Introduction
Dynamic loading is essential for maintaining intervertebral disc health since a major nutritional mechanism is load-induced fluid transport, and intermittent stress can stimulate matrix production. Yet, excessive dynamic loading can be detrimental. Currently, the boundary between therapeutic and injurious spinal stress is undefined. To address this, we have developed an approach that combines mathematical and animal models of dynamic spinal compression. The main objective of this study was to determine whether a three-parameter fluid transport model [1] could accurately predict the disc’s response to compression. Also, we questioned whether model parameters differ between normal and degenerated discs.

Methods
Degeneration was induced in the 10th caudal disc of 34 Swiss Webster mice using a previously reported model of intervertebral disc degeneration (approved by the University Committee on Animal Research) [2]. Static loads were applied by first inserting two pins perpendicularly through each vertebral body adjacent to the study disc. In seventeen animals, calibrated, elastic loops were placed around opposing pins to apply a 1.3 MPa compressive stress to the discs. These remaining animals served as unloaded controls, where the pins were left in place, but not loaded. After one week of loading, the elastics were removed and the mice were allowed unrestricted activity for three weeks. This procedure reproducibly provides a degenerated phenotype.

Compressive creep tests were performed in a bath of room temperature saline (0.15M) using a servo-hydraulic testing system (MTS Bionix 858, Eden Prairie, MN). Five cycles of creep (20min creep, 40min recovery) were applied at stresses of either 0.4MPa (n=10) or 0.8MPa (n=10). The data were then fit to a fluid transport model to determine k, D and G (k, endplate permeability; D, strain dependence due to swelling pressure; G, time dependence due to annular creep) [1]. Proteoglycan content was measured using the DMMB assay (n=10). Histological sections were stained by the HBQ method for analysis of morphology and viewed with a polarizing lens (n=4). Data were analyzed using unpaired t-tests and 2way ANOVA with repeated measures. Critical significance levels were set at p < 0.05.

Results
The fluid transport model fit the creep data well (SSE < .01). A significant decrease in disc height was observed in the degenerated discs (p<0.006). Both D and G demonstrated a significant increasing trend in the degenerated discs (p<0.006, p<0.01) (Figure 1). A significant decrease in k was observed for the loaded discs (p<0.006). There was no significant difference between the parameters when comparing the different compressive loads (0.4 MPa and 0.8MPa). Therefore, the two loading groups were pooled for further analyses. The proteoglycan content was 29% greater in the degenerated discs (p<0.002). This result was consistent with the histological sections, where the nucleus stained more intensely for proteoglycan (Figure 2). Additionally, there was a higher degree of disorganization and fragmentation in the annular fibers of the degenerated disc when viewed using a polarized light (Figure 3).

Discussion
Our results illustrate that a three-parameter fluid transport model accurately describes the disc’s response to compression. These data also demonstrate that degeneration alters the intervertebral disc’s fluid transport properties. That the magnitude of the applied stress does not alter the model parameters suggests these reflect tissue properties rather than merely facilitating a curve fit. Trends observed in the model parameters were reflected in the biochemical and histological data. For example, increases in proteoglycan content in the degenerated discs corresponded to increases in D, the strain dependence due to the swelling pressure of the nucleus pulposus. Also, annular disorganization, which occurred in the degenerative discs, is consistent with an increase in G, the time-dependence due to annular creep.

The model parameters were highly sensitive to assumptions regarding the initial height of the disc as well as its swelling pressure. Specifically, the swelling pressure was difficult to measure due to the small physical size of the disc, and was therefore estimated from the literature. The decrease in endplate permeability, k, does not parallel the effect on endplate permeability observed in degenerated human discs. This result may be due to the relatively small thickness of the mouse endplate with respect to the human endplate.

In the future, we plan to utilize predictions for k, D and G to mathematically model the disc’s in vivo response to complex dynamic loading regimens. The loading amplitude, cycle length and cycle frequency will be varied in order to define regimens that optimize disc nutrition and tissue strain. As a validation, the loading regimens will then be applied in vivo [3]. Measures of disc form and function will be used to assess the outcome. We anticipate that these studies will facilitate development of interventions for humans, such as improved guidelines for manual materials handling.

References

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COMPRESSIVE CREEP BEHAVIOR OF NORMAL AND DEGENERATIVE INTERVERTEBRAL DISCS

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