INTRODUCTION:
A loss of nutrient supply has long been thought to be a major factor leading to disc degeneration and recent in vivo measurements have supported this hypothesis. Solute transport from the blood vessels through the endplate into the disc, measured by following gadolinium [1] or nitrous oxide [2] transport, has found that effective endplate permeability falls significantly in degenerate and scoliotic discs [2]. Computations support the importance of loss of nutrient supply by showing that once endplate permeability falls below a critical level, disc cell viability is compromised [3]. Here we give additional information on transport into pathological human discs in vivo. We measured solute transport into herniated human discs during routine surgical procedures. These measurements were then used as a basis for calculations of critical glucose concentrations and hence cell survival in order to determine which discs could be good candidates for cellular repair strategies.

METHODS:
Measurements were carried out with ethical permission, on 21 intervertebral discs of 19 consenting patients undergoing surgical discectomies for treatment of disc herniations and sciatica. Solute concentrations of nitrous oxide (N₂O, a non-metabolised tracer solute administered as an anaesthetic) were monitored electrochemically using a needle microelectrode [2] inserted 15 mm into the disc during surgery prior to removal of the prolapsed tissue. Disc degeneration grade [4] was obtained from MR images. Disc height was estimated from MR and X-Ray images. Concentrations of N₂O in the discs were used to calculate a solute transport parameter (STP), the ratio of the concentration at the measurement point compared to calculated, ‘ideal’ concentration calculated for diffusion with no transport restriction at the disc-bone interface. Calculations were based on measurements of disc height, time of N₂O administration, and estimated tissue hydration by MRI grade for each disc. A mathematical reaction-diffusion model was then used to predict the viable cell density in the centre of each disc taking 0.5mM as the critical glucose concentration for cell survival [3].

RESULTS:
The age range of the 19 patients was 28-70yrs. All discs were L4-5, or L5-S1 levels. The disc ranged in height from 6-12 mm with an average height of 8.83 mm. All discs were degenerate (45% MR grade 3, 45%/grade 4, 10% MR grade 5). We found no correlation between MR grade, patient age and the solute transport parameter STP (data not shown). Measured values of STP in these herniated discs were very variable ranging from 0.05 to 4.31 (Figure 1). In 7 discs, STP was greater than 0.75, indicative of loss of endplate integrity and/or blood vessel ingrowth. In 9 discs STP was ≤ 0.3. Calculations showed that viable cell density in the tissue falls with increasing disc height and a decrease in endplate permeability (Figure 2) in agreement with results in experimental model systems; STP would have to be ≥ 0.4 to sustain the viable cell densities of 5 million/ml reported in human lumbar discs (Figure 3).

DISCUSSION:
From measurement and calculations, we estimate that nutrient transport was at levels to sustain normal cell activity in only around 25% of herniated discs. However we found that there was a considerable variation in the rate of N₂O transport into these herniated discs and that transport efficiency could not be predicted from standard clinical MR images. By comparing measured STP with model calculations it was estimated that in around 40% of the herniated discs, the fall in nutrient supply would have compromised cell survival (discs with STP<0.3). On the other hand, in around 30% of discs, the STP was much greater than possible by diffusion alone indicating some breach of the transport route to the disc such as structural disruption to the endplate or secondary vascularisation; this situation also provides a poor environment for disc cells which are more active at 5-10% oxygen than 21% oxygen and could potentially stimulate the increase in neural ingrowth seen in some degenerate discs. These results suggest that >70% of herniated discs would not be good candidates for cellular repair strategies because of adverse nutrient transport pathways. The results also indicate that standard diagnostic protocols cannot distinguish potentially viable from non-viable discs. Thus some further diagnostic tool (such as further development of Gd influx measured by MRI or of microelectrode technology) is urgently required if cell therapies for stimulating disc repair are to become a routine clinical treatment.

REFERENCES