INTRODUCTION: Intervertebral disc is the largest avascular tissue in the human body. The disc extracellular matrix is made and maintained by disc cells indicating the importance of cells for disc health. Disc cells, like in other tissues, consume oxygen and glucose to provide energy primarily by glycolysis; breakdown of glucose to produce lactic acid. Disruption in transport of these nutrients and metabolites into and out of the disc could trigger or accelerate disc degeneration as under low oxygen or pH cell metabolism and viability are adversely affected [1,2]. Since these small solutes move through the disc matrix mainly by diffusion [3], concentration gradients develop depending on the balance between the rate of transport through the matrix and cellular activity. Concentration gradients of these species throughout the disc tissue cannot develop independently as their consumptions (oxygen and glucose) or production (lactate) are coupled; for instance pH affects rates of both glucose consumption and lactate production [4]. The present novel numerical study aimed to evaluate the concentrations of oxygen, glucose and lactate in the disc while accounting for the coupling between these species via the pH level in the tissue and the nonlinear concentration-consumption (for glucose and oxygen) and concentration-production (for lactate) relations. The effects of changes in the endplate exchange area (EA) for the transport of nutrients and in the disc geometry as well as tissue diffusivities under mechanical loading on species concentrations were also investigated.

METHODS: To model a human lumbar intervertebral disc, an axisymmetric geometry (height of 11 mm and maximum radius of 21.8mm) with three distinct regions (nucleus, inner annulus and outer annulus) was considered. The two distinct nonlinear partial differential equations governing the diffusion of oxygen and lactate were coupled via the tissue pH which in turn varied depending on the lactate concentration in the tissue. Consumption/production rates of species were evaluated based on the cell density in each region, being largest in the outer anulus and smallest in the nucleus [5]. The ratio between lactate production and glucose consumption was taken as 2.0 throughout the tissue. The effects of changes in the endplate exchange area (EA) for the transport of nutrients and in the disc geometry as well as tissue diffusivities under mechanical loading on species concentrations were also investigated.

RESULTS: Oxygen and glucose concentrations decreased with distance from supply sources via the central areas of end-plates and outer annulus periphery, falling respectively to minimums of 0.71 kPa and 1.5 nmol/mm³ at the disc center in an unloaded disc with EA=50% (Fig. 1). Inversely, the lactic acid concentration was lower at the source supply regions and highest at the disc center reaching a maximum of 4.8 nmol/mm³. The computed pH in the disc ranged from pH 7.0 to pH 7.3. Solute concentrations were substantially influenced by changes in the end-plate exchange area (EA: 5, 10, 25, 50 and 100%) and mechanical loading (under ~1000N axial compression for 2-8 h) on the species concentrations were also investigated. The influence of compression loading on nutrient concentrations was introduced by alterations in the disc geometry as well as tissue diffusivities associated with accompanying fluid loss.

DISCUSSION: It is recognized that any nutrition deficiency disrupts the normal function of disc cells. An insufficient nutrient supply is associated with a lowered oxygen tension/glucose concentration and acidic pH levels (due to raised lactic acid concentrations). It could adversely affect the ability of disc cells to synthesize and maintain the disc’s extracellular matrix, threaten their viability and ultimately lead to disc degeneration [1,2]. In this numerical study, the concentrations of oxygen, glucose and lactate were evaluated in the disc, taking into account the coupling between these species via the pH level in the tissue using recent measurements [4]. The cartilaginous endplate undergoes calcification with aging and disruption in presence of end-plate fractures leading to marked changes in the exchange area at the end-plate as the major pathway for the disc nutrition [6]. The non-linear dependence of species concentrations on end-plate EA reveals its importance and points to a critical threshold below which the disc nutrition may significantly be disrupted. The mechanical loading of the disc appears to have opposing effects on the disc nutrition; on one hand it decreases the disc height which facilitates the transport of nutrients from the end-plates to the disc centre where the nutrients reach their minimum, but on the other it decreases the fluid content that reduces solute diffusivities and, hence, solute transport. The former effect was found to be predominant resulting in an improved solute transport especially in the nucleus region. The solute concentrations (especially for the glucose), however, slightly fell at the anulus-nucleus boundary far away from the sources of supply as compression loading was considered.

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NONLINEAR COUPLED DIFFUSION OF GLUCOSE, OXYGEN AND LACTIC ACID IN THE HUMAN INTERVERTEBRAL DISC

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