ALTERATIONS IN ENDPLATES MARKEDLY INFLUENCE THE NUTRITION OF INTERVERTEBRAL DISCS

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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 nutrition is mainly dependent on the diffusion of nutrients through the central part of cartilaginous endplates, CEP, via a dense hyaline cartilage. Injuries and/or calcification of CEP have been indicated to cause disc degeneration likely by perturbing the transport of nutrients into and their by-products out of the disc [1-3]. Since small solutes move through the disc matrix mainly by diffusion, concentration gradients develop depending on the balance between the rate of transport and cellular activity. These concentration gradients cannot develop independently as their consumptions (oxygen and glucose) and production (lactate) are coupled; for instance pH affects rates of both oxygen consumption and lactic acid production [4]. The present computational study aims to evaluate the nonlinear (concentration versus consumption or production) coupled (via pH level) concentrations of oxygen, glucose and lactate in the disc as the transport via the CEP is perturbed. This is done by either varying the endplate exchange area (via diffusivity) or simulating a central endplate fracture (Schmorl's node).

METHODS: An axisymmetric geometry with four distinct regions (CEP, nucleus, inner and outer anulus) with different properties was used to model a lumbar intervertebral disc (Fig. 1). The 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. 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. The ratio between lactate production and glucose consumption was taken as 2.0 based on measurements [4]. An in-house nonlinear finite element code was developed to solve the coupled nonlinear equations employing a pseudo transient approach with a backward integration scheme. Supply sources were applied at the outer anulus periphery and central CEP adjacent to the nucleus. The effects of changes in the endplate calcification or exchange area (simulated by varying CEP diffusivity) and a central endplate fracture (no transport at a 4mm radius zone) on the species concentrations were investigated.

RESULTS: Oxygen and glucose concentrations decreased with distance from supply sources at the CEP and outer anulus periphery, falling respectively to minimums of 0.5 kPa and 1.2 nmol/mm^3 at the disc mid-height close to the nucleus-anulus boundary. Inversely, the lactic acid concentration was lower at source supply regions and highest at the disc mid-height reaching maximum of 5.3 nmol/mm^3. Solute concentrations were substantially influenced by changes in the endplate exchange area demonstrating a nonlinear relationship with the oxygen critical concentration in the disc mid-height falling rapidly for relative diffusivities <~20% (Fig. 2). This nonlinearity was even more pronounced for glucose as it fell rapidly at relative diffusivities <~50%. A reverse trend was noted for the lactic acid. As the exchange area (i.e., CEP diffusivity) decreased, the location of critical zone (minimum concentrations for glucose and oxygen but maximum for lactate) shifted away from the nucleus-anulus boundary towards nucleus centre (Fig. 3). Presence of a central CEP fracture influenced concentrations especially at disc centre (Fig. 4 for glucose).

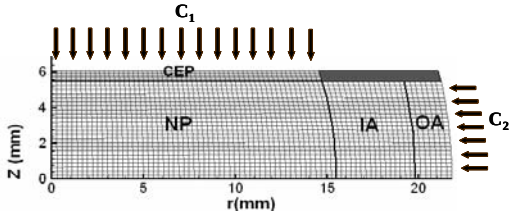
DISCUSSION: Nutritional deficiency associated with lowered oxygen/glucose concentrations and acidic pH levels (due to raised lactic acid concentrations) could adversely affect the ability of disc cells to synthesize and maintain the disc's extracellular matrix. It would hence threaten cells viability leading ultimately to disc degeneration [1,3].

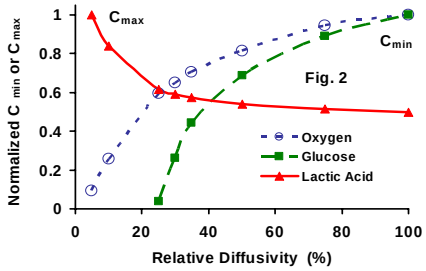
The CEP undergoes calcification with aging and disruptions under mechanical loads, events that significantly affects the exchange area at the endplates recognized as the major pathway for the disc nutrition. The non-linear dependence of species concentrations on endplate exchange area points to a critical threshold below which the disc nutrition may be disrupted significantly, thus supporting the hypothesis that CEP calcification may deprive the cells of crucial nutrients and lead to disc degeneration [1-3]. The oxygen concentration drops dramatically once diffusivity (CEP permeability) falls below ~20% whereas in contrast the lactic acid concentration markedly increases. For glucose, such event occurs earlier when diffusivity drops below 40%. The glucose and not the oxygen appears, hence, to be the limiting nutrient for the survival of disc cells [5]. Results also indicate that such disruptions in nutrient supply shifts the location of critical zones (with minimum nutrients) away from the nucleus/anulus boundary towards the disc center (Fig. 3).

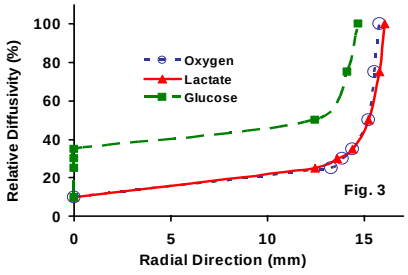
In vitro studies on spinal motion-segments indicate that in normal discs the central bony endplates are the most vulnerable structures to fracture under axial compression [6]. Endplate fractures (Schmorl's node) have frequently been observed in all age groups [7]. Discs with such fractures also tend to exhibit advanced degenerative changes. In conjunction with reported mechanical consequences of such fractures along with loss of disc material into adjacent vertebrae (vertical prolapse) [7,8], the current study suggests that endplate disruptions also markedly interfere with the transport of disc nutrients to cells away from the supply sources. Combination of mechanical and nutritional parameters could, hence, be responsible for the pathogenesis of disc degeneration in presence of disruptions in the CEP.

ACKNOWLEDGEMENT: Work is supported by the NSERC-Canada and Arthritis Research Campaign-UK.

Fig. 1







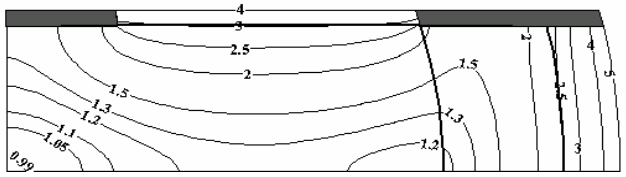


Fig. 4 Glucose Concentration (nmol/mm^3)

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