INTRODUCTION: Understanding the mechanism which leads to low back pain is a critical step to developing novel preventative strategies and therapeutic interventions that target this debilitating disease. Epidemiologic data indicate a strong correlation between incidence of low back pain and repeated mechanical loading of the spine. Low back pain also correlates with degeneration of the intervertebral disc and with sclerotic changes to the subchondral bone and vertebral endplates. While the exact mechanism remains unknown, one of the two general theories by which mechanical loading leads to painful intervertebral disc degeneration is via changes in diffusion of small molecules to the disc through the vertebral endplates, particularly in the region of the central nucleus. If the endplates and subchondral bone respond to the mechanical stimuli and become sclerotic, this can impede diffusion to and from the disc, subsequently creating ischemia and hypoxia. This results in catabolic activity that ultimately causes destruction of the matrix, loss of proteoglycans, and structural failure of the disc.

There are multiple factors that can affect the diffusion of small molecules to the nucleus including biomechanical loading and deformation, fluid flow, ion transport, and concentration gradient (pure diffusion). The purpose of this study was to develop a simplified 2D finite element model to systematically characterize which of the parameters are most significant to determining small molecule diffusion to the central portion of the nucleus.

METHODS: A 2D diffusion model of the intervertebral disc with adjacent endplates and vertebral bodies was developed in COMSOL. Multiphysics. Geometric and physical properties were systematically varied over physiologically relevant ranges taken from the literature. Maximum and minimum physiological values were simulated for each parameter. The concentration of glucose in the center of the nucleus was calculated for each scenario to determine which parameters had the most significant effect on the distribution of glucose. Concentration was calculated based on a variation of Fick’s law, \( \frac{\partial c}{\partial t} + \nabla \cdot (D \nabla c) = R \), where \( \delta_t \) is a time-scaling coefficient, \( c \) is the nutrient concentration in mol/m³, \( D \) is the diffusion coefficient in m²/s, and \( R \) is the reaction rate (mol/(m²s)).

RESULTS: Glucose concentration was most sensitive to changes in endplate characteristics, including thickness (uniform and nonuniform) and coefficient of diffusion, whereas glucose concentration was relatively insensitive to the equivalent changes in anulus characteristics. The most significant parameters are endplate diffusivity, thickness, and diffusivity from the disc, which indicates that endplate analysis via CT scans shows that thickness is not uniform in most cases. These results indicate that accurate endplate geometry is an important parameter in predicting diffusion to the intervertebral disc and the simplifying assumption of uniform endplate geometry may introduce artifacts.

FIGURE 2. Glucose concentration profiles were different for nonuniform endplate thickness (left) and uniform endplate thickness (right). Color indicates glucose concentration, red to blue is high to low. EP, endplate. IVD, intervertebral disc.

DISCUSSION: In this study, we compared several parameters previously established as factors regulating small molecule diffusion into the intervertebral disc, including physical properties of the vertebral endplates, nucleus pulposus, and anulus fibrosis. Of all parameters in this study, endplate thickness and diffusivity were the most significant with non-uniform endplate geometry resulting in characteristically different diffusion rates relative to uniform geometry.

This is the first study to investigate nutrient diffusion through a 2D model with non-uniform endplate thickness. This is clinically relevant in that endplate analysis via CT scans shows that thickness is not uniform in most cases. These results indicate that accurate endplate geometry is an important parameter in predicting diffusion to the intervertebral disc and the simplifying assumption of uniform endplate geometry may introduce artifacts.

Results from this study indicate that glucose diffusion is sensitive to endplate thickness and differences in superior and inferior endplate geometry. These parameters can be controlled in the current model but cannot be varied in 2D axisymmetric models or models symmetric about the transverse axial plane. For more computational-intensive 3D models, endplate geometry is critical factor for accurate prediction of small molecule diffusion. Simplifying assumptions related to the geometry of the endplates should be minimized to maintain high accuracy in these models. It is important to consider that endplate geometry is non-uniform and the superior and inferior endplates of the same disc do not necessarily have the same thickness. Future model refinement will involve further assessment of the key parameters using more sophisticated models of diffusion and patient-specific geometry.

REFERENCES: