Mechanical Loading Rate Modulates Transport into the Cartilaginous Endplate and Intervertebral Disc In Vivo.

Sarah Elizabeth Linley¹, Joshua Peterson¹, Rosemarie Mastropolo¹, Arun Ficker¹, Sarah Frank², Timothy Roberts, MD¹, James Lawrence, MD, MBA³, Joseph Glennon, VMD⁴, Daryl DiRisio, MD⁵, Eric H. Ledet, PhD¹.

¹Rensselaer Polytechnic Institute, Troy, NY, USA, ²Brown University, Providence, RI, USA, ³Albany Medical College, Albany, NY, USA, ⁴Veterinary Specialties Surgical Associates, Pattersonville, NY, USA.

Disclosures:

Introduction: The intervertebral disc is avascular and relies on transport from the adjacent vertebral bodies to receive nutrients and expel waste products. Reduced transport into the disc is thought to contribute to degeneration. Diffusion is believed to be the primary transport mechanism in the disc, but convection (bulk flow) induced by mechanical loading may also contribute to transport. The role of convection in disc transport remains controversial. When loaded, deformation of the disc induces bulk fluid flow. Because the disc is viscoelastic, the amount of deformation is dependent on the rate of the applied load. Thus, loading rate may dictate convective transport. Loading rates that enhance transport into the disc may be an attractive therapeutic strategy to slow or reverse degeneration. However, the extent to which mechanical loading rate affects transport into the disc has not been previously investigated. The purpose of this study was to quantify changes in transport into the intervertebral disc in vivo subjected to cyclic low and high rate loading.

Methods: Using a custom designed in vivo loading apparatus, we applied cyclic axial compression and distraction loading at two distinct loading rates to individual motion segments of the New Zealand white (NZW) rabbit lumbar spine in vivo. Following IACUC approval, 10 skeletally mature male NZW rabbits were administered the small molecule MRI contrast agent gadodiamide (0.3 mmols/kg, IV). Three animals were subjected to low rate, low frequency loading (0.5 Hz, 2 sec/cycle, 200N) for 10 minutes, and three animals were subjected to low rate, high frequency loading (0.5 Hz, 0.2 sec/cycle, 200 N) for 10 minutes. Four animals served as unloaded controls were allowed to sit for 10 minutes without activity. Immediately at the conclusion of the loading or rest period, the animals were euthanized and the lumbar spines harvested. Post-contrast enhanced 7T T1 MRI was used to quantify net transport of gadodiamide into the intervertebral disc. µCT was used to quantify subchondral bone density. The experimental level (L3-L4) of each group was normalized to the level two superior to experimental (L1-L2), and statistical differences were assessed using an ANOVA with Fisher’s post-hoc test. In vitro dynamic compression testing of rabbit lumbar motion segments at 0.5 Hz and 5 Hz was also conducted to determine the frequency dependent stiffness of the rabbit intervertebral disc at high and low rates of loading.

Results: 10 minutes of low rate loading significantly increased gadodiamide transport into the nucleus pulposus by a mean 6.5% compared to the unloaded, control level (Figure 1A). Following the application of the same number of cycles of high rate loading, transport of gadodiamide into the nucleus was decreased by 19.91% compared to control. In the anterior annulus, high rate loading caused a 14.6% decrease in net transport compared to control (Figure 1B). High rate loading affected transport into the cranial endplate to a greater extent than the caudal endplate, with transport reductions of 19.19% and 5.8% compared to control, respectively (Figure 1C). Low rate loading did not have a significant effect on transport into the annulus or cartilaginous endplate. Subchondral bone density was not a factor in the differences in transport observed. In vitro testing of excised rabbit lumbar spine motion segments illustrated that the mean stiffness of the lumbar intervertebral disc at 5 Hz was 493.6 N/mm, which was significantly greater than the mean stiffness of 418.44 N/mm at 0.5 Hz (p<0.05, two sample t-test).

Discussion: Results from this study suggest that small molecule transport into the intervertebral disc is dependent on the rate of applied loading. This is likely due to the viscoelastic properties of the disc. With increasing rate of loading, the stiffness of the disc increases. At low rates of loading, transport into the disc is enhanced, likely due to deformation induced bulk fluid flow. Low rate loading may therefore be beneficial to disc health as it can enhance transport of nutrients into the disc. However, with the application of the same number of loading cycles, high rate loading caused a reduction in gadodiamide concentration in the nucleus, endplates and anterior annulus. The mechanism is likely an increase in hydrostatic pressure in the nucleus with high rate loading, which restricts diffusion into the disc.[1,2] High rate loading may contribute to disc degeneration by restricting nutrient transport into the nucleus and surrounding tissues.

Significance: Our results suggest a nutritional pathway by which mechanical loading may affect disc health. Loading modalities that enhance bulk fluid flow may be beneficial to disc health. High rates of loading that restrict transport into the disc may contribute to degeneration of the disc.

Acknowledgments:


![Graph A](image1.png)

![Graph B](image2.png)

![Graph C](image3.png)

Figure 1. Mechanical loading rate affects transport into the (A) nucleus pulposus (means that do not share a letter are significantly different, p<0.05); (B) annulus fibrosus (*p<0.05,* (C) cartilage endplate (*p<0.05, # = significantly different from all groups, p<0.05).

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