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A composition-based intervertebral disc model to study the effects of extracellular matrix degenerative changes on nutrition

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Introduction

Altered nutrition in the intervertebral disc (IVD) affects cell viability and can generate catabolic cascades that contribute to extracellular matrix (ECM) degradation [1]. Such degradation is expected to affect couplings between disc mechanics and nutrition, possibly contributing to accelerate the degenerative processes. However, the relevance of this hint may depend upon the relation of ECM changes to major biophysical events; e.g. cell nutrition and viability [2], within the mechanically loaded disc, which remains unclear. Thus, this study aims to use composition-based IVD mechanical and transport models to evaluate the influence of disc biochemical composition on nutrition and cell viability.

Materials and Methods

A L4-L5 poro-hyperelastic finite element (FE) model including the nucleus (NP), the annulus (AF), a transition zone (TZ) and the endplates (CEP and BEP) was used (Fig.1) [3]. The Donnan-osmotic pressure was simulated (Eq. 1, 2 and 3) and coupled to a transport and cell viability model [4,5].

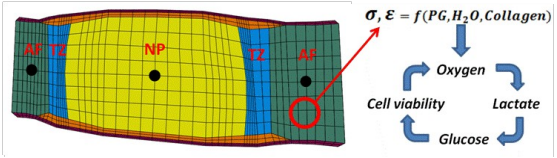

Fig. 1: Composition-based IVD model

$$\Delta\pi = \phi_{int} RT \sqrt{c_{F,exf}^2 + 4\left(\frac{\gamma_{ext}^{\pm}}{\gamma_{int}^{\pm}}\right)^2 c_{ext}^2} - 2\phi_{ext} RT c_{ext} \quad \text{Eq. 1}$$

$$c_{F,exf} = \frac{n_f c_F}{n_{exf}} \quad \text{Eq. 2} \qquad n_{exf} = n_f - \varphi_{ci}\rho_{c,tot} \quad \text{Eq. 3}$$

A cycle of 8 hours of night rest under 150 N compression followed by 16 hours of diurnal activity under 800 N compression was repeated to simulate three days of activity. External pressure was nil. Oxygen, lactate and glucose concentrations were applied at the outer surface of the CEP and at the outer AF. Solute concentrations and cell viability were evaluated along a mid sagittal plane path (Fig.1). A design of experiment (DOE) was performed, using a fractional factorial statistical method. Parameter variations were based on a previous association between IVD Pfirrmann degeneration grades, i.e. I (high level) and III (low level), and AF and NP composition, i.e. initial water content (n_{F0}), initial fixed charge density (c_{F0}) and collagen content (Coll).

Results and discussion

In all cases cell, viability was not affected by any of the parameter combinations defined for the DOE. Nonetheless, the ANOVA revealed that the initial water content was the tissue parameter that affected the most the solute contents, especially glucose content at the anterior AF. Importantly, all solute concentrations decreased when degenerate tissue properties were simulated, and reduced nutrition is known to trigger inflammatory and catabolic responses by disc cells [6]. The ANOVA results also showed that beside water content, altered proteoglycan (c_{F0}) or collagen (Coll) composition within the NP could affect the nutrition of the AF (Fig 2a.). In such a case, the cumulated effects of water and proteoglycan reductions in the NP had a major impact on the posterior AF (Fig. 2b), an important structure that often disrupts along disc degeneration.

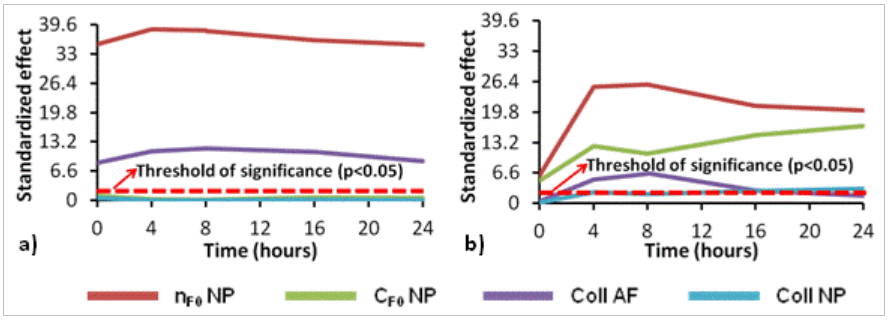

Fig. 2: Standardized effect of composition parameter variations on glucose concentrations for one simulated day, in the AF a) anterior and b) posterior

Conclusions

This study showed that the AF and NP tissue degeneration may not be critical to IVD cell viability but may alter significantly the distribution of nutrients, with early ECM changes. The results give an idea of the propagation of disc degenerative changes: the NP degeneration affects AF nutrition through increased consolidation, exposing particularly the posterior AF. Such a propagation sequence is expected to be important to consider in regenerative medicine.

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