Title

Dorsal Root Ganglia Diffusion Metrics in Patients with Lumbar Radiculopathy Undergoing Injection

Author

Fitch, Chase Hamilton

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Dorsal Root Ganglia Diffusion Metrics in Patients with Lumbar Radiculopathy Undergoing Injection

by

Chase Fitch

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Approved:

DocuSigned by:

Cynthia Chin

C02E7B87A580493...

Chair

DocuSigned by:

Sharmila Majumdar

Sharmila Majumdar

DocuSigned by:

Felix Liu

Felix Liu

DocuSigned by:

Misung Han

Misung Han

DocuSigned by:

Michael Ohliger

Michael Ohliger

EB514B0EC25145F...

Committee Members

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DORSAL ROOT GANGLIA METRICS IN PATIENTS WITH LUMBAR RADICULOPATHY

Chase Fitch

ABSTRACT

Purpose: We compared injected, assumed to be symptomatic, and non-injected, assumed to be asymptomatic, dorsal root ganglia (DRG) in patients receiving lumbar facet and/or nerve injections using DTI MRI data and foraminal stenosis (FS) and canal stenosis (CS) grades.

Materials and Methods: Healthy volunteers (HVs) and patients receiving lumbar facet and/or nerve block injections for pain underwent lumbar MRIs including axial T2-weighted fat-water separated FLEX 3D FSE and axial DTI. Patients were imaged up to a month prior to injection and up to six months after injection. Processing included: DRG segmentation (MD.ai), 3D volume (MorphACE), DTI (spherical harmonic and Constant Solid Angle). ADC, FA and volume were compared between HVs, asymptomatic and symptomatic DRG and correlated with stenosis grades using paired t-tests.

Results: 25 patients and 5 HVs DTI scans were analyzed (34 patients and 10 HVs for volume). There was a sequential increase in DRG volume from cranial-caudal L1-S1 in the HVs ($p<0.001$). Symptomatic DRG had higher FA than asymptomatic DRG before injection ($p<0.01$) and symptomatic DRG FA decreased after injection ($p<0.05$) while asymptomatic DRG FA slightly increased. Severe CS was associated with lower ADC than no or mild CS ($p<0.001$).

Conclusion: Cranial-caudal sequential increase in DRG volume from L1-S1, consistent with cadaver data, may reflect degree of cutaneous and muscle area/volume innervation. Symptomatic DRG have higher FA than asymptomatic DRG that return to asymptomatic levels after injection. This could be due to phospholipase A2 (PLA2) inhibition by corticoid-steroid suppressing nerve cell growth and thus organized diffusion alternatively receptor inhibition. Severe CS could cause arterial flow constriction leading to ischemic DRG and reduced ADC.

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LIST OF ABBREVIATIONS

UCSF	University of California, San Francisco
FS	Foraminal Stenosis
CS	Canal Stenosis
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
T1w	T1-weighted
T2w	T2-weighted
SE	Spin-Echo
DTI	Diffusion Tensor Imaging
SNR	Signal to Noise Ratio
FA	Fractional Anisotropy
ADC	Apparent Diffusion Coefficient
HV	Healthy Volunteer
LR	Lumbar Radiculopathy
DRG	Dorsal Root Ganglia (Ganglion for singular)
FOV	Field of View

BACKGROUND AND INTRODUCTION

Background

Lumbar radiculopathy (LR) is defined as pain radiating down the legs caused by compression of nerve roots originating from the lumbar spine levels (L1-L5) causing radiating pain, shooting pain, and paranesthesia. This affects an estimated 17 million Americans and costs over 100 billion dollars per year (Mokad, et al. 2015). Nerve compression often caused by both foraminal stenosis (FS) and canal stenosis (CS) is most often caused by degenerative disease of the spine osteophytic spurring, disc herniation, tumor, infection or congenital scoliosis. The lies in the center of the vertebra and houses the nerves of the spinal cord. The foramen are the lateral tunnels where nerves exit from the canal. If either of these spaces are constricted, nerves may become compressed and cause pain or other symptoms.

The most common imaging diagnostic tests for LR are X-ray, CT scan and MRI. X-ray and CT scan can be used to see bony abnormalities such as fractures, osteoarthritis, tumor or infection destruction; MRI can additionally view soft tissue structures such as disc herniation and nerve root compression. In the typical clinical MRI for LR, intravenous contrast is not used and T1w SE, T2w SE and T2w fat-saturated SE are standard, however limited to only assessing morphological degeneration. Diffusion tensor imaging (DTI) can track water proton diffusion motion within tissue using tensors to calculate the level and direction of anisotropy. Historically, DTI has been rarely used in the spine as the small

axial area of the spine requires higher resolution and SNR. However, increases in the availability of higher field magnets, more advanced scanners and coils and improvement in pulse sequence designs and image processing have allowed DTI of the spine. Two common DTI metrics include fractional anisotropy (FA), measuring the degree of anisotropy, and apparent diffusion coefficient (ADC), measuring the total diffusion.

Certain metrics have been evaluated for lumbar spine nerve DTI. First, ADC and FA values have not been found to depend on sex and age (Pierpaoli, et al. 1996). Nerve FA values were lower, and ADC values were found higher in those patients with disk herniation, edema, and scar reduction (Eguchi, et al. 2016) while compressed lumbosacral nerves were found to have lower ADC and FA (Li, et al 2016). Lower ADC is also found in ischemic areas in nerves and areas of axonal loss and demyelination. Another study (Li, et al 2019), found lumbar disc herniation could be diagnosed with DTI in lateral nerve roots and DTI could be used to evaluate the spine post-surgery. FA and ADC have been found to correlate with the patient's neurological symptoms and ADC has additionally been found to correlate with functional status; for example, higher ADC generally results from more edema in the nerve indicating more severe injury (Li, et al 2019, Balbi, et al. 2011, Singh, et al. 2022).

The dorsal root ganglia (DRG) reside within the posterior spinal nerve root and house the cell bodies of sensory neurons. Situated within the intervertebral neural foramina, they serve as a crucial link between peripheral nerves and the central nervous system, comprising the brain and spinal cord. DRG play a pivotal role in processing pain signals and are increasingly targeted for interventional pain management including nerve blocks utilizing local anesthetic injections to decrease propagation of pain signals in

overstimulated nerves. In lumbar disc herniation and/or stenosis, the DRG of the compressed nerve root can undergo edematous changes resulting in higher ADC. Patients exhibiting decreased ADC, possibly indicating ischemia, often experience limited improvement in leg symptoms following surgery, suggesting a potential correlation between DRG ADC and neuronal plasticity in the lumbar spine.

Local injections, consisting of an anesthetic (commonly bupivacaine) and corticosteroid, are given at the expected radiculopathy level to reduce inflammation through a biochemical process involving the inhibition of prostaglandins, thromboxanes and leukotrienes production (Coutinho, et al. 2011). These injections result in various levels of pain reduction with some patients having long-term pain reducing effects, while others show little to no immediate effects. On average, patients have moderate immediate pain relief that lasts two weeks to three months (Chou, et al. 2015). These injections have very low complication risk and show no significant differing effects in demographics such as sex, race, age, etc. (Chou, et al. 2015).

We predict that patient's symptomatic DRG undergoing spinal injection interventions for lumbar nerve compression-related pain will demonstrate lower ADC diffusion values compared to healthy volunteers (HVs) and asymptomatic, non-injected DRG. This investigation aims to enhance our understanding of DTI metrics in DRG in patients with lumbar spine pain.

Goals

1. Evaluate inherent differences in DRGs - establish normal values and variations

In the HV group, find and compare ADC averages for each DRG's level and side (L vs R). Use this data, if significance is found, to make normative comparisons to compare different.

2. Confirm the difference in DRG metrics between HV and patients.

Most of the literature supports that ADC and FA is lower in compressed nerves, but not universally. The second aim will compare HVs' DRG to the symptomatic DRG. In addition to ADC and FA values, DRG volume will be compared.

3. Compare the DRG metrics between symptomatic DRG to asymptomatic DRG regarding degree of FS and CS diagnosis.

Compression does not always equate pain. We will determine if diffusion values differ between nerves causing and not causing radiculopathy within individuals reporting of LR. This provides a basis within individuals as ADC, FA and DRG volume values differ from individual to individual. We will then look at how stenosis impacts these values.

4. Evaluate the impact of injection on diffusion metrics.

For the patients with pre and post injection images, compare metrics between the two scans to discover impacts on injection in injected vs non-injected nerves.

METHODS AND MATERIALS

Patients

Patients were recruited from individuals receiving lumbar anesthetic/steroid injections at University of California, San Francisco (UCSF) for lumbar spine pain. Injections were given by UCSF physicians and consisted of bupivacaine and corticosteroid. Patients were excluded if they had tumor, infection, congenital deformity or hardware resulting in extensive artifact obscuring the lumbar vertebrae. Patients were also excluded if they were pregnant, claustrophobic or their scans could not be completed. In addition to imaging, patients were physically examined by UCSF neurologists, surgeons or their physician assistants (PAs) to determine potential lumbar levels causing LR. Some patients also underwent electromyography (EMG) studies. Pain scores were reported by the patient prior immediately before and after the injection from 0 to 10. Pain difference was calculated from before minus after pain score. Mild pain difference was considered 1 to 3 and severe pain difference was considered 4-10.

FS and CS were diagnosed by the injecting physician or by Cynthia Chin MD. The FS grade was marked as affecting the level and side it was diagnosed at; however, the CS grade was marked as affecting the DRG bilaterally, one level below (ex: L4 CS affects the right and left L5 DRG). DRG were labeled symptomatic if they received an injection at that side and level and other DRG were labeled asymptomatic. For facet injections, only the more cranial DRG was considered injected.

MRI Scan Parameters

MRIs were acquired with various parameters and locations. All images were acquired on the General Electric 3T scanner at the China Basin clinic. A coronal T2-weighted Cube FLEX and an axial DTI of the lumbar spine (from T12 through the sacral spine) were acquired. The lumbar DTIs utilized 16 diffusion directions. For patients, images were acquired up to 3 months before injection and between 1 and 3 months after injection.

The axial Cube Flex (3D fast spin echo with Dixon-based fat water separation) was prescribed with 1.2 mm isotropic resolution, 36 x 25.2 cm^2 in-plane FOV, and 300 slices in the axial orientation, with other imaging parameters of 2500 ms TR, 70-80 ms TE, ±166.7 kHz readout bandwidth, and 100 echo train length. These images were reformatted to allow for coronal slice view and segmentation.

The DTI sequence used 2D fat-suppressed single-shot spin-echo echo-planar imaging with 32 x25.6 cm^2 field of view, 64x80 matrix size, 3 cm slice thickness, 118 slices, 9000 ms TR, 45 ms TE, b-value of 600 s/m^2, and 16 diffusion directions.

Image Segmentation

DRG were manually annotated by me and other trained researchers on Cube FLEX and DTI images respectively on MD.ai; the annotations reviewed by Cynthia Chin MD. DRG DTI images were annotated bilaterally from the L1-L5 levels and Cube FLEX were annotated at every visible DRG from L1-S1.

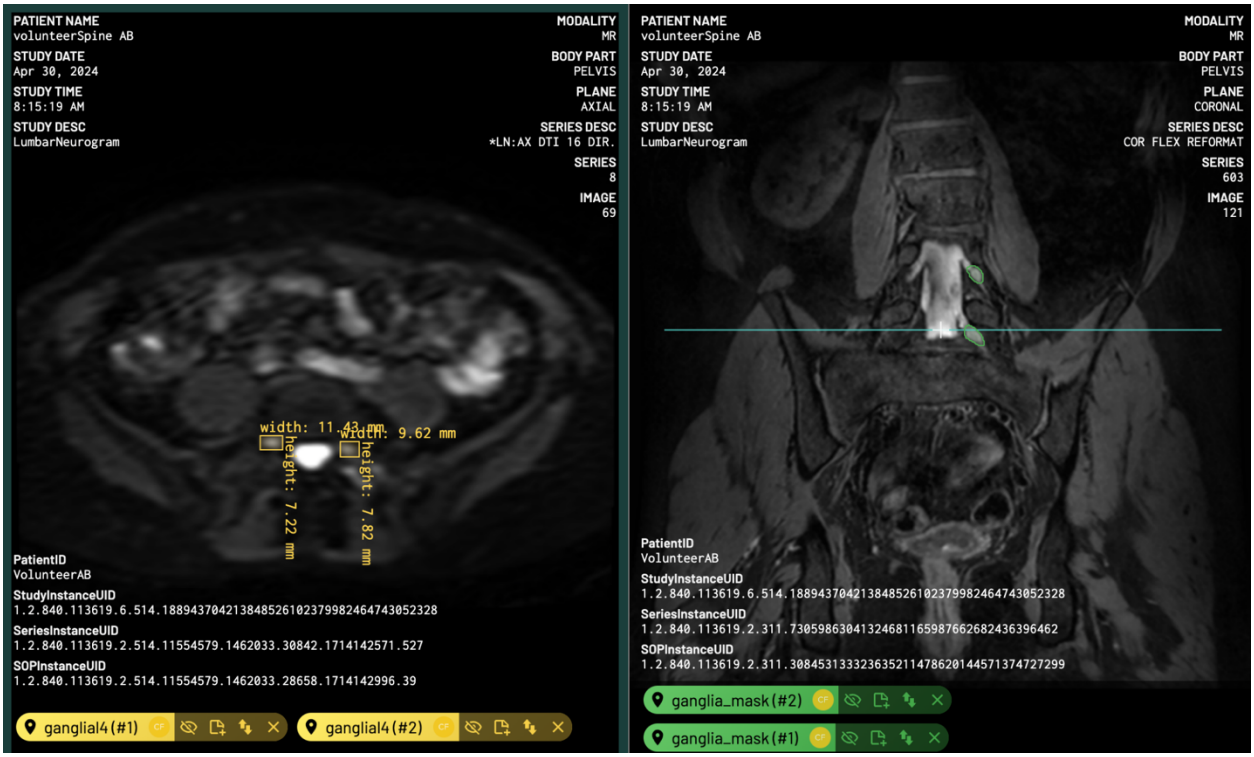


Figure 1. MD.ai Segmentation
MD.ai segmentation view of a healthy volunteer (HV).

DRG Volume

A seed ROI on 2D DRG segmentations were taken from MD.ai on a single reformat coronal T2 FLEX slice and morphological snake region growing was used to extract a 3D volume using Morphological Active Contours without Edges (MorphACE from scikit-image) (Chan & Vese, 2001). This program is a fast, reliable semi-automated morphological snake region growing algorithm using relative differences thresholds (Figure 1).

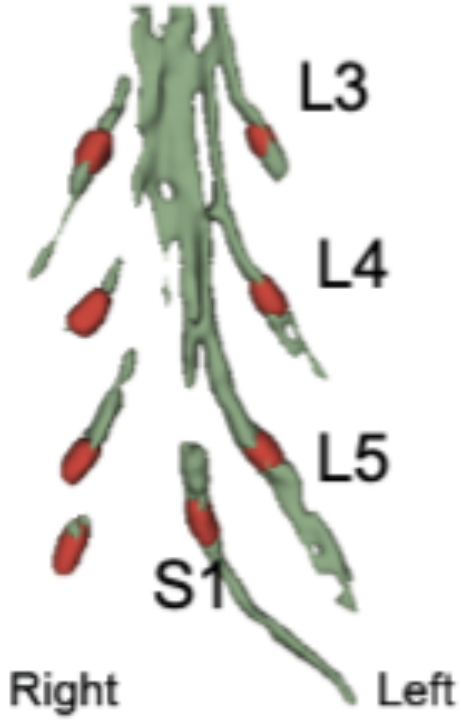


Figure 2. Semi-Automated Segmentation
Developed semi-automatic DRG segmentation incorporating morphological snake techniques in the coronal plane. Figure courtesy Misung Han and Felix Liu ISMRM 2024.

DTI Metrics

MD.ai data was downloaded with annotations in JSON format and images in DICOM format and processed in python, dcm2niix and DIPY. DICOMs were converted into NIFTI files and JSON annotations were converted to binary mask volumes and applied to NIFTI images. Using spherical harmonics and Constant Solid Angle (CAS), a Q-ball modeling method, DTI volumes were constructed into diffusion maps in a methodology modeled after Aganji, et al. (2010). FA and ADC values were calculated from the masked areas by using DIPY to probabilistically determine fiber tracts and extracting DTI values from even spatial intervals along fiber tracts. If present in the DRG volume, these values were included and averaged.

Statistics

We ran a two-tailed t-test to calculate Pearson's correlations between different groups to check for significance difference between volume, ADC or FA comparisons. To test the correspondence between FS and CS, a chi-squared analysis was used with expected values being calculated by multiplying the number of FS by the number of CS for the respective diagnosis level and dividing the product by the total number of DRG diagnosed. All error bars used standard error (STE) for graphs. No standardization was needed for side or lumbar level.

RESULTS

Patients

34 patients and 10 HVs controls imaged and processed for volume data; 25 patients and 5 HV had DTI scans (Figure 3). 6 patients had before and after injection scans. 68% of patients were female; the average age was 64.1 and the range was 21-91. 49 patients were originally recruited. 7 withdrew from the study, 8 were scanned on a different scanner that couldn't be processed and 9 had issues in DTI processing. Of the 25 patients, 13 had facet injections, 9 had nerve blocks, and 3 had both. 80% of patients had either L4 or L5 treated and was the most common level; every level was treated at least once.

Image Segmentation

Certain DRG were not visible due to hardware artifacts, or not included in the imaging volume. Additionally, the L1 and L2 levels occasionally were at the periphery of the window and did not have enough contrast from background to find the DRG. This was not the case when L1 or L2 radiculopathy was expected respectively.

DRG Volume

HV volume significantly increased as the lumbar level became more caudal from L1 to S1; HV volume did not significantly differ between left and right DRG (Figure 4). Absolute DRG volume did not differ significantly. Using DRG volume as a fraction of the S1 volume to correct for patient size, every level was significant from the next at the $p<0.0001$ level. There were no significant differences between patient and HV volume.

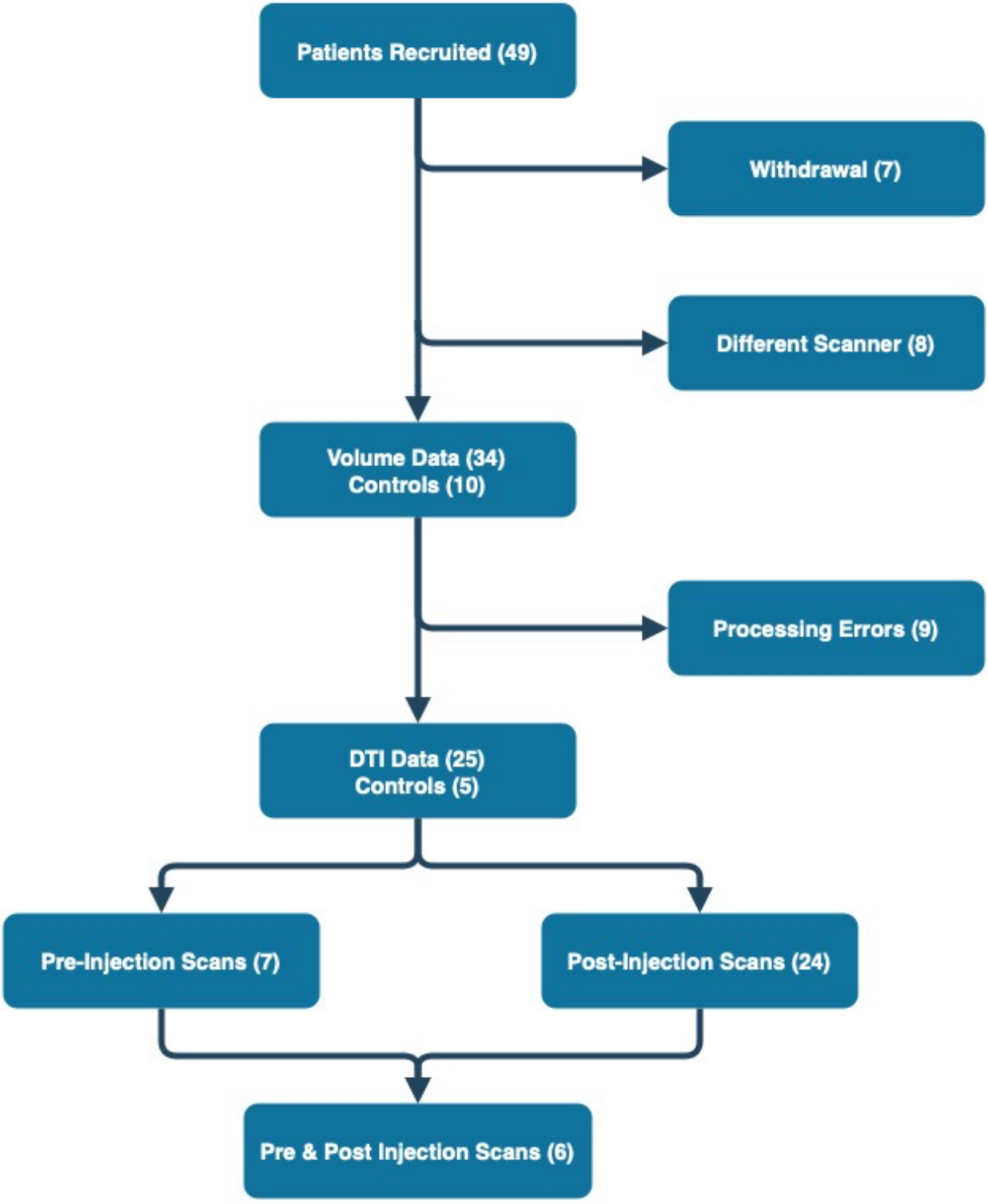
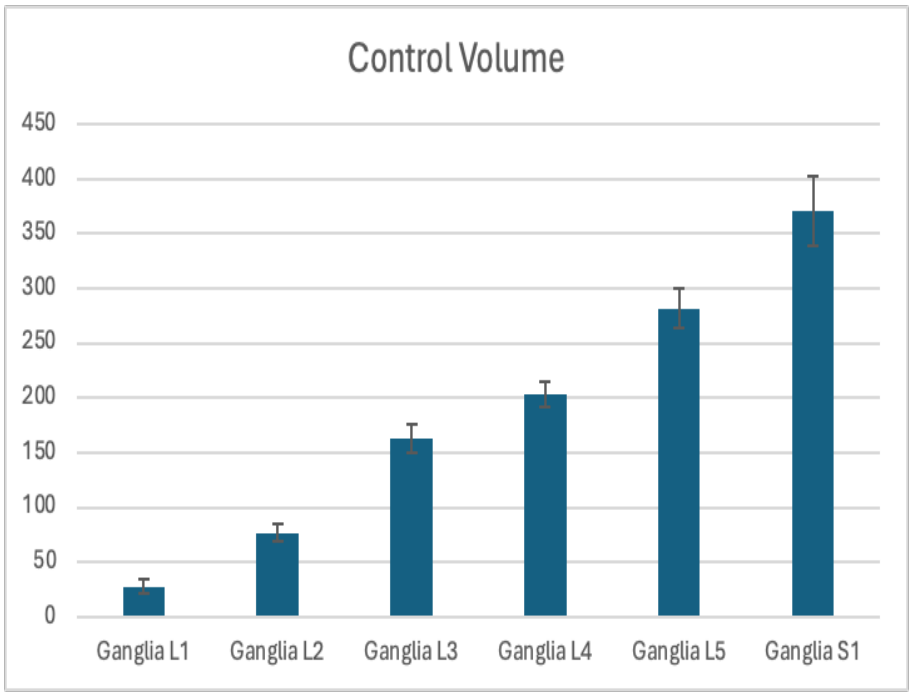


Figure 3. Recruitment flowchart.



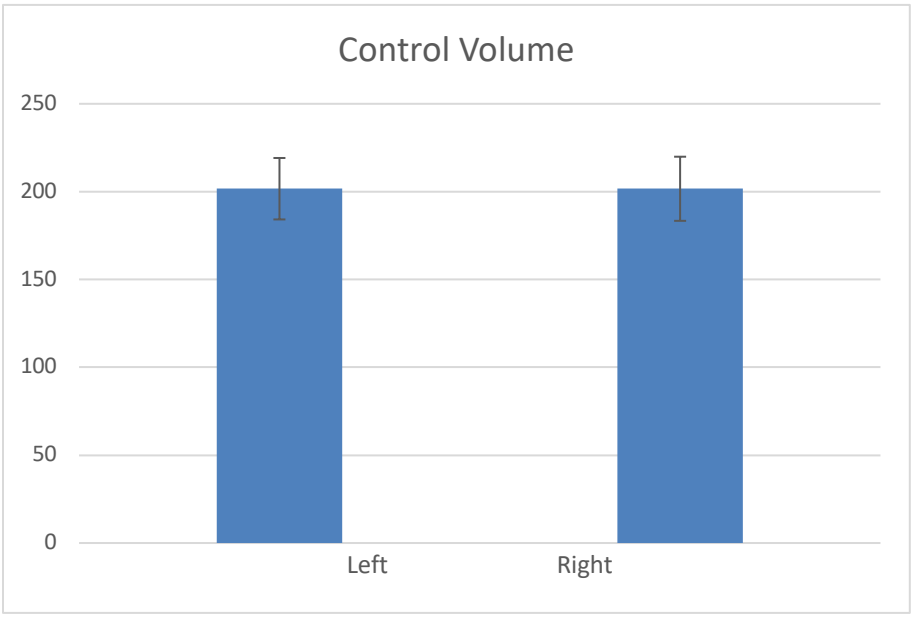


Figure 4. Volunteer Volume
HV volume (n=10 people) for vertebral level and side. Each vertebral level volume was significant at the $p<0.0001$ level compared to any other (when calculated as a ratio to account for subject size) while the side differences had no significant difference.

DTI Metrics

Establishing Normative Values

DTI metrics were acquired (HV n=5 people and patient n=25 people). Comparing vertebral levels in the HVs, DRG had no significant ADC or FA differences, however ADC values were found to decrease cranially to caudally (Figure 5). There were no significance differences comparing left and right in ADC or FA.

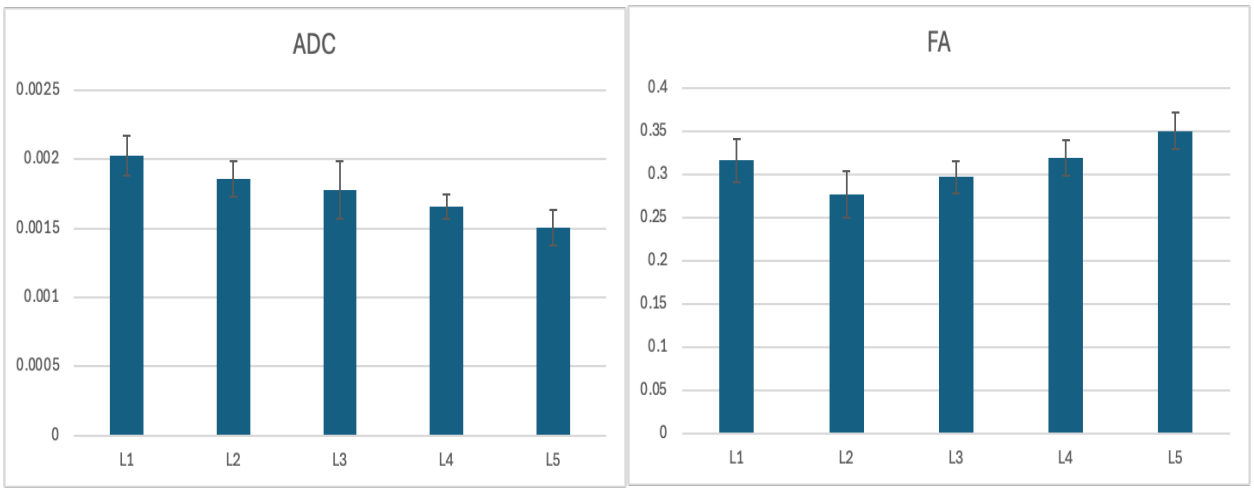


Figure 5. ADC/FA by Vertebral Level
ADC and FA differences between vertebral levels (L1-L5) in healthy volunteers (HVs). There were no significant differences.

Comparing Different Cohorts

There were no significant differences between HV and patients in the aggregate ADC or FA. The pre-scan asymptomatic DRG were found to have significantly lower FA than the HV DRG ($p<0.05$), the post-scan symptomatic DRG ($p<0.01$), and the pre-scan symptomatic DRG ($p<0.05$) (Figure 6).

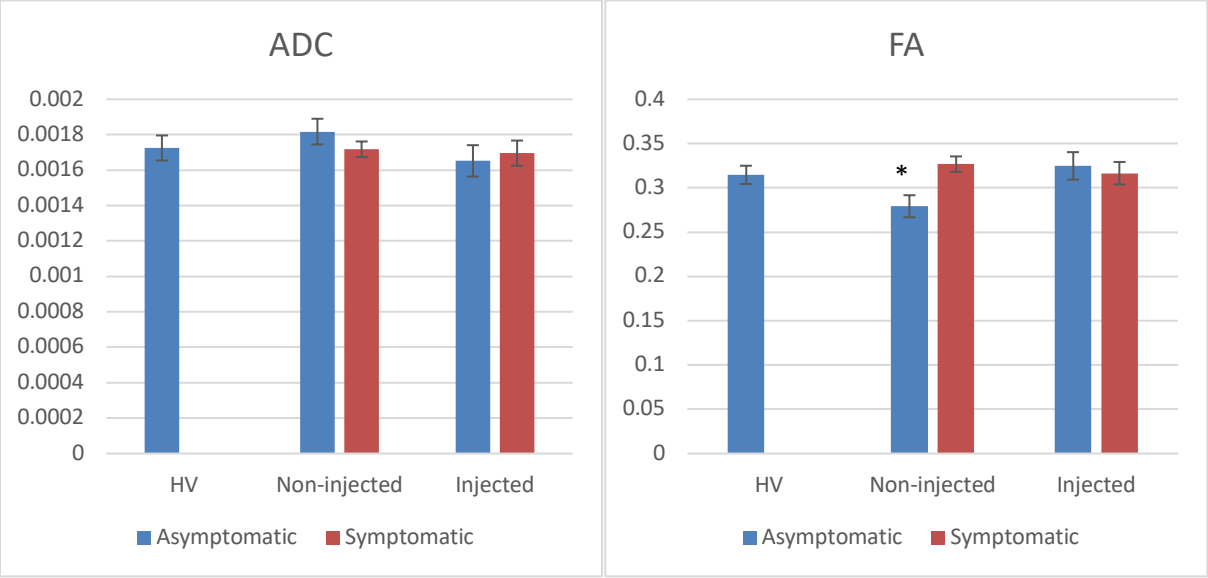


Figure 6. ADC/FA by Injection Status
ADC and FA comparisons between DRG cohort before and after injection. Asymptomatic FA was significantly lower than the HV ($p<0.05$), asymptomatic post-injection ($p<0.01$) and symptomatic pre-injection ($p<0.05$).

Pre vs Post Injection

There were no significant differences in ADC between symptomatic and asymptomatic DRG before and after injection. The symptomatic DRG were found to have significantly higher FA before injection compared to the asymptomatic DRG before injection ($p<0.01$) and the symptomatic DRG after injection ($p<0.05$) (Figure 7). There were no significant differences between injection type or pain score difference.

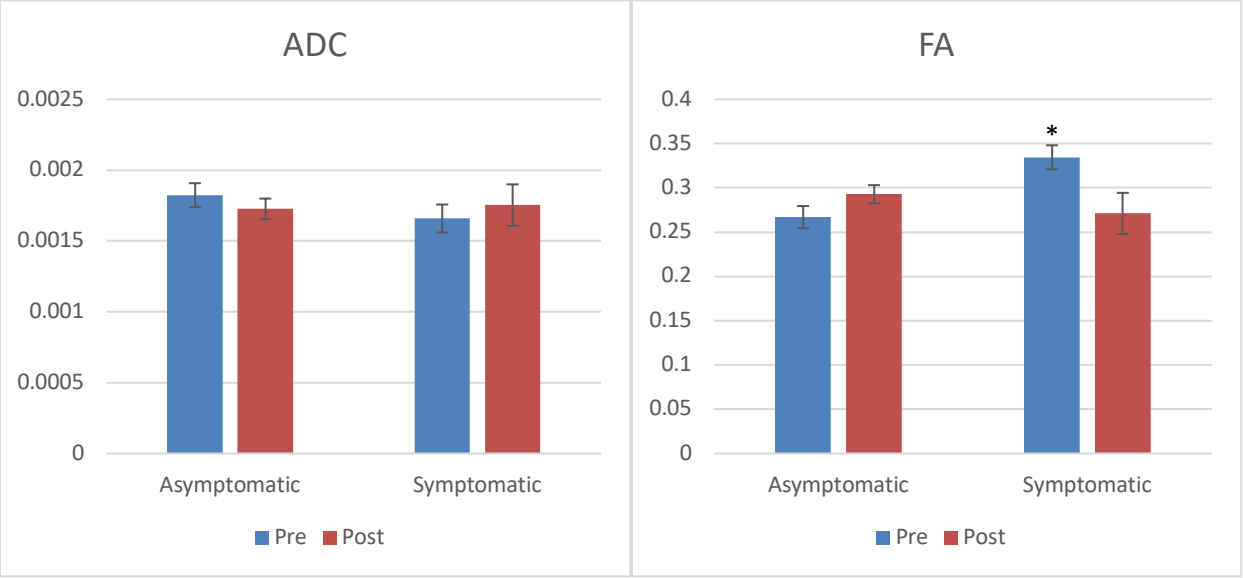


Figure 7. ADC/FA Pre vs Post Injection
ADC and FA values of patients with both pre and post injection. FA of pre-injection symptomatic DRG was significantly higher than pre-injection asymptomatic DRG ($p<0.01$) and post-injection symptomatic DRG ($p<0.05$). There were no significant ADC differences.

Stenosis

Stenosis grades were recorded centrally for CS and bilaterally for FS (**Table 1**). 44% of patients had severe FS (median: 2 severe foramen) and 32% had severe CS (median: 1 severe canal). A chi-squared analysis showed FS and CS were positively correlated at the $p<0.001$ level. In DRG with severe CS, ADC was significantly lower than no (normal) and mild CS ($p<0.001$); there were no significant trends found for FA by FS or CS grade or ADC by FS grade (Figure 8).

Table 1. Foraminal and Canal Stenosis Count

	Foraminal Stenosis →				
Canal Stenosis ↓	mild	moderate	normal	severe	Grand Total
mild	32	10	8	6	56
moderate	13	4	5	4	26
normal	39	5	90	10	144
severe	7	6	6	5	24
Grand Total	91	25	109	25	250

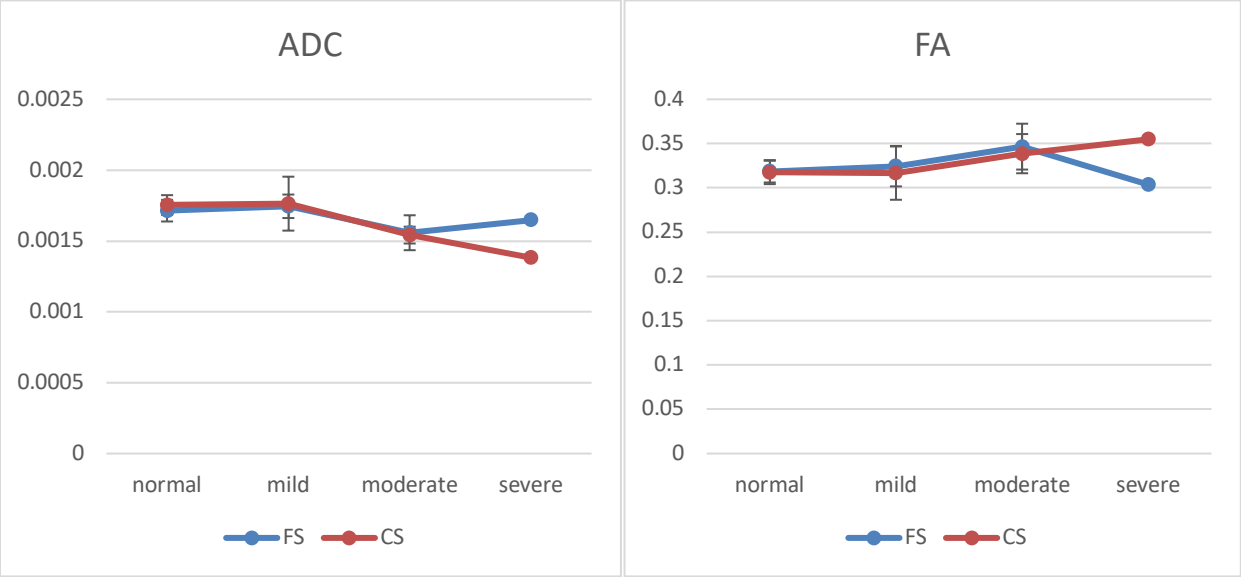


Figure 8. ADC/FA by Stenosis Grade
ADC and FA averages by FS and CS grade. Severe CS ADC was significantly lower than normal and mild CS ADC ($p<0.001$).

DISCUSSION

DRG volume trends are consistent with cadaver data (Haberburger, et al. 2019); DRG volume increased, cranially to caudally, from L1 to S1. It is unclear how the size of the DRG impacts diffusion as we did not find any trends. This could be due to our small HV group size. I would imagine if there were any trends, they would have little impact that would not be explained by other variables. In future studies, we plan to improve processing efficiency and apply to more patient data sets to increase sample size.

We found no significant differences comparing HV, symptomatic and asymptomatic DRG. Symptomatic nerves were found to have higher FA than asymptomatic nerves before injection. The FA of the symptomatic nerves was found to drop after injection. This finding goes against prior literature. It is presumed that increased damage leads pain and this pain is associated with axonal loss and demyelination which would have less FA. Higher FA of asymptomatic nerves is odd and not trivial to explain. A small component of this is due less total diffusion (seen in ADC graph in Figure 7) that likely has an ischemic origin, but this does not explain all the variance. Injections have also been found to decrease FA in the injected nerves while not affecting the non-injected nerves. Again, part but not all the variance is explained by total diffusion (seen in ADC graph in Figure 7), but more explanation is needed. The post scans were around three months after injection where only the corticosteroid should have impact. Corticosteroid can decrease surrounding non-nerve tissue edema, which is often reversely correlated with nerve edema (McKay & Cidlowski). The corticosteroid could impact the receptors between neurons impacting fluid flow or down regulates PLA2 activity (Carassiti et al 2021) causing less cell growth (Sun, et al. 2021). Fewer cells may have less organized fluid flow between them. An

alternative theory is there is over-healing. In an animal model of injured nerves, nuclear clefting, nuclear pores, mitochondrial volumes and lysosomal volumes were increased compared to controls. This results in an increase in the number of pores that protons can travel through in the neuron, thus increasing FA (Kobayshi S, et al. 2004). It is possible that this is occurring in human patients.

Supported by previous literature (Kanematsu R, et al. 2021), L4 and L5 were the most injected levels and the levels with the most FS and CS. FS and CS were also found to correlate with injected level. It is likely that any kind of damage, FS or CS, causes worse stenosis in the canal and foramina. Alternatively, any type of injury or degeneration causes damage to both the foramina and canal. CS grade was found to negatively correlate with ADC. In a canine study, CS was shown to compress arterial blood supply while FS was shown to congest the venous blood supply (Kobayashi S, et al. 2008). It is possible that the ADC in patients with CS resulted from the compression of the arterial blood supply causing ischemia. In future studies, we plan to use a numeric CS parameter, the quotient of the canal diameter over the disc diameter plus canal diameter, to provide a quantitative metric. Along with increased sample size, this trend can be better investigated and potentially related CS and FS to FA as well as ADC for FS.

In the future, we would also like to see how pain score changes relate to the changes in ADC and FA post injection in a larger pre vs post injection data set. We would also like to get the weight, height, age, sex and race data for controls to evaluate these parameters. Size of DRG may influence ADC as more caudal DRG were larger and had less ADC, thus body size, relating to weight, height and sex, could be different and require standardization to accurately compare different DRG between and within individuals. Finally, we would

like to investigate the brain PET-MRI data associated with many of these patients. These scans are already acquired and could relate to the pain scores of the individuals.

REFERENCES

1. Aganj I, Lenglet C, Sapiro G, Yacoub E, Ugurbil K, Harel N. “Reconstruction of the orientation distribution function in single- and multiple-shell q-ball imaging within constant solid angle”, Magnetic Resonance in Medicine. 2010 Aug;64(2):554-66. doi: 10.1002/mrm.22365
2. Balbi V, Budzik JF, Duhamel A, Bera-Louville A, Le Thuc V, Cotten A. Tractography of lumbar nerve roots: initial results. Eur Radiol. 2011 Jun;21(6):1153-9. doi: 10.1007/s00330-010-2049-3. Epub 2011 Jan 16. PMID: 21240648.
3. Carassiti M, Pascarella G, Strumia A, Russo F, Papalia GF, Cataldo R, Gargano F, Costa F, Pierri M, De Tommasi F, Massaroni C, Schena E, Agrò FE. Epidural Steroid Injections for Low Back Pain: A Narrative Review. Int J Environ Res Public Health. 2021 Dec 26;19(1):231. doi: 10.3390/ijerph19010231. PMID: 35010492; PMCID: PMC8744824.
4. Coutinho A.E., Chapman K.E. The anti-inflammatory and immunosuppressive effects of glucocorticoids, recent developments and mechanistic insights. *Mol. Cell. Endocrinol.* 2011;**335**:2–13. doi: 10.1016/j.mce.2010.04.005.
5. Eguchi Y, Oikawa Y, Suzuki M, Orita S, Yamauchi K, Suzuki M, Aoki Y, Watanabe A, Takahashi K, Ohtori S. Diffusion tensor imaging of radiculopathy in patients with lumbar disc herniation: preliminary results. Bone Joint J. 2016 Mar;98-B(3):387-94. doi: 10.1302/0301-620X.98B3.36036. PMID: 26920965.
6. Haberberger RV, Barry C, Dominguez N and Matusica D (2019) Human Dorsal Root Ganglia. *Front. Cell. Neurosci.* 2019 Jun;13:271. doi: 10.3389/fncel.2019.00271
7. Kobayashi S, Takeno K, Miyazzaki T, Kubota M, Shimada S, Yayama T, Uchida K, Normura E, Mwaka E, Baba H. Effects of Arterial Ishecmia and Venous Congestion on The Lumbar Nerve Root in Dogs. Journal of Orthopedic Research. November 2008
8. Li J, Cui H, Liu Z, Sun Y, Zhang F, Sun Y, Zhang W. Utility of diffusion tensor imaging for guiding the treatment of lumbar disc herniation by percutaneous transforaminal endoscopic discectomy. Sci Rep. 2019 Dec 10;9(1):18753. doi: 10.1038/s41598-019-55064-3. PMID: 31822704; PMCID: PMC6904469.

9. Li J, Wang Y, Wang Y, Lv Y, Ma L. Study on lumbosacral nerve root compression using DTI. Biomed Rep. 2016 Sep;5(3):353-356. doi: 10.3892/br.2016.734. Epub 2016 Aug 2. PMID: 27602215; PMCID: PMC4998170.
10. McKay LI, Cidlowski JA. Physiologic and Pharmacologic Effects of Corticosteroids. In: Kufe DW, Pollock RE, Weichselbaum RR, et al., editors. Holland-Frei Cancer Medicine. 6th edition. Hamilton (ON): BC Decker; 2003. Available from: https://www.ncbi.nlm.nih.gov/books/NBK13780/
11. Mokdad A.H., Ballestros K., Echko M., Glenn S., Olsen H.E., Mullany E., Lee A., Khan A.R., Ahmadi A., Ferrari A.J., et al. The State of US Health, 1990–2016: Burden of Diseases, Injuries, and Risk Factors Among US States. *JAMA.* 2018;**319**:1444–1472
12. Pierpaoli C, Jezzard P, Basser PJ, Barnett A, Di Chiro G. Diffusion tensor MR imaging of the human brain. Radiology. 1996 Dec;201(3):637-48. doi: 10.1148/radiology.201.3.8939209. PMID: 8939209.
13. Roger Chou, Robin Hashimoto, Janna Friedly, et al. Epidural Corticosteroid Injections for Radiculopathy and Spinal Stenosis: A Systematic Review and Meta-analysis. Ann Intern Med.2015;163:373-381. [Epub 1 September 2015].doi:10.7326/M15-0934
14. Singh R, Khare N, Aggarwal S, Jain M, Kaur S, Singh HD. A Prospective Study to Evaluate the Clinical and Diffusion Tensor Imaging (DTI) Correlation in Patients with Lumbar Disc Herniation with Radiculopathy. Spine Surg Relat Res. 2022 Dec 12;7(3):257-267. doi: 10.22603/ssrr.2022-0159. PMID: 37309501; PMCID: PMC10257965.
15. Sun GY, Geng X, Teng T, Yang B, Appenteng MK, Greenlief CM, Lee JC. Dynamic Role of Phospholipases A2 in Health and Diseases in the Central Nervous System. Cells. 2021 Oct 30;10(11):2963. doi: 10.3390/cells10112963. PMID: 34831185; PMCID: PMC8616333.
16. Tony Chan and Luminita Vese, Active Contours without Edges,. In IEEE Transactions on Image Processing, 2001, DOI:10.1109/83.902291

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