Simulation and Prediction of Human Intervertebral Disc Degeneration and Repair
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**Introduction:** Degenerative intervertebral disc (IVD) disease is related to low back pain which affects more than 500 million people worldwide. Understanding degenerative processes in human IVD is challenging, due mainly to the complicated interactions among biological, chemical, electrical, and mechanical signals. Simulation and characterization of these signals are crucial for developing effective treatment strategies for degenerated discs. Thus, the objective of this study was to develop a novel multi-physics model for human IVD for simulating and predicting disc degeneration and repair.

**Materials and Methods:** A 3D finite element model for IVDs was developed based on a recently developed, cell-activity-coupled mechano-electrochemical mixture theory. In this model, the disc was considered as an inhomogeneous, porous, mixture consisting of a charged solid phase (with cells), an interstitial fluid phase, and a solute phase (with multiple species of solutes, e.g., Na⁺, Cl⁻, glucose, oxygen, and lactate). The governing equations were cast in terms of solid matrix displacement, cell density, and (electro)chemical potentials of the constituents. The material properties, such as tissue fixed charge density, hydraulic permeability, solute diffusivities were nonlinearly coupled with tissue deformation (or tissue hydration), and cell metabolism and viability were nonlinearly related to nutrient levels in the disc. The degenerative disc disease caused by poor nutrition supply was simulated. The repair of degenerated discs with biological therapies was also investigated.

**Results and Discussion:** Changes in cell density, oxygen concentration, glucose concentration, swelling pressure, glycosaminoglycan (GAG) content, water content, mechanical stress and strain, and disc height during tissue degeneration (up to 55 years) process were simulated. It was predicted that the progression of human IVD degeneration was in general very slow. The model was validated by comparing model predictions on GAG and water distributions in the disc to the experimental results in human IVDs reported in the literature. The predicted water content distributions in the disc were also consistent with T2-weighted MRI images of human IVDs.

This model can be used not only for predicting the progression of degenerative disc disease, but also for conducting in-silico clinical trials on disc repair using biological therapies with increased cell number (e.g., cell implantation), increased matrix anabolic process (e.g., growth factor treatment), or decreased catabolic process. The cell number needed for implantation, the nutrition level needed for survival of implanted cells, timing for treatment, and long-term outcomes of the therapies were investigated with the model. For example, the relationship between cell number and the time needed for degenerated disc to recover its original height was obtained.

The findings from this study provide new insights into nonlinear interactions among biological, chemical, electrical, and mechanical events in the disc during its degenerative or repairing progression. This model can be used to develop new strategies for treating degenerative disc disease and to evaluate the long-term efficacy of therapeutic strategies.

**Translational Impact:** This computational model may be used as a medical device for assisting clinicians to identify disc degeneration and to determine the optimal treatment options. It can also be used to screen drugs for disc repair in-silico, significantly reducing healthcare system cost.

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