

Effect of Mechanical Loading and Endplate Calcification on the Distribution of Glucose in Intervertebral Disc

¹Jackson, A R; ²Huang, C-Y; ¹Gu, W Y

¹Tissue Biomechanics Lab, Univ. of Miami, Coral Gables, FL; ²Stem Cell and Mechanobiology Lab, Univ. of Miami, Coral Gables, FL

Introduction: Because the intervertebral disc (IVD) is the largest avascular structure in the body, important nutrients, such as oxygen and glucose, must be transported to cells from surrounding vasculature. Inadequate nutrient supply is believed to be a primary cause of disc degeneration. However, due to difficulty in measuring nutrient concentrations in IVD *in vivo*, theoretical modeling must be used to supplement experimental results for better understanding of nutritional transport in IVD. The objective of this study was to develop a 3D finite element model of the IVD. Using this model, we investigated the effects of *in vivo* loading conditions and endplate calcification on glucose concentrations in the disc.

Methods: Theoretical Model: A mechano-electrochemical mixture model [1] was used in this study. The IVD was assumed to consist of three major components: solid matrix, fluid (water), and solutes [oxygen (O_2), glucose, lactate, Na^+ , and Cl^-]. Nutrient transport in the disc was coupled to cellular metabolism. Rates of nutrient consumption and lactate production were based on previous studies [2,3].

Finite Element Analysis: Here, we consider a 3D geometry based on that of an L2-L3 disc (Grade I) harvested from a human lumbar spine (41 y.o. M). The IVD was modeled as an inhomogeneous tissue with three distinct regions: annulus fibrosus (AF), nucleus pulposus (NP) and cartilaginous endplate (CEP). The CEP was considered as impermeable above the AF, and as a permeable cartilaginous tissue above the NP. Due to symmetry, only the upper quadrant of the disc was modeled. Tissue properties and nutrients concentrations at tissue boundaries were taken from literature [2,4-6].

The IVD was subjected to *in vivo* loading conditions associated with transition from lying to standing positions; the disc was 19% in tension in the anterior region, and 16% in compression in the posterior region in the standing position [7]. Discs were then subjected to a 10% static compressive load in the standing position, to simulate weight-bearing.

The effect of CEP calcification was also examined, as the endplate is known to become calcified during degeneration. CEP calcification was simulated by reducing the tissue porosity (i.e., water content). A comparison of glucose concentration profiles in the disc with CEP with a porosity of 0.6 (normal) and 0.42 (30% reduction) were investigated.

Results: While the model developed can simultaneously determine stress and strain distributions and solute (Na^+ , Cl^- , O_2 , glucose, lactate) concentrations in IVD tissue, only glucose concentrations are reported here. Typical glucose profiles for IVD in unloaded state for normal and calcified CEP conditions are shown in Fig. 1. There was a ~3% reduction in the minimum glucose concentration in the disc with CEP calcification. Furthermore, CEP calcification more strongly affected glucose concentrations in the NP, which had an 11.2% decrease in the averaged glucose concentration, compared with a 0.7% decrease in the AF. The application of *in vivo* conditions for standing resulted in a marginal (~2%) decrease in the minimum glucose concentration in the disc for both CEP conditions, as compared to supine position (see Fig. 2). This also led to an increase in glucose concentration in the anterior disc, while there was a decrease in the posterior (see Fig. 2). Applying a 10% static

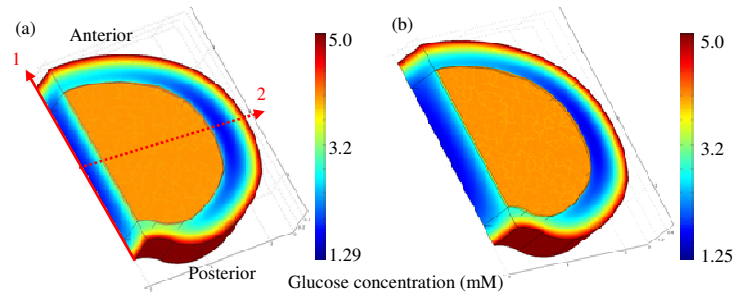


Figure 1: 3D glucose concentration profile for (a) normal and (b) calcified endplate in unloaded state.

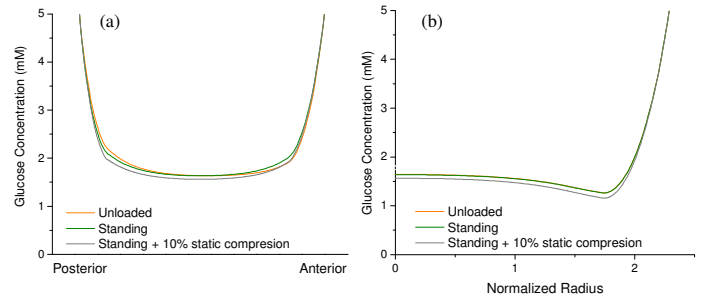


Figure 2: Effect of loading on glucose concentration profile through middle of disc (a) posterior to anterior (line 1 in Fig. 1a) and (b) along disc radius (line 2 in Fig. 1a) for IVD with normal (uncalcified) CEP.

compressive load to the standing conditions led to a further ~9% decrease in minimum glucose concentrations for both normal and calcified conditions as compared to standing conditions for each case.

Discussion: This study demonstrated that CEP calcification may lead to decreased glucose levels in the disc. From Fig. 1, an overall decrease in the glucose in the disc, signified by a larger area of dark blue (low concentrations), is apparent. This supports the hypothesis that CEP calcification leads to reduced nutritional supply to the disc cells.

Furthermore, this study also showed that transition from lying to standing does not cause a large decrease in minimum glucose concentrations in the disc; however, this transition does alter the glucose concentration profile, with an increase in concentration anteriorly and a decrease posteriorly, see Fig 2a. This is because the disc is in tension in the anterior portion, but in compression in the posterior. Tension results in increased water content and glucose diffusivity in this region, while compression has the opposite effect. This may have clinical implications, as most disc herniations occur in the posterolateral region [8]. That is, poor nutritional supply to cells in the posterior disc during standing may lead to regional degeneration of the tissue, giving rise to disc herniation.

Finally, this study demonstrated that the application of compressive strain in the standing position leads to a reduction of the glucose concentrations in the disc, whether the endplate is normal or calcified. This is expected because compressive strain results in reduced tissue water content and nutrient diffusivity, as mentioned previously.

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References: [1] Lai et al, *J Biomech Eng* 113:245-58; [2] Huang & Gu, *J Biomech* 41:1184-96, 2008; [3] Bibby et al, *Spine* 30:487-96, 2005; [4] Huang et al., *Spine* 32:2063-9, 2007; [5] Yao & Gu, *J. Biomech* 40:2071-7, 2007; [6] Soukane et al, *Euro Spine J* 18:254-62, 2008; [7] Wang et al., *J Biomech* 42:705-11, 2009; [8] Martin et al, *Neurosurg Focus* 13(2): E1, 2002.