

## Tight adhesions after spinal cord stimulation observed during dorsal root entry zone lesioning for pain after spinal root avulsion: illustrative cases

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**BACKGROUND** Patients often experience strong shooting pains after spinal root avulsion. The efficacy of spinal cord stimulation (SCS) for this type of pain is inconsistent; however, dorsal root entry zone (DREZ) lesioning (DREZ-lesion) has often proven to be an effective treatment modality. The authors report two cases in which DREZ-lesion was performed to treat pain after spinal root avulsion after implantation of SCS, but the operations were challenging due to strong adhesions.

**OBSERVATIONS** The authors present two cases of patients with pain after spinal root avulsion in whom SCS implantation was only temporarily effective. Patients complained of persistent and paroxysmal shooting pains in the upper extremities. SCS removal and DREZ-lesion were performed, but adhesions in the epidural and subdural space contacting the leads were strong, making it difficult to expose the DREZ.

**LESSONS** Although adhesions around the spinal cord can be caused by trauma, the authors believe that in these cases, the adhesions could have been caused by the SCS leads. There are few previous reports confirming the efficacy of SCS in treating pain after spinal root avulsion; therefore, caution is required when considering SCS implantation.

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**KEYWORDS** spinal root avulsion pain; dorsal root entry zone lesioning; spinal cord stimulation

Pain after spinal root avulsion is often caused by strong traction on the upper limbs or shoulders, as occurs in motorcycle accidents, and is characterized by strong shooting pain (paroxysmal pain). Pain occurs in ~70–90% of patients after spinal root avulsion, and 20% of these cases are intractable.<sup>1,2</sup> Various pain treatments have been attempted, including dorsal root entry zone lesioning (DREZ-lesion), spinal cord stimulation (SCS), motor cortex stimulation, intrathecal analgesic pump implantation, stellate ganglion block, and thalamic deep brain stimulation.<sup>3</sup> DREZ-lesion is effective in treating root avulsion pain, but the efficacy of SCS remains unclear.<sup>4–10</sup> The British Pain Society indicated in 2009 that SCS for root avulsion pain is not responsive.<sup>11</sup> Recent reports suggest that burst or high-frequency SCS may reduce pain, but the long-term effects

are still uncertain.<sup>12,13</sup> SCS is often considered an attractive option because it is minimally invasive; however, recent reviews suggest that DREZ-lesion should be performed for pain after spinal root avulsion because of its efficacy in pain relief.<sup>3,9</sup> We report two cases in which DREZ-lesion was performed in patients with pain after spinal root avulsion who had SCS devices implanted but there was difficulty in exposure of DREZ due to strong spinal cord adhesions.

### Illustrative Cases

#### Case 1

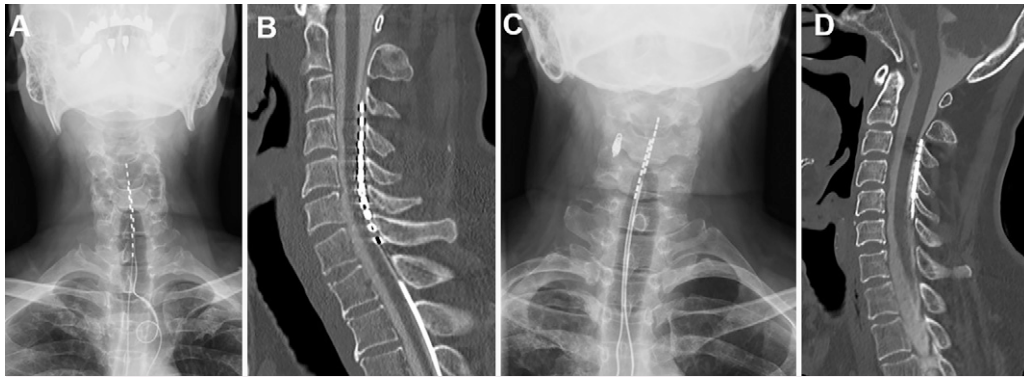
A 40-year-old male who was involved in a motorcycle accident 8 years before his visit to our hospital, presented with spinal root

**ABBREVIATIONS** CT = computed tomography; DREZ = dorsal root entry zone; DREZ-lesion = dorsal root entry zone lesioning; MRI = magnetic resonance imaging; NRS = numerical rating scale; RF = radiofrequency; SCS = spinal cord stimulation; VAS = visual analogue scale.

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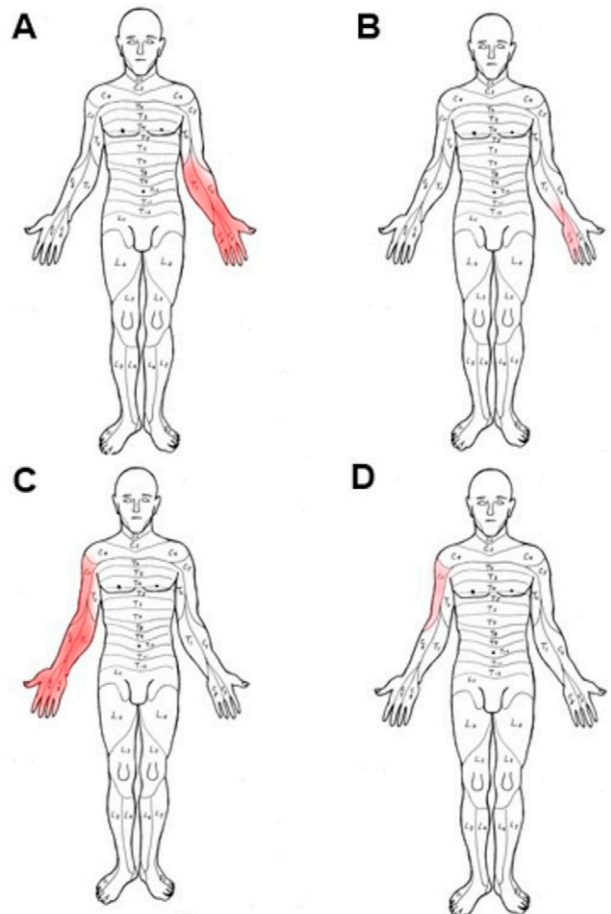
**FIG. 1.** Cervical radiography, CT myelography (sagittal and axial view). SCS leads were implanted before DREZ-lesion. **A and B:** Case 1. **C and D:** Case 2.

avulsion pain in his left upper limb. He had an SCS device implanted at another hospital 3 years before the visit to our hospital (Fig. 1A and B). The persistent pain subsequently improved, but the paroxysmal pain persisted; strong opioids and stellate ganglion blocks did not improve the pain. The prescription at the time of his visit was fentanyl patch (2 mg), tramadol (50 mg), and acetaminophen (3,600 mg). The SCS was not used at the time of the visit because it was no longer effective. The pain presented in the left hand and the ulnar side of the forearm (C6–T1 region) as paroxysmal pain of numerical rating scale (NRS) 5–9 and persistent pain of NRS 4 (Fig. 2A). The patient also had sensory loss in the left forearm, hyperalgesia in the left C5 and T1–2 regions, and severe motor paralysis in the left upper limb. Magnetic resonance imaging (MRI) revealed a pseudomeningocele on the left side of the C5–6, C6–7, and C7–T1 spinal levels. The nerve roots of the left C5–8 were not visualized. Magnetic resonance neurography showed poor visualization of the left spinal nerves of C5–8 (Fig. 3A). A diagnosis of C5–8 avulsion injury was made based on these symptoms and radiological findings. Computed tomography (CT) myelography indicated that the spinal cord was deviated dorsally in the dural canal and contacted the dura mater just beneath the SCS leads (Fig. 4A–D).

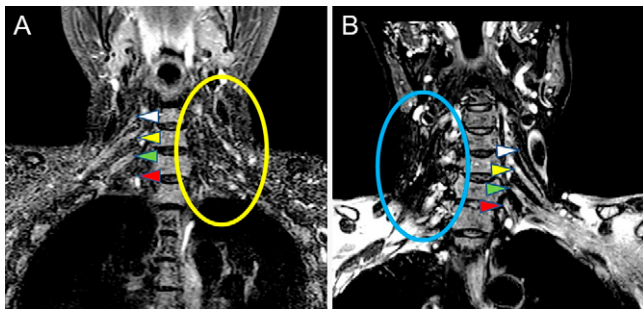
Surgery was performed simultaneously with SCS removal and DREZ-lesion. We performed a hemilaminectomy from C5–7 with a caudal partial laminectomy of C4 and a cranial partial laminectomy of T1 and incised the dura; the ligamentum flavum was tightly adherent to the dura and the dura was thickened. When the dura was incised, the arachnoid membrane immediately beneath the lead was muddy, and the spinal cord at the C7–T1 level was strongly adherent to the dura, making it difficult to expose the DREZ (Fig. 5A–C). Only the DREZ that could be exposed (C5–7) was radiofrequency (RF) coagulated (70°C for 30 s, 51 points at 1 mm intervals), using an RF lesion generator (RFG-3C, Radionics Inc), and an RF lesion needle electrode with a 2 mm tip. Dural reconstruction was performed using muscle flaps and fat. Postoperatively, pain in the area corresponding to the coagulated DREZ (~80% of the total) disappeared, but pain on the ulnar side of the forearm corresponding to the area that could not be coagulated persisted. The persistent pain improved 1.5 years after surgery; however, the patient still experienced NSR 9 paroxysmal pain in the same area (Fig. 2B). His medication regimen remained unchanged (fentanyl patch [3 mg], tramadol [75 mg], and acetaminophen [650 mg]).

### Case 2

The second case was a 50-year-old male who had a motorcycle accident 2 years before his visit to our hospital and presented with spinal root avulsion pain in the right upper limb. He received SCS at another institution 1 year before his visit to our hospital



**FIG. 2.** Range of pain. **A:** Case 1 before DREZ-lesion. **B:** Case 1 after DREZ-lesion. **C:** Case 2 before DREZ-lesion. **D:** Case 2 after DREZ-lesion.



**FIG. 3.** Magnetic resonance neurography (coronal view). **A:** Left C5–8 nerves were not delineated (*yellow circle*) in case 1. **B:** Right C6–8 nerves were not delineated (*blue circle*) in case 2. On the normal side, the *white arrowheads* point to C5, the *yellow arrowheads* to C6, the *green arrowheads* to C7, and the *red arrowheads* to C8.

(Fig. 1C and D). After SCS implantation, the persistent pain was partially reduced, but the paroxysmal pain did not improve. He was referred to the pain clinic and then to the Department of Neurosurgery. When he was referred to our hospital, his medication comprised tramadol (150 mg), acetaminophen (1,300 mg), and pregabalin (300 mg); SCS was no longer effective at the time of his first visit, and there was no change in pain when it was turned off. The painful area was the entire right upper limb (C5–T1 region), with paroxysmal pain of NRS 9 at 30-minute intervals and persistent pain of NRS 4 (Fig. 2C). There was sensory loss in the right C6–7 region, hyperalgesia in the right C5 and T1–2 regions, paresthesia in the left C6 and below, due to Brown–Séquard syndrome, severe motor paralysis in the right upper and lower limbs and left half-blindness due to right occipital lobe infarction caused by traumatic right vertebral artery injury. MRI revealed high-intensity lesions in the right spinal cord at the C6 spinal

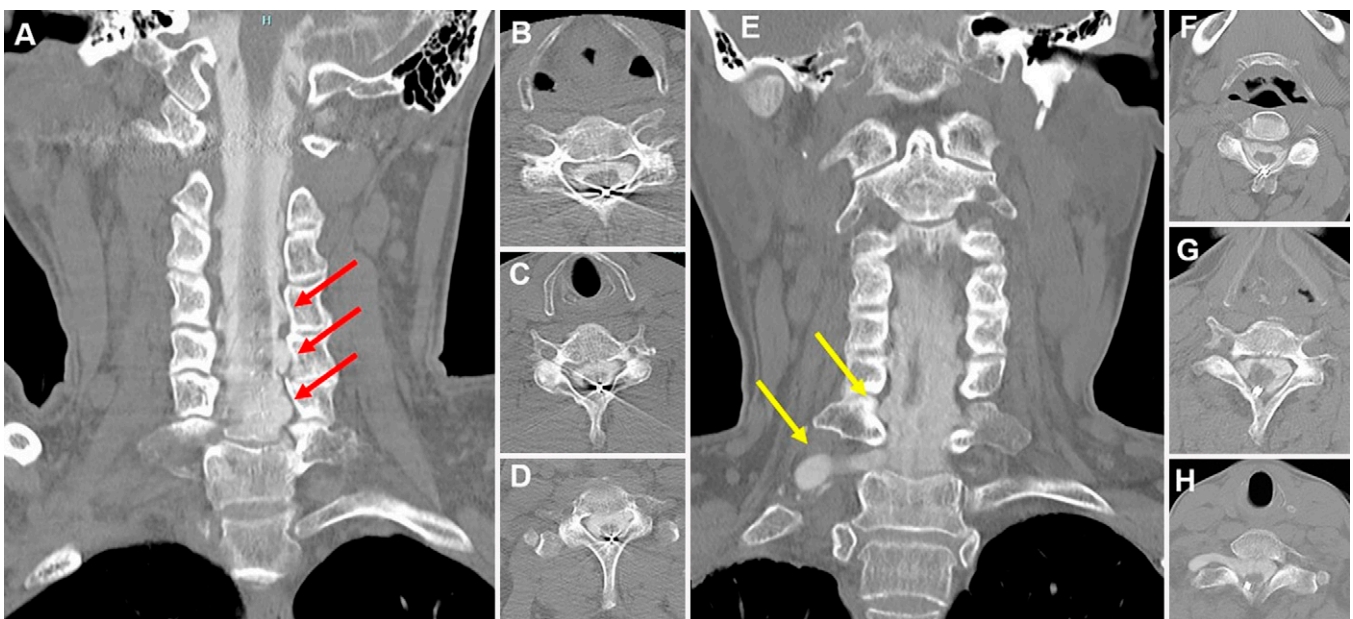
level in T2-weighted images and a pseudomeningocele on the right side of the C6–7 and C7–T1 spinal level, and the nerve roots of the right C6–8 were not visualized. Magnetic resonance neurography showed poor visualization of the right spinal nerves of C6–8, and a diagnosis of C6–8 avulsion injury was made (Fig. 3B). Similar to case 1, CT myelography revealed that the spinal cord was deflected dorsally within the dural canal and contacted the dura just beneath the lead (Fig. 4E–H).

Surgery was performed as in case 1, with SCS extraction and DREZ-lesion. When we performed a hemilaminectomy from C4 to T1 and incised the dura, the ligamentum flavum was adherent to the dura mater. When the dural incision was made, the arachnoid was cloudy and partially adherent to the spinal cord (Fig. 5D–F). Although it was time-consuming to carefully detach the ligamentum flavum and arachnoid, we were able to expose the entire DREZ, and RF coagulation (70°C for 30 seconds, 49 points at 1 mm intervals, using an RF lesion generator (RFG-3C) and an RF lesion needle electrode with a 2 mm tip was performed as planned. After surgery, paroxysmal and persistent pain in the right upper extremity disappeared. Paroxysmal pain recurred 8 months after surgery; at 18 months following surgery, persistent NRS 4 pain and paroxysmal NRS 6 pain remained on the outer side of the upper arm (Fig. 2D). However, the extent and degree of pain improved from preoperative levels, and the patient was extremely satisfied with the surgical outcome. Medication was reduced to tramadol (112.5 mg), acetaminophen (975 mg), and pregabalin (150 mg).

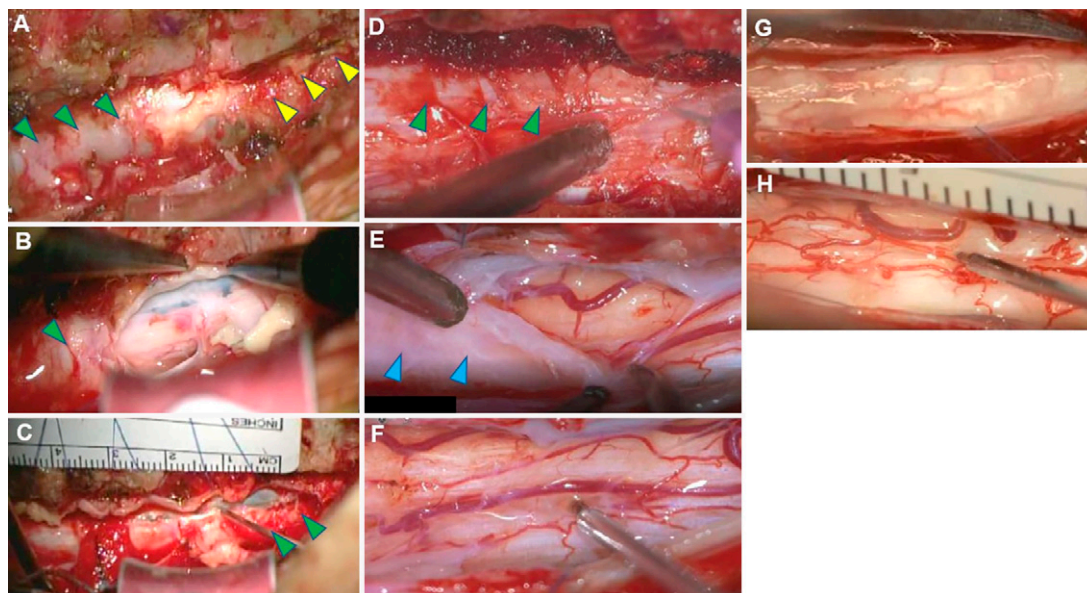
## Discussion

### Observations

We encountered two cases of DREZ-lesion after SCS implantation. In both cases, the SCS is ineffective, and the DREZ-lesion was difficult to complete because of strong adhesions around the SCS lead. It is known that SCS causes epidural adhesions, and



**FIG. 4.** CT myelography. Pseudomeningoceles were revealed at the level of C5–6, C6–7, C7–T1 in case 1 (**A**, *red arrow*) and C6–7, C7–T1 in case 2 (**E**, *yellow arrow*). The spinal cord was deflected dorsally and contacted the dura mater just beneath the SCS leads. **A–D:** Case 1. **E–H:** Case 2. **A and E:** Coronal view. **B–D and F–H:** Axial view. **B and F:** C5–6 level. **C and G:** C6–7 level. **D and H:** C7–T1 level.



**FIG. 5.** Surgical view. Case 1: The dura mater (green arrowhead) and the ligamentum flavum (yellow arrowhead) were thickened and tightly adherent (A). The arachnoid just below the SCS lead was thickened and muddy (B). The dura mater and spinal cord at the C7–T1 level were tightly adherent, and it was difficult to expose the DREZ at C8 level (C). Case 2: The dura mater (green arrowhead) and the ligamentum flavum were adherent (D). The arachnoid was cloudy (blue arrowhead) (E), and the arachnoid and dura were tightly adherent (F). Normal view: **G and H:** Normal clear and soft arachnoid.

there are reports that the previous implantation affects the degree of epidural adhesions and prolongation of operative time for reimplantation.<sup>14</sup> In this case, the SCS was suspected to cause the adhesions between the dura mater and the ligamentum flavum.

There are many reports examining the pain-relieving effects of spinal root avulsion suggesting that DREZ-lesion is more effective than SCS. In the previous study, the 5-year postoperative analgesic efficacy of DREZ-lesion for pain after root avulsion (>50% improvement in visual analogue scale [VAS]) was 84.6% for paroxysmal pain and 73.1% for persistent pain, with a higher analgesic efficacy for paroxysmal pain.<sup>15</sup> In our report, 2.5 years after DREZ-lesion surgery, VAS exhibited >50% improvement for paroxysmal pain in 7 of 10 patients, whereas paroxysmal pain disappeared in 5 patients, and persistent pain disappeared in 2 patients.<sup>7</sup>

On the other hand, in studies investigating the effect of SCS on pain after spinal root avulsion, some have reported that it is effective in all cases,<sup>16–18</sup> whereas others have indicated that it is not effective.<sup>19–21</sup> There are no reproducible reports. In our experience, SCS was ineffective.

The difference in the pain relief effect could be due to the nature of the pain after spinal root avulsion. Spinal root avulsion causes intractable pain due to afferent pathway blockage and damage to the spinal dorsal horn neurons, which can be divided into persistent and paroxysmal pain according to the underlying mechanism.<sup>7</sup> Paroxysmal pain is believed to be caused by overactivity in layer V of the dorsal horn of the spinal cord due to disruption of inhibitory pathways, whereas persistent pain is believed to result from degeneration of the neurons damaged by avulsion, central sensitization (increased release of glutamate and substance P in presynaptic A-delta and C fibers and altered sensitivity of postsynaptic N-methyl-D-aspartate receptors), and involvement of the limbic system and

cerebral cortex, suggesting involvement of both the brain and spinal cord.<sup>7,22–28</sup>

DREZ-lesion is a treatment that prevents overactivity by destroying the superficial layers I–V of the dorsal horn of the spinal cord. Based on the underlying mechanism, it is understandable that DREZ-lesion is effective for paroxysmal pain, but its effectiveness may be limited in persistent pain which includes a supra-spinal component.

SCS is based on the gate control theory published by Melzack and Wall<sup>29</sup> in 1965, whereby electrically stimulated dorsal funiculus retrogradely stimulate A $\beta$  fibers that transmit tactile information and inhibit A $\delta$  fibers that transmit pain information.<sup>28</sup> However, in the case of root avulsion, the dorsal horn neurons are damaged and contact between the dorsal funiculus and A $\beta$  fibers is physically broken; therefore, the stimulation provided by SCS may not be conducted retrogradely to the A $\delta$  fibers, and the pain-relieving effect may not be exerted.<sup>30,31</sup>

For these reasons, DREZ-lesion should be performed preferentially for pain after spinal root avulsion, particularly for paroxysmal pain.

The first limitation of this report is that the epidural adhesions may be traumatic. The adhesions between the arachnoid and dura mater and between the dura mater and the ligamentum flavum were strong and difficult to dislodge during surgery (Fig. 5A–H). Most reports examining traumatic changes after avulsion injury describe pseudomeningocele and none describe adhesions inside or outside the dura.<sup>32</sup> The present cases had pseudomeningocele, but the adhesion sites were different from that of a pseudomeningocele, suggesting that SCS leads may have caused the adhesions. We performed DREZ-lesion in other patients, but none possessed such strong intradural and extradural adhesions as in these cases.

Another limitation is that there are no reports of subdural adhesions after SCS implantation. However, the dorsal deviation of the spinal cord on CT myelography suggests adhesion between the spinal cord and the dura mater beneath the SCS leads, and the dorsal deviation of the spinal cord on axial section imaging is associated with intradural adhesions in tethered cord syndrome.<sup>33</sup> There is a possibility that irritation owing to SCS will affect and cause the inflammation to spill over into the subdural area. If the dorsal deviation of the spinal cord is observed on preoperative imaging, it would be important to pay attention to subdural adhesions.

## Lessons

In spinal root avulsion, SCS is not very effective for paroxysmal pain. In many patients, paroxysmal pain is more severe and is more problematic than persistent pain. Because previous SCS can make subsequent DREZ-lesion difficult due to adhesions within and outside the dura, caution is required when considering SCS.

## References

- Nashold BS Jr, Ostdahl RH. Dorsal root entry zone lesions for pain relief. *J Neurosurg.* 1979;51(1):59–69.
- Parry CB. Pain in avulsion of the brachial plexus. *Neurosurgery.* 1984;15(6):960–965.
- Gebreyohanes AMH, Ahmed AI, Choi D. Dorsal root entry zone lesioning for brachial plexus avulsion: a comprehensive literature review. *Oper Neurosurg (Hagerstown).* 2021;20(4):324–333.
- Sindou M. *Study of the dorsal root entry zone. Implications for pain surgery.* Lyon: Med Thesis, University of Lyon Press; 1972.
- Nashold BS Jr, Urban B, Zorub DS. Phantom pain relief by focal destruction of the substantia gelatinosa of Rolando. In: Bonica JJ, Albe-Fessard DG, eds. *Advances in Pain Research and Therapy.* Raven Press; 1976:959–963.
- Emery E, Blondet E, Mertens P, Sindou M. Microsurgical DREZotomy for pain due to brachial plexus avulsion: long-term results in a series of 37 patients. *Stereotact Funct Neurosurg.* 1997;68(1-4 Pt 1): 155–160.
- Ali M, Saitoh Y, Oshino S, et al. Differential efficacy of electric motor cortex stimulation and lesioning of the dorsal root entry zone for continuous vs paroxysmal pain after brachial plexus avulsion. *Neurosurgery.* 2011;68(5):1252–1258.
- Meena R, Doddamani RS, Agrawal D, Chandra PS. Dorsal root entry zone (DREZ) lesioning for brachial neuralgia. *Neurol India.* 2020;68(5):1012–1015.
- Montalvo Afonso A, Ruiz Juretschke F, González Rodríguez R, et al. DREZotomy in the treatment of deafferentation pain: review of results and analysis of predictive factors for success. *Neurocirugía (Astur: Engl Ed).* 2021;32(1):1–9.
- Dauleac C, Brinzeu A, Fenniri I, Sindou M, Mertens P. Microsurgical DREZotomy for Treatment of Brachial Plexus Avulsion Pain. *World Neurosurg.* 2021;148:177.
- The British Pain Society. Spinal cord stimulation for the management of pain: recommendations for best clinical practice. The British Pain Society; 2009. Accessed January 5, 2021. [https://www.britishpainsociety.org/static/uploads/resources/files/book\\_scs\\_main\\_1.pdf](https://www.britishpainsociety.org/static/uploads/resources/files/book_scs_main_1.pdf)
- Dombovy-Johnson ML, Hagedorn JM, Wilson RE, Canzanello NC, Pingree MJ, Watson JC. Spinal cord stimulation for neuropathic pain treatment in brachial plexus avulsions: a literature review and report of two cases. *Neuromodulation.* 2020;23(5):704–712.
- Lopez L, Sdrulla AD. Success with dorsal root entry zone lesioning after a failed trial of spinal cord stimulation in a patient with pain due to brachial plexus avulsion. *Pain Rep.* 2021;6(4):e973.
- Kin K, Agari T, Yasuhara T, et al. The factors affecting the difficulty of percutaneous cylindrical electrode placement for spinal cord stimulation. *World Neurosurg.* 2018;113:e391–e398.
- Aichaoui F, Mertens P, Sindou M. Dorsal root entry zone lesioning for pain after brachial plexus avulsion: results with special emphasis on differential effects on the paroxysmal versus the continuous components. A prospective study in a 29-patient consecutive series. *Pain.* 2011;152(8):1923–1930.
- Bennett MI, Tai YM. Cervical dorsal column stimulation relieves pain of brachial plexus avulsion. *J R Soc Med.* 1994;87(1):5–6.
- Piva B, Shaladi A, Saltari R, Gilli G. Spinal cord stimulation in the management of pain from brachial plexus avulsion. *Neuromodulation.* 2003;6(1):27–31.
- Lai HY, Lee CY, Lee ST. High cervical spinal cord stimulation after failed dorsal root entry zone surgery for brachial plexus avulsion pain. *J Surg Neurol.* 2009;72(3):286–289.
- García-March G, Sánchez-Ledesma MJ, Diaz P, et al. Dorsal root entry zone lesion versus spinal cord stimulation in the management of pain from brachial plexus avulsion. *Acta Neurochir Suppl (Wien).* 1987;39:155–158.
- Sindou MP, Mertens P, Bendavid U, García-Larrea L, Mauguière F. Predictive value of somatosensory evoked potentials for long-lasting pain relief after spinal cord stimulation: practical use for patient selection. *Neurosurgery.* 2003;52(6):1374–1384.
- Wolter T, Kieselbach K. Cervical spinal cord stimulation: an analysis of 23 patients with long-term follow-up. *Pain Physician.* 2012;15(3):203–212.
- Teixeira MJ, da Paz MG, Bina MT, et al. Neuropathic pain after brachial plexus avulsion—central and peripheral mechanisms. *BMC Neurol.* 2015;15:73.
- Parry WCB. Pain in avulsion lesions of the brachial plexus. *Pain.* 1980;9(1):41–53.
- Fujioka H, Shimoji K, Tomita M, Denda S, Hokari T, Tohyama M. Effects of dorsal root entry zone lesion on spinal cord potentials evoked by segmental, ascending and descending volleys. *Acta Neurochir (Wien).* 1992;117(3-4):135–142.
- Guenot M, Bullier J, Rospars JP, Lansky P, Mertens P, Sindou M. Single-unit analysis of the spinal dorsal horn in patients with neuropathic pain. *J Clin Neurophysiol.* 2003;20(2):143–150.
- Sindou MP, Blondet E, Emery E, Mertens P. Microsurgical lesioning in the dorsal root entry zone for pain due to brachial plexus avulsion: a prospective series of 55 patients. *J Neurosurg.* 2005;102(6): 1018–1028.
- Nickel FT, Seifert F, Lanz S, Maihöfner C. Mechanisms of neuropathic pain. *Eur Neuropsychopharmacol.* 2012;22(2):81–91.
- Sdrulla AD, Guan Y, Raja SN. Spinal cord stimulation: clinical efficacy and potential mechanisms. *Pain Pract.* 2018;18(8):1048–1067.
- Melzack R, Wall PD. Pain mechanisms: a new theory. *Science.* 1965;150(3699):971–979.
- Denny-Brown D, Kirk EJ, Yanagisawa N. The tract of Lissauer in relation to sensory transmission in the dorsal horn of spinal cord in the macaque monkey. *J Comp Neurol.* 1973;151(2):175–200.
- Ovelmen-Levitt J, Johnson B, Bedenbaugh P, Nashold BS Jr. Dorsal root rhizotomy and avulsion in the cat: a comparison of long term effects on dorsal horn neuronal activity. *Neurosurgery.* 1984;15(6): 921–927.
- Rahimizadeh A, Ehteshami S, Yazdi T, Rahimizadeh S. Remote paraparesis due to a traumatic extradural arachnoid cyst developing 2 years after brachial plexus root avulsion injury: case report and review of the literature. *J Brachial Plex Peripher Nerve Inj.* 2015; 10(1):e43–e49.
- Vernet O, O’Gorman AM, Farmer JP, McPhillips M, Montes JL. Use of the prone position in the MRI evaluation of spinal cord retethering. *Pediatr Neurosurg.* 1996;25(6):286–294.

**Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**

Conception and design: Hosomi. Acquisition of data: Hosomi, Kimoto, Emura, Mori. Analysis and interpretation of data: Hosomi, Kimoto. Drafting the article: Kimoto. Critically revising the article: Hosomi, Kimoto, Mori, Oshino, Kishima. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Hosomi. Study supervision: Hosomi, Saitoh, Kishima.

**Supplemental Information****Previous Presentations**

Results from this study were partly presented at the 60th Annual Meeting of the Japan Society for Stereotactic and Functional Neurosurgery, January 23, 2021, online, and the 35th Annual Meeting of the Japan Neuromodulation Society, May 8, 2021, online.

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