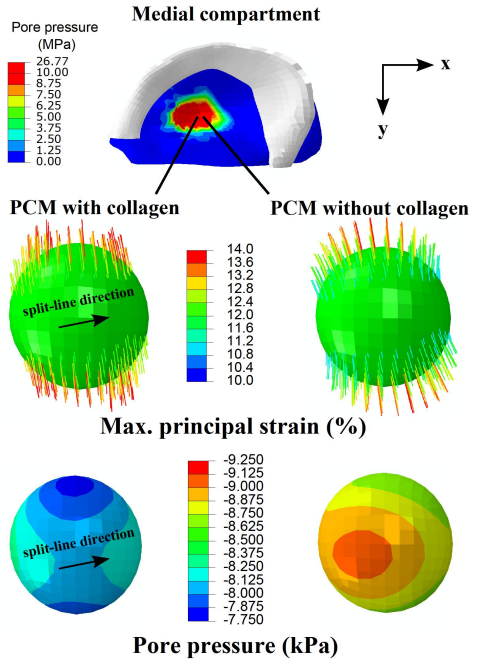

Figure 2: Maximum principal strain and pore pressure in the cell. Importance of the split-lines and PCM collagen fibrils is evident.

The cell elongated more in the model with the collagen fibrils present in the PCM, especially perpendicular to the split-lines (Table 1). The fibrils in the PCM produced more of an inhomogeneous strain distribution in the PCM with both compression and tension in the x-y plane. Stresses in the cell and especially in the PCM were greater in the model with the collagen fibrils in the PCM, while pore pressures were greater without the fibrils in the PCM.

DISCUSSION

For the first time, two-stage multiscale modeling was applied to investigate the importance of the split-line orientations of the collagen fibrils in the ECM and circumferentially oriented fibrils in the PCM on chondrocyte strains and stresses. Consistent with an earlier tissue level study [2], cell deformations were minimized along the split-line direction of the collagen fibrils. On the other hand, the fluid pressure distribution within the cell was inhomogeneous and maximized along the split-line direction. Direction-dependent changes in these parameters were due to the fact that cartilage is stiffer along the split-line direction, effectively preventing both tissue and cell expansion while simultaneously amplifying fluid pressure in the same direction.

Similarly as in a previous *in vitro* model simulation [3], the cell elongated more in the model with the collagen fibrils in the PCM. Perpendicular to the split-lines, the fibrillar PCM pulled the cell more effectively, as was indicated by almost a negligible PCM strain coupled with a substantial cell strain in that direction. On the other hand, the ECM was very stiff in the direction parallel to the split-lines, preventing the PCM from expanding. Thus, the collagen fibril tension in the PCM caused compressive deformations in some locations of the PCM along the ECM split-lines, having also a subsequent effect on cell morphology in that direction. Interestingly, the collagen fibrils in the PCM reduced the fluid pressure in the cell, indicating a possible protective mechanism for the cell [4].

In conclusion, the multiscale model showed that the split-line patterns of cartilage and the collagen fibrils in the PCM modulate cell strains and stresses in a human knee joint under impact loading. Therefore, the current modeling approach could be used in the future to assess cartilage mechanobiology and cell viability of a patient.

Table 1: Direction-dependent changes in cell morphology and volume, and local pore pressures, logarithmic strains and stresses in chondron submodels with and without the collagen fibrils in the PCM.

Parameter	Chondron with PCM collagen		Chondron without PCM collagen	
	Cell	PCM	Cell	PCM
Change in height - z (%)	6.3	8.9	6.1	7.9
Change in width - x (%)	7.0	-2.2	6.6	0.3
Change in depth - y (%)	13.1	1.2	11.6	4.4
Change in volume (%)	12	2.0	12	4.0
Strain z (%)	4.4	9.1	4.7	7.9
Strain x (%)	7.3	-2.4	8.2	0.3
Strain y (%)	14.3	1.1	12.9	4.2
Stress z (kPa)	0.57	27.8	0.64	2.35
Stress x (kPa)	2.35	62.1	2.23	3.82
Stress y (kPa)	3.13	31.4	2.90	4.72
Pore pressure z (kPa)	-8.5	-7.7	-9.6	-8.4
Pore pressure x (kPa)	-8.7	-7.9	-9.4	-8.3
Pore pressure y (kPa)	-8.4	-7.6	-9.3	-8.2

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REFERENCES

[1] Shirazi, R et al., *J Biomech*, 41:3340-3348, 2008.
[2] Mononen, ME et al., *J Biomech*, 45:579-587, 2012.
[3] Julkunen, P et al., *Med Biol Eng Comput*, 47:1281-1290, 2009.
[4] Guilak, F et al., *Ann N Y Acad Sci*, 1068:498-512, 2006.