Dorsal Root Entry Zone Lesioning: Systematic Review

Lesionamento da zona de entrada da raiz dorsal: Revisão sistemática

Giovanna Zambo Galafassi1, Paulo Henrique Pires Aguiar2,4, André Akira Takahashi1, Jorge Roberto Pagura5

1 Faculdade de Medicina do ABC, Santo André, SP, Brazil
2 Department of Research and Innovation, Laboratório de Biologia Celular e Molecular, Faculdade de Medicina do ABC, Santo André, SP, Brazil
3 Department of Neurosurgery, Hospital Santa Paula, São Paulo, SP, Brazil
4 Department of Neurology, Pontifícia Universidade Católica de São Paulo, Sorocaba, SP, Brazil
5 Department of Neurology and Neurosurgery, Faculdade de Medicina do ABC, Santo André, SP, Brazil

Address for correspondence Giovanna Zambo Galafassi, Faculdade de Medicina do ABC, Rua Pirassununga, 190, apto 42, Valparaíso, Santo André, SP, 09060020, Brazil (e-mail: giovannagalafassi@gmail.com).

Abstract

Introduction Dorsal root entry zone (DREZ) lesioning (DREZ-otomy) is considered an effective treatment for chronic pain due to spinal cord injuries, brachial and lumbosacral plexus injuries, postherpetic neuralgia, spasticity, and other conditions. The objective of the technique is to cause a selective destruction of the afferent pain fibers located in the dorsal region of the spinal cord.

Objective To identify and review the effectiveness and the main aspects related to DREZ-otony, as well as the etiologies that can be treated with it.

Methods The PubMed, MEDLINE and LILACS databases were used as bases for this systematic review, having the impact factor as the selection criteria. The 23 selected publications, totaling 1,099 patients, were organized in a table for systematic analysis.

Results Satisfactory pain control was observed in 70.1% of the cases, with the best results being found in patients with brachial/lumbosacral plexus injury (70.8%) and the worst, in patients with trigeminal pain (40% to 67%).

Discussion Most of the published articles observed excellent results in the control of chronic pain, especially in cases of plexus injuries. Complications are rare, and can be minimized with the use of new technologies for intraoperative monitoring and imaging.

Conclusion DREZ-otomy can be considered a great alternative for the treatment of chronic pain, especially in patients who do not tolerate the side effects of the medications used in the clinical management or have refractory pain.

Keywords
► neuropathic pain
► dorsal root entry zone
► radiculopathy
► spinal cord

Resumo

Introdução O lesionamento da zona de entrada da raiz dorsal (dorsal root entry zone, DREZ), ou DREZ-otomia, é considerado um tratamento eficaz para a dor crônica decorrente de lesões medulares, lesão dos plexos braquial e lombossacral, neuralgia...
Introduction

Neurosurgical procedures should be considered as a possible treatment for chronic pain refractory to pharmacotherapy and other treatments. Over 100 million adults in the United States are afflicted with chronic pain conditions by different causes (chronic diseases, peripheral nerve disorders and primary pain disorders) that play an important role in the patient’s quality of life. Chronic neuropathic pain seems like a disease in itself, without any benefit or protective significance that characterizes the role of nociceptive pain in the human body. This illness imposes economic burdens to individuals and society, which can be observed in studies that suggest that patients with chronic pain experience worse health-related quality of life than the general population. Moreover, some epidemiological studies have also reported the negative effect that chronic pain has on health conditions, since it can be associated with more symptoms of anxiety and depression, and poorer sleep quality.

The lesion of the dorsal root entry zone (DREZ) is considered an effective procedure to treat this type of pain. The goal of DREZ lesioning is to create a selective destruction of neurons and fibers that enter the DREZ and, by this mean, cut off the pain circuit and relieve the symptoms. The idea that characterizes the DREZ-otomia and its principal etiologies that can be treated by this procedure, e revisar os principais aspectos relacionados à técnica.

Métodos As bases de dados do PubMed, MEDLINE e Lilacs foram utilizadas na realização desta revisão sistemática, tendo o impacto como critério de seleção. As 23 publicações selecionadas, totalizando 1.099 pacientes, foram organizadas numa tabela para análise sistemática.

Resultados Controle satisfatório da dor foi observado em 70,1% dos casos, sendo que os melhores resultados foram encontrados em pacientes com lesão dos plexos braquial/lombossacro (70,8%), e os piores, em pacientes com dor neuropática do nervo trigémeo (40% a 67%).

Discussão A maioria dos artigos publicados encontrou ótimos resultados no controle da dor crônica, principalmente na dor relacionada à lesão de plexos. As complicações são raras, podendo ser minimizadas com o emprego das novas tecnologias de monitoração intraoperatoria e imagem existentes.

Conclusão A drezotomia pode ser considerada uma ótima alternativa para o tratamento da dor crônica, especialmente em pacientes que não toleram os efeitos colaterais das medicações utilizadas no manejo clínico ou apresentam dor refratária.

Methods

The PubMed, MEDLINE and LILACS databases were searched for manuscripts related to the DREZ operation. All relevant articles were included in the present review. Additionally, the reference sections of these articles were evaluated, and papers that provided important information regarding the subject were included. The results and conclusion of these articles were summarized in a chart. All types of studies were included, including other literature reviews. Articles that did not provide data regarding the effectiveness of the technique were not included. The selection protocol followed the flowchart in Fig. 1.
Results

In total, 23 articles were included in the present review, totaling 1,099 patients. The articles retrieved were written between 1986 and 2017. All data collected was summarized in Table 1, including the conclusion, year and number of patients evaluated.

Out of the 23 articles, 10 performed the procedure for the improvement of chronic pain related to spinal cord injury, 4, due to phantom pain, 13, due to lesion of the brachial or lumbosacral plexuses, 4, due to postherpetic neuralgia, 2, due to cauda equina lesion, 3, due to hyperspastic states, 3, due to facial pain of multiple causes, 3, due to peripheral nerves, 1, due to deafferentation pain syndromes, and 2 for the control of cancer pain (Table 1).

For cervical DREZ lesioning, the highest percentage of good or excellent pain relief was found regarding cancer pain, hyperspastic states and cervical root avulsion. Plexus injuries, spinal cord injury, peripheral nerve injury and hyperspastic states were the etiologies related to the best results with conus medullaris DREZ lesion (Table 1).

Nucleus caudalis DREZ lesion was the technique with the fewer number of patients (n = 41). All of them underwent surgery due to facial pain. The median percentage of good or excellent pain relief was of 60% (range: 40% to 73%). Due to the small sample, these results may not show the actual effectiveness (Table 1).

Discussion

Considerations Regarding the Nonsurgical Management of Pain

There is a vast range of pharmacological and nonpharmacological treatments available, including different mechanisms to control the pain pathway. In general, the pharmacological treatment is well tolerated by the patients; nevertheless, some of those treatments have potentially complicated side effects.

Antiepileptics, such as gabapentin and pregabalin, can be considered the most popular drugs to treat neuropathic pain. Pregabalin is approved for the management of pain due to diabetic peripheral neuropathy, postherpetic neuralgia, fibromyalgia, and neuropathic pain due to spinal cord injuries. Recently, the combination of intravenous ketamine and oral gabapentin was evaluated in a double-blinded, randomized, controlled trial on complicated neuropathic pain. This study showed an important improvement in pain scores in comparison to the placebo group. Anticonvulsants, like phenytoin...
### Table 1: Systematic review of studies on lesioning of the dorsal root entry zone (DREZ)

<table>
<thead>
<tr>
<th>Study</th>
<th>DREZ lesioning methods</th>
<th>Target</th>
<th>Etiology</th>
<th>Patients (n)</th>
<th>Pain relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedman and Nashold, 1986</td>
<td>Radiofrequency thermocoagulation</td>
<td>Cervix or conus medullaris</td>
<td>Spinal cord injury</td>
<td>56</td>
<td>50%</td>
</tr>
<tr>
<td>Saris et al., 1988</td>
<td>Radiofrequency thermocoagulation, probe with 0.5 mm of diameter, and 2 mm in depth</td>
<td>Conus medullaris</td>
<td>Phantom pain</td>
<td>9</td>
<td>67%</td>
</tr>
<tr>
<td>Young, 1990</td>
<td>Radiofrequency method using a 0.5–2-mm stainless steel electrode with control of electric current and duration</td>
<td>Cervix or conus medullaris</td>
<td>Brachial or lumbosacral plexuses injuries, spinal cord injury, phantom pain, postherpetic neuralgia, and cauda equina injury</td>
<td>21</td>
<td>67%</td>
</tr>
<tr>
<td></td>
<td>CO2 Laser</td>
<td></td>
<td></td>
<td>20</td>
<td>45%</td>
</tr>
<tr>
<td></td>
<td>Radiofrequency method using 0.25–2-mm stainless steel electrode with control of the electrode temperature and duration</td>
<td></td>
<td></td>
<td>37</td>
<td>68%</td>
</tr>
<tr>
<td>Sindou, 1995</td>
<td>Microsurgical DREZ-otomy, 45° ventromedially, and 2–3-mm deep</td>
<td>Cervix</td>
<td>Cancer pain</td>
<td>46</td>
<td>87%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Conus medullaris</td>
<td>Cancer pain</td>
<td>35</td>
<td>78%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cervix or conus medullaris</td>
<td>Brachialplexus injuries, spinal cord injury, peripheral nerve lesion, phantom pain, postherpetic neuralgia</td>
<td>139</td>
<td>87%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Conus medullaris</td>
<td>Hyperspastic states</td>
<td>42</td>
<td>82%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cervix</td>
<td>Hyperspastic states</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>Bullard and Nashold, 1997</td>
<td>Radiofrequency thermocoagulation</td>
<td>Nucleus caudalis</td>
<td>Facial pain</td>
<td>25</td>
<td>67%</td>
</tr>
<tr>
<td>Rath et al., 1997</td>
<td>2-mm bare-tipped thermocontrolled electrode</td>
<td>Cervix</td>
<td>Cervical root avulsion</td>
<td>23</td>
<td>82%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cervix or conus medullaris</td>
<td>Spinal cord injury</td>
<td>23</td>
<td>48%</td>
</tr>
<tr>
<td>Samii et al., 2001</td>
<td>Radiofrequency thermocoagulation</td>
<td>Cervix</td>
<td>Brachialplexus injuries</td>
<td>47</td>
<td>63%</td>
</tr>
<tr>
<td>Sindou et al., 2001</td>
<td>Microsurgical DREZ-otomy, 3 mm in depth on average, with 35° of ventromedial obliquity</td>
<td>Cervix or conus medullaris</td>
<td>Spinal cord and/or cauda equina injuries</td>
<td>44</td>
<td>60%</td>
</tr>
<tr>
<td>Delgado-López et al., 2003</td>
<td>Radiofrequency</td>
<td>Nucleus caudalis</td>
<td>Facial pain</td>
<td>5</td>
<td>40%</td>
</tr>
<tr>
<td>Sindou et al., 2005</td>
<td>2-mm deep and made at a 45° angle ventrally</td>
<td>Cervix</td>
<td>Brachialplexus injuries</td>
<td>55</td>
<td>66%</td>
</tr>
<tr>
<td>Spaic et al., 2005</td>
<td>Microsurgical DREZ-otomy, 2-mm deep, and made at a 45° angle ventrally</td>
<td>Thorax or conus medullaris</td>
<td>Spinal cord injuries</td>
<td>24</td>
<td>77%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14</td>
<td>85%</td>
</tr>
<tr>
<td>Study</td>
<td>DREZ lesioning methods</td>
<td>Target</td>
<td>Etiology</td>
<td>Patients (n)</td>
<td>Pain relief</td>
</tr>
<tr>
<td>-------</td>
<td>------------------------</td>
<td>--------</td>
<td>----------</td>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Prestor, B. 2006</td>
<td>Radiofrequency thermocoagulation</td>
<td>Cervix</td>
<td>Brachial plexus avulsion</td>
<td>26</td>
<td>96%</td>
</tr>
<tr>
<td>Chen and Tu, 2006</td>
<td>Radiofrequency thermocoagulation</td>
<td>Cervix</td>
<td>Brachial plexus injuries</td>
<td>60</td>
<td>60%</td>
</tr>
<tr>
<td>Teixeira et al., 2007</td>
<td>Radiofrequency lesions using a thermocouple electrode spaced by 2 mm along the DREZ</td>
<td>Cervix</td>
<td>Radiation-induced brachial plexopathy</td>
<td>8</td>
<td>75%</td>
</tr>
<tr>
<td>Zhang et al., 2008</td>
<td>Radiofrequency thermocoagulation</td>
<td>Cervix or conus medullaris</td>
<td>Deafferentation pain syndromes</td>
<td>23</td>
<td>74%</td>
</tr>
<tr>
<td>Hong et al., 2008</td>
<td>2.5-mm deep radiofrequency electrode at in the Lissauer tract and obliquely oriented at 45°</td>
<td>Cervix</td>
<td>Upper-extremity spasticity</td>
<td>9</td>
<td>67%</td>
</tr>
<tr>
<td>Kanpolat et al., 2008</td>
<td>Radiofrequency electrode at 45° and 2-mm depth to the spinal cord</td>
<td>Cervix or conus medullaris</td>
<td>Brachial plexus avulsion, phantom limb pain, painful spasticity after spinal cord injury, tumor and postherpetic neuralgia</td>
<td>44</td>
<td>77%</td>
</tr>
<tr>
<td>Ruiz-Juretschke et al., 2011</td>
<td>Radiofrequency thermocoagulation</td>
<td>Cervix</td>
<td>Spinal cord injury, brachial plexus avulsion and other peripheral nerve injuries</td>
<td>13</td>
<td>77%</td>
</tr>
<tr>
<td>Awad et al., 2013</td>
<td>Radiofrequency thermocoagulation</td>
<td>Cervical</td>
<td>Brachial plexus injuries, spinal cord injuries</td>
<td>19</td>
<td>69%</td>
</tr>
<tr>
<td>Haninec et al., 2014</td>
<td>Radiofrequency electrode with a tip 2 mm deep</td>
<td>Cervix</td>
<td>Brachial plexus injury</td>
<td>48</td>
<td>70.8%</td>
</tr>
<tr>
<td>Liu et al., 2015</td>
<td>Microsurgical DREZ-otomy assisted with spinal cord stimulation</td>
<td>Thorax and conus medullaris</td>
<td>Postherpetic neuralgia</td>
<td>6</td>
<td>83%</td>
</tr>
<tr>
<td>Chivukula et al., 2015</td>
<td>Radiofrequency thermocoagulation</td>
<td>Nucleus caudalis</td>
<td>Facial pain</td>
<td>16</td>
<td>68.75%</td>
</tr>
<tr>
<td>Takai and Taniguchi, 2017</td>
<td>Microsurgical tumor forceps with blunt dissection technique at a depth of 4–5 mm from the surface of the DREZ.</td>
<td>Cervix</td>
<td>Brachial plexus injuries</td>
<td>10</td>
<td>90%</td>
</tr>
</tbody>
</table>
and carbamazepine, and other older-generation antiepileptic drugs (phenobarbital and valproic acid) have unfavorable metabolic and interaction profiles; thus, they are being less and less prescribed nowadays.  

Tricyclic antidepressants can modulate afferent pain pathways by increasing the levels of serotonin and noradrenaline in the central nervous system. Tricyclics have proven to be effective in the treatment of several chronic pain conditions, and can also be considered a first-line treatment in patients with neuropathic pain. Although these medications tend to be well-tolerated, various side effects are described, which are caused by the serotonergic, noradrenergic, and anti-histaminergic properties of these drugs. These adverse effects include: bladder retention, prolonged QT interval, sedation etc.  

Cannabinoids have received a lot of attention in recent years. This is due to studies that have shown their analgesic effects for non-cancerous pain. While cannabinoids tend to be well-tolerated with mild, transient side effects, more studies are required to prove the effectiveness and security of these drugs for the treatment of neuropathic pain.  

**Surgical Treatment**  
Lesioning of the DREZ is a well-established surgical treatment for neuropathic pain. This procedure can be considered effective, safe and well-tolerated by most patients, justifying its frequent use.  
Since the first description, DREZ lesioning evolved considerably. Created as a method for pain control for patients with chronic pain following brachial plexus avulsion, it can be used for many conditions, such as deafferentation pain, postparaplegia pain, painful spasticity, facial pain, cancer pain, postherpetic neuralgia, and brachial and sacral plexus avulsions.  
The effectiveness of DREZ lesioning is based on the physiopathology of these diseases. They have in common neuropathic pain, which can be caused by imbalances between excitatory and inhibitory somatosensory signaling, alterations in ion channels, and variability in the way that pain messages are modulated in the central nervous system.  
The dorsal root of the spinal cord contains the axons from the primary afferent fibers originated in nociceptive receptors, which are responsible for the connection between the peripheral nervous system and the central nervous system. These neurons can ascend or descend a few vertebral levels through the tract of Lissauer. They enter the spinal cord through the dorsal root, where neurotransmitters are liberated, activating the second-order neurons located in the dorsal root. The second-order neurons ascend in the spinal cord through the lateral spinothalamic tract and spinal lemniscus until they reach the primary somatosensory cortex, where the information is processed. Considering these anatomo-physiological aspects, it is simpler to understand why the destruction of the dorsal root has the potential to modulate neuropathic pain.  
However, DREZ lesioning does not affect only pain fibers. The procedure has the ability of interrupting the unmyelinated and small myelinated fibers (considered tonogenic by their nociceptive input), as well as the large myelinated fibers going to the ventral horn, which are situated laterally and centrally in the DREZ respectively. At the end, the targets for lesioning are the central portion of the dorsal rootlets, the lateral part of the tract of Lissauer, and mainly the first five dorsal layers of the dorsal horn, where the (deafferented) hyperactive neurons are located (which are involved in the physiopathology of neuropathic pain) or where the excitatory segmental circuitry of the dorsal horn is situated (which is involved in spasticity) .  
The procedure is performed in prone position, and, depending on the level of the spinal cord, it may require a three-point cranial fixation device to align and immobilize the spine and skull. The laminectomy level should be determined based on the symptomatology, which generally follows specific dermatomes, demanding the bilateral destruction of fibers. Hemilaminectomies can be used for postherpetic neuralgia, or less frequently for single-dermatome pain or unstable spine. Patients undergoing a conus medullaris DREZ generally have laminectomies from levels D10 to L1, while patients undergoing nucleus caudalis or solitarius lesions undergo a small suboccipital craniectomy and Cl-C2 laminectomies.  
The dura mater and arachnoid are opened in the midline. Some structures, like the serpiginous vessels (Fig. 2), may be present along the sulcus, so they must be retracted to enable a proper visualization of the region. Once the DREZ is located (Fig. 3), the electrode can be introduced. Radiofrequency lesions are generally made at 75°C for 15 seconds, at 1 mm intervals along the intermediolateral sulcus, including the entire altered zone. The electrode should penetrate 2.0 mm deep and be held at a 25° angle into the dorsal nerve rootlet (Fig. 4).
procedure is extended to the segments corresponding to the pain territory, including one level above and one below.\textsuperscript{20}

Takai and Taniguchi\textsuperscript{23} described a posterior horn lesion using a microsurgical tumor forceps with a dissection technique at a depth of 4 mm to 5 mm from the surface of the DREZ. This new technique is based on recent findings regarding neuropathic pain suggesting the involvement of deeper layers of the gray matter of the spinal cord in pain conduction.\textsuperscript{22} This justifies the performance of deeper lesions on the posterior horn.

Another interesting fact regarding DREZ lesioning is the worse results found in conditions with diffuse pain. This seems to be related to the delimitation of the appropriate lesion level, which can be difficult depending on the case. Chun et al.\textsuperscript{21} described a modified DREZ lesioning procedure performed on both the complete injury zone (directly-injured cord level following spine injury) and the incomplete injury zone (indirectly-injured cord level identified on magnetic resonance imaging by signal change). This technique showed better results for diffuse pain than the original one, so they concluded that DREZ lesioning should be performed from the injured level up, including all abnormal rootlets above the level of the injury.

Sindou and Jeanmonod\textsuperscript{24} reported a series of 53 patients with harmful spasticity in one or both lower limbs. These patients underwent MDT for their painful state or abnormal postures (either hyperextention or flexion). Spasticity and spasms decreased or were abolished in most patients, 75% and 88.2% of them respectively. Abolition of sensation was found in less than 10% of the patients. This study showed that MDT has the potential to significantly improve the quality of life of the patients. In 2017, Sithinamursuwon et al.\textsuperscript{25} published a study comparing DREZ lesioning and selective dorsal rhizotomy in fifteen spasticity patients. They concluded that DREZ lesioning is more effective to reduce spasticity, but more destructive than selective dorsal rhizotomy. Due to this, they suggested that DREZ lesioning should be preferred for bed-ridden patients, while selective dorsal rhizotomy, for ambulatory patients.

In 2016, Sindou and Georgoulis\textsuperscript{26} published a case series of 3 patients with focal dystonia who underwent cervical microsurgical DREZ-otomy. They noticed that all patients maintained the relief of hypertonia, the sustained abnormal dystonic postures remained absent, and most of the functional benefit was still present at the last follow-up. No patient suffered total loss of tactile sensation and proprioception. However, thermal and nociceptive sensations almost disappeared in all three patients. Moreover, patients did not develop neuropathic pain.\textsuperscript{26}

The complications associated with DREZ lesioning can be separated into two different groups: over-lesioning and under-lesioning. The most common complications regarding over-lesioning are paralysis and dysesthesia, due to the destruction of adjacent pathways in the spinal cord (the lateral corticospinal, rubrospinal and spinocerebellar tracts, and the dorsal fasciculus). Genito-sphincterian deficits are another possible complication.\textsuperscript{19} On the other hand, ineffective pain control represents the under-lesioning complications.

To minimize the complications, it is imperative to choose the right spinal cord level, size of the lesion and angle of insertion. Henssen et al.\textsuperscript{27} conducted a study in 2019 to measure the angle between the DREZ and the posterior median sulcus (PMS). They made 11.7-T post-mortem magnetic resonance images and compared them to polarized light imaging microscopy to determine the fiber orientation of the dorsal horn tracts. The median angles between the DREZ and the PMS were of 40.1° (left hemicord) and 39.8° (right hemicord). With these results, they concluded that an insertion angle of 25° should be recommended for DREZ lesioning.

Another study, conducted in 2019 by Monaco et al.,\textsuperscript{28} described a real-time imaging technique to optimize DREZ lesioning using intraoperative ultrasound (US), which can determinate the exact location of the gray matter and dorsal horn. The US enables a correct positioning of the needle during the puncture, a proper angular adjustment, and a controlled depth.

\textbf{Conclusion}

Lesioning of the DREZ is an effective and safe procedure that should be considered a treatment for neuropathic pain due to diverse etiologies. Even though the pharmacological treatment is a possibility for the non-complicated cases, the surgical procedure is related to better results and fewer side effects. Thus, the treatment must be individualized, considering the quality of life and the decision of the patient.

\textbf{Conflict of Interests}

The authors have no conflicts of interest to declare.

\textbf{References}

Drezotomy: Systematic Review  
Galafassi et al.


