

## ORIGINAL ARTICLE

### Treatment of neuropathic deafferentation pain using DREZ lesions; long-term results<sup>☆</sup>

F. Ruiz-Juretschke<sup>\*</sup>, F. García-Salazar<sup>†</sup>, R. García-Leal, C. Fernández-Carballal, B. Iza, J.M. Garbizu, S. García-Duque, T. Panadero

*Servicio de Neurocirugía, Hospital General Universitario Gregorio Marañón, Madrid, Spain*

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#### KEYWORDS

Brachial plexus  
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Pain;  
Spinal injury

#### Abstract

**Introduction:** Deafferentation pain secondary to spinal cord injury, brachial plexus avulsion and other peripheral nerve injuries is often refractory to conventional treatments. This study evaluates the long-term efficacy of spinal DREZ (*Dorsal Root Entry Zone*) lesions for the treatment of neuropathic pain syndromes caused by deafferentation.

**Patients and methods:** A series of 18 patients with refractory deafferentation pain treated with radiofrequency DREZ lesions is presented. The immediate and long-term efficacy was measured with the Visual Analogue Scale (VAS) before and after treatment, the patient's subjective evaluation, the percentage of patients returning to work and the reduction in pain medication.

**Results:** Pain on the VAS significantly decreased from 8.6 preoperatively to 2.9 ( $p < .001$ ) at release. Over the long-term, with a mean follow-up of 28 months (6-108) pain remained at 4.7 on the VAS ( $p < 0.002$ ). The percentage of patients with moderate to excellent pain relief was 77% at discharge and 68% at the last follow-up. Pain medication was reduced in 67% of the patients and 28% returned to work. The best results were obtained in patients with brachial plexus avulsion, with a significant long-term pain relief in all cases.

**Conclusions:** Radiofrequency DREZ lesion is an effective and safe treatment for refractory neuropathic pain caused by deafferentation.

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<sup>☆</sup>No work similar to this manuscript has been published or submitted to another journal for publication. Some of the data included in this work were reported at the 14th Annual Conference of the Spanish Neurology Society (SENEC) held in Seville in May 2009.

<sup>\*</sup>Corresponding author.

E-mail: doc.fer@gmx.de (F. Ruiz-Juretschke).

<sup>†</sup>Dr. Francisco García Salazar, the driving force behind pain surgery at our department and the lead surgeon in all the cases presented in this series, died on October 5th, 2009, during the preparation of this manuscript. R.I.P.

**PALABRAS CLAVE**

Avulsión plexo  
braquial;  
Desaferentización;  
*Dorsal root entry zone*;  
Dolor;  
Lesión medular

## Tratamiento del dolor neuropático por desaferentización mediante lesión DREZ, resultados a largo plazo

**Resumen**

**Introducción:** El dolor por desaferentización secundario a lesiones medulares, avulsión del plexo braquial y otras lesiones de nervios periféricos, es a menudo refractario a tratamientos convencionales. Este trabajo evalúa la eficacia a largo plazo de la cirugía de lesión DREZ (*Dorsal Root Entry Zone*) en diversos síndromes de dolor neuropático por desaferentización.

**Pacientes y métodos:** Se presenta una serie de 18 pacientes con dolor refractario por desaferentización tratados mediante lesión DREZ con radiofrecuencia. La eficacia inmediata y a largo plazo se valoró mediante la escala visual analógica (EVA) preoperatoria y postoperatoria, la valoración subjetiva del paciente, la reincorporación laboral y la reducción de la medicación analgésica.

**Resultados:** El dolor en la EVA disminuyó significativamente de 8,6 antes de la cirugía a 2,9 de media al alta ( $p < 0,001$ ). A largo plazo, con un seguimiento medio de 28 meses (6-108), el dolor se mantuvo en 4,7 en la EVA ( $p < 0,002$ ). El porcentaje de pacientes con un alivio moderado a excelente del dolor fue de 77% al alta y 68% a largo plazo. El 67% de los pacientes redujo la medicación analgésica y el 28% se reincorporó al trabajo. Los mejores resultados se obtuvieron en los pacientes con avulsión del plexo braquial con una mejoría significativa del dolor a largo plazo en todos los casos.

**Conclusiones:** La lesión DREZ por radiofrecuencia es un tratamiento eficaz y seguro para el dolor neuropático refractario por desaferentización.

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**Introduction**

The DREZ region (*dorsal root entry zone*) was described by Sindou and includes: the medial portion of the dorsal root, Lissauer's tract, and the posterior horn of the spinal cord<sup>1</sup>. Several different studies carried out in animals and in patients with spinal cord section have demonstrated paroxysmal neuronal hyperactivity in this region, which might be the physiopathological basis of deafferentation pain.<sup>1</sup> In 1972, Sindou and Fisher published the technique of microsurgical injury to the DREZ region as treatment for neuropathic pain in a patient with infiltration of the brachial plexus due to a Pancoast tumour.<sup>2</sup> Shortly afterward, Nashold introduced the technique of DREZ lesion by thermocoagulation using radiofrequency for pain associated with avulsion of the brachial plexus.<sup>3</sup> Since then, the DREZ lesion technique has been used to treat neuropathic pain in different situations such as: avulsion of the cervical roots of the brachial plexus, postherpetic neuralgia, spinal cord injury, cancer and peripheral nerve injury. In this work, we report our experience and outcomes long term with the technique of DREZ lesion for the treatment of the neuropathic pain.

**Patients and methods**

A review was made of all patients with neuropathic deafferentation pain refractory to other treatments and treated by means of spinal DREZ lesion at the Gregorio Marañón General University Hospital between 1994 and

2009. During this period, 19 DREZ lesion procedures were performed on 18 patients (7 men and 11 women) with a mean age of 52 years (27-77). The epidemiological, clinical, and surgical data were collected from the clinical history. Evolution of pain was recorded on the basis of the progressive data collected at follow-up visits to the neurosurgery clinic and pain clinic, as well as by telephone interviews of patients not monitored at our centre.

The aetiology of the neuropathic pain was: avulsion of the brachial plexus (8 patients), neoplastic infiltration of the brachial plexus (3 patients), spinal cord trauma (2 patients), and neuropathic pain in other locations (5 patients). The metameric level of pain distribution was cervical in 13 cases, dorsal in 4 cases, and lumbosacral in one case. The mean time between the onset of pain and DREZ surgery was 6 years (1-17). During that time, patients were treated with any number of medical therapies without achieving pain control, as well as various different surgical procedures: stimulation of posterior tracts (11), intrathecal morphine pump (3), neurolysis of the brachial plexus (2), amputation (3), thalamic deep brain stimulation (1). The patients' clinical characteristics are illustrated in table 1.

The surgical technique was carried out under general anaesthesia with the patient lying face down in 15 cases and sitting in 3. The Mayfield craniostat was used in the 11 cases in which the approach was via the cervical spinal cord. The spinal cord was exposed by means of a bilateral laminectomy of all the segments involved and included a rostrally located segment and another, caudally located one. The segments to be injured were determined on the basis of the dermatomes with radiating pain, bearing in

**Table 1** Clinical characteristics and pain response to DREZ lesion, cases ordered by type of painful syndrome

	Age/ sex	Injury	DREZ levels	VAS		
				Prior	On discharge	Final
1	41/ M	Brachial plexus avulsion	C5-C8	7	0	0
2	73/ F	Brachial plexus avulsion	C5-T1	9	0	5
3	36/ M	Brachial plexus avulsion	C5-T1	10	0	0
4	38/ M	Brachial plexus avulsion	C5-T1	8	2	2
5	50/ M	Brachial plexus avulsion	C4-C7	9	0	2
6	38/ F	Brachial plexus avulsion	C5-T1	10	0	4
7	27/ M	Brachial plexus avulsion	C5-T1	8	0	3
8	52/ F	Brachial plexus avulsion	C5-T1	8	3	3
9	64/ F	CRPS in the hand	C6-C7	8	4	NA
10	29/ F	Causalgia of the abdominal wall	T12-L1	8	0	7
11	52/ F	CRPS in the hand	C5-T1	10	10	10
12	66/ F	Causalgia of the lower limb	Unilateral conus	8	8	8
13	48/ F	Costal causalgia	T6-T8	10	0	2
14	56/ F	Neoplasm of the plexus (Breast)	C4-T1	9	3	5
15	69/ F	Neoplasm of the plexus (Sarcoma)	C5-T1	10	10	10
16	60/ M	Neoplasm of the plexus (Pancoast t.)	C4-C6	6	6	6
17	77/ M	D9-D11 spinal cord trauma	Bilateral T10-T12	6	0	NA
18	60/ F	D10-D12 spinal cord infarct	Bilateral T10-L1	10	6	8

VAS: visual analogue scale; NA: not available; CRPS: complex regional pain syndrome.

mind the shift of the spinal cord levels with respect to the spinal levels, especially in the thorax where the roots exit the conjoining foramina 1 or 2 levels further down. Using microscopic vision, the dura was opened along the midline and both sides of the roots were identified at the level of the intermediolateral sulcus. It is particularly important for the DREZ zone to be located bilaterally in plexus avulsions, since the absence of roots on the injured side together with arachnoid fibrosis, which hinders dissection and can rotate the spinal cord, may disorient the surgeon. Once the intermediolateral sulcus has been identified and the arachnoids dissected, the DREZ lesion was performed as per the parameters put forth by Nashold at 75°C for 15 seconds with a 2-mm radiofrequency electrode (Radionics, Burlington, MA).<sup>3</sup> The lesions were performed at 1-mm intervals, proceeding from caudal to rostral, generating more than 50 lesions over an extension from C5 to T1 (fig. 1). It is important for the electrode to be inserted in the lateral portion of the DREZ at a 45° angle so as to reach the dorsal horn without injuring the posterior cords or the pyramidal pathway. Once the procedure had been performed, the dura was sutured hermetically and the wound closed by anatomical planes. All patients received peri- and post-operative prophylactic steroid therapy with dexamethasone.

The outcome was measured subjectively according the patient's own assessment, considering an excellent result to be the absence of pain; a good outcome was when the pain relief was greater than 75% moderate, when it was 25-75% and poor, if the relief obtained by the surgery was less than 25%. Likewise, pre-operative pain was recorded using the Visual Analogue Scale (VAS), as was immediate post-operative pain on discharge of the patient from

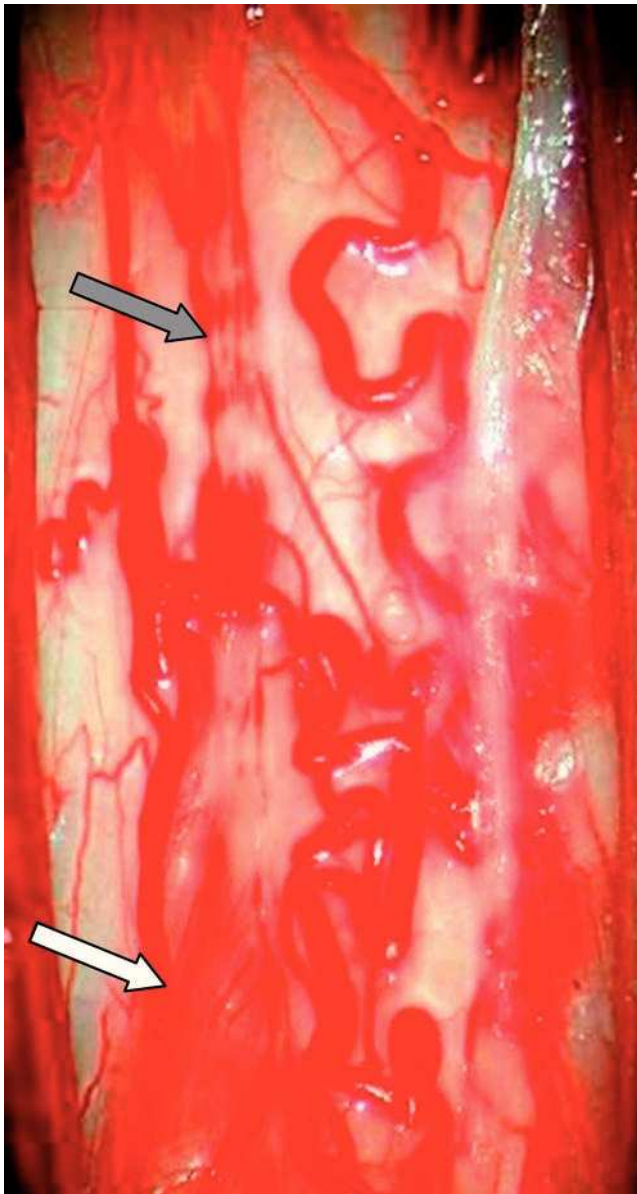
hospital and late post-operative pain at the time of the last check-up. The mean pain scores according to the VAS were compared using a non-parametric Wilcoxon test for matched pairs, considering a  $p < 0.05$  as significant. The other indicators of a good outcome analyzed were significant reduction in pain relief medication (by at least a level on the WHO pain treatment scale) and return to work activities.

Finally, treatment-associated mortality and morbidity were recorded.

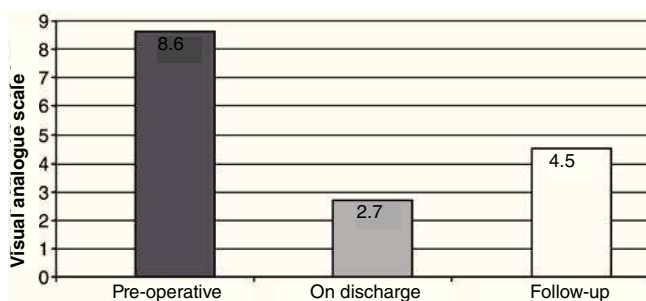
## Results

The mean level of pain prior to the surgery according to the VAS was 8.6 and fell significantly to 2.9 at the time of discharge ( $p < 0.001$ ). At the last follow-up visit after a mean of 28 months (6-108), the mean VAS score was 4.7 ( $p < 0.002$ ) (fig. 2). Two patients were lost to follow-up, one of whom died during the post-operative period. The patient-reported result was excellent in 10 cases, good in 3, moderate in 1, and poor in 4 in the immediate post-operative measurement, although the long-term result was deemed to be excellent in 3, good in 6, moderate in 3, and poor in 6. Pain relief medication could be decreased in 66.7% of the patients and 27.8% of the patients were able to go back to work.

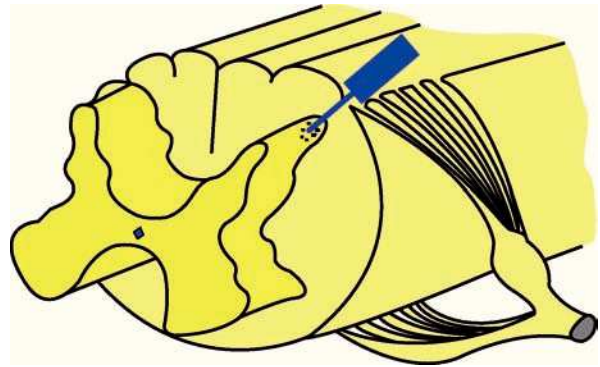
Post-operative neurological complications were recorded in four patients (22.2%). In 3 cases, these complications consisted of a temporary alteration of proprioceptive sensation and vibratory sensation due to posterior cord involvement, without this getting in the way of walking. A permanent spinal cord injury occurred in only one case: a patient with pain secondary to post-surgical dorsal



**Figure 1** Intra-operative image of a left cervical DREZ lesion for avulsion of the brachial plexus, the arrow in grey points to the radiofrequency injuries at the level of the intermediolateral sulcus in which the avulsed roots are missing. The white arrow points to intact low cervical roots.



**Figure 2** Comparison of pain prior to surgery, on discharge, and long term according to the mean value on the visual analogue scale.



**Figure 3** Schematic view of the DREZ technique using radiofrequency injury.

myelopathy in whom a bilateral low dorsal DREZ was performed. Furthermore, minor complications appeared associated to the wound in two patients in the form of CSF fistulae that resolved with bed rest and lumbar drainage in both cases. One patient died as a result of nosocomial pneumonia 9 days after surgery.

## Discussion

The DREZ region is an important centre of integration of painful stimuli. The dorsal roots enter the intermediolateral sulcus and divide into 4-10 rootlets. Nociceptive fibres are located in the lateral portion of the dorsal roots; their neuronal somas are located in the spinal ganglion, and they end in the dorsal horn. Before making synapses in Rexed's areas 1, 2 and 5 of the dorsal horn, the nociceptive fibres extend over several segments caudo-cranially, forming a sheath that surrounds the posterolateral end of the dorsal horn: Lissauer's tract. Lissauer's tract is known to have a modulating ability and it is known that injury to its medial portion through which nociceptive fibres pass reduces painful excitability.<sup>4</sup> Spinal cord deafferentation pain is believed to be due to spontaneous hyperactivity of the nociceptive neurons originating in the spinal-thalamic pathway, as well as the spinal-reticular pathway at the level of the dorsal horn, in addition to hyperexcitability of these neurons by having lost their inhibitory afferences.<sup>3,5</sup> A paroxysmal increase in the spontaneous activity of the dorsal horn has been measured in animal and human studies,<sup>6,7</sup> as has increased response to nociceptive stimuli.<sup>8</sup> The DREZ lesion is a neuroablative technique targeting the lateral portion of the dorsal roots, the medial portion of Lissauer's tract, and the dorsal horn, preserving the lemniscal proprioceptive fibres and the inhibitory portion of Lissauer's tract<sup>2</sup> (fig. 3).

The first indication established for the DREZ technique was deafferentation pain in patients with avulsion of the brachial plexus. These patients displayed chronic central neuropathic pain that was intractable in 20-30% of cases. Pain is established in the first ten days in half the cases and it is rare for it to begin after the first 6 months.<sup>9</sup> There are typically two components: a chronic burning or stabbing pain that does not ordinarily follow a clear metameric

distribution and is located more often than not in the forearm and the hand, and brief paroxysmal pain on top of the previous pain.<sup>3,9,10</sup> The pain becomes disabling and fails to respond to analgesics, opiates, or peripheral or sympathetic blockades. Response to anti-epileptic drugs and to transcutaneous electrical stimulation tends to be partial and insufficient. Different types of ablative surgeries, such as cordotomy, thalamotomy, or cingulotomy and stimulation techniques of the posterior cords or deep brain nuclei have yielded poor outcomes.<sup>10</sup> Amputation of the limb provides no relief whatsoever.<sup>3,5</sup> At present, neurotization techniques of the brachial plexus are capable of giving back some degree of protective sensitivity to the extremity and several series report improvement in deafferentation pain.<sup>11</sup> The DREZ technique has demonstrated good outcomes in patients with brachial plexus injury due to avulsion with significant pain improvement, considering relief as >50% on the VAS, in 58-100% of cases following surgery.<sup>5,9,10,12-16</sup> Moreover, functional improvement has been seen on anxiety and depression scales, as well as return to work in more than one third of the patients.<sup>5,16</sup> Our series offers comparable outcomes with long-term improvement of pain in 100% of the patients with injury brachial plexus due to avulsion. The outcomes of the long-term follow-up in the literature reveal relapse of pain in 13-20% of patients after 5 years, although significant relief is sustained in more than 60% of cases.<sup>14,17</sup> No association has been demonstrated between treatment efficacy and pain duration, although a higher long-term relapse rate has been observed in patients with duration of pain less than three years.<sup>5,14</sup>

Deafferentation pain appears in 10-25% of all spinal cord injuries, distinguishing segmental pain with metameric distribution at the levels of the injured spinal cord (*end-zone pain*) and diffuse caudal pain at the level of spinal cord injury. Different studies have shown efficacy rates of 41-75% with a response that is clearly superior in patients with segmental pain.<sup>9,15,18-21</sup> Diffuse pain below the level of injury only improves in 16-29% of the cases and should not be contemplated when indicating this surgery. Several authors have described greater efficacy in cases with partial spinal cord injury.<sup>22,23</sup> DREZ lesion provides some added benefits in spinal cord injury with decreased spasticity in the extremities and in the vesical detrusor muscle by interrupting the myotatic reflex.<sup>24</sup>

Other applications of DREZ lesion are postherpetic neuralgia, peripheral nerve injury, complex regional pain syndrome, and injury of the brachial plexus due to tumour infiltration or radiotherapy. Most of the published data have come from small, heterogeneous series that do not enable us to establish any degree of efficacy in these indications. Most authors agree that it is less efficacious in cases of tumour injury to the brachial plexus and other peripheral nerve injuries; it lasts less and is less predictable.<sup>13,15,25,26</sup> Our results are not favourable in these indications, with significant improvement in 38%; hence, as things stand at the present time, we also consider other alternatives for these types of pain, such as cordotomy in predominantly nociceptive cancer pain.

The DREZ lesion technique has been published with multiple technical variations, from micro-coagulation as

proposed by Sindou and thermocoagulation by radiofrequency described by Nashold, later modified by Friedmann and Thomas, to laser or ultrasound ablative techniques.<sup>9,10,12,27</sup> Currently there are several authors defending bipolar coagulation under microscopic control, arguing that it requires no extra instrumentation and that the destruction of the DREZ zone would be more complete than with separate injuries using radiofrequency thereby increasing efficacy, although there are no comparative studies.<sup>16,25</sup> In our experience, the radiofrequency technique has an efficacy rate similar to what one finds in the literature with a low rate of complications. A benefit has been seen in the use of monitoring and locating techniques for the DREZ by means of motor and somatosensory evoked potentials.<sup>14,28</sup> The direct recording of transcutaneous potentials at the level of the spinal cord above and below the lesion enables intra-operative assessment of the integrity of the posterior cords, the lateral corticospinal sheath, and the spinocerebellar sheath. In addition, spontaneous or evoked spinal cord activity recording in the DREZ region allows this region to be located more precisely and increases the efficacy of the procedure. The lack of neuromonitoring is a technical limitation of our series that we hope to correct in future cases.

We had a 22% rate of complications with neurological impairment in this series; the neurological impairment was transitory in three of the patients who presented proprioceptive sensory disorders. The sensory and motor deficit got worse and prevented the patient from walking in only one case of bilateral low dorsal DREZ lesion in a patient with prior spinal cord injury. This is in line with the morbidity rates of 15-30% reported in recent series, mainly comprising transient sensory disorders due to injury to the posterior cord in most cases, which do not prevent walking.<sup>5,13,14,16</sup>

In conclusion, DREZ spinal lesion through radiofrequency is a treatment that targets neuropathic deafferentation pain. It is especially indicated in avulsion of the brachial plexus and segmental pain secondary to spinal cord injury, with more variable efficacy in other indications. The safety profile can be considered acceptable bearing in mind that it is a salvage technique in cases of disabling intractable pain.

## Conflict of interest

There is no conflict of interest or external source of funding in this work.

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