New Method for the Quantitative Assessment of Sensory Disturbances in Cervical Myelopathy: Application for Neurological Level Diagnosis

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Abstract:

Introduction: Cervical myelopathy frequently manifests as sensory disturbances, including numbness, and their distribution pattern aids in neurological level diagnosis. However, the objective assessment of sensory disturbances is challenging. In this study, we attempted to quantitatively evaluate sensory symptoms in patients with cervical myelopathy according to lesion level using PainVision®.

Methods: Dermal sensations were evaluated in patients (n = 158) and healthy volunteers (n = 100) using PainVision® PS-2100, which measured the current perception threshold (CPT). The results were analyzed for their correlation with magnetic resonance imaging (MRI) data, visual analog scale (VAS) scores, and patient functional status assessed by the Japanese Orthopaedic Association (JOA) and JOA Cervical Myelopathy Evaluation Questionnaire (JOACMEQ) scores.

Results: Forearm and palm CPT values were significantly higher in patients with cervical myelopathy (both sites, $P < 0.001$) and were negatively correlated with the JOA score (forearm, $r = -0.33$; palm, $r = -0.35$; $P < 0.001$) and the JOACMEQ scores for upper extremity function (forearm, $r = -0.37$; palm, $r = -0.39$; $P < 0.001$), lower extremity function (forearm, $r = -0.39$; palm, $r = -0.40$; $P < 0.001$), and quality of life (forearm $r = -0.27$, $P = 0.0025$); however, no correlation was observed with the VAS score. Stratification of patients according to their lesion levels determined by MRI revealed that the C3/C4 subgroup had significantly higher forearm CPT values than the C4/C5 ($P = 0.024$) and C5/C6 ($P = 0.0013$) subgroups and higher palm CPT values than the C5/C6 subgroup ($P = 0.009$).

Conclusions: Quantitative measurements of sensory disturbances using the PainVision® device correspond to the degree of patient functional disability and the lesion level. This indicates that both the distribution and intensity of sensory abnormalities are important for neurological level diagnosis in patients with cervical myelopathy.

Keywords:

cervical myelopathy, neurological level diagnosis, sensory disturbance, PainVision®, current perception threshold, magnetic resonance imaging, cervical spine

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Introduction

Cervical myelopathy is a common age-related degeneration of the cervical spinal cord due to compression caused by herniated disks, spondylotic spurs, ossification of the posterior longitudinal ligaments, or spinal stenosis[1]. The condition is manifested by neurological symptoms, such as neck and limb pain, abnormal gait, falls due to limb weakness, paresthesia, and sphincter dysfunction, which lead to severe functional disability. Decompression surgery is the most effective treatment, and timely diagnosis is essential to inhibit disease progression[2,3]. Currently, magnetic resonance imaging (MRI) remains the gold standard test for the disease[4]; however, due to the nonspecific nature of the neurological signs, there may be a time lag between the preliminary diagnosis and MRI examination[5,6]. Furthermore, the MRI results may not have strong association with the neurological functions, and cases of asymptomatic spinal cord compression revealed by MRI are common[6,7]. Therefore, diagnosing cervical myelopathy without neurological evaluation is challenging, and MRI findings should be complemented with motor, reflex, and sensory assessments[8,9].

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Table 1. Demographic and Clinical Characteristics of Patients with Cervical Myelopathy and Healthy Controls.

Parameter	Cervical myelopathy group	Healthy group	*P*-value*
Patients (n)	158	100	-
Male to female ratio, n (%)	120:38 (76/24)	76:24 (76/24)	0.99
Age (years, mean±SD)	65.6±12.3	65.5±14.0	0.89
BMI (kg/m^2, mean±SD)	23.6±3.4	23.1±3.3	0.44
Diagnosis			
Cervical spondylotic myelopathy (n)	146	-	-
Ossification of the posterior longitudinal ligament (n)	12	-	-

*Mann-Whitney *U*-test; BMI, body mass index; SD, standard deviation

A review of 35 studies revealed that bilateral sensory complaints in the hands may suggest cervical cord pathology and should be considered as an MRI indicator[10]. Paresthesia, such as numbness, is often the first manifestation of cervical myelopathy, and upper limb sensory disturbances are the most commonly reported symptoms[6]. Moreover, several studies indicated that sensory testing can reveal the spread of lesions along the sagittal section of the spinal cord and determine the neurological level of disk compression and spinal cord enhancement[11-14]. Localization of the main lesion to a specific intervertebral level can help distinguish cervical myelopathy from nonstenotic conditions, such as amyotrophic lateral sclerosis and multiple sclerosis; it may also help determine the most appropriate site for targeted surgery, which is important to minimize complications, especially in the elderly[13,14]. Although MRI can reveal spinal cord compression at several levels, it may not determine the principal lesion responsible for the symptomatology[15]. In this respect, neurological signs (e.g., tendon reflexes, muscle weakness, and sensory disturbances) may contribute to an accurate diagnosis[12-14]; among them, sensory symptoms in the arms are considered as the most reliable indicator of cervical myelopathy[13]. However, few studies have provided comprehensive analysis of the sensory abnormalities characteristic for cervical myelopathy, possibly due to the lack of quantitative sensory tests.

PainVision® PS-2100 (Nipro Corporation, Osaka, Japan) was developed to quantitatively evaluate pain and sensory perception. The device causes painless, selective stimulation of Aβ and Aδ sensory fibers by sending pulses of electric current along the surface of the body and recording the participant's sensory threshold. PainVision® has been proven useful for evaluating pain severity in different pathological conditions, including cancer and low back pain[16-18], but its application for sensory assessment in patients with cervical myelopathy has not been previously reported.

This study aimed to determine whether the PainVision® device can be used to quantify the magnitude of sensory disturbance and increase the accuracy of neurological level diagnosis in patients with cervical myelopathy. To this end, the sensory threshold assessed by PainVision® was compared between patients and healthy individuals and analyzed for correlation with MRI data and patient functional status.

Materials and Methods

Study population

We examined 158 patients (120 men, 38 women; mean age 65.6 ± 12.3 years) with cervical myelopathy indicated for surgery; among them, 146 were diagnosed with cervical spondylotic myelopathy and 12 with ossification of the posterior longitudinal ligament (Table 1). The diagnosis was made by highly experienced spinal surgeons based on symptomatology, neurological findings, radiography results, and MRI findings. Only patients exhibiting strong T2-weighted MRI signals at single intervertebral levels were included. The control group comprised 100 age- and sex-matched healthy volunteers (76 men, 24 women; mean age 65.5 ± 14.0 years) without evidence of cervical myelopathy or cervical radiculopathy after neurological examination (Table 1). Patients and healthy individuals with histories of cervical spine surgery, symptomatic cerebral infarction, diabetic neuropathy, or upper extremity entrapment neuropathy were excluded; patients with high-intensity MRI signals at multiple intervertebral levels were also not considered.

MRI

Standard MRI analyses were conducted using a 1.5-T Magnetom® Symphony Tim System (Siemens Healthineers, Munich, Germany). The MRI scans consisted of T2-weighted sequences in the sagittal and axial planes of the cervical spine. The intervertebral level responsible for the neuropathy was determined as the level showing a strong intramedullary signal on T2-weighted images, i.e., maximum spinal cord compression (Fig. 1A). If spinal cord compression was also observed at other levels (Fig. 1B), the responsible lesion was determined by highly experienced spinal surgeons based on symptomatology, neurological findings, and MRI; cases exhibiting inconsistencies between MRI and other test results were excluded from the analysis. Patients were divided into C3/C4, C4/C5, C5/C6, and C6/C7 subgroups according to the levels of cervical cord compression, and their sensory measurements were compared.

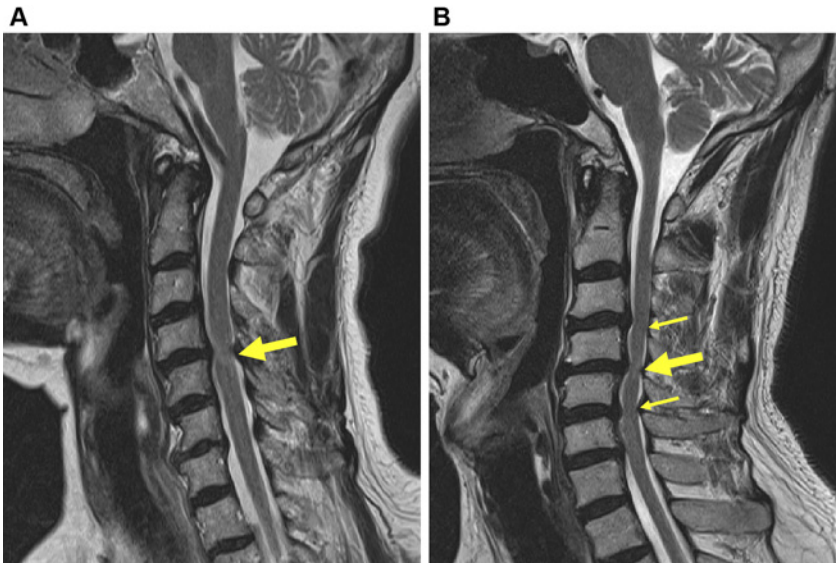

Figure 1. Level diagnosis based on T2-weighted MRI results. (A) An MR image showing one strong intramedullary signal at the C4/C5 level. (B) An MR image showing one strong signal at the C4/C5 level (thick arrow) and weak signals at the C3/C4 and C5/C6 levels (thin arrows); in such cases, the responsible lesion was determined by highly experienced spinal surgeons based on symptomatology and neurological examinations.

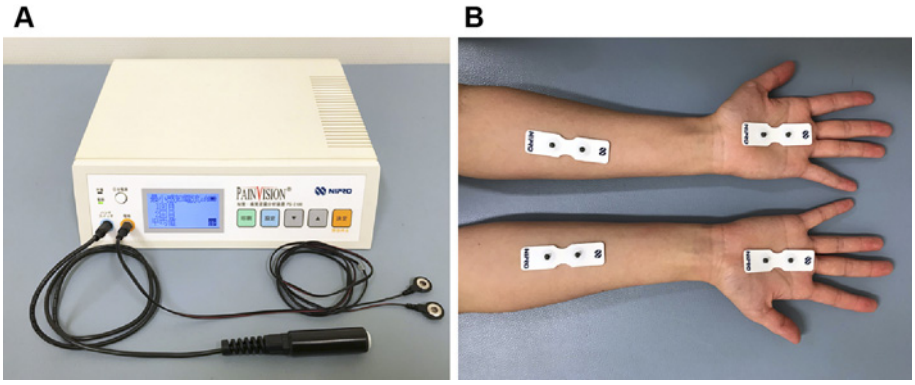

Figure 2. Quantitative assessment of sensory perception using PainVision®. (A) Overall view of the PainVision® PS-2100 apparatus. (B) Electrodes were patched to the surfaces of patient forearms or palms, and the lowest perceptible current (current perception threshold [CPT]) was measured.

Sensory evaluations

PainVision®

Objective (quantitative) evaluations of sensory disturbances (paresthesia) were conducted using PainVision® PS-2100 according to the manufacturer's instructions. Electrodes were placed on flat body surfaces, free of hair; in this study, the measurements were performed in the forearms and palms as the most suitable sites. The electrode plates were affixed to the proximal one-third of the flexor side of the forearm, slightly closer to the ulna, and to the center of the palm (Fig. 2). The electric signal was slowly increased within the range of 0-150 μA (50 Hz; pulse width, 0.3 m); the lowest perceptible current sensed as electrical stimulation[19] was defined as the current perception threshold (CPT) and recorded. Each measurement was performed three times, and the average bilateral CPT values were calculated for the forearm and palm.

Visual analog scale (VAS)

Numbness in the upper and lower extremities and neck pain were evaluated using a unidimensional VAS. The patients were asked to mark sensation intensity on a continuous straight line, using a range from 0 mm (none) to 100 mm (extreme).

Table 2. Correlation of CPT Measurements with JOA, JOACMEQ, and VAS Scores.

Scoring system	Parameter	Score, mean±SD	Forearm CPT		Palm CPT	
			r	*P*	*r*	*P*
JOA	Overall score	9.2±2.7	**-0.33**	**<0.001**	**-0.35**	**<0.001**
JOACMEQ	Cervical spine function	68.0±26.1	-0.14	0.12	-0.13	0.14
	Upper extremity function	62.3±26.7	**-0.37**	**<0.001**	**-0.39**	**<0.001**
	Lower extremity function	44.0±31.8	**-0.39**	**<0.001**	**-0.40**	**<0.001**
	Bladder function	67.7±24.7	-0.11	0.23	-0.17	0.062
	Quality of life	39.6±18.0	**-0.27**	**0.0025**	-0.16	0.087
VAS	Upper extremity numbness	68.5±28.6	0.026	0.78	-0.16	0.088
	Lower extremity numbness	41.9±33.8	0.13	0.16	-0.16	0.087
	Neck pain	41.2±31.7	-0.09	0.27	-0.12	0.16

CPT, current perception threshold; JOA, Japanese Orthopaedic Association; JOACMEQ, JOA Cervical Myelopathy Evaluation Questionnaire; VAS, visual analog scale; SD, standard deviation

Functional evaluation

Japanese Orthopaedic Association (JOA) scoring system

The JOA scoring system is a 17-point, investigator-administered tool used to assess the functional disability of patients with cervical myelopathy. The score is calculated based on six domains (motor dysfunction of the upper extremities, motor dysfunction of the lower extremities, sensory dysfunction of the upper extremities, sensory dysfunction of the lower extremities, sensory dysfunction of the trunk, and dysuria) and ranges from 0 (complete dysfunction) to 17 (no loss of function).

JOA Cervical Myelopathy Evaluation Questionnaire (JOACMEQ)

The JOACMEQ is a self-administered questionnaire that includes 24 questions regarding cervical spine function, upper and lower extremity function, bladder function, and quality of life. The patients rated their conditions, separately for each domain, from 0 (worst) to 100 (best).

Ethical statement

This study was approved by our institutional ethics committee. Informed oral or written consent was obtained from all patients after explanation of the study aim and protocol.

Statistical analysis

The results were analyzed using SPSS®, version 22.0 (IBM, Chicago, IL, USA). The data are expressed as mean ± standard deviation. CPT value comparisons (control *vs*. patient group and C3/C4 *vs*. C4/C5, C5/C6, and C6/C7 subgroups) were performed using the Mann-Whitney *U*-test. The correlations between the PainVision® results and those from the other tests were determined using bivariate analysis, based on Pearson's correlation coefficient. $P < 0.05$ was considered statistically significant.

Results

There were no differences in the demographic characteristics between the patient and healthy control groups (Table 1). The analysis of the PainVision® measurements revealed that the levels of sensory perception among patients with cervical myelopathy were significantly lower than those among control individuals, as evidenced by higher CPT values in the forearms (16.7 ± 10.3 μA *vs.* 11.8 ± 3.2 μA; $P < 0.001$) and palms (33.2 ± 12.6 μA *vs*. 23.0 ± 6.9 μA; $P < 0.001$). Comparison of the CPT values with the JOA and JOACMEQ scores revealed negative correlation of forearm and palm CPTs with the JOA scores ($r = -0.33$ and $r = -0.35$, respectively; $P < 0.001$), as well as with the JOACMEQ scores for upper ($r = -0.37$ and $r = -0.39$, respectively; $P < 0.001$) and lower ($r = -0.39$ and $r = -0.40$, respectively; $P < 0.001$) extremity function (Table 2). Furthermore, the forearm CPT values were negatively correlated with the JOACMEQ quality of life score ($r = -0.27$, $P = 0.0025$). However, there was no association between CPT values and VAS scores for neck pain or extremity numbness (Table 2).

Next, 158 patients with cervical myelopathy were stratified according to the level of neuropathy determined by MRI (Fig. 3) into four subgroups: C3/C4 (n = 38), C4/C5 (n = 65), C5/C6 (n = 49), and C6/C7 (n = 6), and their CPT values were compared with those of healthy individuals. Statistical analysis revealed that all patient subgroups had higher CPTs than the control group in both the forearm (Table 3) and palm (Table 4), and the differences were statistically significant for all neuropathy levels, except C6/C7 ($P = 0.076$ for the palm, Table 4); nevertheless, the C6/C7 patients also exhibited a tendency toward elevated CPTs. These results indicate that cervical myelopathy at all levels leads to decreased sensory perception.

Intergroup comparisons of forearm and palm CPT values revealed that patients with more cranial levels of myelopathy (C3/C4 subgroup) had overall stronger paresthesia than the other subgroups. Thus, there was a significant increase in

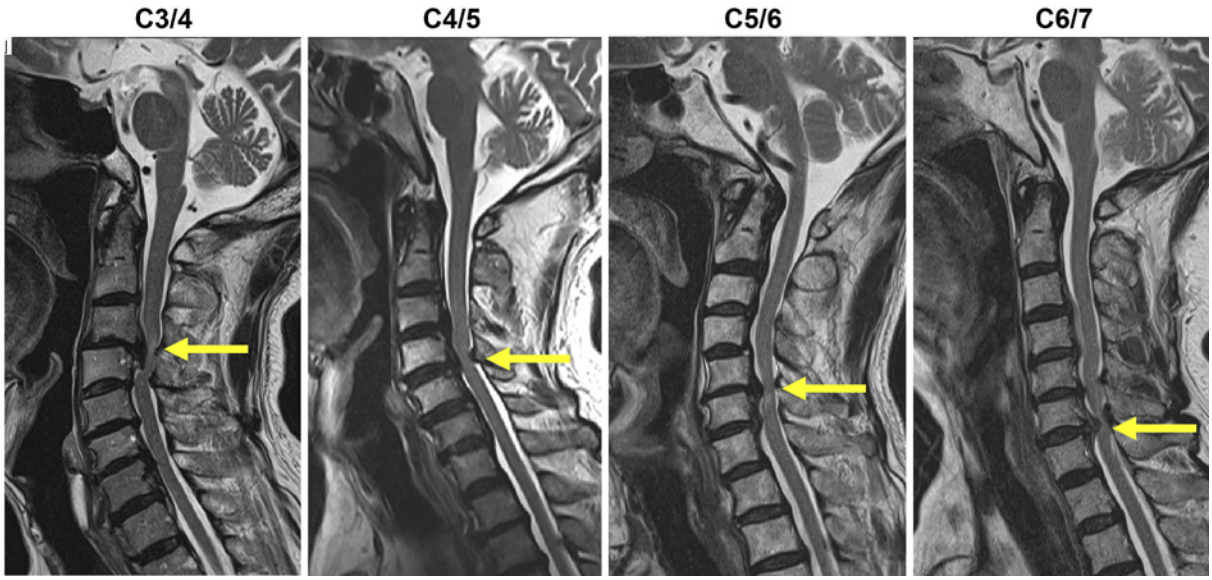

Figure 3. Preoperative MRI scans in patients with cervical myelopathy at different intervertebral levels. Arrows point to the level of obvious cord compression, indicated by a high-intensity signal on T2-weighted images: C3/C4, C4/C5, C5/C6, and C6/C7.

Table 3. Comparison of Forearm CPT Measurements between Groups.

Control CPT (μA, mean±SD)	Cervical myelopathy		*P*-value*	
	Level group (n)	CPT (μA, mean±SD)	*vs.* control	*vs.* C3/C4 group
11.8±3.2	Total (158)	16.7±10.3	**<0.001**	-
	C3/C4 (38)	21.6±15.3	**<0.001**	-
	C4/C5 (65)	16.4±9.5	**<0.001**	**0.024**
	C5/C6 (49)	13.6±4.3	**0.012**	**0.0013**
	C6/C7 (6)	15.3±3.1	**<0.001**	0.47

CPT, current perception threshold; SD, standard deviation
*Mann-Whitney *U*-test

Table 4. Comparison of Palm CPT Measurements between Groups.

Control CPT (μA, mean±SD)	Cervical myelopathy		*P*-value*	
	Level group (n)	CPT (μA, mean±SD)	*vs.* control	*vs.* C3/C4 group
23.0±6.9	Total (158)	33.2±12.6	**<0.001**	-
	C3/C4 (38)	35.8±10.1	**<0.001**	-
	C4/C5 (65)	35.0±15.1	**<0.001**	0.24
	C5/C6 (49)	29.8±10.4	**<0.001**	**0.009**
	C6/C7 (6)	27.8±7.0	0.076	0.094

CPT, current perception threshold; SD, standard deviation
*Mann-Whitney *U*-test

the mean forearm CPT values in C3/C4 patients compared with those in C4/C5 and C5/C6 patients (P = 0.024 and P = 0.0013, respectively; Table 3) and a significant increase in the palm CPT values compared with those in C5/C6 patients (P = 0.009; Table 4). The C3/C4 subgroup also tended to have higher CPTs compared with the C6/C7 subgroup, but the difference was not statistically significant (P > 0.05; Table 3, 4).

Discussion

In this study, we used the PainVision® device to quantitatively analyze sensory disturbances in patients with cervical myelopathy caused by spinal cord lesions at different levels. The results revealed that CPT values were significantly correlated with disease severity assessed by the multidimensional JOA and JOACMEQ scores commonly used to evalu-

ate the functional status of patients with cervical myelopathy. However, the absence of a correlation between the CPT values and the VAS score was unexpected, although similar results were obtained in a study of chemotherapy-induced vascular pain[20]. Most importantly, CPT values were higher when the level of myelopathy was more cranial. Thus, patients with lesions at the C3/C4 level had a higher CPT than those with lesions at more caudal intervertebral levels, C4/C5, C5/C6, and C6/C7. However, the difference between the C3/C4 and C6/C7 subgroups was not significant, probably because there were few patients with spinal cord compression at the C6/C7 level, who are known to represent only 4% of all cervical myelopathy cases[11]. These findings indicate a level-dependent loss of sensory perception and are consistent with the distribution of sensory deficits proposed by Seichi et al.[13] for neurological level diagnoses. Thus, our study shows that sensory disturbances serving as biomarkers for the neurological level diagnosis can be identified not only by their distribution but also by their intensity, which can be measured using PainVision®.

In patients with cervical myelopathy, the neurological level diagnosis is important for identifying the intervertebral compression site most appropriate for surgery[15]. However, making decisions based only on MRI results is difficult[7]. Kokubun[11] proposed the neurological level diagnosis of patients with cervical myelopathy, postulating that in most cases, the intervertebral level of the lesion can be determined through neurological evaluation and the dermatome pattern of sensory disturbance. Hirabayashi et al.[12] revealed that a single level might be responsible for specific neural signs and symptoms. Thus, disk compression at the C3/C4, C4/C5, or C5/C6 levels could cause numbness in all fingers, in the 1st to 3rd fingers, or in the 3rd to 5th fingers, respectively, whereas compression at the C6/C7 level was not associated with numbness. A study of 50 patients who underwent successful surgery for cervical compressive myelopathy at a single intervertebral level revealed a 66% agreement between MRI results and neurological signs; the highest correlation was observed for the extent of hand numbness (62%), followed by the pinprick response (40%), deep tendon reflexes (36%), and muscle weakness (19%)[14]. Similar results were reported by Seichi et al.[13], who analyzed the correlation between neurological parameters and cervical MRI results, showing that the distribution of sensory deficits in the upper extremities was a more reliable parameter for level diagnosis than muscle strength or deep tendon reflex.

Despite the indicated diagnostic importance of sensory signs, there is a lack of objective data regarding sensory disturbances in patients with cervical myelopathy, possibly due to the limitations of the existing tests. Sensory perception can be analyzed using subjective methods, such as VAS or numerical rating scales[21,22]; however, these tests are biased and may depend on patient mood and physical status. Objective methods, such as the pin prick (pain/temperature sensation), tissue paper, Semmes-Weinstein monofilament, Ipswich touch (touch sensation), and tuning fork C128 (vibration) tests[23,24], are very useful for diagnosing the spread of lesions in the transverse plane of the spinal cord. However, they are not easy to administer, requiring time, patience, and understanding, and do not yield quantifiable results. These limitations can be overcome using the PainVision® device, which selectively stimulates Aβ fibers (touch/pressure receptors) and Aδ fibers (mechanical/pain/temperature receptors), thus reproducing objective sensory tests on thermal nociception and tactile perception. The PainVision® test is quantitative, noninvasive, painless, rapid, and easy to conduct and does not require lengthy instruction or special training. Thus, the device can provide quantitative analyses of sensory disturbances in patients with cervical myelopathy. Furthermore, the device could be used to compare disease severity among patients and to assess individual patient neurological conditions before and after treatment, which may not be possible with conventional sensory tests. PainVision® has been previously employed in clinical practice to evaluate peripheral neuropathy, low back pain, and postherpetic neuralgia[15,18,25]; however, it has not been used to measure sensory deficits in patients with cervical myelopathy. Our results reveal that PainVision® can provide objective, quantitative data that are useful for determining neurological levels, as evidenced by the good correlation of CPT measurements with the functional status and the level of cervical cord compression revealed by MRI. In addition, the test can be conducted quickly, taking approximately 10 min per patient to measure CPT in four sites. Although we did not find a correlation between CPT values and VAS scores, this can be attributed to the subjective nature of the VAS, in which similar ratings by different patients may not necessarily reflect similar experiential intensities[26].

To the best of our knowledge, this is the first report of quantification of sensory disturbances in patients with cervical myelopathy. However, our study has several limitations. We used the PainVision® device to provide objective sensory evaluations of pain/temperature/tactile sensations, but did not examine the correlation with conventional objective sensory tests (pin prick, monofilament, tuning fork, etc.). Furthermore, we analyzed only patients with single lesions that exhibited strong intramedullary signals on the T2-weighted images, excluding those with multiple high-intensity areas; however, the latter also need to be evaluated to determine the correlation between neurological deficits and intervertebral compression levels. These limitations can be addressed in future studies. It should also be noted that the fairly high price of the PainVision® device (about 1,500,000 JPY or 14,000 USD) may, at present, hinder its wider application.

In conclusion, our findings reveal that the PainVision® device provides a useful quantitative method to evaluate sensory disturbances in patients with cervical myelopathy, leading to improved neurological level diagnoses for targeted decompression surgery. The device may be helpful in providing outcome measure to assess disease severity and treatment efficacy.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

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Author Contributions:

• Study conception and design: Takeshi Inoue, Shigeru Soshi

• Data acquisition: Takeshi Inoue, Makoto Kubota

• Data analysis and interpretation: Takeshi Inoue, Shigeru Soshi, Makoto Kubota

• Drafting of the manuscript: Takeshi Inoue, Shigeru Soshi

• Critical revision: Takeshi Inoue, Shigeru Soshi, Keishi Marumo

Informed Consent: Informed consent was obtained from all participants in this study.

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