

Tensile mechanical analysis of anisotropy and velocity dependence of the spinal cord white matter: a biomechanical study

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Graphical Abstract *Biomechanical study of white matter*



Abstract

In spinal cord injuries, external forces from various directions occur at various velocities. Therefore, it is important to physically evaluate whether the spinal cord is susceptible to damage and an increase in internal stress for external forces. We hypothesized that the spinal cord has mechanical features that vary under stress depending on the direction and velocity of injury. However, it is difficult to perform experiment because the spinal cord is very soft. There are no reports on the effects of multiple external forces. In this study, we used bovine spinal cord white matter to test and analyze the anisotropy and velocity dependence of the spinal cord. Tensile-vertical, tensile-parallel, shear-vertical, and shear-parallel tests were performed on the white matter in the fibrous direction (cranial to caudal). Strain rate in the experiment was 0.1, 1, 10, and 100/s. We calculated the Young's modulus of the spinal cord. Results of the tensile and shear tests revealed that stress tended to increase when external forces were applied parallel to the direction of axon fibers, such as in tensile-vertical and shear-vertical tests. However, external forces those tear against the fibrous direction and vertically, such as in tensile-parallel and shear-parallel tests, were less likely to increase stress even with increased velocity. We found that the spinal cord was prone to external forces, especially in the direction of the fibers, and to be under increased stress levels when the velocity of external forces increased. From these results, we confirmed that the spinal cord has velocity dependence and anisotropy. The Institutional Animal Care and Use Committee of Yamaguchi University waived the requirement for ethical approval.

Key Words: anisotropy dependence; external force; mechanistic analysis; spinal cord injury; straining rate; stress; velocity dependence; white matter

Chinese Library Classification No. R446; R364; R741

Introduction

Spinal cord diseases such as cervical spondylotic myelopathy, posterior longitudinal ligament ossification, and spinal cord tumors, like traumatic injuries do, often present with symptoms associated with a mechanical insult to the spinal cord, resulting in tissue damage that affects patients' activities of daily life (Iyer et al., 2016; Eckert and Martin, 2017; Kretzer, 2017; Pepke et al., 2018; Boody et al., 2019; Ottenhausen et al., 2019).

Because spinal cord disorders are associated with injuries

of gray matter and white matter (Bhattacharyya, 2018), it is important to understand the mechanical properties of these tissues. The mechanical properties of spinal cord gray matter, white matter, and the saddle (the nerve root and the cauda equina) have been characterized in tension (Ichihara et al., 2003, 2004, 2015), indentation (Koser et al., 2015), pipette aspiration (Ozawa et al., 2001), unconfined compression (Jannesar et al., 2018), compression analysis (Nishida et al., 2020), and age-related mechanical effects of gray matter and white matter (Okazaki et al., 2018).

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Spinal cord injuries occur when strong external forces, such as a car accident or a fall, are applied to the spinal cord (Eckert and Martin, 2017). Initial mechanical trauma includes traction, compression forces and stretch injury (McDonald and Sadowsky, 2002; Henderson et al., 2005). Such forces are known to cause spinal cord injury, but few studies have examined how velocity and anisotropy affect the white matter. We hypothesize the spinal cord has mechanical features that vary under stress according to the direction and velocity of the injury. An understanding of this feature could provide clues for interpreting preoperative and postoperative images of intraspinal stress and to the manipulations to watch out during surgery.

Thus, we conducted a study using bovine white matter to test the anisotropy and velocity dependence of the spinal cord. The objective of our study was to examine the mechanical properties of the spinal cord regarding speed and direction and to address the lack of information in the literature.

Materials and Methods

Animals

The Holstein cows were killed through exsanguination at a meat center in one author's prefecture; it is a licensed institute. The experiment involved the use of spinal cords that tested negative for bovine spongiform encephalopathy and were sourced within 6 hours of slaughter. The spinal cord was wrapped in gauze dipped in saline and placed in plastic. It was then immersed in ice water in a cooler box and transported to the laboratory within 30 minutes. The spinal cord was investigated at 22°C as reported earlier (Ichihara et al., 2003). The experiment was completed within 12 hours of animal slaughter. The experiment was completed within 12 hours of slaughter. The specimens and instruments used for this experiment were prepared under the instruction and supervision of the Hofu City Public Health Center and the Yamaguchi Prefecture Department of Sanitation. Our study used spinal cords of cows that were slaughtered for food. The Institutional Animal Care and Use Committee of Yamaguchi University waived the requirement for ethical approval. The university's regulations provide for review of research that uses living animals.

We used only spinal cords collected from Holstein cows, because of their relatively high availability. Experiments were conducted using spinal cords from 10 vertebrae of Holsteins that were between 20 and 22 months of age. The section of the spinal cords that we used covered from the first cervical vertebra to the first thoracic vertebra. Both ends of the cord were cut off because they could have been injured by the tensile load that was applied to the neck of cows during slaughter (**Figure 1A**).

After a semicircular polyethylene terephthalate agent was inserted into the trabeculae between the pia mater and the arachnoid membrane of the spinal cord, the fibrous tissue connecting the arachnoid membrane and the pia mater were cut off to excise the spinal cord (**Figure 1B**). Next, the spinal cord was spread, starting at the dorsal median sulcus. The gray matter was damaged in the spreading stage, so only the white matter could be cleanly expanded (**Figure 1B**).

A test sample was prepared that took into account the direction of the axon fibers (**Figure 2A**). The size of the cross-sectional area was required to calculate the stress. The length of the test specimen was about 1 cm and the test site had a gage length of 4 mm. The site grasped during the test was the edge. The width and thickness of samples were measured with an optical transmission sensor (IG-010, Keyence, Tokyo, Japan) at three different points and with a gage length of 4 mm (**Figure 2B**).

The spinal parenchyma was soft and watery. A tensile jig was needed to hold the test sample in place. We created a separate jig with a plastic clip. The test sample was sandwiched and fixed in place with enough force to prevent the test sample from being crushed. Shaped cushioning material (Sanwa Co., Ltd., Fukuoka, Japan) was attached between the test sample and the jig to prevent slippage caused by moisture in the test sample during the tensile test (**Figure 3A**).

Test equipment and test methods

Tensile test

On the basis of the velocity and displacement data provided by the personal computer (PC) via serial communication, the host controller sent control pulses to the servo controller (SRCD10+RGU-2 Yamaha, Iwata, Japan). Next, a servomotor (T9H 20BK-400, Yamaha) applied a hammer attached to the actuator of the slider to perform a tensile test. The displacement data of the test sample were measured by a rotary encoder coaxially mounted on a servomotor. The data were then loaded into a PC through a servo controller, a host controller, and an encoder board (PCI-6204, Interface, Hiroshima, Japan). The load data of the test samples were measured by a load cell (LTS-100GA, Kyowa Electronic Instruments Co., Ltd., Tokyo, Japan), and then were loaded into a PC via a dynamic strainmeter (DPM-700B, Kyowa Electronic Instruments) and an analog-to-digital conversion board (PCI-3171A, Interface; **Figure 3B and C**).

Tensile tests were performed at crosshead speeds of 0.4, 4, 40, and 400 mm/s (strain rates of 0.1, 1, 10, and 100/s) with a gauge length of 4 mm and at a sampling frequency of 5 kHz.

Shear test

On the basis of the velocity and displacement data given to the PC via serial communication, the host controller gave control pulses to the servo controller (RDX X05-1475544, Yamaha). Next, a hammer attached to the actuator (FLIP-X T5LH20-200, Yamaha) was placed horizontally on the slider to break the test sample and the shear test was performed. The displacement data of the test sample was measured by a rotary encoder coaxially attached to the servomotor and imported into a PC via a servo controller, a host controller, and an encoder board (PCI-6204, Interface). The load data of the test samples were measured as voltage data by a load cell (LTS-100GA, Kyowa Electronic Instruments) and imported into a PC via a dynamic strainmeter (DPM-700B, Kyowa Electronic Instruments) and an analog-to-digital conversion board (DPM-700B and PCI-3171A, respectively; Interface).

We designed a shear test apparatus to cause shearing upon hammer impact. The slider was fixed so that the test could not be performed at a constant speed because of the movement of the slider (**Figure 4**).

Shear tests were performed at crosshead speeds of 0.4, 4, 40, and 400 mm/s (strain rates of 0.1, 1, 10, and 100/s) with a gauge length of 4 mm and at a sampling frequency of 5 kHz.

Diffuse axonal damage was reported to occur with a shear strain of 10% to 50% and a strain rate of 10 to 50/s (Margulies et al., 1990; Morrison et al., 1998). We set the strain and strain rate in accordance with the protocols of those two studies. Elastic modulus (Young's modulus) of the specimen was calculated in the range of strain 10–50% assumed in traffic traumatic brain injury with reference to the two studies. The calculations were made in the range of 0.1 to 0.5 strains. The difference in stress between 0.1 and 0.5 strains was obtained by referring to the literature and dividing that value by 0.4.

Tensile-vertical (TV), tensile-parallel (TP), shear-vertical (SV), and shear-parallel (SP) tests were performed on white matter in the direction of the fibers (Figure 5).

Statistical analysis

The sex, age and collection site (spinal cord) were the same for all experimental animals. Therefore, one-way analysis of variance was performed between the elastic modulus for strain rates of 0.1, 1, 10, and 100/s and the direction of the test (TV, TP, SV, and SP) for velocity-dependence and anisotropic analyses. Statistical analysis was performed with StatFlex software version 6 (Artec Co., Ltd., Osaka, Japan). *P* values < 0.05 were considered statistically significant. Bars represent the mean ± standard deviation.

Results

The cross-sectional areas of the spinal cord specimen are shown in Table 1. Data on stress and its standard deviation at 0.1 and 0.5 strains for test samples of white matter subjected to tensile and shear tests at different rates of strain are shown in Table 2. The standard deviation of Young's modulus values and the number of test samples are shown in Table 3.

Stress-strain curve of the four types of moduli are presented in Figure 6. The stress increased with increasing strain rate

in all test conditions. Stress was found to be strain rate-dependent. Figure 7 shows the effect of the test method (A; SV, B; TV, C; SP, and D; TP) on strain rate (0.1, 1, 10, and 100/s). The vertical and horizontal axes represent Young's modulus values and strain rates, respectively. TV showed no significant difference from 0.1 to 10/s, but at 100/s, the stress significantly increased ($P < 0.05$) over the stresses at other speeds (Figure 7A). TP showed no significant difference from 0.1 to 10 mm/s, but the stresses increased at 100/s more than at the other speeds ($P < 0.001$; Figure 7B). SV showed no significant difference in white matter stress with increasing velocity (Figure 7C). SP showed no significant difference from 0.1 to 1/s, but there was a significant difference from 1 to 10/s ($P < 0.05$), and a speed of 100/s increased the stress more than the other speeds ($P < 0.001$; Figure 7D).

The results for each test at each strain rate are shown in Figure 8. Under the 0.1/s condition, TV ($P < 0.05$) and SP ($P < 0.01$) each increased the stress for SV with a significant difference. TP showed a significant increase in stress for all directions ($P < 0.001$; Figure 8A). Under the 1/s condition, the stresses of TV ($P < 0.05$) and SP ($P < 0.001$) for SV each increased with a significant difference. TP showed a significant increase in stress for all directions ($P < 0.001$; Figure 8B). Under the 10/s condition, SP ($P < 0.001$) significantly increased the stress with respect to SV. For TV, SP ($P < 0.001$) increased the stress significantly, whereas TP significantly increased the stress for all directions ($P < 0.001$; Figure 8C). Under the 100/s condition, the stresses were significantly increased for TV ($P < 0.05$), SP ($P < 0.001$), and TV ($P < 0.001$), and for SV and TP ($P < 0.001$) in all directions ($P < 0.001$; Figure 8D).

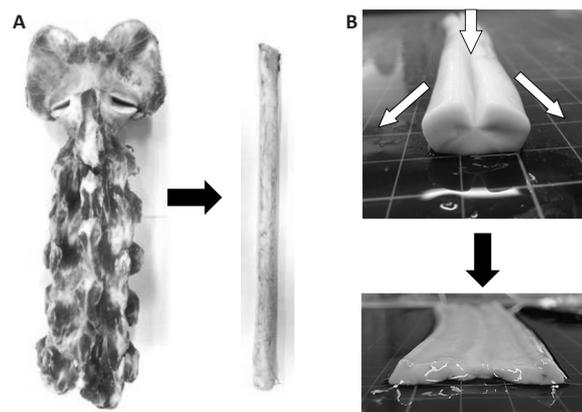


Figure 1 | Spine and spinal cords collected from Holstein cows. (A) Both ends of the cord were cut off because they could have been injured by the tensile load that was applied to the neck of the cows during slaughter. (B) Next, each spinal cord was spread, starting at the dorsal median sulcus (white arrows; entry into the spinal cord, direction of deployment).

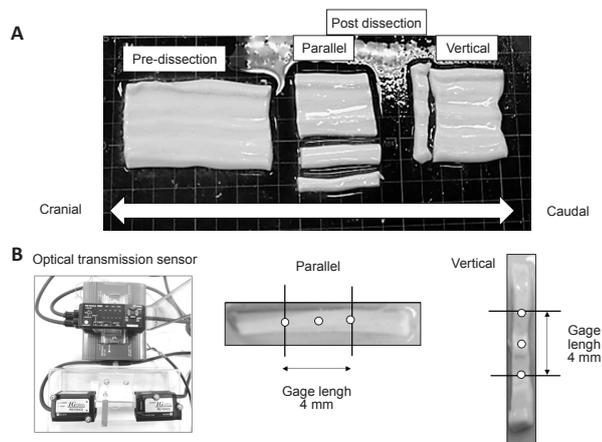


Figure 2 | Method for preparing spinal cord specimens from Holstein cattle. (A) A test sample was prepared taking into consideration the direction of axon fibers. (B) The width and thickness of the samples were measured with an optical transmission sensor, at 3 points (white circle) with a gage length of 4 mm.

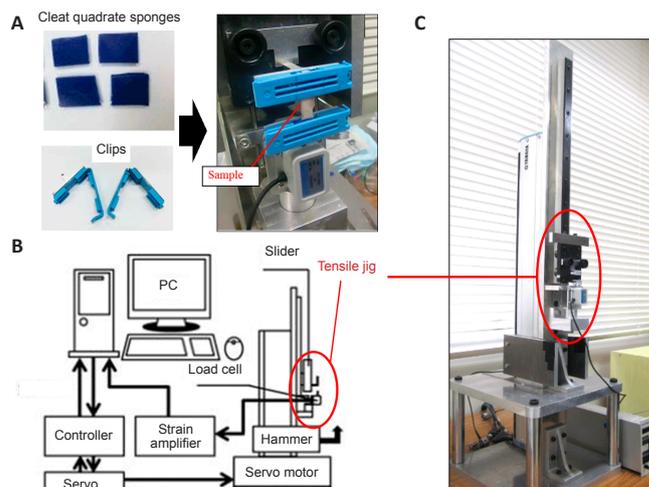


Figure 3 | The tensile jig. (A) Cleat quadrate sponges, clips, and tensile jig grasped white matter. (B) Diagram of the test device. (C) Photograph of the test device.

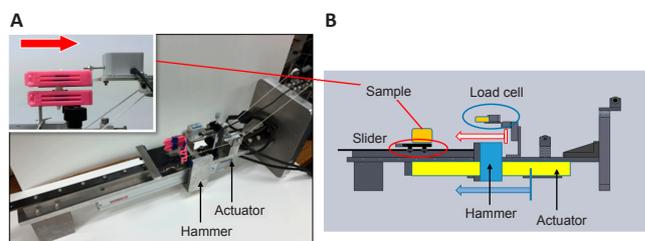


Figure 4 | Setup of the shear test and diagram. (A) White matter, shear jig, and shear test device. (B) Diagram of shear test device.

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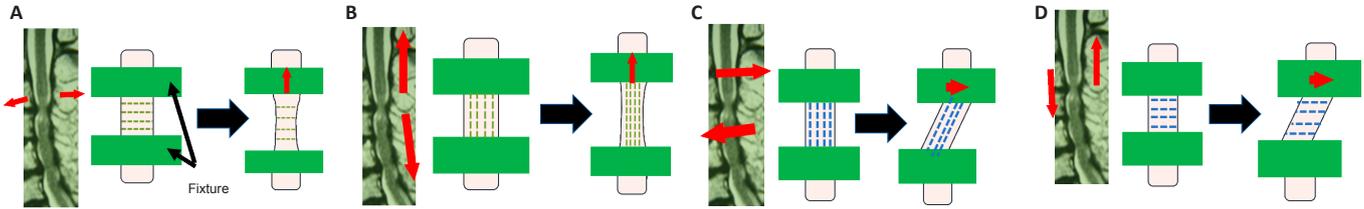


Figure 5 | Tensile and shear tests on white matter of cows.

MRI showed the injury direction of spinal cord. The dotted lines indicate the direction of axon fibers. (A) Tensile-vertical. Injury in the direction of splitting axon fibers. (B) Tensile-parallel. Injury in the direction of pulling axon fibers (stretch injury). (C) Shear-vertical. Torsional force injury to axon fibers. (D) Shear-parallel. Shear force injury to axon fibers.

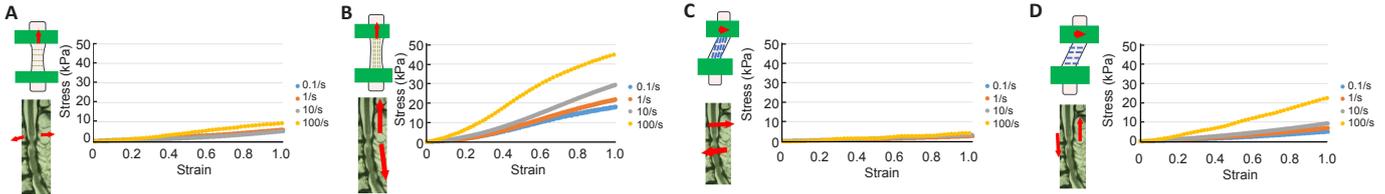


Figure 6 | Stress-strain curve for each strain rate.

The vertical axes are the stress (kPa), and the horizontal axes are the strain rate respectively. Although the stresses increased with increasing strain rate under all test conditions, each result had characteristics. (A) Tensile-vertical (TV). The difference in speed was not strong. (B) Tensile-parallel (TP). The stress was the strongest, and velocity dependence was observed. (C) Shear-vertical (SV). The stress was the lowest and it had the least impact. (D) Shear-parallel (SP). The second largest increase in stress was observed, especially at a strain rate of 100/s.

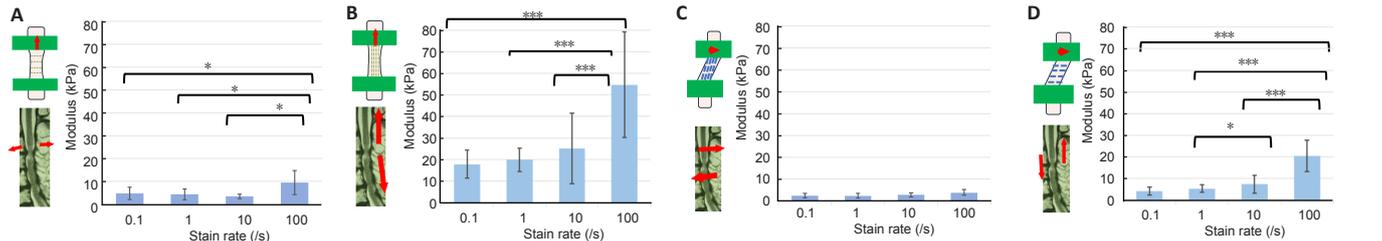


Figure 7 | Each strain rate-dependence analysis for the effect of the test method (TV, TP, SV, and SP).

The vertical axes are the Young's modulus (kPa), and the horizontal axes are the strain rate. One-way analysis of variance was performed under the effect of the modulus of elasticity at the strain rate of 0.1, 1, 10, and 100/s in the direction of the test [TV (A), $n = 47$; TP (B), $n = 55$; SV (C), $n = 49$; and SP (D), $n = 78$]. $*P < 0.05$, $***P < 0.001$. Bars represent the mean \pm standard deviation. TP: Tensile-parallel; TV: tensile-vertical; SP: shear-parallel; SV: shear-vertical.

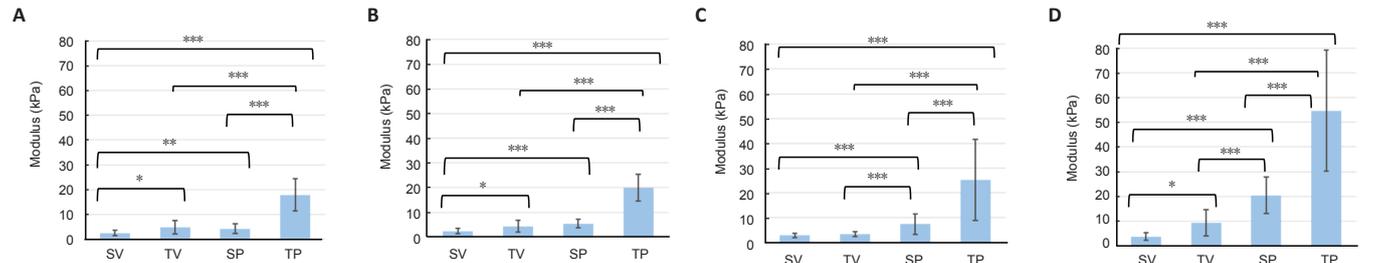


Figure 8 | Effect of the anisotropy analysis for the effect of each strain rate.

The vertical axes are the Young's modulus (kPa), and the horizontal axes are the direction of the fibers. One-way analysis of variance was performed under the effect of the modulus of elasticity on the direction of the test (TV, TP, SV, and SP) at the strain rates of 0.1, 1, 10, and 100/s (A–D). (0.1; $n = 53$, 1; $n = 61$, 10; $n = 65$, and 100; $n = 50$). $*P < 0.05$, $**P < 0.01$, $***P < 0.001$. Bars represent the mean \pm standard deviation. TP: Tensile-parallel; TV: tensile-vertical; SP: shear-parallel; SV: shear-vertical.

Table 1 | Cross section area at 3 points (white circles shown in Figure 2B) with a gage length of 4 mm in the spinal cord specimen harvested from cows

Test direction	Cross section area (mm ²)		
	Point 1	Point 2	Point 3
Parallel	11.6 \pm 2.49	11.0 \pm 3.20	10.9 \pm 3.22
Vertical	10.5 \pm 2.83	10.5 \pm 2.96	10.7 \pm 3.00

Data are expressed as the mean \pm standard deviation.

Table 2 | Characterizations of stress-strain of the spinal cord harvested from cows at a strain of 0.1 and 0.5 mm/s

Strain (mm/s)	Strain rate (/s)	Tensile test (kPa)		Shear test (kPa)	
		Vertical stress	Parallel stress	Vertical stress	Parallel stress
0.1	0.1	0.522 \pm 0.208	0.568 \pm 0.269	0.251 \pm 0.159	0.293 \pm 0.247
	1	0.418 \pm 0.284	0.552 \pm 0.340	0.234 \pm 0.110	0.409 \pm 0.153
	10	0.284 \pm 0.136	0.789 \pm 0.673	0.356 \pm 0.355	0.582 \pm 0.493
	100	0.585 \pm 0.634	2.51 \pm 3.33	0.177 \pm 0.131	1.22 \pm 0.961
0.5	0.1	2.41 \pm 1.11	7.72 \pm 2.82	1.23 \pm 0.594	1.99 \pm 0.838
	1	2.14 \pm 0.937	8.53 \pm 2.44	1.20 \pm 0.494	2.56 \pm 0.819
	10	1.65 \pm 0.358	11.0 \pm 7.01	1.50 \pm 0.623	3.56 \pm 1.98
	100	4.35 \pm 2.66	24.4 \pm 12.2	1.69 \pm 0.633	9.42 \pm 3.51

Data are expressed as the mean \pm standard deviation.

Table 3 | Elastic modulus of the spinal cord specimen harvested from cows

Strain rate (/s)	Tensile test				Shear test			
	Vertical		Parallel		Vertical		Parallel	
	Young's modulus (kPa)	n						
0.1	4.72±2.71	13	17.9±6.49	12	2.46±1.12	10	4.23±1.87	18
1	4.31±2.36	13	19.9±5.42	14	2.41±1.09	14	5.39±1.76	20
10	3.42±0.971	12	25.5±16.4	15	2.86±0.917	17	7.46±4.12	21
100	9.41±5.28	9	54.7±24.6	14	3.77±1.52	8	20.5±7.34	19

Data are expressed as the mean ± standard deviation.

Discussion

We used bovine white matter to test and analyze the anisotropy and velocity dependence of the spinal cord. The tests were performed on the white matter in the fibrous direction (cranial to caudal) changing strain rate. Results of the tensile and shear tests showed that stress tends to increase when external forces are applied parallel to the direction of axon fibers. However, external forces those tear against the fibrous direction and vertically were less likely to increase stress even with increased velocity. We found the spinal cord to be prone to external forces, especially in the direction of the fibers, and to be under increased stress levels when the velocity of external forces increased.

The pathogenesis of spinal cord injury can be divided into primary and secondary injuries. Primary injury is a direct result of external forces at the time of occurrence, whereas secondary injury consists of the subsequent ischemia, inflammation, and apoptosis (Tator and Fehlings, 1991).

We focused mainly on primary damage: direct traumatic forces to the spinal cord (such as trauma, herniated discs, spinal tumors, intraoperative manipulation) and external forces caused by spinal alignment changes and other events (intervertebral instability, impingement, and adjacent intervertebral disorders). Direct injuries, such as herniation of discs, cervical ossification of the posterior longitudinal ligament, and trauma, are relatively easy to see on static medical images. There is the situation in cases of paralysis in which kyphosis develops after posterior decompression of the cervical and thoracic ossification of the posterior longitudinal ligament (Nishida et al., 2017; Ma et al., 2018; Uei et al., 2018; Kim et al., 2020). Such dynamic factors of the spinal cord (Miyazaki et al., 2017) can be evaluated with kinematic magnetic resonance imaging and spinal cord contrast-enhanced computed tomography, but this is difficult on the patient and is laborious for the health-care provider, so the attending physician must be able to assess the stress in the spinal cord from X-rays and static images. Furthermore, transient neurological deficits have been reported in surgical procedures for spinal tumors that directly manipulate the spinal cord (Ottenhausen et al., 2019). This may be due in part to the incision of the spinal cord for resection of the tumor and to direct external forces during retraction. Clinically, as mentioned above, there are reports that speculate on the damage to the spinal cord.

The soft tissue of living organisms is nonlinear, anisotropic, incompressible and incompressible heterogeneous material with high water content. Because of this, it exhibits viscoelastic behavior. Thus, in the weak tensile range, it responds to deformation and the strain curve rises sharply as the strain is increased. A similar behavior was observed in the white matter experiment. The results for the strain curve differ depending on the internal structure of the biological tissue. Previous experiments have been performed on the

brain, blood vessels, lungs, articular cartilage and skin (Azuma and Hasegawa, 1973; Sato et al., 1979; Vawter, 1983). These tissues are also anisotropic, with collagen and elastin oriented along the Langer fibrils in the skin and providing high tension in this direction. The spinal cord has also been shown to have axonal fibers in the long axis direction (Naidich, 2011). Findings in the literature concerning the effect of tissue type on the time-independent mechanical properties of the spinal cord are varied.

The mechanical properties of spinal cord grey and white matter have been studied in tension (Ichihara et al., 2003, 2004), indentation (Koser et al., 2015), pipette aspiration (Ozawa et al., 2001) and unconfined compression (Jannesar et al., 2018). Ichihara et al. (2003) and Koser et al. (2015) reported that grey matter was stiffer than white matter. On the other hand, Koser et al. (2015) measured anisotropy and showed that grey matter behaved like an isotropic material. Specifically, the transverse direction was 1.6 times stiffer than the axial direction. Also, Ozawa et al. (2001) found no difference between tissue types, possibly because they used low-peak strains.

Sharkey (2018) quantified the *in vivo* mechanical properties of the spinal cord and found white matter to be stiffer than grey matter. Nishida et al. (2015) reported that different neural tissues showed varying stiffnesses and tensile strengths, with the cauda equina being 17 and 47 times harder than spinal cord gray and white matter, respectively. Nishida et al. (2020) also reported compression analysis of the gray and white matter. Okazaki et al. (2018) demonstrated age-related differences in the hardness of neural tissues from older and younger cows. Clearly, the published results vary depending on the type of animals, tensile strength and strain rate. Although all of the results to date are valuable, there is still a need for continued experimentation in this area.

We investigated the effects of velocity and anisotropy on the spinal cord, as well as the external forces that tend to increase intraspinal stress. The tensile and shear tests showed that stress tends to increase when external forces are applied parallel to the direction of axon fibers such as TP and SP. The tests conducted here confirmed that spinal white matter is anisotropic. Moreover, stress tends to increase with increasing strain rate, confirming that spinal white matter has velocity dependence. For TV and SV, the strain rate is irrelevant. However, for SP the strain rate is over 100/s, indicating the possibility of damage caused by low strain rates in PV. We believe the anisotropy and velocity dependence of the spinal cord are two causes of paralysis that are more likely to occur with acute external forces than with chronic compression. The external forces that tear vertically against the fibrous direction are less likely to increase stress, even with increased velocity. The spinal cord was found here to be somewhat durable, even with the anterior compression and retractions experienced during surgery.

There are some limitations to our study. First, our results are variable, and the cross-sectional area of the vertically cut specimens was not uniform. Therefore, the content of the anterior, lateral, and posterior funiculi are not uniform, and analysis of each part was not done. Also, the number of our experiments was low. Baba et al. (1997) reported that cell population in the anterior horn starts to decrease when the cross-sectional area of the cord is decreased by 30% due to compression and reaches a plateau when the area is decreased by 50%. In clinical practice, it is not known how much strain and strain rate damage will produce spinal cord injury. The present study evaluated only the anisotropic and velocity-dependent features. It is thus impossible to explain the relationship between tensile/shear injury and spinal cord function. Furthermore, increased stress does not represent a spinal cord injury. Finally, gray matter was not assessed.

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These limitations mean that age-related changes in the spinal cord and the effects of blood flow were not factored into our findings.

Conclusion

Mechanistic analysis of anisotropy and velocity dependence of spinal white matter showed that spinal white matter is prone to damage by external forces, especially in the direction of the fibers (cranial to caudal), and that there is an increase in stress when the velocity of the external forces increases. These findings may be helpful in understanding the mechanics of spinal cord injury, the stresses occurring in the spinal cord preoperatively and postoperatively, and how to most carefully manipulate the spinal cord intraoperatively.

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Conflicts of interest: No benefits in any form have been received or will be received by a related commercial party directly or indirectly to the subject of this article.

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Institutional review board statement: The Institutional Animal Care and Use Committee of Yamaguchi University waived the requirement for ethical approval. The regulations of the university provide review of researches that use living animals. Our study used spinal cords of cows that were slaughtered for food. Therefore, our study was excluded from ethical review.

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References

- Azuma T, Hasegawa M (1973) Distensibility of the vein: from the architectural point of view. *Biorheology* 10:469-479.
- Baba H, Maezawa Y, Uchida K, Imura S, Kawahara N, Tomita K, Kudo M (1997) Three-dimensional topographic analysis of spinal accessory motoneurons under chronic mechanical compression: an experimental study in the mouse. *J Neurol* 244:222-229.
- Bhattacharyya S (2018) Spinal cord disorders: myelopathy. *Am J Med* 131:1293-1297.
- Boody BS, Lendner M, Vaccaro AR (2019) Ossification of the posterior longitudinal ligament in the cervical spine: a review. *Int Orthop* 43:797-805.
- Eckert MJ, Martin MJ (2017) Trauma: spinal cord injury. *Surg Clin North Am* 97:1031-1045.
- Henderson FC, Geddes JF, Vaccaro AR, Woodard E, Berry KJ, Benzel EC (2005) Stretch-associated injury in cervical spondylotic myelopathy: new concept and review. *Neurosurgery* 56:1101-1113.
- Ichihara K, Taguchi T, Sakuramoto I, Kawano S, Kawai S (2003) Mechanism of the spinal cord injury and the cervical spondylotic myelopathy: new approach based on the mechanical features of the spinal cord white and gray matter. *J Neurosurg* 99:278-285.
- Ichihara K, Taguchi T, Hashida T, Ochi Y, Murakami T, Kawai S (2004) The treatment of far-out foraminal stenosis below a lumbosacral transitional vertebra: a report of two cases. *J Spinal Disord Tech* 17:154-157.

- Iyer A, Azad TD, Tharin S (2016) Cervical spondylotic myelopathy. *Clin Spine Surg* 29:408-414.
- Jannesar S, Allen M, Mills S, Gibbons A, Bresnahan JC, Salegio EA, Sparrey CJ (2018) Compressive mechanical characterization of non-human primate spinal cord white matter. *Acta Biomater* 74:260-269.
- Kim SY, Hyun SJ, Kim KJ, Jahng TA (2020) Surgical outcomes according to dekyphosis in patients with ossification of the posterior longitudinal ligament in the thoracic spine. *J Korean Neurosurg Soc* 63:89-98.
- Koser DE, Moeendarbary E, Hanne J, Kuerten S, Franze K (2015) CNS cell distribution and axon orientation determine local spinal cord mechanical properties. *Biophys J* 108:2137-2147.
- Kretzer RM (2017) Intradural spinal cord tumors. *Spine (Phila Pa 1976)* 42 Suppl 7:S22.
- Ma L, Liu FY, Huo LS, Zhao ZQ, Sun XZ, Li F, Ding WY (2018) Comparison of laminoplasty versus laminectomy and fusion in the treatment of multilevel cervical ossification of the posterior longitudinal ligament: a systematic review and meta-analysis. *Medicine (Baltimore)* 97:e11542.
- Margulies SS, Thibault LE, Gennarelli TA (1990) Physical model simulations of brain injury in the primate. *J Biomech* 23:823-836.
- McDonald JW, Sadowsky C (2002) Spinal-cord injury. *Lancet* 359:417-425.
- Miyazaki M, Notani N, Ishihara T, Kanezaki S, Tsumura H (2017) Surgical outcomes after laminoplasty for cervical spondylotic myelopathy: a focus on the dynamic factors and signal intensity changes in the intramedullary spinal cord on MRI. *Clin Neurol Neurosurg* 162:108-114.
- Morrison B, 3rd, Meaney DF, McIntosh TK (1998) Mechanical characterization of an in vitro device designed to quantitatively injure living brain tissue. *Ann Biomed Eng* 26:381-390.
- Naidich TP (2011) Chapter 5, The normal spinal cord and meninges. In: *Imaging of the spine* (eds), pp 107-146. New York: Elsevier.
- Nishida N, Kanchiku T, Ohgi J, Ichihara K, Chen X, Taguchi T (2015) Mechanical properties of nerve roots and rami radicales isolated from fresh pig spinal cords. *Neural Regen Res* 10:1869-1873.
- Nishida N, Kanchiku T, Kato Y, Imajo Y, Suzuki H, Yoshida Y, Ohgi J, Chen X, Taguchi T (2017) Cervical ossification of the posterior longitudinal ligament: factors affecting the effect of posterior decompression. *J Spinal Cord Med* 40:93-99.
- Nishida N, Jiang F, Ohgi J, Tanaka A, Imajo Y, Suzuki H, Funaba M, Sakai T, Sakuramoto I, Chen X (2020) Compression analysis of the gray and white matter of the spinal cord. *Neural Regen Res* 15:1344-1349.
- Okazaki T, Kanchiku T, Nishida N, Ichihara K, Sakuramoto I, Ohgi J, Funaba M, Imajo Y, Suzuki H, Chen X, Taguchi T (2018) Age-related changes of the spinal cord: a biomechanical study. *Exp Ther Med* 15:2824-2829.
- Ottenhausen M, Ntoulas G, Bodhinayake I, Ruppert FH, Schreiber S, Förschler A, Boockvar JA, Jödicke A (2019) Intradural spinal tumors in adults-update on management and outcome. *Neurosurg Rev* 42:371-388.
- Ozawa H, Matsumoto T, Ohashi T, Sato M, Kokubun S (2001) Comparison of spinal cord gray matter and white matter softness: measurement by pipette aspiration method. *J Neurosurg* 95:221-224.
- Pepke W, Almansour H, Richter M, Akbar M (2018) Spondylotic cervical myelopathy: indication of surgical treatment. *Orthopade* 47:474-482.
- Sato M, Hayashi K, Niimi H, Moritake K, Okumura A, Handa H (1979) Axial mechanical properties of arterial walls and their anisotropy. *Med Biol Eng Comput* 17:170-176.
- Sharkey LR (2018) An inverse finite element approach to modeling the rat cervical spinal cord: for use in determining the mechanical properties of the grey and white matter. Vancouver, British Columbia, Canada: University of British Columbia.
- Tator CH, Fehlings MG (1991) Review of the secondary injury theory of acute spinal cord trauma with emphasis on vascular mechanisms. *J Neurosurg* 75:15-26.
- Uei H, Tokuhashi Y, Oshima M, Maseda M, Nakahashi M, Nakayama E (2018) Efficacy of posterior decompression and fixation based on ossification-kyphosis angle criteria for multilevel ossification of the posterior longitudinal ligament in the thoracic spine. *J Neurosurg Spine* 29:150-156.
- Vawter DL (1983) Poisson's ratio and incompressibility. *J Biomech Eng* 105:194-195.

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