



# Safety of Conventional and Pulsed Radiofrequency Lesions of the Dorsal Root Entry Zone Complex (DREZC) for Interventional Pain Management: A Systematic Review

Mila Pastrak · Ognjen Visnjevac · Tanja Visnjevac · Frederick Ma · Alaa Abd-Elseyed

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## ABSTRACT

**Study Design:** Systematic literature review.

**Objective:** The goal of this systematic review is to assess the clinical safety and potential complications of conventional and pulsed radiofrequency ablations targeting dorsal root entry zone complex (DREZC) components in the treatment of chronic pain.

**Background:** There is a growing popularity for the use of radiofrequency ablation (RFA)

techniques targeting DREZC components by pain management physicians for an increasing variety of indications. To date, we lack a systematic review to describe the safety and the type of complications associated with these procedures.

**Methods:** This was a systematic literature review. This systematic search was limited to peer-reviewed literature using “radiofrequency ablation” as a search keyword using PubMed’s database for manuscripts published between inception and December 2020. Abstracts that involved the application of radiofrequency currents, of any modality, to DREZC components for the treatment of pain were included for full-text review. Search was limited to original data describing clinical outcomes following RFA performed for pain indications only, involving the DREZC components outlined above, in human subjects, and written in English. The primary outcomes were complications associated with conventional RFA and pulsed radiofrequency ablation (PRF). Complications were categorized as type 1 (persistent neurological deficits or other serious adverse events, defined as any event that resulted in permanent or prolonged injury; type 2 (transient neuritis or neurological deficits, or other non-neurological non-minor adverse event); type 3 (minor adverse events (e.g., headache, soreness, bruising, etc.).

**Results:** Of the 62 selected manuscripts totaling 3157 patients, there were zero serious adverse events or persistent neurological deficits

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M. Pastrak  
School of Medicine, University College Cork, Cork,  
Ireland  
e-mail: apastrak19@gmail.com

O. Visnjevac · T. Visnjevac · F. Ma  
Faculty of Health Sciences, McMaster University,  
Hamilton, ON, Canada

T. Visnjevac  
e-mail: tvisnjevac@gmail.com

F. Ma  
e-mail: DrMa@bloorpain.com

O. Visnjevac  
Bloor Pain Specialists, Toronto, ON, Canada

O. Visnjevac  
Cleveland Clinic Canada, Toronto, ON, Canada  
e-mail: DrV@bloorpain.com

A. Abd-Elseyed (✉)  
Anesthesiology, University of Wisconsin School of  
Medicine and Public Health, Madison, WI, USA  
e-mail: abdelsayed@wisc.edu

reported. A total of 36 (1.14%) transient neurological deficits, cases of transient neuritis, or non-minor adverse events like uncomplicated pneumothorax were reported. A total of 113 (3.58%) minor adverse events were reported (bruising, transient site soreness, headache).

**Conclusions:** This systematic review indicates that the use of RFA lesion of the DREZC for interventional pain management is very safe. There were no serious adverse effects with a sizable sample of randomized controlled trial (RCT), prospective observational, and retrospective studies.

**Keywords:** Radiofrequency ablation; Dorsal root ganglia; Neuralgia

### Key Summary points

This systematic review evaluated safety and complication rates of RFA and PRF lesions of DREZC components for various pain indications.

A total of 62 manuscripts were included in this review.

Among a total of 3157 cases, there were zero serious adverse events resulting in permanent injury. A total of 36 (1.14%) transient neurological deficits, cases of transient neuritis, or non-minor adverse events like uncomplicated pneumothorax were reported. A total of 113 (3.58%) minor adverse events were reported (bruising, transient site soreness, headache).

This systematic review indicates that the use of RFA lesion of the DREZC for interventional pain management is very safe.

## INTRODUCTION

Chronic pain is defined as pain that persists or recurs for longer than 3 months and is associated with significant emotional distress and/or

significant functional disability [1]. The prevalence of chronic pain is approximately 25–30% of the worldwide population. It arises from numerous etiologies including tissue damage, inflammation, nerve injury, or dysfunction of the nervous system [2]. Chronic pain is a debilitating condition associated with symptoms such as unprovoked pain sensation, paresthesia, dyesthesia, allodynia, or hyperalgesia [1]. A growing body of literature supports a relationship between peripheral nerve damage as well as the primary role of the plasticity and modality of dorsal root ganglia (DRG) neurons in chronic pain states [3, 4].

DRG are large collections of primary afferent sensory neurons located on the distal end of dorsal spinal roots [3]. DRG neurons are pseudo-bipolar neurons; while a peripheral neural branch innervates the target organ, a central branch carries the somatosensory information to the spinal cord where it synapses with secondary sensory neurons to transmit information to the central nervous system (CNS) [3]. The primary afferent sensory neurons are transducing information by C-fibers, A-delta, and A-beta nerve fibers from nociceptors, thermoreceptors, chemoreceptors, and proprioceptors [5]. Following peripheral nerve injury or sensitization, primary sensory neurons demonstrate maladaptive molecular changes in DRG cell bodies and in their axons, thereby resulting in development or propagation of neuropathic pain states [3–5]. Ion channel modifications in DRG that are in part contributing to these effects include proliferation of voltage-dependent sodium channels, downregulation of voltage-gated potassium channels, and increased expression of the calcium channels [5]. Changes occurring at the DRG neuron levels can result in peripheral sensitization, ectopic neuronal activity, presynaptic modulation as well as increased neuronal excitability in the spinal cord [5]. Further, hyperexcitability and ectopic firing of cell bodies at the DRG level can increase central sensitization and reduce central inhibition that are crucial for the onset and maintenance of chronic pain [5].

The critical role of the DRG neurons in pain transduction and preservation of persistent pain states has long been recognized, focusing

attention on these tissues as targets for therapeutic interventions [4]. The dorsal sensory pathway's linear anatomical organization and accessible location have made the DRG and the neighboring dorsal rootlets, dorsal root entry zone, as well as the dorsal rami and their branches, which are collectively referred to as the dorsal root entry zone complex (DREZC), an attractive target for neuromodulation [4, 6]. DREZC components, which are part of the dorsal sensory pathway, have been the target of pain relief interventions including radiofrequency ablation (RFA) and steroid injections [4–8]. Biological changes in neurological tissues exposed to RFA can occur as a result of the thermal effects and/or the high intensity electric field, and can be either ablative or neuro-modulatory lesions [4–8].

While the DRG, being central in pain signal processing and propagation of chronic pain states, is a logical target component of the DREZC, it is technically difficult to accurately discern whether the tips of each RFA cannula are adjacent to the DRG or adjacent its neighboring DREZC components, since the DRG cannot be visualized using fluoroscopy, the most commonly used modality for RFA procedures [6]. DRGs also vary in number, from one to three per spinal level, and in location (intraspinal, intraforaminal, or extraforaminal), none of which can be visualized or reliably identified using fluoroscopy [6].

As such, there is an element of potential error in all past publications reporting interventions of the DRG, specifically. As a result of the anatomical differences of individualized components of this linear dorsal afferent sensory pathway (the dorsal rami, DRG, the dorsal rootlets, and the dorsal root entry zone) and limitations to accurately localize each of these components with common clinically available tools (such as fluoroscopy), the more sensitive and inclusive term DREZC has been utilized herein to refer to RFA lesions targeting the DRG or dorsal rami [6]. The goal of this systematic review is, thus, to assess the clinical safety and potential complications of conventional and pulsed RFA targeting DREZC components in the treatment of chronic pain.

## METHODS

### Study Design

Systematic literature review, PRISMA method.

### Search Strategy

This systematic search was limited to peer-reviewed literature using “radiofrequency ablation” as a search keyword using PubMed's database for manuscripts published between inception and December 2020.

### Study Selection

Abstracts that involved the application of radiofrequency currents, of any modality, to DREZC components for the treatment of pain were included for full-text review.

### Inclusion Criteria

Search was limited to original data describing clinical outcomes following RFA performed for pain indications only, involving the DREZC components outlined above, in human subjects, and written in English.

### Exclusion Criteria

Exclusion criteria included the following:

- Technical reports or basic science investigations not describing clinical outcomes following RFA procedures
- Manuscripts describing RFA not targeting DREZC components
- Manuscripts describing the use of RFA for non-pain indications (i.e., cardiac, dermatology, cancer)
- Review articles
- Case reports

### Data Collection

Two trained research assistants employed by author OV performed the initial identification and screening, confirming each other's findings. All authors subsequently assessed these

**Table 1** Summary of complications following conventional or pulsed RFA of the dorsal root entry zone complex (DREZC)

Indication	Study type	Treatment arm complications			Sham/placebo arm complications		
		Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
Cervicobrachial pain	C-RFA RCT ( <i>n</i> = 20) Van Kleef et al., 1996	–	–	9/9 (100%)	–	1/11 (9%)	3/11 (27%)
	C-RFA RCT ( <i>n</i> = 61) Slappendel et al., 1997	–	6/32 (19%)	–	NA	NA	NA
	P-RFA RCT ( <i>n</i> = 23) Van Zundert et al., 2007	–	–	–	–	–	–
	C-RFA Pros ( <i>n</i> = 20) Van Kleef et al., 1993	–	7/20 (35%)	12/20 (60%)	NA	NA	NA
	C-RFA Pros ( <i>n</i> = 54) Samwel et al., 2000	–	–	–	NA	NA	NA
	P-RFA Pros ( <i>n</i> = 15) Choi et al., 2011	–	–	–	NA	NA	NA
	P-RFA Pros ( <i>n</i> = 20) Yang et al., 2020	–	–	–	NA	NA	NA

**Table 1** continued

Indication	Study type	Treatment arm complications			Sham/placebo arm complications			
		Type 1	Type 2	Type 3	Type 1	Type 2	Type 3	
Cervicogenic headache	C-RFA RCT ( <i>n</i> = 30) Haspeslagh et al., 2006	–	–	–	NA	NA	NA	
	P-RFA Retro ( <i>n</i> = 139) Li et al., 2019	–	–	–	NA	NA	NA	
	P-RFA Retro ( <i>n</i> = 114) Lee et al., 2020	–	–	–	NA	NA	NA	
	C-RFA Pros ( <i>n</i> = 15) Van Suijlekom et al., 1998	–	–	1/15 (7%)	NA	NA	NA	
	P-RFA Pros ( <i>n</i> = 20) Li et al., 2020	–	–	3/20 (15%)	NA	NA	NA	
	Cervical disk herniation pain	P-RFA RCT ( <i>n</i> = 34) Halim et al., 2017	–	–	3/17 (18%)	NA	NA	NA
		Chronic cervical pain	P-RFA Retro ( <i>n</i> = 18) Van Zundert et al., 2003	–	–	–	NA	NA
P-RFA Retro ( <i>n</i> = 59) O’Gara et al., 2020	–		–	1/59 (2%)	NA	NA	NA	

**Table 1** continued

Indication	Study type	Treatment arm complications			Sham/placebo arm complications		
		Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
Cervical or lumbar pain	P-RFA Retro ( <i>n</i> = 154)	–	–	–	NA	NA	NA
	Chao et al., 2008						
Lumbosacral radicular pain, chronic low back pain, lumbar facet syndrome	C-RFA Pros ( <i>n</i> = 122)	–	–	27/122 (22%)	NA	NA	NA
	Pevsner et al., 2003						
	C-RFA RCT ( <i>n</i> = 31)	–	–	–	–	–	–
	Van Kleef et al., 1999						
	C-RFA RCT ( <i>n</i> = 83)	–	9/43 (21%)	29/44 (66%)	NA	NA	NA
	Geurts et al., 2003						
	P-RFA RCT ( <i>n</i> = 100)	–	–	–	–	–	–
	Lin et al., 2010						
	C-RFA RCT ( <i>n</i> = 84)	–	3/84 (4%)	–	NA	NA	NA
	Cohen et al., 2010						
C-RFA RCT ( <i>n</i> = 56)	–	–	–	NA	NA	NA	
Alkemeier et al., 2013							
P-RFA RCT ( <i>n</i> = 31)	–	–	2/16 (13%)	–	–	2/15 (13%)	
Shanthanna et al., 2014							

Table 1 continued

Indication	Study type	Treatment arm complications			Sham/placebo arm complications		
		Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
	P-RFA RCT ( <i>n</i> = 18)	–	–	–	NA	NA	NA
	Hashemi et al., 2014						
	P-RFA RCT ( <i>n</i> = 62)	–	6/31 (19%)	–	–	4/31 (13%)	–
	Koh et al., 2015						
	P-RFA RCT ( <i>n</i> = 28)	–	–	–	NA	NA	NA
	Holanda et al., 2016						
	P-RFA RCT ( <i>n</i> = 55)	–	–	–	NA	NA	NA
	Arsanious et al., 2016						
	C-RFA RCT ( <i>n</i> = 60)	–	–	–	–	–	–
	Van Tilburg et al., 2016						
	P-RFA RCT ( <i>n</i> = 60)	–	–	–	NA	NA	NA
	Lee et al., 2018						
	P-RFA RCT ( <i>n</i> = 50)	–	–	–	NA	NA	NA
	De et al., 2019						
	P-RFA RCT ( <i>n</i> = 150)	–	–	–	–	–	–
	Moussa et al., 2020						
	P-RFA Retro ( <i>n</i> = 279)	–	–	–	NA	NA	NA
	Van Wijk et al., 2001						
	P-RFA Retro ( <i>n</i> = 13)	–	–	–	NA	NA	NA
	Teixeira et al., 2005						

**Table 1** continued

Indication	Study type	Treatment arm complications			Sham/placebo arm complications		
		Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
	P-RFA Retro ( <i>n</i> = 60)	–	–	–	NA	NA	NA
	Van Boxem et al, 2011						
	C-RFA/P-RFA Retro ( <i>n</i> = 50)	–	–	1/50 (2%)	NA	NA	NA
	Nagda et al., 2011						
	P-RFA Retro ( <i>n</i> = 60)	–	–	–	NA	NA	NA
	Kim et al., 2018						
	P-RFA Retro ( <i>n</i> = 82)	–	–	–	NA	NA	NA
	Park et al., 2019						
	C-RFA Pros ( <i>n</i> = 40)	–	–	5/40 (13%)	NA	NA	NA
	Stolker et al., 1993						
	P-RFA/C-RFA Pros ( <i>n</i> = 76)	–	–	–	NA	NA	NA
	Simopoulos et al., 2008						
	P-RFA Pros ( <i>n</i> = 127)	–	–	–	NA	NA	NA
	Tsou et al., 2010						
	C-RFA Pros ( <i>n</i> = 58)	–	–	11/58 (19%)	NA	NA	NA
	Shabat et al., 2013						
	P-RFA Pros ( <i>n</i> = 65)	–	–	–	NA	NA	NA
	Van Boxem et al, 2015						
	P-RFA Pros ( <i>n</i> = 10)	–	–	–	NA	NA	NA
	Das et al., 2018						



**Table 1** continued

Indication	Study type	Treatment arm complications			Sham/placebo arm complications		
		Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
Post herpetic neuralgia	P-RFA/C-RFA Pros ( <i>n</i> = 118) Abdurrahman et al., 2018	–	3/118 (3%)	–	NA	NA	NA
	P-RFA Pros ( <i>n</i> = 30) Tortora et al., 2021	–	–	–	NA	NA	NA
	P-RFA/C-RFA Quasi ( <i>n</i> = 25) Trinidad et al., 2015	–	–	–	NA	NA	NA
	P-RFA Quasi ( <i>n</i> = 50) Marliana et al., 2020	–	–	–	NA	NA	NA
	P-RFA RCT ( <i>n</i> = 116) Huang et al., 2018	–	–	–	NA	NA	NA
	P-RFA RCT ( <i>n</i> = 150) Ding et al., 2019	–	2/150 (1%)	–	NA	NA	NA
	P-RFA Retro ( <i>n</i> = 42) Kim et al., 2017	–	–	1/20 (5%)	NA	NA	NA
	P-RFA Retro ( <i>n</i> = 58) Kim et al., 2017	–	–	–	NA	NA	NA
	P-RFA Pros ( <i>n</i> = 49) Kim et al., 2008	–	–	–	NA	NA	NA
	P-RFA Controlled ( <i>n</i> = 90) Wan et al., 2016	–	–	5/90 (6%)	NA	NA	NA

**Table 1** continued

Indication	Study type	Treatment arm complications			Sham/placebo arm complications		
		Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
Neuropathic pain	P-RFA RCT ( <i>n</i> = 10) Moore et al., 2020	–	–	–	–	–	–
	P-RFA RCT ( <i>n</i> = 41) Vigneri et al., 2020	–	–	–	–	–	–
	P-RFA Retro ( <i>n</i> = 28) Shabat et al., 2006	–	–	6/28 (21%)	NA	NA	NA
	Chest malignancy pain	–	Reported but not quantified	Reported but not quantified	NA	NA	NA
Post-mastectomy pain	P-RFA RCT ( <i>n</i> = 64) Hetta et al., 2020	–	–	–	NA	NA	NA
	Post knee arthroplasty pain	–	–	–	NA	NA	NA
Cerebral palsy spasticity	C-RFA Pros ( <i>n</i> = 17) Vles et al., 2010	–	–	2/17 (12%)	NA	NA	NA

*RCT* randomized controlled trial, *Pros* prospective observational study, *Retro* retrospective chart review or series, *Quasi* quasi controlled study, *NA* not applicable, *AE* adverse event, *C-RFA* conventional (continuous heat) radiofrequency ablation, *P-RFA* pulsed (discontinuous heat) radiofrequency ablation. Dashed lines indicate a value of 0/*n* (0%). – = zero events reported in this category. Type 1 = Persistent neurological deficits or other serious adverse events. Type 2 = Transient neuritis or neurological deficits, or other non-neurological non-minor adverse event. Type 3 = Minor adverse events (e.g., headache, soreness, bruising, etc.)

reports for eligibility and inclusion, and obtained confirmation from at least one colleague as to the eligibility of each manuscript.

### Data Extraction

Data was extracted from these reports into a spreadsheet by the two trained research

assistants employed by author OV, then subsequently verified by authors OV and MP. The primary outcomes were complications, which were subcategorized into the following:

- Type 1 = Persistent neurological deficits or other serious adverse events, defined as any event that resulted in permanent or prolonged injury.

- Type 2 = Transient neuritis or neurological deficits, or other non-neurological non-minor adverse event.
- Type 3 = Minor adverse events (e.g., headache, soreness, bruising, etc.).

### Variables Measured

The following parameters were measured:

- Indication for DREZC ablation
- Type of radiofrequency ablation (conventional or pulsed)
- Location of the treatment (anatomic targets)
- Complications associated with the treatment
- Duration of the complications associated with the procedure

### Effect Measures and Synthesis of Data

Data for the above complications were tabulated to note prevalence rates of each type of complication (Table 1), but no quantification of results was planned as it was expected there would be significant heterogeneity in the data. Missing data were noted as such.

### Reporting Bias

No attempts were made to assess risk of bias due to missing results arising from reporting biases as the authors felt such efforts would be largely subjective.

### Ethics Compliance

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

## RESULTS

A total of 39,207 manuscripts from PubMed published between inception and December 2020 were identified in the initial literature search and the majority were excluded (Fig. 1).

A total of 62 manuscripts were included for qualitative analysis: 25 were randomized controlled trial (RCT) studies, 16 were retrospective studies, 19 were prospective studies, and two were quasi experimental studies, collectively reporting outcomes for a total of 3157 patients. The characteristics of the included studies are detailed in Tables 2, 3, 4, and 5.

### Randomized Controlled Clinical Trials

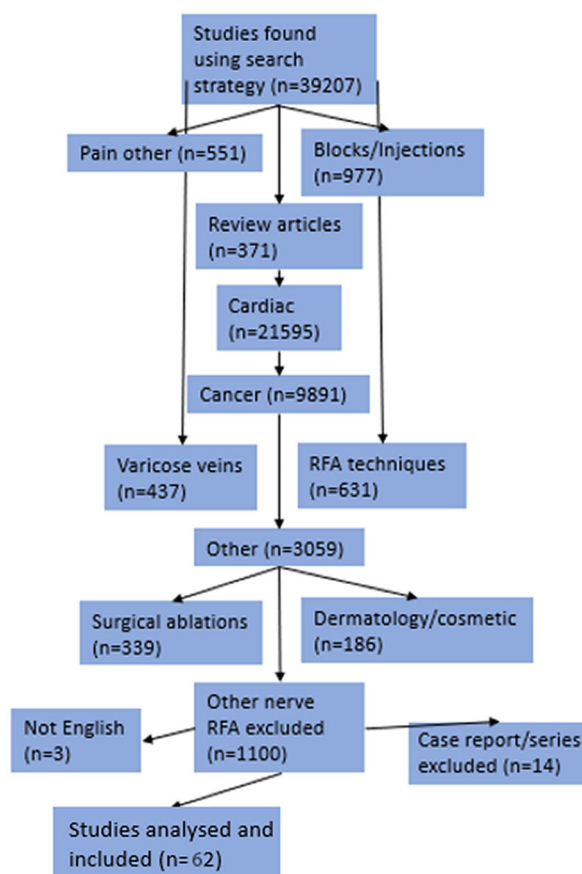
Twenty-four RCT studies were analyzed, including nine RCTs using conventional RFA and 15 studies with pulsed mode RFA (Table 2) [9–32]. Of the nine conventional RFA RCTs, two pertained to cervicobrachial pain, one pertained to cervicogenic headache, one pertained to lumbosacral radicular pain, one pertained to thoracic radicular pain, and four pertained to chronic low back pain or lumbar facet joint pain. A total of 402 patients were exposed to conventional RFA between 40 and 80 °C. Two studies for cervicobrachial pain showed that RFA lesions adjacent to the DREZC were associated with mild complications post treatment [9, 10]. In a randomized trial that exposed nine patients to conventional RFA at 67 °C, seven patients complained of a burning sensation in the treated dermatomes that receded spontaneously after 3 weeks [10]. In the same study, one patient also had mild hypoesthesia of the upper arm which decreased after 3 months [10]. Another randomized study for cervicobrachial pain reported complaints of neuritis and a slight loss of muscle strength in a small number of patients at 6 weeks post treatment that resolved spontaneously during a 3-month follow-up period [9]. Interestingly, an RCT trial that implemented conventional RFA for cervicogenic headache in 15 patients was not associated with any serious complications [11].

A randomized, double blind, sham-controlled study in 45 patients using conventional RFA for chronic lumbosacral radical pain reported discrete loss of motor function and change in sensation in 29 patients [12]. Another study that described the effect of conventional RFA of the DREZC in 78 patients suffering from thoracic refractory pain due to chest

malignancies also reported adverse events post therapy, including back pain ( $n = 9$ ), soreness ( $n = 15$ ), and hematoma ( $n = 3$ ) whereas major complications were neuritis ( $n = 11$ ), sensory deficit ( $n = 8$ ), and anesthesia dolorosa ( $n = 2$ ) [13]. Notably, however, in this study, RFA of thoracic T2–T8 DREZC lesions with combined fluoroscopy and CT-guidance that was applied to 40 out of 78 patients showed significantly lower incidence of adverse events in comparison to patients that were treated with standard fluoroscopy (15% vs. 37%, respectively) [13]. No infection, motor deficits, or pneumothorax was recorded in this clinical trial [13]. In an RCT that treated 15 patients with conventional RFA at the dorsal rami (components of the DREZC) of L3, L4, and L5 for chronic low back pain, no complications associated with the procedure

were reported [14]. In another trial with conventional RFA on dorsal ramus for low back pain, two of 151 treated patients experienced significant worsening of back pain while one patient had a new radiating pain in their leg after the procedure [15]. All symptoms in affected patients spontaneously resolved after 3 months [15]. In a third RCT using conventional RFA on the dorsal ramus to treat chronic low back pain in 56 patients, no adverse events were reported during the 6-month observation period [16]. Similarly, the application of conventional RFA to the medial branch of the dorsal ramus to 30 patients with lumbar facet joint pain was not encountered with serious adverse events during the trial [17].

Of the 15 published RCTs with pulsed RFA of DREZC components (Table 2), three studies



**Fig. 1** Flow diagram of study selection. Adapted from Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA]; Moher et al., 2009. RFA = radiofrequency ablation; Pain other = manuscripts not

describing clinical use of RFA, but describing some other aspect of pain pathophysiology or clinical pain management

**Table 2** Randomized controlled clinical trial data: complications following conventional or pulsed RFA of the dorsal root entry zone complex (DREZC)

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Van Kleef et al., 1996	20 pts. 9 pts had RFA at 67 °C; 11 pts had sham treatment. Cervicobrachial pain	CRF	Significant reduction in VAS score in treatment group; Treatment group 8/9 pts successful vs. sham 2/11 pts successful	Treatment group: 1 pt had mild burning pain during RF procedure, 7 pts had burning sensation in the treated dermatome (subsided 3 weeks post treatment), 1 pt had slight pain of the upper arm (subsided 3 months post treatment) Sham: 3 pts had non-radiating pain at injection site, 1 pt had slight hypoesthesia of the thumb (subsided 3 months post treatment)	3 months
Slappendel et al., 1997	61 pts. 32 pts had RFA at 67 °C, 29 pts were a control with RFA at 40 °C. Cervicobrachialgia	CRF	Significant reduction in VAS score in both groups. 3 pts in the 67 °C group had an increase in pain (VAS > 3 points), none in the 40 °C group	Treatment group: 6 pts had neuritis after 6 weeks. Control: 5 pts had neuritis after 6 weeks and 2 pts had minimal loss of muscle strength	3 months
Van Kleef et al., 1999	31 pts. 15 had RFA of DRG at L3, L4, and L5. 16 had same procedure but no current. Chronic low back pain	CRF	Significantly more successful pts in the RFA treated group at 8 weeks, 3, 6, and 12 months	None	12 months

**Table 2** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Geurts et al., 2003	83 pts. 45 pts had RFA at 67 °C, 36 pts had treatment with local anesthetic. Chronic lumbosacral radicular pain	CRF	No difference between the two groups. Lumbosacral RFA of DRG was not effective	Treatment related pain (> 60% of pts), change in sensitivity (15–20%) and a discrete loss of motor function (7–15%) was evenly distributed between both groups	3 months
Haspelslagh et al., 2006	30 pts. 15 pts had RFA at 67 °C treatment, 15 pts had steroid and anesthetic injections. Cervicogenic headache	CRF	No significant difference in VAS between groups. No difference in number of headache days, headache intensity and mean health scores between the groups	None	3 months
Van Zundert et al., 2007	23 pts. 11 pts RFA, 12 pts had sham RFA intervention. Chronic cervicobrachial pain	PRF	Statistically significant improvement in treated pts vs. sham pts of global perceived effect (82% vs. 33%) and VAS (82% vs. 25%). No significant reduction in pain medication intake	None	3 months
Lin et al., 2010	100 pts. 29 had PRF on DRG. 36 received electroacupuncture therapy. 35 received control. Chronic low back pain	PRF	RFA treatment group had significant improvement compared to electroacupuncture therapy at 1 month	None	1 month
Cohen et al., 2010	84 pts. All pts had conventional RFA on L5 dorsal rami. Low back pain	CRF	54 pts had pain relief at 1 month. 36 pts had pain relief at 3 months	1 month after denervation 2 pts experienced significant worsening of back pain. 1 pt had new radiating pain in their leg. All symptoms were resolved by 3 months	3 months

**Table 2** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Lakemeier et al., 2013	56 pts. 27 had RFA of dorsal ramus. 29 had steroid injection. Chronic low back pain	CRF	No significant differences between the groups. Both had pain relief	None	6 months
Shanthanna et al., 2014	31 pts. 16 had RFA; 15 pts had sham RFA intervention. Chronic lumbar radicular pain	PRF	No significant differences in VAS pain reduction between the groups	2 pts had mild headache and back pain for 1 day	3 months
Hashemi et al., 2014	80 pts. 40 pts had PRF on dorsal ramus. 40 had triamcinolone and bupivacaine. Low back pain due to degenerative spondylolisthesis	PRF	Significantly lower ODI and NRS scores in PRF treated group	None	12 months
Koh et al., 2015	62 pts. 31 pts had RFA; 31 pts had sham RFA intervention. Chronic lumbosacral radicular pain	PRF	Treated group had significantly higher success in pain reduction vs. sham (at 2 months: 48.4% vs. 19.4%; at 3 months: 38.7% vs. 9.7%). No significant differences in secondary outcome variables (NRS, ODI, MQS scores)	6 pts in treatment group and 4 pts control group had transient pain aggravation at 2–3 days post procedure; temporary pain during needle insertion and paresthesia during sensory stimulation in several treated patients	3 months
Holanda et al., 2016	28 pts. 11 pts had RFA; 7 pts had lidocaine injection; 10 pts had laser irradiation. Chronic low back pain	PRF	Laser and lidocaine groups had 100% pain reduction, pulsed RF had a 62.5% pain reduction (measured on VAS)	None	1 month
Arsanious et al., 2016	55 pts. 26 had thermal radiofrequency neurotomy. 29 pulsed RFA and thermal radiofrequency neurotomy. Lumbar facet joint pain	PRF	Statistically significantly lower pain reported by pts with combination treatment at 1 day post procedure	Pain associated with the procedure up to 2 days	48 h

**Table 2** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Van Tilburg et al., 2016	60 pts. 30 pts had RFA of the medial branch of the dorsal ramus. 30 pts had sham RFA intervention. Lumbar facet joint pain	CRF	No statistically significant differences were reported	None	3 months
Halim et al., 2017	34 pts. 17 pts had RFA; 17 pts had percutaneous nucleoplasty. Contained cervical disk herniation	PRF	Significant pain improvement in both groups	3 pts in RFA group had mild transient headaches and muscle stiffness 3 pts in percutaneous nucleoplasty group had mild difficulties swallowing	3 months
Huang et al., 2018	116 pts. 58 pts had CT-guided RFA and gabapentin; 58 pts had gabapentin Post-herpetic neuralgia—neck and thoracic area	PRF	Significantly lower VAS, enhanced T cell immunity and inhibited inflammatory response in RFA group vs. control	None	6 months
Lee et al., 2018	60 pts. 30 pts had DRG block before RFA treatment; 30 pts had RFA without DRG block. Chronic low back pain	PRF	Successful outcome on pain index score, pain medication reduction, or pt satisfaction in both groups	None	6 months
Ding et al., 2019	150 pts. 50 pts with acute stage disease, 50 pts with subacute stage disease and 50 pts with chronic stage disease had CT-guided RFA. Herpes zoster neuralgia—thoracic area innervation	PRF	Significant reduction in VAS scores in all groups. Patients with acute stage disease had the largest VAS decrease and decrease in anti-epileptic medication followed by subacute and chronic disease stage pts	2 cases of pneumothorax complications were observed; no infection or apparent dyspnea	12 months



**Table 2** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Reyad et al., 2019	78 pts. 40 pts had RFA at 80 °C under CT fluoroscopy guidance; 38 pts had RFA under fluoroscopy guidance only. Thoracic refractory pain—chest malignancies	CRF	Significantly reduced VAS scores in both groups relative to baseline and were lower in CT-guided RFA vs. fluoroscopy guidance group	Back pain, soreness, hematoma, neuritis, anesthesia dolorosa and sensory deficits were observed in both groups; per-patient adverse events occurrence was significantly lower in the CT-guided group	3 months
De et al., 2019	50 pts. 25 had pulsed RFA. 25 had local anesthetic. Lumbar radicular pain	PRF	Significant reduction in VAS scores for pulsed RFA group compared to local anesthetic	None	6 months
Moore et al., 2020	10 pts. 5 pts had RFA; 5 pts had sham. Chronic radicular neuropathic pain—cervical and lumbosacral	PRF	Significant reduction in NRS pain score at 3 months, reduced TNF $\alpha$ concentration and CD3 <sup>+</sup> count in CSF in RFA group vs. sham	None	6 months
Vigneri et al., 2020	41 pts. 21 pts had RFA and epidural adhesiolysis; 20 pts had sham stimulation followed by epidural adhesiolysis. Chronic lumbosacral neuropathic pain	PRF	Significant NRS score reduction in RFA group at 1 and 6 months post treatment; 1 month post treatment RFA pts had a > 50% pain reduction compared to 25% of epidural adhesiolysis pts; 6 months post treatment pulsed-RF pts had a 48% pain reduction compared to 10% of epidural adhesiolysis pts	None	6 months

**Table 2** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Moussa et al., 2020	150 pts. 50 pts had RFA of DRG; 50 pts had RFA denervation of medial dorsal branch; 50 pts did not receive treatment; all 150 pts received local anesthetic and steroid injection. Lumbar facet syndrome	PRF	3 months post treatment VAS significantly improved in all groups, most notably in RFA group. 1 year post treatment the control group lost improvement. 2 years post treatment RFA of DRG maintained significant improvement vs. medical branch denervation group	None	3 years
Hetta et al., 2020	64 pts. 32 pts had RFA on thoracic DRG; 32 pts had RFA on thoracic PVN. Chronic postmastectomy pain	PRF	Significantly higher number of pts who had > 50% reduction in VAS received pulsed RFA on DRG at 4 and 6 months. Significantly higher pt satisfaction at 3 and 6 months post treatment with RFA on DRG	None	6 months

were for patients with cervical pain syndromes [18–20]. In one RCT that implemented pulsed RFA in 11 patients with chronic cervicobrachial pain, no treatment-associated complications were observed [18]. In a smaller RCT study, five patients treated with pulsed RFA for the reduction of radicular pain in cervical and lumbar dermatomes also did not report complications or adverse events during the extended follow-up period [19]. Another RCT study in 34 patients with cervical disk herniation was associated with mild and transient headache as well as muscle stiffness in some patients post procedure [20].

There were also nine RCTs of pulsed RFA lesions to DREZC components in patients with

chronic lumbar or lumbosacral pain [21–29]. One RCT that evaluated pulsed RFA and electroacupuncture on low back pain did not report any associated complications over 1 month after therapy in 100 patients [21]. Another RCT including 30 patients with chronic lumbar radicular pain treated with pulsed RFA found no serious short-term and long-term side effects, but did note two of 16 patients treated with RFA complained of minor headache and a transient increase in back pain which did not last beyond 1 day [22]. In an RCT study that used three cycles of pulsed RFA of the lumbar DREZC in 31 patients with chronic lumbosacral pain, several patients reported temporary pain during needle insertion and paresthesia during sensory

**Table 3** Retrospective studies: complications following conventional or pulsed RFA of the dorsal root entry zone complex (DREZC)

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Van Wijk et al., 2001	279 patients had RFA. Chronic spinal pain radiating to the leg	PRF	59% experienced greater than 50% pain relief, at 2 months; 58% continued to have pain relief for a variable period of 2–70 months	None	70 months
Van Zundert et al., 2003	18 pts. Pulsed RFA performed at C2 on 4 pts, at C3 on 2 pts, C4 on 2 pts, C5 on 4 pts, C6 on 3 pts, and C7 on 3 pts. Chronic cervical pain	PRF	72% and 33% of pts had successful pain reduction 8 weeks and 1 year post treatment, respectively	None	Up to 2.5 years
Teixeira et al., 2005	13 pts. All received pulsed RF to DRG of affected segmental nerve or segmental nerve at S1 foramen. Acute lumbar radicular pain	PRF	NRS score significantly decreased by 7.83 to 2.25 in the first 2 weeks with a final score of 0.27 after 15.8 months	None	Up to 23 months

**Table 3** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Cohen et al., 2006	49 pts. 13 pts RFA of DRG; 15 pts had RFA of intercostal nerves; 21 pts had pharmacotherapy. Chronic postsurgical thoracic pain	PRF	No statistical difference between groups at 6 weeks follow-up. Statistical difference between groups at 3 months follow-up. RFA DRG (53.8% success rate) was significantly greater than pulsed RF intercostal nerves (6.7%)	RFA DRG: 1 pt had pneumothorax (treated with observation) RFA intercostal nerve: 1 pt had pneumothorax (hospitalized) Pharmacotherapy: 7 pts. 2 treated with gabapentin (sedation). 1 treated with gabapentin (tremors). 2 treated with nortriptyline (sedation), 1 treated with nortriptyline (dizziness and urinary retention). 1 treated with desipramine (persistent nightmares)	3 months
Chao et al., 2008	154 pts. 49 pts with cervical had RFA. 116 pts with lumbar pain RFA. Cervical and lumbar radicular pain	PRF	53.06% of pts in the cervical group and 50.86% of pts in the lumbar group had an improvement of > 50% in pain 1 week post treatment. 55.10% of pts in the cervical group and 44.83% of pts in the lumbar group had an improvement of > 50% in pain 3 months post treatment	None	Up to 1 year

**Table 3** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Van Boxem et al., 2011	60 pts. All pts RFA. Lumbosacral radicular syndrome	PRF	2 months: 18/60 pts with > 50% pain relief; 6 months: 14/60 pts with significant pain reduction; 1 year: 8/60 pts with significant pain reduction  Need for medication was significantly more reduced in pts with pain relief	None	12 months
Nagda et al., 2011	50 pts. All received conventional/pulsed RFA. Lumbar radicular pain	CRF/PRF	All pts had > 50% pain relief	1 pt had transient thigh numbness following a second treatment	Several years
Kim et al., 2017	42 pts. 20 pts had RFA; 22 pts had continuous epidural block. Herpes zoster–post acute pain	PRF	NRS levels were significantly lower in the RFA group at 1, 3, and 6 months; 1 month: RFA group had a significant decrease in analgesic dose compared to pre-procedure; Anticonvulsant dose was significantly lower in RFA at 4, 5, and 6 months	1/20 pts had pain at the procedure site 8/22 pts in the continuous epidural group had evidence of mild complications (headache, catheter insertion site pain, dizziness, constipation, motor weakness, dysuria)	6 months

**Table 3** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Albayrak et al., 2017	39 pts. 17 had transcutaneous electrical nerve simulation and exercise treatment; 22 pts had transcutaneous electrical nerve simulation exercise treatment, and RFA DRG. Persistent pain after total knee arthroplasty	PRF	Significant reduction in DN4 score at 15 days and 1 month for RFA group  Significant reduction in WOMAC and patient satisfaction in transcutaneous electrical stimulation group	None	Up to 1 year
Kim et al., 2017	58 pts. 29 pts had RFA for acute herpes zoster; 29 pts had RFA for post-herpetic neuralgia. Acute herpes zoster and post-herpetic neuralgia	PRF	Pain intensity was decreased in all pts. Pts with acute herpes zoster had significantly lower NRS, significantly lower Pregabalin and oral morphine use. Statistically significant success rate in acute vs. post-herpetic neuralgia group (82.7% vs. 17.2%)	None	3 months
Kim et al., 2018	60 pts. All underwent RFA. Post treatment: group 1 (good analgesia, 28); group 2 (poor analgesia, 32). Chronic lumbosacral radicular pain	PRF	Significantly more pts in group 1 with comorbid musculoskeletal pain (10 vs. 2)  20 pts in group 1 had statistically sig. positive response to prior ESIs compared to 14 in group 2	None	6 weeks
O’Gara et al., 2020	59 pts. All received cervical DRG RFA. Chronic cervical radicular pain	PRF	40 pts had a > 50% reduction in pain; 7 pts had a complete reduction in pain	1 pt had temporary flare-up post treatment, resolved within 2 weeks	12 months

**Table 3** continued

First author, year	Patients, indication	Treatment	Efficacy	Side effects	Follow-up
Li et al., 2019	139 pts. 87 pts had RFA and ESI; 52 pts had ESI only. Cervicogenic headache	PRF	Significant reduction in pain for both groups  RFA + ESI group had significantly lower VAS score, pain medication intake, panic attack frequency, higher ability to work, higher social function, physical function, emotional function, cognitive function, and global health score	None	2 years
Park et al., 2019	82 pts. All received electromyography/nerve conduction prior to RFA (group 1, 2, 3). Intractable lumbosacral radicular pain	PRF	Group 1: normal findings, 28 pts; group 2: radiculopathy, 31 pts; group 3: neuropathy, 23 pts, had significantly lower pain relief than groups 1 and 2 with RFA  Post-treatment pain scores were significantly lower across all groups	None	12 months
Lee et al., 2020	114 pts. 45 pts had C2 DRG RFA; 66 pts had C2 DRG block. Cervicogenic headache	PRF	40% of C2 DRG RFA pts had > 50% pain relief 6 months post treatment	None	6 months
Shabat et al., 2006	28 pts. All had RFA. Neuropathic spinal pain	PRF	4 weeks: 24/28 pts had significant pain relief; 3 months: 23/28 pts had significant pain relief; 1 year: 19/28 pts had significant pain relief	6 pts experienced mild discomfort in the treated area, resolved 3 weeks post treatment	12 months

**Table 4** Prospective studies: complications following conventional or pulsed RFA of the dorsal root entry zone complex (DREZC)

First author, year	Patients	Treatment	Efficacy	Side effects	Follow-up
Van Kleef et al., 1993	20 pts had RFA DRG at C4, C5, or C6. Cervical pain syndrome	CRF	75% of pts responded to treatment and had pain relief. 33% of pts had a recurrence of pain	12 pts had burning pain at 3 weeks, resolved by 6 weeks 7 pts had hyposensitivity in dermatome at 3 weeks, resolved by 6 weeks except in 1 pt which resolved after 6 months	9 months
Stolker et al., 1993	40 pts. All had CRF of dorsal ramus. Chronic thoracic spinal pain	CRF	19 pts were pain free, 14 pts had > 50% pain relief, 7 pts had no pain relief at 2 months	5 pts had postoperative pain	18–54 months
Van Suijlekom et al., 1998	15 pts. All had CRF of the dorsal ramus at C3 to C6. Cervicogenic headache	CRF	Significant reduction in headaches per week in 12 pts	1 pt had burning pain in the neck after the lesion which resolved after 2 weeks	14 months
Samwel et al., 2000	54 pts. All RFA of DRG. Cervicobrachialgia	CRF	Significant reduction in VAS scores. Significant correlation between psychological dysfunction and pain reduction	None	3 months
Pevsner et al., 2003	122 pts. All had RFA of dorsal ramus. 98 had thoracolumbar region pain. 24 had cervical spine pain	CRF	77 pts had improvement in pain	No major complications 27 pts developed discomfort at the site of operation, resolved spontaneously by 1 month	12 months



**Table 4** continued

First author, year	Patients	Treatment	Efficacy	Side effects	Follow-up
Simopoulos et al., 2008	76 pts. 37 pts had RFA. 39 pts received PRF and CRF. Chronic lumbar radicular pain	PRF/CRF	No significant difference between the groups. 70% of pts treated with PRF and 82% of pts treated with PRF + CRF had a successful pain reduction	None	8 months
Kim et al., 2008	49 pts. All had 3 cycles of RFA. Post-herpetic neuralgia	PRF	Significant reduction in VAS score at 1, 2, and 3 months	None	3 months
Tsou et al., 2010	127 pts. 78 pts had RFA at L2 for low back pain and 49 pts had RFA at L3–S1 for lower limb pain. Chronic low back pain with or without lower limb pain	PRF	37/78 pts and 34/74 had > 50% pain improvement at 3 months and 1 year, respectively 27/49 and 20/45 had > 50% pain improvement at 3 months and 1 year, respectively	None	3 years
Vles et al., 2010	17 pts. All had RFA. Hip flexor/adductor spasms and pain for cerebral palsy	CRF	Significant improvement in pain, ease of care, and spasticity	2 pts had a temporary pain increase post procedure; treated by gabapentin	6 months
Choi et al., 2011	15 pts. All had RFA. Cervical radicular pain	PRF	Significant reduction in VAS score. Significant reduction in NDI score at 3 months. 11/15 pts had pain relief of > 50% at 3 months	None	3 months

**Table 4** continued

First author, year	Patients	Treatment	Efficacy	Side effects	Follow-up
Shabat et al., 2013	58 pts. All had RFA at dorsal ramus. Low back pain	CRF	43 pts had had significant pain relief at 1 month, 38 pts at 3 months	11 pts developed discomfort at the site of operation that spontaneously resolved at 1 month	12 months
Van Boxem et al., 2015	65 pts. All RFA at L5 or S1. Chronic intractable lumbosacral radicular pain	PRF	Pain relief (> 50%) was achieved in 56.9% at 6 weeks, 52.3% at 3 months and 55.4% at 6 months	None	6 months
Xie et al., 2016	27 pts. All CT-guided RFA. Refractory pain induced by rib metastasis of lung cancer	CRF	3 days post treatment: NRS scores significantly decreased in all pts; 1 month post treatment: NRS scores significantly decreased in 25 pts; 3 months post treatment: NRS scores significantly decreased in 21 pts	3 days post procedure: 15 pts had chest wall numbness 1 month post procedure: 12 pts had chest wall numbness 3 months post procedure: 12 pts had chest wall numbness	3 months
Das et al., 2018	10 pts. All had 2 cycles of RFA. Chronic lumbosacral radicular pain	PRF	9/10 pts had significant pain relief	None	3 months
Abdurrahman et al., 2018	118 pts. 75 had pulsed RFA at the dorsal ramus. 43 had conventional RFA. Lumbar facet joint pain	PRF or CRF	The number of procedural repetitions was higher in those with pulsed RFA	2 pts exposed to pulsed RFA developed neuropathic pain after 3 repetitions 1 pt exposed to 2 repetitions of CRF developed neuropathic pain	24 months

**Table 4** continued

First author, year	Patients	Treatment	Efficacy	Side effects	Follow-up
Yang et al., 2020	20 pts. All had bipolar RFA of cervical DRG. Cervical radicular pain	PRF	Significantly lower NRS scores at 1, 2, and 3 months	None	3 months
Li et al., 2020	20 pts. All ultrasound-guided RFA of the C2. Chronic headache	PRF	Significantly lower VAS score at 1, 3, and 6 months. Significantly lower BPI score	1 pt had transient cervicalgia, resolved after 24 h 3 pts had transient dizziness for 30 min	6 months
Tortora et al., 2021	30 pts. All CT guided RFA. Lumbosacral radicular pain	PRF	Significantly lower VAS score. Significantly lower ODI score. Significantly lower RDQ score	None	1 month
Wan et al., 2016	90 pts. All had bipolar pulsed RF. Post-herpetic neuralgia	PRF	Significantly lower VAS score and SF-36 score at 1, 4, 8, and 12 weeks post procedure	Pain, high blood pressure, and tachycardia. 5 pts had ecchymoma, with rapid recovery	3 months

stimulation as well as pain aggravation at 2–3 days post procedure that resolved spontaneously without any sequelae; however, no serious adverse events were noted [23]. Similarly, pulsed RFA on the dorsal ramus, a component of the DREZC, on 55 patients with lumbar facet joint pain reported transient pain (up to 2 days) post procedure [24]. An RCT with a single treatment of RFA on lumbar DREZC in 11 patients reported no treatment-related side effects [25]. Another RCT study that also used pulsed RFA lesions of the DREZC in the treatment of low back pain in 60 patients had no associated complications [26]. A study in 25 patients with lumbar radicular pain that combined transforaminal epidural bupivacaine injection with three cycles of pulsed RFA did not report complications with either treatment modality [27]. An RCT that tested effectiveness of combining pulsed RFA on lumbosacral

DREZCs with epidural adhesiolysis showed that pulsed RFA application for the neuropathic pain due to lumbosacral radiopathy was not associated with any complications [28]. An RCT study of 150 patients with chronic lumbar facet syndrome treated with pulsed RFA of the DREZC or radiofrequency denervation of the medial dorsal branch also noted no complications arising as a result of either treatment [29].

There was one study that examined RCT of pulsed RFA lesions of thoracic DREZCs for postmastectomy pain syndrome [30]. Analgesic efficacy of pulsed RFA lesions was evaluated on the DREZC and compared to RFA of their corresponding paravertebral somatic nerves. Both RFA treatments had no side effects; nevertheless the authors acknowledged the inherent risk of performing thoracic foraminal interventions and the technical difficulty of targeting thoracic DREZC components [30].

**Table 5** Quasi and controlled clinical studies: complications following conventional or pulsed RFA of the dorsal root entry zone complex (DREZC)

First author, year	Patients	Treatment	Efficacy	Side effects	Follow-up
Trinidad et al., 2015	25 pts. 19 had pulsed RF of DRG. 3 had conventional RF of medical branch. 3 had a combination of pulsed RF and conventional RF. Lumbar radicular pain	PRF/CRF	1 month: all groups had a significant decrease in NRS and ODI scores. 84% of pts reported significant satisfaction with the treatment	Mild pain at the site of puncture for several days post procedure, resolved spontaneously	1 year
Marliana et al., 2020	50 pts. 25 were treated with pulsed RF at DRG. 25 were control (orally administered sodium diclofenac). Chronic lumbar radicular pain	PRF	Significant decrease in VAS score and ODI score in treatment group compared to control at 1, 2, and 4 weeks post procedure	None	4 weeks

The efficacy of pulsed RFA was also tested on herpes zoster neuralgia in two RCT studies [31, 32]. A study in 150 patients with acute, subacute, and chronic herpes zoster neuralgia targeted the DREZC with CT-guided pulsed RFA [31]. Two cases of uncomplicated pneumothorax were observed among 150 patients [31]. The second RCT for the post-herpetic neuralgia in 168 patients of which 58 were exposed to pulsed RFA combined with gabapentin had no associated complications [32].

### Retrospective Studies

There were 15 studies with a retrospective design that used pulsed RFA and one study that evaluated the combination of pulsed and conventional RFA (Table 3) [33–48]. Of the five retrospective studies of pulsed RFA on cervical DREZCs, two studies evaluated the treatment on cervicogenic headache and three studies evaluated the treatment of chronic cervical pain syndromes [33–37]. A case–control study that evaluated 139 patients of which 87 patients had RFA in combination with epidural steroid injection at the C2 level for cervicogenic headache had no complications associated with the RFA intervention [33]. In another retrospective

cervicogenic headache analysis of 45 patients that received RFA lesions to DREZC components of C2, no post-procedure complications were recorded throughout the study [34]. In a retrospective study of 59 patients who underwent RFA therapy for chronic cervical radicular pain, a single patient experienced a pain flare-up post procedure that spontaneously resolved after 2 weeks [35] while a retrospective review of 18 patients who underwent RFA for chronic cervicobrachial pain did not show any adverse events [36]. Likewise, a study of 154 patients treated with pulsed RFA as a result of cervical and lumbar radicular pain did not report any complications [37].

In a retrospective data analysis of 279 patients who received RFA for chronic lumbar radicular pain, the authors did not report complications associated with RFA for lumbar radicular pain in any of the treated patients [38]. Another study in 13 patients with acute lumbar radicular pain who were possible candidates for disk surgery, RFA of the DREZC was not associated with any side effects up to 12 months post treatment [39]. In another study that examined RFA in 60 patients with lumbosacral radicular pain syndrome, no complications were reported [40]. A retrospective

analysis of 50 patients that were exposed to multiple conventional and pulsed RFA treatments showed a single adverse event of transient thigh numbness which resolved after 1 week [41], whereas a study that retrospectively analyzed 60 patients with chronic lumbosacral radicular pain had no complications related to pulsed RFA [42]. In a retrospective study that included 82 patients with intractable lumbosacral radicular pain who had poor clinical outcomes after lumbar spinal surgery and subsequently underwent pulsed RFA of the DREZC, the authors did not report any complications associated with the RFA procedure [43]. In another retrospective study that analyzed 28 patients with neuropathic spinal pain who had pulsed RFA rhizotomy of the DREZC no major complications were noted. However, in this study a small number of patients reported mild discomfort in the treated area that resolved spontaneously within 3 weeks [44]. Twenty-two patients with persistent postsurgical pain after knee arthroplasty who received pulsed RFA of the L4 DREZC in combination with transcutaneous electrical nerve stimulation reported no associated complications [45].

In a retrospective study that evaluated 49 patients with chronic postsurgical thoracic pain, 15 patients who received pulsed RFA on the intercostal nerves and 13 patients who had of DREZC RFA were compared with 21 patients who were treated pharmacologically [46]. One patient had an adverse event of a small pneumothorax that was detected during a routine scan after pulsed RFA of the DREZC [46]. The pneumothorax was found to not be related to the procedure and was treated conventionally. The second case of pneumothorax required hospitalization and was reported in a patient that was treated with RFA on the intercostal nerves [46].

There were two retrospective studies of pulsed RFA of the DREZC for the management of acute and post-herpetic herpes zoster neuralgia [47, 48]. The first study examined 42 patients, 22 that received continuous epidural block and 20 who were treated with pulsed RFA of the DREZC [47]. Only one patient in the pulsed RFA treatment group had pain at the site of the procedure [47]. The second study

evaluated 58 patients who were treated with pulsed RFA of the DREZC either at the acute herpes zoster or post-herpetic neuralgia: no complications were reported [48].

### Prospective Studies

There were 18 prospective design studies of which eight studies were conventional RFA, eight were pulsed RFA, and two studies used a combination of pulsed RFA with conventional RFA modalities (Table 4) [49–66].

Four prospective studies applied conventional RFA lesions to cervical DREZCs [49–52]. The first study followed 20 patients for 6 months and 17 patients for 9 months post DREZC lesioning [49]. A total of 12 patients experienced burning pain whereas seven patients had hyposensitivity in the dermatome, both of which resolved within 3 weeks post treatment [49]. Additionally, one patient experienced prolonged hyposensitivity up to 6 months post treatment [49]. The second prospective study that treated cervicogenic headache with conventional RFA on the dorsal ramus reported that one of 15 patients had burning pain post procedure which resolved after 2 weeks [50]. The third study in 54 patients with cervicobrachialgia did not have complications post procedure [51]. The fourth study treated 122 patients with conventional RFA on the dorsal ramus of either in the thoracolumbar region or cervical spine [52]. There were no major complications associated with the procedure; however, 27 patients reported discomfort at the site of operation which resolved spontaneously after 1 month [52].

A conventional RFA study in 17 patients with hip flexor/adductor spasms and pain from cerebral palsy found that two patients had an increase in pain post procedure, which was temporary and treated with gabapentin [53].

Another prospective study that used conventional CT-guided RFA in patients with refractory pain induced by rib metastasis of lung cancer reported that 15 out of 27 patients had chest wall numbness at 3 days post procedure and 12 patients had chest wall numbness both at 1 and 3 months post procedure [54].

Interestingly, a study that reported on 58 elderly patients, aged 80 and older, treated with conventional RFA on the dorsal ramus, a DREZC component, for low back pain did not have any major complications post procedure, but the authors noted that 11 patients developed discomfort at the site of intervention that resolved spontaneously by 1-month follow-up [55]. Another study that also used conventional RFA on the dorsal ramus to treat chronic thoracic spinal pain reported transient postoperative pain in five of the 40 patients [56].

In a study that treated 76 patients for chronic lumbar radicular pain, 37 of which had pulsed RFA and 39 who had pulsed RFA and conventional RFA, no neurological deficits were observed in either treatment group [57]. In a study that treated 118 patients with lumbar facet joint pain, of which 75 patients had pulsed RFA and 43 patients had conventional RFA on the DREZC [58], the authors reported that two patients treated with pulsed RFA developed neuropathic pain after three repetitions while one patient treated with conventional RFA developed neuropathic pain after two repetitions [58].

Of the eight pulsed RFA manuscripts, one pertained to chronic headache, two pertained to cervical radicular pain, four pertained to lumbosacral radicular pain, and one pertained to post-herpetic neuralgia [59–66]. In 20 patients suffering from chronic headaches treatment with ultrasound-guided pulsed RFA was not associated with any major complications, but the authors reported that one patient had transient cervicgia which resolved within 24 h and three cases of transient dizziness [59]. In another study cervical DREZC RFA, none of the 15 patients exposed to RFA experienced any side effects following treatment [60]. Similarly, treatment with bipolar pulsed RFA for cervical radicular pain was not related to any complications in 20 treated patients [61].

A total of four prospective studies evaluated pulsed RFA intervention in 232 cumulative patients for the treatment of chronic lumbar and lumbosacral radicular pain [62–65]. Pulsed RFA DREZC lesions were performed from L2 to S1 levels and there were no complications reported in any of the four manuscripts [62–65].

Similarly, in a prospective study that evaluated three cycles of pulsed RFA in 49 patients for the treatment of post-herpetic neuralgia, the authors did not report any associated complications [66]. Another prospective study involving 90 patients with post-herpetic neuralgia who were treated with high voltage, long duration, bipolar pulsed RFA, the side effects included high blood pressure, pain, and tachycardia [67]. Notable bruising was present in five patients post treatment that spontaneously recovered during the follow-up period [67].

### Quasi and Controlled Clinical Studies

There were two quasi studies and one controlled clinical study (Table 5) [68, 69]. Both quasi studies focused on lumbar radicular pain, one of which combined pulsed RFA and conventional RFA, whereas the second study only used pulsed RFA as the treatment modality. The first quasi study treated 25 patients with pulsed RFA, conventional RFA, or a combination of pulsed RFA and conventional RFA [68]. No major complications were reported; however, a few patients experienced mild pain at the site of puncture post procedure, which spontaneously resolved after several days [68]. In the second study 25 patients were exposed to pulsed RFA and had no reported complications [69].

## DISCUSSION

Given the significance of the DREZC components in the development and propagation of chronic pain, RFA modalities have been recognized as a clinically important approach for interventional pain management. RFA lesioning of the DREZC components is a minimally invasive procedure with the potential to afford more permanent and complete denervation. Of the 62 selected manuscripts totaling 3157 patients, there were zero serious adverse events or persistent neurological deficits reported. A total of 36 (1.14%) transient neurological deficits, cases of transient neuritis, or non-minor adverse events like uncomplicated pneumothorax were reported. A total of 113 (3.58%)



minor adverse events were reported (bruising, transient site soreness, headache).

Initial clinical investigations have shown that conventional RFA could be used safely with low incidence of post-procedural neuropathic pain. In recent years, pulsed RFA treatment administered to DREZC has generated compelling evidence of its efficacy in clinical practice for a variety of pain syndromes (Tables 2, 3, 4, and 5). Although conventional and pulsed RFA on DREZC are deemed distinct, both techniques were applied to treat similar pain syndromes including cervicogenic headaches, cervical radicular pain, discogenic pain, lumbar radicular pain, and pain associated with the sacroiliac joint [4, 7, 8, 11, 12, 19, 20, 22, 23, 27, 28, 33–35, 37, 39–43, 50, 57, 59–64, 67, 68]. Further, RFA treatment strategy has been shown to be beneficial in treating disease states such as acute and post-herpetic neuralgia and refractory pains post cancer surgery [13, 30–32, 47, 54].

RFA is a minimally invasive treatment option with good results for a variety of pain states and, herein, we have demonstrated that it has an excellent safety profile. Of the few adverse events, most reported only minor procedure site-related adverse events, like soreness or bruising. There were, however, two cases of pneumothorax reported among 150 patients treated for herpes zoster neuralgia [31], but these were considered uncomplicated and not hemodynamically compromising.

Notably, it is important to note that the studies selected for analysis were not designed with the primary outcome of safety and, thus, were not powered to detect complications of RFA lesions of the DREZC. Nonetheless, collectively, among the 3157 patients in the 62 analyzed manuscripts, no serious adverse events manifested.

## CONCLUSION

This systematic review indicates that RFA lesions of the DREZC for interventional pain management are quite safe. There were no serious adverse effects with a sizable sample of RCT, prospective observational, and retrospective studies.

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