# Penetration of Solutes into the Intervertebral Disc after Intravenous Injection

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## INTRODUCTION

In the intervertebral disc, the largest avascular structure in the body, diffusion plays a crucial role governing the transport of nutrients, metabolic wastes, drugs, antibiotics and various tracers between the blood vessels outside the disc and the tissue/cells throughout the disc. The significance of the transport routes from endplates and annulus periphery on nutrient transport in relation to cell function and disc degeneration has been recognized [1]. In addition, there is now an increasing interest in delivery of solutes via blood to the disc, following intravenous injection. For effective therapeutic action, pharmaceutical agents and antibiotics must reach throughout the disc at minimum necessary concentration levels; albeit conditions governing successful intravenous delivery remain as yet unknown. *In vivo* measurements have however confirmed very low concentration levels at disc centre following intravenous administration [2, 3]. Another area of interest is the delivery of imaging contrast agents to the disc as a diagnostic tool to differentiate healthy from degenerate discs [4].

In this study and in continuation of our earlier works, the penetration time-history of sulphate particles from blood supply at the endplates and annulus periphery during post intravenous injection period is investigated by a transient finite element study. The model closely simulates in vivo measurements on sulphate concentrations in discs of adult dogs following injection into blood [3]. The effect of endplate calcification seen in aging, scoliosis, and degenerate discs [5] on sulphate concentration profiles is also investigated. It is hypothesized that the concentration levels at disc centre are low at all times compared to those in the blood and that they further fall as endplates calcify.

## METHOD

An axisymmetric model of an adult dog lumbar disc is developed and used to simulate the in vivo measurements of sulphate penetration profiles in dogs at different times after initial intravenous administration [3]. With the diameter and height of 19.5 mm and 4.5 mm, respectively, the disc is divided into 3 regions (nucleus, inner/outer annuli) with distinct properties. The continuity equation and Fick's law yield the Poisson's equation governing the transient diffusion while accounting also for the incorporation of sulphate [3]. The finite element mesh is made of ~6000 bilinear quadrilateral elements. The blood-disc partition coefficient $K_L$ at the source boundaries is 0.25 above the nucleus, 0.42 above the inner annulus and 0.88 at the annulus periphery [3] while the endplate above the outer annulus is impermeable. The tissue diffusivity is taken as 0.011 $cm^2$/hr in the nucleus and 0.010 $cm^2$/hr in the annulus [3]. The source temporal profile at the disc external boundaries in contact with blood vessels follows, based on measurements, the relation $m = m_o K_L e^{\lambda t}$ where $m_o$ is the initial (t = 0) sulphate concentration in plasma in counts/g plasma and $\lambda$ = -0.246 /hr is the decay constant [3]. Concentration profiles are normalised to $m_o$ as done in measurements to compare results between dogs [3]. Analyses are carried out up to 6 hours post injection in accordance with measurements.

The endplate permeabilities of 0.82 above the nucleus and 0.35 above the inner annulus that were estimated via flux calculations with foregoing partition coefficients [3] are used in this study for the reference model. To investigate the effect of endplate blockage on concentration profile histories, these values are then either increased to 1 to simulate fully permeable endplates or reduced by 50% or 75% to simulate calcification and degeneration. The commercial finite element program COMSOL is used.

## RESULTS

Simulated sulphate concentrations using experimental parameters were in agreement with measured values (Figs. 1 and 2). They followed blood concentrations at source supply, fell with time at the outer annulus where concentrations were highest and decreased substantially from there to the nucleus where minimum concentrations as low as 5% of that initially in the plasma ($m_o$) were computed. Solute concentrations were markedly influenced by changes in the endplate permeability (Fig. 1). They were highest everywhere in the disc and at all times when the endplate was taken as completely permeable but decreased with the fall in endplate permeability reaching lowest values in the case with 25% permeable endplate. The endplate blockage influenced primarily the concentrations in the nucleus region (Fig. 2).

## DISCUSSION

This work aimed to compute the time-history of the concentration profile in the intervertebral disc following intravenous injection of a small anionic solute. Despite the axisymmetric geometry of the model, predicted profiles were in satisfactory agreement with in vivo measurements recorded up to 6 hours post injection [3]. No attempts were however made to adjust input data to further improve the quality of fit. Results demonstrated a fall in concentrations with time in accordance with concentration decay in blood; concentrations also fell when moving away from the supply source at the outer annulus periphery towards the nucleus whereas not much variation was observed in the nucleus itself. The concentration level in the nucleus relative to that in the blood reached as low as 5% in the reference model and 1% in the case with 25% endplate calcification. These levels would depend, among other parameters, also on the disc size and solute size/charge. Current results explain the reported observation of antibiotics in larger concentrations in the annulus and much lower concentrations in the nucleus [3].

Alterations in the endplate permeability had a profound effect on concentration profiles at all times and specially in the nucleus region, demonstrating its crucial role on the delivery of nutrients, drugs, and injected solutes into the disc as confirmed earlier from simulation [1] and *in vivo* [4] studies. Thus the degeneration state of the intervertebral disc has important implications in the success of drug/antibiotic delivery as their efficacy requires some minimum inhibitory concentration levels. Future expansion of this work is expected to shed light on the diagnostic application of imaging following injection of contrast media (e.g., gadolinium) into blood stream [4].

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**REFERENCES** 1) Shirazi-Adl et al, J Biomech, in press. 2) Walters et al, Spine 31:391, 06. 3) Urban et al, Bioreheology 15:203, 78. 4) Rajasekaran et al, JMRI 25:410, 07. 5) Benneker et al, Spine 30:167, 05.

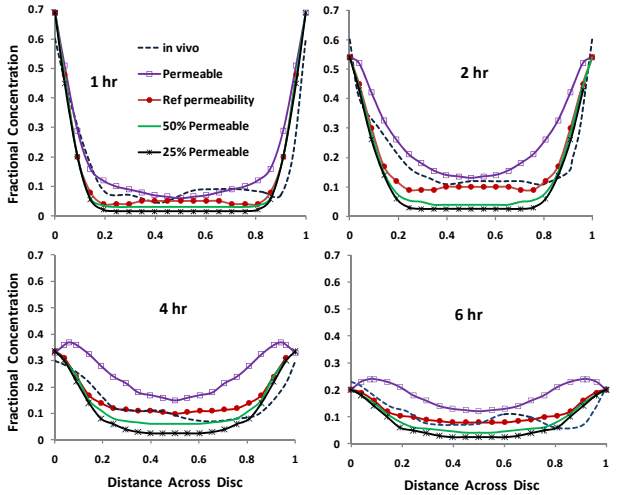


**Fig. 1-** Measured and computed fractional sulphate concentration profiles across the disc mid-height at various times after injection.

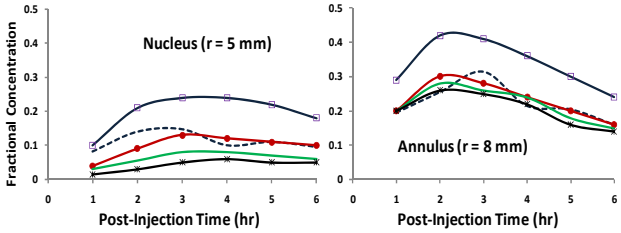


**Fig. 2-** Concentration profiles versus time at disc mid-height locations.