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Radiofrequency Applications to Dorsal Root Ganglia

A Literature Review

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Application of radiofrequency currents to the dorsal root ganglia, in the treatment of various pain syndromes, has been clinically practiced for more than 30 yr. The clinical efficacy and the safety of this technique, however, remain poorly understood. The authors reviewed the literature on this modality of pain relief to determine its clinical efficacy, safety, and mechanisms of action. The two modalities in common clinical use were pulsed and continuous mode radiofrequency. These techniques were generally found to be safe, and the majority of the observational studies reported their clinical efficacy. Five randomized controlled trials evaluated their clinical use; these trials were relatively short-termed and small in size, and their results were variable. The mechanism of action of these techniques was unclear. Larger controlled clinical trials evaluating the long-term effects of these techniques and basic science research to determine their precise mode of action are needed.

APPLICATION of radiofrequency currents of various modalities to the dorsal root ganglia (RF-DRG), in the treatment of various painful conditions, has been practiced for more than 30 yr. Of the three previous review articles[1–3] related to this topic, two[1,2] provided an overall review of all the radiofrequency procedures used in the treatment of spinal pain, and the reviews were limited to two randomized controlled trials (RCTs).[4,5] The third article primarily discussed the role of dorsal root ganglia (DRG) in the causation of cervical radicular symptoms.[3] The aim of this article is to comprehensively review the available literature on RF-DRG in the treatment of pain, to determine the evolution of this technique, its mode of action, its efficacy, and its safety.

Materials and Methods

The MEDLINE, EMBASE, and Cochrane databases were searched for key words *radiofrequency and dorsal root ganglion*, *DRG and radiofrequency*, *RF-DRG*, *pulsed radiofrequency and dorsal root ganglion*, *DRG and pulsed radiofrequency*, and *PRF-DRG*; this search yielded 49 articles. To limit the review to peer-reviewed literature, conference proceedings and abstracts were not sought. Studies that involved application of radiofrequency currents, of any modality, to the spinal nerve roots or DRG, in the treatment of pain, were included in the review. Editorials, letters, and any duplicate articles were not included. Twenty-six of the retrieved articles met the above criteria and were further reviewed. An additional 6 pertinent articles were identified after the review of 26 initially identified articles. To understand the evolution of this technique, elucidate its mechanisms of action, and tabulate the adverse effects, all the identified clinical and laboratory studies were reviewed.[1–32] A meta-analysis of the clinical data obtained was not possible because of the small number of RCTs on diverse clinical conditions that studied heterogeneous patient populations. The best evidence synthesis method[33] was therefore used to assess the outcomes of the literature reviewed.

The best evidence synthesis method seeks to provide the best available evidence on the topic at hand, disregarding the lesser-quality evidence in favor of the better-quality one. This method of research review is especially suited when pooling across the published studies is not possible because of a small number of trials reporting on a large number of study categories. The standards for the evidence and the study selection criteria are predetermined and are objective, consistent, and germane to the topic being reviewed. After the study selection criteria are established, the study inclusion techniques are exhaustively inclusive, similar to a meta-analysis. Unlike a meta-analysis, however, detailed descriptions of the best evidence on the topic are provided, to give readers the opportunity to verify the original literature and formulate their own independent conclusions.

In determining the best evidence for the efficacy of RF-DRG, we considered the randomized controlled data as the best evidence available, and these studies were therefore further critically analyzed. The internal validity of the RCTs identified was based on the validated criteria in pain research proposed by Jadad *et al.*[34] The four levels of best evidence (table 1) used in this review, and

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Table 1. Qualitative Analysis

Level of Evidence	Best Scientific Evidence
A	Strong evidence: consistent findings in multiple relevant high-quality RCTs
B	Moderate evidence: consistent findings in one relevant high-quality RCT plus one or more relevant low-quality RCTs
C	Limited evidence: consistent findings in one relevant high-quality RCT or more than one relevant low-quality RCT
D	Inconclusive evidence: one relevant low-quality RCT, no relevant RCTs, or RCTs with inconsistent or inconclusive outcomes

The rating system is based on the published methods used by Niemisto *et al.*[2]
RCT = randomized controlled trial.

the 5-point Jadad scale used for qualitative study analysis (table 2), were similar to the ones used in the previous related reviews.[1,2] Identification of an item on the Jadad scale in a trial rendered it a positive score, whereas its absence was marked as zero; a trial scoring 3 or more points was graded as a high-quality trial, whereas a trial scoring 2 or fewer points was regarded as a low-quality trial.[1]

Results

Of the 32 articles reviewed (fig. 1), there were 3 review articles,[1–3] 24 clinical studies[4–26] (one publication[9] had 2 clinical studies), and 6 laboratory studies.[27–32] Fifteen clinical studies were of conventional or continuous mode radiofrequency application to the DRG (continuous RF-DRG),[4–7,9–15,18,19,23,24] and 9 were of pulsed mode RF-DRG.[8,9,16,17,20–22,25,26] There were 5 RCTs,[4–8] 4 of continuous RF-DRG[4–7] and 1 of pulsed RF-DRG.[8] Three RCT pertained to cervicobrachial pain,[4,5,8] 1 pertained to cervicogenic headache,[6] and 1 pertained to lumbosacral radicular pain.[7] There was 1 nonrandomized controlled trial of both pulsed and continuous RF-DRG use.[9] There were 9 uncontrolled studies of prospective design,[9–17] of which 6 were of continuous RF-DRG[10–15] and 3 were of pulsed RF-DRG[9,16,17] use. Of the 5 retrospective studies encountered,[18–22] 2 used continuous RF-DRG[18,19] and 3 used pulsed RF-DRG.[20–22] There were 4 case reports or case series, 2 each of continuous[23,24] and pulsed RF-DRG.[25,26] Two of the studies[5,26] had duplicate articles that were not included in this review.

Table 2. Criteria for Assessment of the Randomized Controlled Trials

Item	Methodologic Criteria*
A	Study was described as randomized
B	Methodology for appropriate random allocation was described
C	Study was described as double-blinded
D	Successful double-blinding was described
E	Withdrawals or dropouts were accounted for

The rating system is based on the published methods used by Geurts *et al.*[1]
* Presence of each item renders a + score.

Prospective Controlled Clinical Trials

Of the 6 prospective controlled trials (table 3), 2 were RCTs of continuous RF-DRG in the treatment of cervicobrachial pain. The trial by Van Kleef *et al.*[4] included 20 patients with cervical radicular symptoms; 9 patients received the continuous RF-DRG, whereas 11 received the sham treatment: the electrode was placed in a manner identical to that used in the treatment group, but no radiofrequency current was applied. Patients were evaluated before and at 8 weeks after the treatment, using greater than 2-point reduction of pain on the visual analog scale (VAS) as the criterion for success. The mean VAS scores decreased from 6.4 to 3.3 in the treatment group and increased from 5.9 to 6.0 in the sham treatment group. Eight patients (88.8%) in the treatment group and 2 patients (18.1%) in the sham group were reported to have successful results, which were statistically significant ($P = 0.0027$, Fisher exact test). The treatment group also showed greater improvement on the Multidimensional Pain Inventory and McGill Pain Questionnaires, with respective changes of 1.7 and 11.2 in the treatment group compared with 0.1 and 0.4 in the control group. The authors concluded that continuous RF-DRG provided significant short-term pain relief in patients with cervicobrachial pain. This was a relatively small study of only 20 patients. Although this trial was randomized and double-blinded, the randomization techniques were not adequately described. The trial also lacked the description of any analgesic drugs used, and only short-term results at 8 weeks were reported.

Slappendel *et al.*[5] published the second RCT of continuous RF-DRG in patients with cervicobrachial pain. It included 61 patients; 32 patients received continuous RF-DRG with the electrode tip heated to 67°C (group 1), and 29 received continuous RF-DRG with electrode tip temperature of 40°C (group 2). The patients were evaluated with VAS scores, and subjectively in terms of "better," "equal," or "worse" pain. In group 1, the mean VAS scores decreased from 6.7 to 4.8 at 6 weeks and increased to 5.0 at 3 months; in group 2, the mean VAS scores decreased from 6.3 to 4.9 at 6 weeks and to 4.4 at 3 months. Clinically significant pain relief (> 2-point reduction in VAS scores) was reported in 15 patients in each of the groups at 3 months— 47% and 51% of the patients in groups 1 and 2, respectively. No statistically

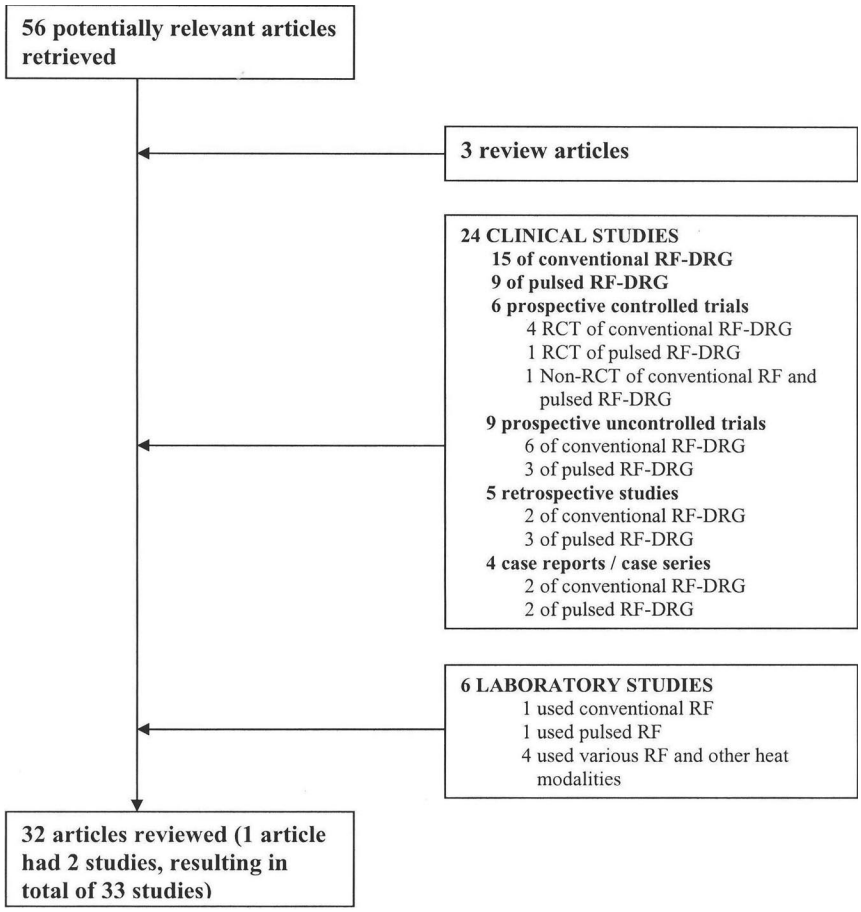

Fig. 1. Flowchart of the publications analyzed in this review. RCT = randomized controlled trial; RF = radiofrequency; RF-DRG = radiofrequency of dorsal root ganglia.

significant difference in the reduced pain scores was found between the two groups. This was a multicenter trial, and 63 patients were included after screening 314 patients, with dropout rate of only 2 patients at 3 months; it was randomized and double-blinded. However, the criteria for a successful outcome were not defined, and only short-term results at 3 months were reported. This trial lacked a placebo control group, and the results of the two treatment groups were compared only to historic controls, the placebo control group in the trial by Van Kleef *et al.*[4] and the diagnostic nerve root blocks.

Haspeslagh *et al.*[6] published an RCT of continuous RF-DRG in the treatment of cervicogenic headache; 30 patients with severe chronic cervicogenic headache were randomized to two equal groups, a radiofrequency group (group 1) and a local nerve injection group (group 2). The patients in group 1 received radiofrequency lesioning of the facet joints (C3–C6), and at 8 weeks, the patients with continued pain that responded positively to a series of diagnostic nerve root blocks received continuous RF-DRG at the affected level. The patients with continued pain at 8 weeks in this group who did not respond to the diagnostic nerve root blocks received transcutaneous electrical nerve stimulation therapy. The patients in group 2 received local anesthetic and steroid injection of the greater occipital nerve; this was repeated at 8 weeks in the unresponsive patients. At 16 weeks, the nonresponsive patients in both groups received transcutaneous electrical nerve stimulation therapy. The primary outcome measures used were VAS and global perceived effect (GPE), and success was defined as a greater than 2-point reduction on the VAS and/or GPE score of greater than +2. The 8-week, 16-week, and 1-yr success rates for group 1 were 80, 66.7, and 53.3%, respectively, compared with 66.7, 55.3, and 50% for group 2. There was no statistically significant difference in the success rates between the two groups, and the authors concluded that the sequential radiofrequency treatments of facet joints and DRG had similar efficacy to the local nerve injections in the treatment of cervicogenic headaches. Although this trial used multiple outcome measures, kept record of the medications used, and followed up patients for a year, this was a relatively small trial, with only 15 patients in each study group, it had a high dropout rate of almost 33%, and the randomization and double-blinding techniques were not adequately described.

Geurts *et al.*[7] published an RCT of continuous RF-DRG application in patients with chronic lumbar radicular pain. Of the 83 patients included in the trial, 45 received the continuous RF-DRG, and 38 received the sham treat-

Table 3. Prospective Controlled Trials on Radiofrequency of the Dorsal Root Ganglion

Study and Methods	Patients and Treatments	Results and Comments	Authors' Conclusions	Study Limitations
Conventional (continuous) RF of DRG				
Van Kleef *et al.*[4] (1996) P, R, DB, sham controlled	20 pts with CBP; 9 had SL CRF-DRG at 67°C for 60 s and 11 had ST	At 8 wk, 88% of pts in the treatment gp and 18.1% in the ST gp had successful results (> 2-point reduction of pain on the VAS; $P = 0.0027$)	CRF-DRG provided significant short-term pain relief in pts with CBP	A small trial of 20 pts. Randomization was not adequately described. It lacked the description of any analgesic drugs used. Only short-term results at 8 wk were reported
Slappendel *et al.*[5] (1997) P, R, DB	61 pts with CBP; 32 had SL CRF-DRG at 67°C and 29 had CRF-DRG at 40°C, both for 90 s	At 3 mo, > 2-point reduction of VAS scores was reported in 47% of pts with CRF-DRG at 67°C and 51% of pts with CRF-DRG at 40°C	The efficacy of CRF-DRG was similar at 40°C and at 60°C	There was no placebo control gp. Results of the two treatment gps were compared only with a historic control. The criteria for successful outcome were not defined. Only the short-term results at 3 mo were reported. Clinically significant reduction of pain scores at 3 mo was observed in only half of the pts
Haspeslagh *et al.*[6] (2006) P, R, DB	30 pts with CGH. Gp 1: 15 pts had RF of the cervical FJs. At 8 wk, symptomatic pts with +ve DNB had CRF-DRG; pts with −ve DNB had TENS therapy. Gp 2: GON block was done in 15 pts and repeated at 8 wk in symptomatic pts. At 16 wk, symptomatic pts in both gps had TENS therapy	The 8-wk, 16-wk, and 1-yr success rates for the RF gp were 80, 67, and 53%, respectively, compared with 67, 55, and 50% for the nerve block gp	Sequential RF treatments of cervical FJs and DRG were similar in efficacy to the occipital nerve blocks	A small trial of 30 pts. A high dropout rate of 33%. The randomization and blinding techniques were not fully described. There was no placebo control gp. Only 3 of 15 pts in the RF gp had CRF-DRG. The results reported were of the combined efficacy of FJ RF and CRF-DRG
Geurts *et al.*[7] (2003) P, R, DB, sham controlled	83 pts with LRP; 45 had SL CRF-DRG at 67°C for 90 s and 38 had ST	At 3 mo, 16% of pts in the CRF-DRG gp and 25% in the ST gp had successful results ($P = 0.43$)	CRF-DRG for LRP was not an effective treatment	Only short-term results at 3 mo were reported. Pts with neurologic deficits were excluded
Pulsed RF of DRG				
Van Zundert *et al.*[8] (2007) P, R, DB, sham controlled	23 pts with CBP; 11 had SL PRF-DRG and 12 had ST	At 3 mo, 82% of pts in the PRF-DRG gp and 25–33% (using VAS or GPE success criteria, respectively) in the ST gp had successful results ($P = 0.02$–0.03)	PRF-DRG might provide pain relief in pts with CBP	A small trial of 23 pts. No. of pts recruited was short of the intended target (42 pts). Although the trial was extended for 6 mo, significance in favor of PRF was reached only at 3 mo. The two study gps had dissimilar characteristics

(*continued*)

Table 3. Continued

Study and Methods	Patients and Treatments	Results and Comments	Authors' Conclusions	Study Limitations
Sluijter *et al.*[9] (1998) P	60 pts with RP; 36 had PRF-DRG and 24 had CRF-DRG at 42°C for 60 s	At 6 wk, 86% of pts in the PRF-DRG gp and 12% in the CRF-DRG at 42°C gp had > 50% improvement in their GPE scores	PRF-DRG was more efficacious than CRF-DRG at 42°C in the treatment of RP	This trial was not randomized, blinded, or placebo controlled. Only short-term results at 6 wk were reported. The trial compared PRF to a form of thermal RF (CRF at 42°C) not used in routine clinical practice

− ve DNB = less than 50% reduction of visual analog scale (VAS) after the diagnostic nerve block; + ve DNB = greater than 50% reduction of VAS after diagnostic nerve block; CBP = cervicobrachial pain; CGH = cervicogenic headache; CRF = conventional/continuous radiofrequency; CRF-DRG = conventional/continuous radiofrequency of dorsal root ganglia; DB = double-blind; DRG = dorsal root ganglia; FJ = facet joint; GON = greater occipital nerve; gp = group; GPE = global perceived effect patient evaluation; LRP = lumbar radicular pain; P = prospective; PRF = pulsed radiofrequency; PRF-DRG = pulsed radiofrequency of dorsal root ganglia; pt = patient; RF = radiofrequency; R = randomized; RP = radicular pain; SL = single-level; ST = sham treatment; TENS = transcutaneous electrical nerve stimulation.

ment. The outcome measures included VAS, Analgesic Rating Scale, and Short Form-36 quality-of-life questionnaire. The success was defined as either reduction in the VAS scores by 50% or reduction of the combined VAS and Analgesic Rating Scale scores by 25%, and increase of Short Form-36 scores by 25%. At 3 months, the mean VAS leg pain score decreased from 6.1 to 5.4 in the treatment group and from 6.2 to 4.2 in the sham-treated group. Seven patients (16%) in the continuous RF-DRG group and 9 patients (25%) in the sham-treated group were considered to have successful results ($P = 0.43$). The authors concluded that continuous RF-DRG was not an effective treatment for chronic lumbar radicular pain and recommended against its routine use. This was a large multicenter trial, with 1,001 patients screened over a period of 2½ yr. Of the 83 patients included in the trial, only 3 dropped out at 3 months. This trial was placebo controlled, and adequate conduct of randomization and double-blinding was described. Multiple outcome measures evaluating multiple domains, including pain, physical impairment, and analgesic use, were used and were included in the final outcome evaluation. This trial, however, reported short-term results at 3 months and excluded patients with sciatica who had neurologic deficits.

The only RCT of pulsed radiofrequency (PRF) application to the DRG was published by Van Zundert *et al.*[8] It included 23 patients with chronic cervicobrachial pain. Eleven of these patients received pulsed RF-DRG, and 12 received sham treatment. Using GPE and VAS, success was defined as a greater than 2-point reduction in VAS and greater than 50% improvement in GPE scores. At 3 months, 9 patients (82%) in the treatment group and 3–4 patients (25–33%) in the ST group had statistically significant ($P = 0.02–0.03$) successful results; the two values indicate respective successes based on VAS and GPE criteria. Reduction of pain medication use was also noted in the PRF group, but no significance was reached at 3 months. This was a placebo-controlled trial, and the procedures for random allocation and double-blinding were well described. Although this was a multicenter study and 256 patients were originally screened, and only 1 patient dropped out during the study period, only 23 patients were recruited over a period of 2½ yr. The number of patients eventually studied was well short of the intended target of 42 patients, making the study results statistically less powerful. Although the study period was extended for 6 months and multiple outcome measures were used measuring, pain, general well-being, analgesic use, and physical disability, statistical significance in favor of PRF was reached only in pain and overall well being at 3 months. The two study groups also had dissimilar characteristics, and patients in the control group were older (52 *vs.* 42 yr) and had significantly higher pretreatment VAS scores (76.2 *vs.* 55.7). Based on the above weaknesses, the authors could only conclude that PRF of cervical DRG "might" provide pain relief at 3 months in patients with cervicobrachial pain.

The first publication of PRF use was published by Sluijter *et al.*[9] It included a prospective nonrandomized controlled trial that compared pulsed RF-DRG with continuous RF-DRG with maximum electrode temperature of 42°C. Of the 60 patients with radicular pain of unspecified nature included in the trial, 36 received the pulsed RF-DRG, and 24 received the continuous RF-DRG at 42°C. At 6 weeks, 31 patients (86%) in the pulsed RF-DRG group and 3 patients (12%) in the continuous RF-DRG at 42°C group reported greater than 50% improvement in their GPE scores. The authors concluded efficacy of pulsed RF-DRG in comparison with continuous RF-DRG at 42°C at 6 weeks. Although this was a prospective controlled trial, it was not randomized, blinded, or placebo-controlled; only short-term results at 6 weeks were reported; and it compared pulsed RF-DRG with a form of continuous RF-DRG (continuous RF-DRG at 42°C) not used in routine clinical practice.

Table 4. Prospective Uncontrolled Trials on Radiofrequency of the Dorsal Root Ganglion

Study and Methods	Patients and Treatments	Results and Comments	Authors' Conclusions
Conventional (continuous) RF of DRG			
Sluijter and Koetsveld-Baart[10] (1980)	20 pts with CBP had SL CRF-DRG at 75°C for 60 s	At 3 and 9 mo, > 70% pain relief reported in 65% of pts	CRF-DRG provided gratifying results in the treatment of CBP
Sluijter[14] (1981)	60 pts had lumbar and 45 had cervical SL CRF-DRG at 70°C for 60 s	40% of pts had "good" results (Patients' Opinion Score) at 3–21 mo of follow-up	CRF-DRG had worthwhile success rate
Vervest and Stolker[11] (1991)	24 pts with CBP had CRF-DRG at 67°C for 90 s; 41 lesions performed in 24 pts	At 2 mo, 80% of pts had "good" results. At 1.5 yr, similar results in 85% of pts	CRF-DRG was safe and provided long-term relief of CBP
Niv and Chayen[15] (1992)	50 pts with malignant pain had CRF-DRG at 70°C for 90 s at 1–3 lumbar or thoracic levels	At 3- and 12-mo follow-up, 62% and 48% of pts, respectively, were "virtually pain free."	CRF-DRG is very effective in pts with localized pain, with minimal side effects
Van Kleef *et al.*[12] (1993)	20 pts with CBP had SL CRF-DRG at 67°C for 60 s	> 50% pain relief (NRS) in 50% of pts at 3 mo, 30% at 6 mo, and 22% at 9 mo	Good initial relief of CBP by CRF-DRG. Tendency for the pain to recur at 3–9 mo
Stolker *et al.*[13] (1994)	45 pts with TSP had 1- or 2-level CRF-DRG at 67°C for 90 s	> 50% pain relief (using 5-point oral analog scale) in 80% of pts for up to 2 yr	CRF-DRG had long-term efficacy in chronic TSP
Pulsed RF of DRG			
Sluijter *et al.*[9] (1998)	15 FBS pts with LRP had SL PRF-DRG	> 2-point reduction of VAS in 53% of pts at 6 mo and 40% of pts at 1 yr	PRF is safe with wider applicability, warranting RCTs
Pevzner *et al.*[16] (2005)	28 pts with LRP and CBP had PRF-DRG	At 3 mo, 2 pts had "excellent," 12 had "good," and 9 had "fair" pain relief	PRF-DRG was safe and effective for LRP and CBP
Shabat *et al.*[17] (2006)	28 pts with spinal neuropathic pain had PRF-DRG	> 30% reduction of pain (VAS) in 82% of pts at 3 mo and 68% of pts at 1 yr	PRF is a safe and effective in the treatment of spinal neuropathic pain

CBP = cervicobrachial pain; CRF-DRG = conventional radiofrequency lesioning of dorsal root ganglia; DRG = dorsal root ganglia; FBS = failed back surgery; LRP = lumbar radicular pain; NRS = numeric rating scale; PRF = pulsed radiofrequency; PRF-DRG = pulsed radiofrequency lesioning of dorsal root ganglia; pt = patient; RCT = randomized controlled trial; RF = radiofrequency; SL = single-level; TSP = thoracic segmental pain; VAS = visual analog scale.

Prospective Uncontrolled Trials

Of the 6 prospective uncontrolled trials of continuous RF-DRG application (table 4), 4 described its use in one spinal region. In 3 such studies, continuous RF-DRG was used in the treatment of cervicobrachial pain.[10–12] The study by Sluijter and Koetsveld-Baart[10] included 20 patients; 65% of these patients had greater than 70% pain relief at 3 and 9 months of follow-up. Vervest and Stolker[11] reported 24 patients; 80% of them had "excellent" to "good" pain relief at 2 months; these patients were followed up for 1.5 yr, along with a group of patients who received facet radiofrequency, and "excellent" to "good" results were reported for 84.6% of the patients in the group. Van Kleef *et al.*[12] followed up 20 patients for 6 months and 17 patients for 9 months after continuous RF-DRG. Using a numeric rating scale, greater than 50% pain relief was reported in 50% of patients at 3 months, 30% at 6 months, and 22% at 9 months. In a study by Stolker *et al.*,[13] continuous RF-DRG was used in the treatment of thoracic segmental pain. Of the 45 patients studied, 91% obtained greater than 50% pain relief at 2 months on a five-grade oral analog scale; 80% of the patients continued to experience the pain relief for 24 months. The authors reported long-term efficacy of continuous RF-DRG in the treatment of chronic thoracic segmental pain.

There are 2 prospective uncontrolled studies where the use of continuous RF-DRG is described in two spinal regions (table 4). Sluijter[14] published a study of 105 patients with cervicobrachial and lumbar radicular pain; 60 patients had lumbar and 45 had cervical continuous RF-DRG. Using patients' opinions as "good," "fair," and "poor," "good" results were reported in almost 40% of patients, at follow-up periods that varied from 3 to 21 months. Niv and Chayen[15] studied 50 patients with lumbar and thoracic segmental pain of malignant origin. Continuous RF-DRG was applied at the affected segmental levels, followed by injection of 40 mg methylprednisolone. At 3 months, 31 patients (62%) were "virtually pain free" and 14 patients (28%) had "fair" pain relief; 48% of the patients continued to be "virtually pain free" at 12 months.

There are 3 prospective uncontrolled trials of pulsed RF-DRG application (table 4).[9,16,17] Sluijter *et al.*[9] reported 15 failed back surgery patients with chronic uni-

lateral lumbar radicular pain who received pulsed RF-DRG at the affected segmental levels. At 6 months, greater than 2-point reduction in VAS scores was reported in 8 patients (53%); 6 of these patients (40%) continued to have the pain relief at 12 months. Pevzner *et al.*[16] reported 28 patients with lumbar and cervical radicular pain who received pulsed RF-DRG. At 3 months, 2 patients had "excellent," 12 had "good," 9 had "fair," and 5 had no pain relief. The study by Shabat *et al.*[17] evaluated 28 patients with chronic neuropathic spinal pain who had pulsed radiofrequency of the suspected DRG. No diagnostic blocks were performed, and the involved vertebral level was determined solely by the clinical and the imaging findings. At 3 months, 82% of the patients reported reduction of VAS scores by more than 30%, a trend that continued for 1 yr (68%). All of the patients had concurrent treatments that included injection of 80 mg methylprednisolone before the pulsed RF-DRG, oral antiinflammatory medications, and physical therapy after the procedure. The nature and etiology of the spinal neuropathic pain was not elucidated.

Retrospective Studies

Of the 5 studies of retrospective design (table 5), 2 used continuous RF-DRG, 1 for lumbar radicular pain and 1 for thoracic segmental pain. The study by Van Wijk *et al.*[18] was a retrospective data analysis of 279 patients who received continuous RF-DRG for chronic lumbar radicular pain. A 4-point pain perception scale—pain free, moderate pain relief (> 50% pain relief), no change in pain, and increased pain—was used to monitor patients' outcome. At 2 months, 164 patients (59%) experienced greater than 50% pain relief, which continued in 96 patients (58%) for a variable period of 2–70 months (mean, 22.9 months). The authors concluded that continuous RF-DRG provided long-term pain relief. The study by Van Kleef *et al.*[19] analyzed 43 patients with chronic thoracic segmental pain of variable etiology who received continuous RF-DRG at the affected segment. Twenty-seven of the patients had pain limited to one or two segments, whereas 16 patients had multisegmental pain. At 8 weeks, 14 patients (52%) with one- or two-segment pain had greater than 50% pain relief, which continued at 9 months in 10 patients (37%); only 3 patients (18%) with pain in more than two segments obtained similar pain relief at both 8 weeks and 9 months.

There were 3 retrospective studies of pulsed RF-DRG use (table 5), 1 each in the treatment of cervicobrachial, thoracic segmental, and lumbar radicular pain. Van Zundert *et al.*[20] performed a retrospective review of 18 patients who underwent pulsed RF-DRG for chronic cervicobrachial pain. Using GPE scores, 72% of the patients reported greater than 50% pain relief at 2 months, 56% of the patients maintained this pain relief for 3–11 months, and in 33% of the patients the pain relief lasted for more than a year. The study by Cohen *et al.*[21] retrospectively analyzed 49 patients with chronic postsurgi-

Table 5. Retrospective Studies on Radiofrequency of the Dorsal Root Ganglion

Study and Methods	Patients and Treatments	Results and Comments	Authors' Conclusions
Conventional (continuous) RF of DRG			
Van Kleef *et al.*[19] (1995)	43 pts with TSP had SL CRF-DRG at 67°C for 60 s; 27 pts had 1- or 2-level and 16 pts had > 2-level SP	> 50% pain relief for 8 wk and 9 mo in 52% and 37% of pts with 1- or 2-level SP and 18% of pts with > 2-level SP, respectively	CRF-DRG provided short- and long-term relief of pain in pts with 1- or 2-level TSP
Van Wijk *et al.*[18] (2001)	279 pts with LRP had CRF-DRG at 67°C for 90 s	> 50% pain relief observed in 58% of pts at 2–70 mo	CRF-DRG provided useful, safe, and long-term treatment for LRP
Pulsed RF of DRG			
Van Zundert *et al.*[20] (2003)	18 pts with CBP had SL PRF-DRG	> 50% pain relief (GPE) seen in 72% of pts at 2 mo, 56% for 3–11 mo, and 33% for > 1 yr	PRF-DRG provided satisfactory long-term pain relief in the majority of pts with CBP
Teixeira *et al.*[22] (2005)	13 pts with LRP due to HD had PRF-DRG at 1 or 2 levels	> 5-point improvement (NRS) in 92% of pts at 1 yr	PRF-DRG is an alternative to ESI in the treatment of HD
Cohen *et al.*[21] (2006)	49 pts with TSP; 28 had PRF (15 of the ICN and 13 of the DRG) and 21 had MM	At 6 wk, > 50% pain relief noted in 62, 21, and 27% of pts who received PRF-DRG, PRF-ICN, and MM, respectively. At 3 mo, these results were 54, 7, and 20%, respectively	PRF-DRG had superior results compared with ICN-PRF and MM

CBP = cervicobrachial pain; CRF-DRG = conventional radiofrequency lesioning of dorsal root ganglia; DRG = dorsal root ganglia; ESI = epidural steroid injection; GPE = global perceived effect; HD = herniated disk; ICN = intercostal nerve; LRP = lumbar radicular pain; MM = medical management; NRS = numeric rating scale; PRF = pulsed radiofrequency; PRF-DRG = pulsed radiofrequency lesioning of dorsal root ganglia; PRF-ICN = pulsed radiofrequency applied to the intercostal nerve; pt = patient; RF = radiofrequency; SL = single-level; SP = segmental pain; TSP = thoracic segmental pain.

cal thoracic segmental pain. Twenty-eight patients who received PRF of either the intercostal nerves (n = 15) or the DRG (n = 13) were compared with 21 patients who were treated pharmacologically. At 6 weeks, 62% of the patients who received pulsed RF-DRG reported greater than 50% pain relief, compared with 21% in the intercostal pulsed radiofrequency group and 27% in the medically managed group; at 3 months, these percentages were 54, 7, and 20%, respectively. Teixeira *et al.*[22] analyzed 13 patients with lumbar radicular pain who were possible candidates for disk surgery; 9 of these patients exhibited motor and sensory deficits of the involved dermatomes. Significant improvements in the numeric rating scale scores (> 5 points) were reported in 12 patients (92%) at 1 yr, and the planned surgery was avoided; resolution of the neurologic deficits was reported in all of the patients. The authors recommended pulsed RF-DRG as an alternative to epidural steroid injections for the treatment of herniated disk. No diagnostic blocks were performed in this study, and the level of DRG lesioning was based only on clinical and imaging findings.

Case Reports and Case Series

Of the 4 case reports or case series encountered (table 6), 2 pertained to continuous[23–24] and 2 pertained to pulsed RF-DRG.[25–26] Uematsu *et al.*[23] used continuous radiofrequency for pain and for other symptoms. Of the 17 patients reported, 13 had chronic pain symptoms, 3 had spastic paraplegia, and 1 had Raynaud disease. At 3–48 months, "excellent" to "good" pain relief was reported in 5 patients (38%), relief of spasticity was reported in 2 of 3 patients, and temporary improvement in symptoms was reported in the patient with Raynaud disease. Nash[24] reported a series of 26 patients with chronic radicular pain of diverse etiology who received continuous RF-DRG at the involved sacral, lumbar, thoracic, or cervical levels. Using "excellent," "good," and "no improvement" criteria, "excellent" to "good" results were reported in 15 of 26 patients. Munglani[25] reported the use of pulsed RF-DRG in 3 patients with lumbar radicular pain and 1 patient with thoracic segmental pain. Marked reduction in pain was reported in these patients for 1–7 months. Rozen and Parvez[26] reported 5 patients with chronic inguinal pain after herniorrhaphy. Pulsed RF-DRG of the affected segments resulted in 75–100% pain relief, which lasted for 6–9 months.

Laboratory Studies

We encountered 6 laboratory studies that pertained to RF-DRG (table 7). In a goat model, De Louw *et al.*[27] studied the effects of continuous radiofrequency on the DRG by observing the morphologic changes and by measuring the monoclonal antibody MIB-1, with enhanced MIB-1 activity indicating a microglial proliferative and cellular injury response.[35] DRG lesions were created in the left lumbar region by applying continuous radiofrequency at 67°C for 60 s (treatment group). Proximity of the electrode to the DRG was determined by motor stimulation thresholds; a motor response at less than 0.2 V was considered intraganglionic, and a response at greater than 0.6 V indicated an extraganglionic electrode placement. Motor response was sought at less than 0.2 V (average, 0.1 V) at the L5 level and at greater

Table 6. Case Series and Case Reports on Radiofrequency of the Dorsal Root Ganglion

Study and Methods	Patients and Treatments	Results and Comments	Authors' Conclusions
Conventional (continuous) RF of DRG			
Uematsu *et al.*[23] (1974)	13 pts with chronic segmental pain from diverse etiologies had CRF-DRG at 1–5 segmental levels	At 3–48 mo, "excellent" to "good" pain relief was reported in 38% of pts	CRF-DRG was described as a simple technique for interrupting nerve root function
Case series			
Nash[24] (1986)	26 pts with radicular pain had CRF-DRG at 1–3 segmental levels	"Excellent" to "good" results were reported in 15 of 26 pts	CRF-DRG was beneficial in 15 of 26 patients
Case series			
Pulsed RF of DRG			
Munglani[25] (1999)	3 pts with LRP and 1 with TSP had PRF-DRG at 1–3 segmental levels	"Marked reduction in pain" was reported in the pts for 1–7 mo	Results were reported as anecdotal but remarkable
Case reports			
Rozen and Parvez[26] (2006)	5 pts with chronic IP after herniorrhaphy had PRF-DRG at 3 segmental levels	75–100% pain relief was reported in all cases and lasted for 6–9 mo	"Minimally invasive neurodestruction" was reported
Case reports			

CRF-DRG = conventional radiofrequency lesioning of dorsal root ganglia; DRG = dorsal root ganglia; IP = inguinal pain; LRP = lumbar radicular pain; PRF-DRG = pulsed radiofrequency lesioning of dorsal root ganglia; pt = patient; RF = radiofrequency; TSP = thoracic segmental pain.

Table 7. Laboratory Studies on Radiofrequency of the Dorsal Root Ganglion

Study	Methods	Results	Authors' Conclusions
De Louw *et al.*[27] (2001)	Goat model. CRF (67°C for 60 s) to left-sided lumbar DRG (motor response at < 0.2 V at the L5 level and at > 0.6 V at the L1–L4 levels). Sham treatment to right-sided lumbar DRG. Morphologic appearance and measurement of monoclonal antibody (MIB-1) at 2 wk	In the treatment gp, the L5 lesions were small (1.8–2.0 mm), were intraganglionic, and showed damage to all fiber types; the L1–L4 lesions were larger, were extraganglionic, and showed no fiber damage, but showed increased labeling for MIB-1 antibody	The intraganglionic CRF lesions destroyed the large myelinated nerve fibers, whereas the extraganglionic lesions affected the microglial cells without directly affecting the nerve fibers
Higuchi *et al.*[28] (2002)	Rat C6 DRG. 3 gps: PRF, CRF at 38°C, and sham-treated animals. Measurement of the IEG, c-fos, reactive neurons at 3 h	Significant relative increase in c-fos immunoreactive neurons in dorsal horn laminae I and II in the PRF-treated rats	PRF-DRG activated pain processing neurons in the dorsal horn. This effect was not mediated by tissue heating
Van Zundert *et al.*[29] (2005)	Rat C5 and C6 DRG. 4 gps: sham treatment, CRF at 67°C, PRF for 2 min, and PRF for 8 min. Measurement of the IEG, c-fos, reactive neurons at 7 days	Equal increases in c-fos immunoreactive neurons in CRF at 67°C and PRF gps; no such increase in sham-treated gp	PRF-DRG caused longer-term neuronal activation
Podhajsky *et al.*[31] (2005)	Rat L5 DRG. 5 gps: 3 gps received PRF, CRF, or conductive heat probe at 42°C for 120 s; a sham-treated gp and a CRF at 80°C gp. Light microscopic observations made at 2, 7, and 21 days	No change in sham gp, minimal changes in all three gps with temperature increased to 42°C, and wallerian degeneration in CRF at 80°C gp	Heat is the primary determinant of any tissue response to PRF. PRF-DRG did not rely on thermal injury for its nociceptive effects
Erdine *et al.*[32] (2005)	Rabbit L1, L2, and L3 DRG. 4 gps: CRF at 67°C, PRF, sham treatment, and control (no intervention) gps. Light and electron microscopic observations made at 2 wk	On electron microcopy, changes were more severe in the CRF at 67°C gp than in the PRF gp; no changes in sham and control gps	PRF-DRG was less destructive than CRF-DRG at 67°C
Hamann *et al.*[30] (2006)	Rat L4 anterior primary ramus or sciatic nerve, exposed to PRF, sham treatment, or axotomy. Microscopic observation and measurement of protein ATF-3 at 1–14 days	ATF-3 expression was up-regulated, indicating cellular stress, in PRF and axotomized animals	PRF-DRG caused cellular stress unrelated to thermal damage

ATF-3 = activating transcription factor 3; CRF = continuous radiofrequency; CRF-DRG = continuous radiofrequency to the dorsal root ganglia; DRG = dorsal root ganglia; gp = group; IEG = immediate early gene; PRF = pulsed radiofrequency; PRF-DRG = pulsed radiofrequency to the dorsal root ganglia.

than 0.6 V (range, 0.9–1.6 V) at the L1–L4 levels. The electrodes were placed similarly on the right side, but no radiofrequency current was applied (sham group). The control group comprised DRG that received no intervention and were procured from goats killed for unrelated experiments. Light microscopic observations, 2 weeks later, showed that in the treatment group, lesions made at the L5 level were small (1.8–2.0 mm) and intraganglionic, with complete loss of myelin of all fiber sizes, whereas the lesions made at L1–L4 levels were larger (2–2.8 mm) and extra ganglionic, and no abnormal morphology was seen in the treated DRG. The DRG MIB-1 antibody activity was significantly increased in the treatment group; it was higher in the sham-treated group and was insignificant in the control group. The authors concluded that the intraganglionic continuous radiofrequency lesions destroyed the large myelinated nerve fibers, whereas the extraganglionic continuous radiofrequency lesions affected the microglial cells without directly affecting the large nerve fibers.

Three studies measured markers of cellular stress (table 7).[28–30] In a rat model, Higuchi *et al.*[28] compared the effects of pulsed RF-DRG, continuous RF-DRG at 38°C, and sham treatment, by measuring expression of immediate early gene c-fos in the dorsal spinal horn neurons; presence of the c-fos immunoreactive neurons indicated neuronal activation.[36] Three hours after application of these radiofrequency modalities, a significant increase in c-fos immunoreactivity was observed in the pulsed RF-DRG group, compared with the continuous RF-DRG at 38°C and the sham-treated group. The authors concluded that the pulsed RF-DRG activated pain-processing neurons in the dorsal horn; this effect was attributed to higher voltages and electromagnetic force delivered during PRF, and was independent of any tissue heating. Van Zundert *et al.*,[29] in a similar study in a rat model, measured c-fos immunoreactivity at 7 days. The study groups included pulsed RF-DRG for 120 s, pulsed RF-DRG for 8 min, continuous RF-DRG at 67°C for 60 s, and a sham-treated group. An equal increase in c-fos immunoreactive neurons was observed in the various treatment groups, irrespective of the radiofrequency modality, whereas no such increase was seen in the sham-treated group. The authors concluded that the results of this study showed late or sustained effect of PRF on the DRG. Also in a rat model, Hamann *et al.*[30] measured activating

transcription factor 3 in the DRG; an increase in the activating transcription factor 3–positive neurons indicated cellular stress.[37] The study groups included a pulsed RF-DRG group (PRF to the L4 anterior ramus), a sciatic nerve PRF group, an axotomy group (the L4 anterior ramus was transected), and a sham-treated group. No increase in activating transcription factor 3–positive neurons was observed in the sham-treated group or when the PRF was applied distally to the sciatic nerve, a moderate increase was seen in the pulsed RF-DRG group, and a marked increase was observed in the axotomy group. The authors concluded that PRF caused cell stress without overt thermal injury; however, they did not rule out the possibility that individual PRF pulses might generate enough heat to cause the cellular stress.

In 2 studies (table 7), DRG morphology was observed after exposing them to various radiofrequency and heat modalities. In a rat model, Podhajsky *et al.*[31] applied four modalities to the DRG that included PRF, continuous radiofrequency (CRF) at 42°C, CRF at 80°C, and conductive heat at 42°C (conductive heat probe heated to 42°C). Light microscopic observations made at 2, 7, and 21 days showed that the tissue response to the temperature increased to 42°C was irrespective of the heating modality; each caused edema at 2 days that persisted through 7 days and was resolved by 21 days. In contrast, lesions made at 80°C consistently caused thermal lesions, characterized by wallerian degeneration. In a similar study, Erdine *et al.*[32] exposed rabbit DRG to PRF and CRF at 67°C; the study also included a sham-treated group (electrode placement on the DRG but no radiofrequency applied) and a control group (no intervention). At 2 weeks, there was no difference in the light microscopic appearances of the DRG in all of the above groups, and the electron microscopic appearance showed no pathologic changes in the DRG of the sham-treated and control groups. However, the electron microscopic appearance in both the CRF at 67°C and PRF groups showed damage to the cellular substructure, which was greater in the CRF at 67°C group. The authors suggested that PRF was more destructive than CRF at 67°C.

Technique

In the first publication of percutaneous radiofrequency application to the sensory spinal nerve roots, Uematsu *et al.*[23] described the technique of cervical, thoracic, and lumbar dorsal rhizotomy. They placed a 17-gauge radiofrequency electrode in the respective intervertebral foramen (IVF) under fluoroscopic guidance; proximity to the target spinal nerve root was further facilitated by the electrical stimulation—1-ms electrical pulses at 2 Hz, between 0.5 and 2.0 V, were used to elicit pain and muscle contractions in the appropriate dermatomes. Subsequently, Sluijter, Koetsveld-Baart, and Mehta[10,38] described their technique of electrode placement, which varied considerably from the one introduced by Uematsu *et al.*[23] To improve patient tolerance, thinner electrodes in the range of 22–23 gauge were used. For precise electrode tip positioning under fluoroscopic guidance, detailed location of the DRG in relation to the x-ray imaging was described: On anteroposterior x-ray projection, the DRG was described to lie immediately behind the lateral aspect of the facet column at all spinal levels; on lateral x-ray projection, it was localized to the dorsocranial quadrant of the IVF in the lumbar and thoracic region, and dorsocaudal quadrant of the IVF in the cervical region. The criteria used for electrical stimulation by these authors were also different: High-frequency electrical currents between 50 and 100 Hz were used to elicit paresthesia, whereas low-frequency currents between 2 and 5 Hz were used to elicit the motor response. To ensure proximity to the DRG, the sensory threshold was kept less than 0.6 V, whereas proximity to the motor nerve root was avoided by keeping the motor threshold greater than 1.5–2 times the sensory threshold. To delineate the DRG position in relation to the electrode tip and to exclude the intradural electrode positioning, a radiculogram before the radiofrequency lesioning was also obtained. Later, Van Kleef *et al.*[19] recommended using greater than 0.4 V of electrical currents during sensory stimulation to avoid intraganglionic electrode placement. The majority of the subsequent studies of both continuous and pulsed RF-DRG adapted the technique of electrode placement described by these authors with little variation.

Except Uematsu *et al.*,[23] who performed lumbar RF-DRG in the lateral recumbent position, the prone position was used for both lumbar and thoracic RF-DRG by most authors (fig. 2). An anterolateral approach, with the patient in the supine position, was used in all of the studies of cervical RF-DRG (fig. 3). Using anteroposterior and lateral fluoroscopic views, the radiofrequency electrode was advanced superomedially from a lateral position in most of the early studies of lumbar and thoracic RF-DRG.[9,13–15,18,38] An oblique fluoroscopic view that

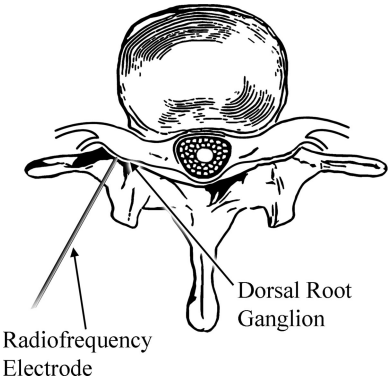

Fig. 2. Diagrammatic representation of axial vertebral view at lumbar level, showing appropriate placement of radiofrequency electrode *via* the intervertebral foramen. Note the introduction of the electrode from a posterolateral position.

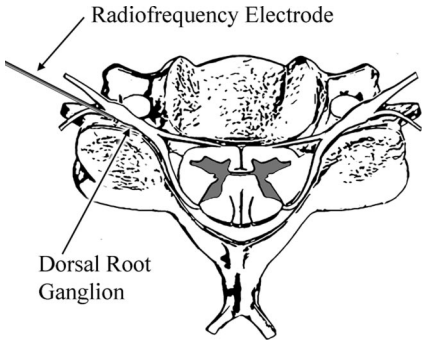

Fig. 3. Diagrammatic representation of axial vertebral view at cervical level, showing appropriate placement of radiofrequency electrode *via* the intervertebral foramen. Note the introduction of the electrode from an anterolateral position.

allowed maximum visualization of the IVFs, with coaxial advancement of the electrode, was used in the later studies of lumbar[7] and thoracic[13,21] RF-DRG. Almost all of the studies of the cervical RF-DRG used oblique fluoroscopic views, with coaxial advancement of the electrode.[4–6,10–12,14,20,38] Haspeslagh *et al.*[6] further elaborated the technique of their oblique view in the cervical region; they aligned the vertebral disk plates and rotated the C-arm in the oblique position until the contralateral pedicles were noted to be projecting posterior to the anterior line of the vertebral bodies. Contact was made with a bony landmark before the IVF was entered in almost all the studies. In the lumbar region, this landmark was either the junction of the transverse process and the facet column[14,38] or the vertebral lamina[24]; in the thoracic region, it was the junction of the transverse process and the caudal portion of the vertebral body[23]; and in the cervical region, it was the posterior and caudal border of the IVF.[4–6,10–12,20,38] In almost all of the studies, after this bony contact was made, the electrode was advanced in the anteroposterior projection, and the target for the electrode tip was the mid-facet column[4–6,10–12,20]; this target was further described as either a line connecting the mid-facet joints[14,38] or the inferomedial aspect of the superior pedicle bounding the IVF.[13,24] On the lateral x-ray projection, the electrode tip was placed in the dorsocranial quadrant of the IVF in the lumbar and thoracic region and in the dorsocaudal quadrant of the IVF in the cervical region. Because of difficult access from the corresponding IVF, the technique of RF-DRG for the first sacral (S1) and upper thoracic (T1–T7) segments was different from the one described above. The S1 DRG was found to be located significantly higher and medial to the S1 IVF,[14,38] and the upper thoracic DRG (T1–T7) were deemed inaccessible because of the presence of ribs and pleura.[13] At these sites, the respective DRG was first identified by obtaining a radiculogram through the corresponding IVF, and the electrode was placed through a burr hole drilled in to the osseous structure directly dorsal to the DRG.[13,14]

During CRF, the electrical current density is greatest around the electrode tip, and the radiofrequency lesion generated is elliptical, with its long axis formed by the uninsulated electrode tip. Therefore, to effectively coagulate the target nerve during CRF application, the electrode tip is typically placed parallel to the long axis of the target nerve.[39] During PRF application, however, the greatest electrical current density is distal to the electrode tip,[9] and placing the electrode parallel to the target nerve is deemed unnecessary. Despite these differences, however, no difference was found between the techniques of electrode placement for pulsed and continuous RF-DRG.

The Target

Uematsu *et al.*[23] modeled their technique after surgical rhizotomy[40] and primarily targeted the sensory spinal nerve roots. However, later publications emphasized direct lesioning of the DRG, arguing that an extraganglionic radiofrequency lesion would be no different than peripheral nerve lesioning.[10,14,24,38] To avoid deafferentation symptoms, Van Kleef *et al.*[19] proposed lesioning adjacent to and not inside the DRG. The segmental level for radiofrequency application was identified by a single set of diagnostic nerve blocks in most of the studies, and comparative blocks as a diagnostic criterion were not used. In two studies,[17,22] no diagnostic nerve blocks were used, and the treatment levels were determined entirely by clinical and imaging findings. To avoid motor disturbances and deafferentation symptoms, as observed after the surgical sectioning of multiple sensory spinal nerve roots,[40] treatment at a single segmental level was advocated by majority of the authors.[4,5,7–10,12,14,19] Citing overlapping innervation of the adjacent dermatomes,[15,41] radiofrequency was applied at multiple segments in several of the studies: CRF was applied at two to seven levels by Uematsu *et al.*,[23] one to five levels by Nash,[24] and one to three levels by Niv and Chayen,[15] whereas PRF was applied at one to three levels by Teixeira *et al.*,[21] Munglani *et al.*,[25] and Rozen *et al.*[26]

Temperatures, Durations, and Modes

The electrode tip was heated to 67°C in the majority of the studies of continuous RF-DRG[4,5,7,11–13,18,19]; the electrode temperature selected was 70°C in 2 studies[14,15] and 75°C in 1 study.[10] The electrode temperatures were used variably in studies by Uematsu *et al.*[23] (50°–70°C) and Nash (70°–80°C).[24] The duration of continuous RF-DRG varied, and both 60 s[4,10,12,14,19] and 90 s[5,7,11,13,15,18] were selected with almost equal frequency; in 2 studies, continuous RF-DRG was applied for 120 s.[23,24] The majority of the studies of pulsed RF-DRG used the protocol described by Sluijter *et al.*[9]: Radiofrequency current was applied for 20 ms, at 2 Hz, for 120 s, with maximum tissue temperature increased to 42°C. In 2 studies, the duration of pulsed RF-DRG application was longer than 2

min; Teixeira *et al.*[22] and Cohen *et al.*[21] applied PRF for 3 and 8 min, respectively.

Complications

Pain and dysesthesias, which resolved spontaneously in a few weeks to months, were reported in a small number of treated patients in several of the studies of continuous RF-DRG.[4,5,10–15,19,24] Transient sensory loss in the treated dermatomes was also reported in some studies of continuous RF-DRG.[4,10,12,13,19] The continuous RF-DRG study by Slappendel *et al.*[5] was the only study that reported motor disturbances, minor weakness in hand strength that was present at 3 months in 3 of 61 patients. Aside from minor immediate postprocedural pain,[9,25] none of the studies of pulsed RF-DRG reported any significant side effects or complications.

Discussion

Historic Perspectives

Surgical sectioning of the sensory spinal nerve roots for the relief of pain was first reported as early as late 19th century.[42] The associated dysesthesias, deafferentation symptoms, and loss of function, however, led to gradual abandoning of these techniques. In the 1930s, neurolytic agents, alcohol,[43] and phenol[44] were introduced to chemically destroy the sensory spinal nerve roots, but the unpredictability of the neurolytic effects limited their use to terminally ill patients. In 1974, after the use of thermal radiofrequency for trigeminal neuralgia,[45] Uematsu *et al.*[23] percutaneously applied radiofrequency to the sensory spinal nerve roots to create a controlled thermal lesion that would safely interrupt the afferent spinal pain pathways. Based on the observations of Brodkey *et al.*,[46] which showed that temperatures above 45°C caused tissue destruction, Uematsu *et al.*[23] increased the electrode temperatures above these levels by applying the radiofrequency currents uninterruptedly—continuous RF-DRG. For selective analgesia, however, these and several subsequent investigators[10,14,23,24] relied on the findings of Letcher and Goldring,[47] which showed selective destruction of the small pain fibers but sparing of the larger sensory and motor fibers at the peripheral zones of the thermal radiofrequency lesions. Optimal electrode tip temperatures and lesioning durations were therefore sought in several of the early studies of RF-DRG. In 1991, Vervest and Stolker[11] first quoted the findings of Smith *et al.*,[48] which reported uniform nerve fibers damage in the radiofrequency lesions created between 45° and 75°C. In 1998, Sluijter *et al.*[9] applied PRF to the DRG. During pulsed RF-DRG, thermal tissue injury was avoided by limiting the peak electrode temperature to 42°C or less, and radiofrequency currents were applied at higher voltages to maximize the delivery of electromagnetic force. These two opposing goals were achieved by applying the radiofrequency currents in a pulsatile manner, and short heat bursts (20 ms) were interspersed by relatively long cooling periods (480 ms), allowing time for the heat to dissipate in between the radiofrequency pulses.

General Overview

Identified as an enlargement on the dorsal spinal root and located at a variable distance from its takeoff from the central thecal sac, the DRG contain the cell bodies of the afferent spinal nerves. In the lumbar region, the DRG are classified as intraspinal, intraforaminal, and extraforaminal, based on their location in relation to the boundaries of the IVF. The majority of the lumbar DRG were found to be intraforaminal, except the S1 DRG was found to be intraspinal in 80% of individuals.[49] The size of the lumbar DRG also progressively increases from the first lumbar to the S1 level. In the cervical region, the DRG have been classified as proximal or distal based on their location, proximal or distal to the interpedicular line. Although cervical DRG were found at a progressively greater distance from the thecal sac, from upper to lower levels, no clear trend was found for the proximal or distal types.[50]

Radicular pain has traditionally been attributed to compression of the spinal nerve root by a herniated disk, causing antidromic spread of impulses along the peripheral nerve.[51] Compression neuropathies, however, are often painless,[52] and in experimental conditions, sustained response was not generated by direct compression of the sensory nerve roots.[53] These observations cast doubts on the assumption that the sensory nerve root compression was the main cause of radicular pain. Spontaneous[54] and enhanced[55] DRG activity, however, was observed in response to the injury in experimental conditions. In addition, inflammatory mediators released at the site of herniated disk material have been shown to modulate the Na^+, K^+, and Ca^{2+} ion channels on the DRG surface, causing its ectopic and sustained firing.[3] Such sustained DRG discharges have also been linked to sensitization of the spinal dorsal horn cells and the resulting state of hyperalgesia.[56] Based on these observations, the DRG are considered the most likely focus of ectopic impulse origin in patients with radicular pain, and the prime target for neurodestructive and neuromodulatory pain treatments.

Mechanisms of Pain Relief

The proposed mechanism of pain relief from RF-DRG is neuronal dysfunction and/or nerve fiber damage, resulting in interruption of the afferent nociceptive impulses. However, none of the clinical or laboratory studies we reviewed provided evidence supporting this assumption. The basic science study by De Louw *et al.*[27] reported small (< 2.0-mm) intraganglionic thermal le-

sions, or larger extraganglionic lesions and a possible DRG cell injury response; these findings do not equate to interruption of the nociceptive impulses and the consequent pain relief. Van Kleef *et al.*[12] recorded sensory evoked potentials and electromyography 1 week before and at 3–4 weeks after the continuous RF-DRG and reported no difference in the results, supporting only the assumption that continuous RF-DRG spared the large sensory and motor nerve fibers. Because no thermal lesion is created during PRF, its mode of action is even less obvious. The proposed mechanisms for PRF effect have ranged from cellular dysfunction from high electromagnetic fields[9,57] and heat bursts[30,57] to neuromodulation.[58] The experimental studies by Higuchi *et al.*,[28] Van Zundert *et al.*,[29] and Hamann *et al.*[30] showed that pulsed RF-DRG caused neuronal activation. The study by Erdine *et al.*[32] also suggested that PRF can cause damage to the cellular substructure of the DRG. However, it is unclear whether either the neuronal activation or the structural cell damage was caused by the transient heat bursts or the high electromagnetic fields generated during the PRF application.[30,57] In addition, the significance of these findings in relation to the interruption of nociceptive impulses remains unclear.

Critical Overview

Although Uematsu *et al.*[23] targeted the sensory spinal nerve roots, majority of the later authors recommended direct (intraganglionic) lesioning of the DRG for the following reasons: (1) to make denervation more permanent, by targeting the neuronal cell bodies; (2) to make denervation more complete, by targeting the sensory fibers in the anterior spinal roots; and (3) to reduce the incidence of postprocedural neuropathic pain, by preventing neuronal hyperactivity by direct DRG lesioning.[10,14,24,38] These assumptions were supported only by the experimental findings of DRG cell hyperactivity observed after peripheral nerve lesions[59] and the presence of sensory fibers in the motor nerve roots.[60] Although the two techniques of RF-DRG are deemed distinct, both continuous and pulsed RF-DRG were used to treat similar pain syndromes. Only 1 clinical study compared continuous with pulsed RF-DRG,[9] and even this study used a mode of continuous RF-DRG—continuous RF-DRG with maximum temperature of 42°C—not used in routine clinical practice. Despite their high false-positive rates,[61] a single set of diagnostic spinal blocks was used almost exclusively, and none of the studies we reviewed used comparative diagnostic blocks.

Efficacy

Although the majority of the uncontrolled clinical studies of RF-DRG reported the efficacy of both continuous and pulsed RF-DRG, results of the controlled clinical trials varied. Of the 2 RCTs of continuous RF-DRG in patients with cervicobrachial pain, the trial by Van Kleef *et al.*[4] scored 4 out of 5 points (table 8) on the 5-point Jadad scale—it lacked the description of random patient allocation—and was graded as a high-quality trial; it reported short-term efficacy of the continuous RF-DRG in the treatment of cervicobrachial pain. The second trial, by Slappendel *et al.*,[5] scored 5 out of 5 points on the Jadad scale (table 8) and was graded as a high-quality trial. This trial concluded that the two treatment groups (RF-DRG at 67°C and at 40°C) had equal clinical efficacy; the efficacy of either of the groups, however, is unclear. In addition to the lack of a placebo control group, the overall pain relief for the two groups was not significant; at 3 months in either group, less than 52% of the patients experienced clinically significant pain relief (> 2 points on the VAS), and less than 12% of the patients had complete pain relief. Based on the studies by Brodkey *et al.*,[46] the effects of 40°C lesion on nervous tissue should be minimal and reversible. Therefore, if one of the study groups (40°C) were considered as a placebo group, the other would be shown to have no clinical effect. The results of this trial therefore do not provide conclusive evidence of the efficacy of continuous RF-DRG. Using the best evidence synthesis method (table 1), with positive results in one high-quality RCT, there is thus level C or limited evidence of short-term efficacy of continuous RF-DRG in the treatment of cervicobrachial pain (table 9).

Table 8. Grading of the Randomized Controlled Trials

Study	A	B	C	D	E	Study Grade
Van Kleef *et al.*[4]	1	0	1	1	1	4/5: High-quality trial
Slappendel *et al.*[5]	1	1	1	1	1	5/5: High-quality trial
Haspeslagh *et al.*[6]	1	0	0	0	1	2/5: Low-quality trial
Geurts *et al.*[7]	1	1	1	1	1	5/5: High-quality trial
Van Zundert *et al.*[8]	1	1	1	1	1	5/5: High-quality trial

The only RCT of RF-DRG use in the treatment of cervicogenic headaches was by Haspeslagh *et al.*[6] This trial concluded that the sequential continuous radiofrequency treatments of the facet joints and the DRG were as effective as the local nerve blocks in the treatment of cervicogenic headaches. Because of the lack of appropriate randomization and blinding, this trial scored only 2 out of 5 points on the 5-point Jadad scale and was graded as a low-quality trial (table 8). In addition to the lack of a placebo control group, the results reported were of the combined efficacy of facet joint radiofrequency and continuous RF-DRG. With only 3 of 15 patients in the treatment group receiving the continuous RF-DRG, this trial did not directly evaluate the efficacy of continuous RF-DRG, and its results were therefore regarded as inconclusive. With inconclusive results in one low-quality RCT trial, there is therefore level D or incon-

Table 9. Best Evidence Synthesis for the Efficacy of RF-DRG

Syndrome	Study	Qualitative Analysis	Results	Best Evidence
Cervicobrachial pain				
	Conventional (continuous) RF-DRG			
	Van Kleef *et al.*[4]	4/5; the study lacked description of random patient allocation. High-quality trial	Short-term efficacy of the continuous RF-DRG	
	Slappendel *et al.*[5]	5/5. High-quality trial	Continuous RF-DRG at 67°C and at 40°C had equal clinical efficacy. With undetermined clinical efficacies for either of the modalities, the results of this trial were considered inconclusive	With positive results in one high-quality RCT, there is level C or limited evidence of short-term efficacy of continuous RF-DRG in the treatment of cervicobrachial pain
	Pulsed RF-DRG			
	Van Zundert *et al.*[8]	5/5. High-quality trial	With significantly different pretrial group characteristics, the results were regarded as possible short-term clinical efficacy of pulsed RF-DRG	With possible positive results in one high-quality RCT, there is level C or limited evidence of possible short-term efficacy of pulsed RF-DRG in the treatment of cervicobrachial pain
Cervicogenic headaches	Haspeslagh *et al.*[6]	2/5; the study lacked adequate randomization and blinding. Low-quality trial	The results were of the combined efficacy of the facet joint RF and the RF-DRG. Only 3 of 15 patients in the treatment group received RF-DRG. This trial did not directly evaluate the efficacy of RF-DRG, and its results therefore provided inconclusive evidence of the efficacy of RF-DRG in the treatment of cervicogenic headaches	With inconclusive results in one low-quality RCT trial, there is level D or inconclusive evidence of the efficacy of continuous RF-DRG in the treatment of cervicogenic headaches
Lumbar radicular pain	Geurts *et al.*[7]	5/5. High-quality trial	Continuous RF-DRG was not effective in the treatment of chronic lumbar radicular pain	With negative results from one high-quality RCT, there is level C or limited evidence against the use of continuous RF-DRG in the treatment of lumbar radicular pain

RCT = randomized controlled trial; RF = radiofrequency; RF-DRG = radiofrequency application to the dorsal root ganglia.

clusive evidence (table 1) of the efficacy of continuous RF-DRG in the treatment of cervicogenic headaches (table 9).

The trial by Geurts *et al.*[7] was the only RCT of RF-DRG use in the treatment of lumbar radicular pain. It reported that continuous RF-DRG was not effective in the treatment of chronic lumbar radicular pain and recommended against its routine use. This trial scored 5 out of 5 points on the Jadad scale and was ranked as a high-quality trial (table 8). With negative results from one high-quality RCT, there is thus level C or limited evidence (table 1) against the use of continuous RF-DRG in the treatment of lumbar radicular pain (table 9).

The trial by Van Zundert *et al.*[8] in the treatment of cervicobrachial pain was the only RCT of pulsed RF-DRG encountered. With different pretrial characteristics of

the two study groups, this trial reported only possible short-term clinical efficacy of pulsed RF-DRG in the treatment of cervicobrachial pain. This trial scored 5 out of 5 on the 5-point Jadad scale and was graded as a high-quality trial (table 8). With possible positive results in one high-quality RCT, it provided level C or limited evidence (table 1) of possible short-term efficacy of pulsed RF-DRG in the treatment of cervicobrachial pain (table 9).

Conclusion

The two primary modalities of radiofrequency application to the DRG used in the clinical practice include continuous RF-DRG, with electrode temperatures in thermodestructive range, and pulsed RF-DRG. Although the uncontrolled studies reported the clinical efficacy of both continuous and pulsed RF-DRG, the controlled clinical data provided results that were variable depending on the pain syndrome being treated and the mode of RF-DRG used. For continuous RF-DRG, limited evidence of short-term efficacy existed in the treatment of cervicobrachial pain, the evidence was inconclusive in the treatment of cervicogenic headaches, and limited evidence against its use existed in the treatment of lumbar radicular pain. For pulsed RF-DRG, limited evidence of possible short-term efficacy existed in the treatment of cervicobrachial pain. The complications reported from continuous RF-DRG were limited mainly to sensory disturbances that were infrequent and self-limiting, and no notable complications of pulsed RF-DRG were reported. Although proximity to the DRG was sought in all of the studies of RF-DRG, its exact target, the optimal number of treated segments, and the preferred mode, whether continuous or pulsed radiofrequency, are not clear. The mechanisms of action of both pulsed and continuous RF-DRG remain poorly understood. More basic science research and larger, long-term outcome, controlled clinical trials are needed to clearly understand the efficacy and the mechanism(s) of action of RF-DRG.

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