**Randomized Trial**

# Pulsed Dose Radiofrequency Before Ablation of Medial Branch of the Lumbar Dorsal Ramus for Zygapophyseal Joint Pain Reduces Post-procedural Pain

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**Background:** One of the potential side effects with radiofrequency ablation (RFA) includes painful cutaneous dysesthesias and increased pain due to neuritis or neurogenic inflammation. This pain may require the prescription of opioids or non-opioid analgesics to control post-procedural pain and discomfort.

**Objectives:** The goal of this study is to compare post-procedural pain scores and post-procedural oral analgesic use in patients receiving continuous thermal radiofrequency ablation versus patients receiving pulsed dose radiofrequency immediately followed by continuous thermal radiofrequency ablation for zygopophaseal joint disease.

**Study Design:** This is a prospective, double-blinded, randomized, controlled trial. Patients who met all the inclusion criteria and were not subject to any of the exclusion criteria were required to have two positive diagnostic medial branch blocks prior to undergoing randomization, intervention, and analysis.

**Setting:** University hospital.

**Methods:** Eligible patients were randomized in a 1:1 ratio to either receive thermal radiofrequency ablation alone (standard group) or pulsed dose radiofrequency (PDRF) immediately followed by thermal radiofrequency ablation (investigational group), all of which were performed by a single Board Certified Pain Medicine physician. Post-procedural pain levels between the two groups were assessed using the numerical pain Scale (NPS), and patients were contacted by phone on post-procedural days 1 and 2 in the morning and afternoon regarding the amount of oral analgesic medications used in the first 48 hours following the procedure.

**Results:** Patients who received pulsed dose radiofrequency followed by continuous radiofrequency neurotomy reported statistically significantly lower post-procedural pain scores in the first 24 hours compared to patients who received thermal radiofrequency neurotomy alone. These patients also used less oral analgesic medication in the post-procedural period.

**Limitations:** These interventions were carried out by one board accredited pain physician at one center. The procedures were exclusively performed using one model of radiofrequency generator, at one setting for the PDRF and RFA. The difference in the number of levels of ablation was not considered in the analysis of the results.

**Conclusion:** Treating patients with pulsed dose radiofrequency prior to continuous thermal radiofrequency ablation can provide patients with less post-procedural pain during the first 24 hours and also reduce analgesic requirements. Furthermore, the addition of PDRF to standard thermal RFA did not prolong the time of standard thermal radiofrequency ablation procedures, as it was performed during the typically allotted time for local anesthetic action.

**Key words:** Low back pain, facet joint disease, medial branch block, Radiofrequency ablation, thermal radiofrequency, pulsed dose radiofrequency, PDRF, zygapophyseal joint

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Low back pain has an incidence of 80% in the general population, with upwards of 30% of the population having complaints of chronic low back pain (1-8). Of the population with chronic low back pain, 15 – 52% have lumbar facet disease, also known as zygapophyseal joint disease (1-7). Lumbar facet joint disease is a chronic pain condition causing low back pain in a facetogenic pattern, based on the zygapophyseal joint effected (3-7). Unlike lumbar radiculopathies, lumbar facetogenic pain rarely refers past the knee (5-8). Common clinical features of facetogenic pain include pain relieved by slight flexion, pain exacerbated with extension and facet loading, and the absence of increased pain with cough or straight leg raise (2).

The diagnosis of facet joint disease is accomplished through a combination of history, physical exam, and diagnostic imaging, often including computed tomography (CT) or magnetic resonance imaging (MRI) (1-9). Pain relief with local anesthetic blocks of the medial branches of the dorsal rami of the affected zygapophyseal joint is the only way to confirm facet syndrome (3-13).

Each lumbar zygapophyseal joint receives its innervation from the medial branches of the dorsal rami at its own level and the level above (4,6,14). The Spine Intervention Society (SIS) has developed an algorithm requiring confirmation of facet joint mediated pain by performing 2 diagnostic medial branch blocks, using a different local anesthetic for each block (4). Patients experiencing true facetogenic pain will have complete relief of their pain following medial branch block for the duration of the local anesthetic (4). With successful diagnostic medial branch blocks and proper needle placement, a prospective cohort study by Dreyfuss et al (5) found that radiofrequency neurotomy of the medial branch nerves of the lumbar facet joints provided at least 80% relief in 60% of patients at 12 months, and at least 60% relief in 80% of patients at 12 months.

The standard procedure for the management of lumbar facet disease is thermal radiofrequency ablation (RFA) that consists of generating a lesion at 80° Celsius for 60 – 90 seconds (6,7). This has been shown to provide maximal thermal coagulation of the lumbar medial branch of the dorsal ramus (8). One of the potential side effects with RFA includes painful cutaneous dysesthesias and increased pain due to neuritis or neurogenic inflammation (9). This pain may require the prescription of opioids or non-opioid analgesics to control post-procedural pain and discomfort. Although pain medications are commonly used to treat post-procedural pain, the availability of alternative options with fewer side effects and risk factors has led to further research.

Pulsed dose radiofrequency (PDRF) was first introduced in 1996 (12). PDRF has been used in treatment of many pain conditions including facetogenic pain, neuralgia, and radicular pain (10,14,15). Research has demonstrated that PDRF selectively targets small diameter C and A$\delta$ nociceptive fibers (16,17). It therefore has been used commonly for peripheral nerve neurotomy (14). Due to its effect on these fibers, it is considered to have an immediate effect on nociceptive pain. PDRF alone is not used independently for neurotomy of the medial branches of the dorsal rami, as it has not been shown to provide a consistent lesion (18).

To the best of our knowledge no studies have compared the pain levels following the addition of PDRF immediately prior to thermal RFA. This study looked at the effects of the addition of PDRF to RFA on post-procedural pain and the requirement of oral analgesic medication usage in the first 48 hours following the procedure.

## Methods

IRB approval was obtained at our institution. Inclusion criteria for this study were as follows: patients with previously diagnosed back pain from facet joint disease, pain for 6 months or greater, with an average pain level of 4 or greater on a numerical pain scale (NPS) where 0 indicates no pain, 5 indicates moderate pain, and 10 indicates severe unbearable pain, and pain not alleviated with conservative therapy including pharmacotherapy or physical therapy.

In addition, each patient possessed decision-making capacity, was able to attend follow-up appointments, and agreed to complete all required documents. Each patient was invited to participate in the study in the pain clinic by an investigator and an explanation of the study was provided. Informed consent was then obtained.

Exclusion criteria were applied to those who participated in other trials during the study period and other trials involving back pain in the past. Patients with poorly controlled systemic diseases including cardiovascular, hepatic, renal, hematologic, and/or neurologic conditions, severe depression, coagulopathies, and/or were on anticoagulants were excluded. Patients who had other significant sources of chronic pain, complex regional pain syndrome (CRPS), fibromyalgia,

rheumatoid arthritis, or chronic fatigue syndrome were excluded. Patients who reported consuming greater than 2 alcoholic drinks and patients who reported recreational drug use were also excluded.

Patients who met the inclusion criteria and were enrolled were required to have 2 positive diagnostic medial branch blocks in order to be randomly assigned to one of the treatment groups. Diagnostic medial branch blocks were performed once with 0.5 mL of 1.5% lidocaine and once with 0.5 mL of 0.5% bupivacaine. The authors chose to maintain tight diagnostic criteria using double comparative diagnostic blocks to prevent the false-positive results from obscuring the accuracy of enrolling patients with true zygapophyseal joint disease. A positive diagnostic medial branch block was defined as greater than 80% pain relief for at least 2 hours with lidocaine and at least 4 hours with bupivacaine.

Sixty patients were initially recruited to participate in this study. Five were excluded due to the failure of the dual diagnostic medial branch blocks. The remaining 55 patients were randomly assigned to either the standard therapy group (group 1) or the investigational group (group 2). Patients in group 1 (n = 26) received only thermal radiofrequency neurotomy (RFN) of the medial branches supplying the effected zygapophyseal joint, while patients in group 2 (n = 29) received PDRF lesioning followed by thermal RFN. Five patients in group 1 and 3 patients in group 2 were lost to follow-up (Fig. 1).

## The Procedure

All of the procedures were performed in a hospital-based procedure suite at the Pain Clinic at our institution. A single Board Certified Pain Medicine physician performed all the procedures. This allowed for minimization of variation based on differences of technique between different physicians.

Patients were placed in the prone position on a fluoroscopy table, the skin over the lumbar region was prepped and draped using sterile technique with 4% Chlorhexidine gluconate as an antiseptic solution. The target of the lumbar median branch block was identified using fluoroscopy in the anteroposterior (AP), oblique, and lateral views according to SIS guidelines. A 27 gauge (G) needle was used to infiltrate the skin of the target areas with 1% lidocaine, for each target nerve. A 21 G, 100 mm needle with 5 mm active tip (Baylis Medical Company Inc.) was introduced towards the most superior and medial part of the transverse process. The target for RFN was the junction of the superior
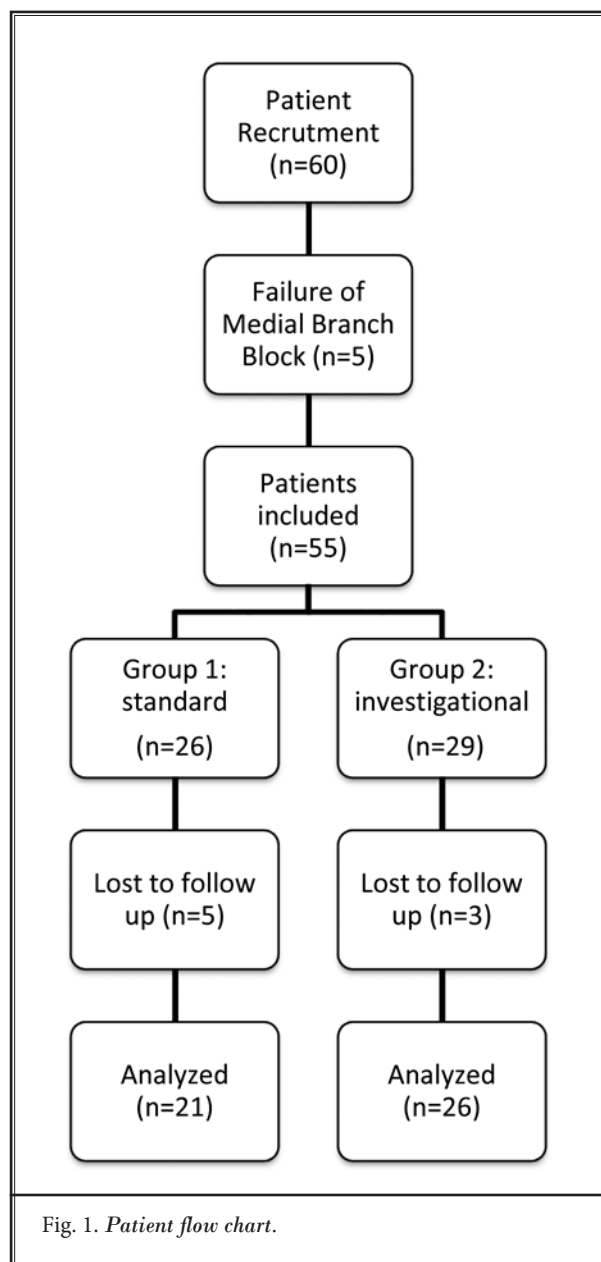


Fig. 1. *Patient flow chart.*

articular process and the transverse process. At the level of dorsal ramus, the target needle was directed towards the junction of the superior edge of the sacral ala and superior articular process.

Confirmation of the position of needle was performed in AP, oblique, and lateral views to ensure that the tip of the needle did not pass beyond the anterior edge of the superior articular process towards the neural foramina. The oblique view confirmed the needle

orientation was parallel to the course of the medial branch nerve. After confirmation that the needle was in the appropriate position, a radiofrequency generator (NeuroTherm® NT2000iX radiofrequency generator) to was used to stimulate the target nerve. The electrode was set to stimulate the target nerve with a pulse of 1-msec duration at 5 Hz. The patient was asked to report pain or pressure sensation that was similar to the pain that they normally experience. If the sensory stimulation did not reproduce their pain at 0.6 V or less then the needle was repositioned and the sensory stimulation would be repeated until a positive sensory stimulation below 0.6 V could be elicited. Motor stimulation was obtained to confirm that there was no muscle contraction in the lower extremity on the side of the procedure.

Once the electrode was in the optimal position, 2 mL of 0.25% bupivacaine was infiltrated in each needle before radiofrequency therapy was applied. The investigational group (Group 2) underwent PDRF treatment immediately after infiltration with bupivacaine. The pulsed wave was set for the tip of the electrode at 42°Celsius (C) at 2 Hz and the lesion occurred for 240 pulses. At the same point in the procedure, group 1 experienced a pause in the procedure of 120 seconds to normalize the procedure length between the 2 groups and remove the duration of PDRF as a confounder. Both groups then underwent radiofrequency neurotomy at 80°C for 90 seconds. This procedure was repeated at each segmental level based on the previous levels of the medial branch blocks.

To obviate bias, the patients, physician, and the co-investigator collecting the data were all blinded. Patients were blinded as to which group they were assigned. The physician was blinded to the results as the study progressed. The co-investigator collecting the data was aware of which group the participants were assigned, but was blinded as to which group received RFA alone and which received both PDRF and RFA. Prior to the procedure, all patients were interviewed by the same co-investigator to explain the process of the study and provided a copy of the NPS questionnaire. Patients were contacted by phone on post-procedural days 1 and 2 in the morning (AM) and afternoon (PM) by the same co-investigator to complete an IRB approved questionnaire. Patients were asked to rate their pain using the NPS in the morning, after waking up from sleep, and evening, before going to bed at night. Patients were also asked what medication and dosage they used for pain control during the first 48 hours.

## Statistical Analysis

Descriptive statistics were conducted to summarize the 2 groups with regard to pain at different time points. A repeated measure analysis of variance programmed in SAS (PROC MIXED) was used to test for changes in pain levels over time between the 2 groups. Fisher's exact test was used to compare pain medication usage in both groups on post-procedure day 1 and 2. All the statistical analyses were conducted using SAS 9.3.1. A P-value of $\leq 0.05$ was considered statically significant.

## Results

Sixty patients were enrolled in the study. Five patients were subsequently excluded for having non-diagnostic medial branch blocks. The remaining 55 patients were randomly assigned to either group 1 or group 2. Seventy-five levels of ablation were performed in group 1 and 85 levels of ablation were performed in group 2 (Table 1). Patients in group 1 had a median

Table 1. *Levels of radiofrequency ablation*.

| Levels of Ablation | Group 1 (standard) | | Group 2 (investigational) | |
|---|---|---|---|---|
| | (n=procedures) | (n=levels) | (n=procedures) | (n=levels) |
| Left L2-5 | 1 | 4 | | |
| Left L3-5 | 7 | 21 | 6 | 18 |
| Right L2-5 | 1 | 4 | 2 | 8 |
| Right L2-4 | 2 | 6 | | |
| Right L3-5 | 12 | 36 | 16 | 48 |
| Right L4-5 | 1 | 2 | 1 | 2 |
| Bilateral L5 | 2 | 2 | 3 | 3 |
| Bilateral L3-5 | | | 1 | 6 |
| TOTAL | 26 | 75 | 29 | 85 |

age of 52.4 years, median body mass index (BMI) of 36.6 kg/m2, and a median pain level of 6.96 ± 2. Patients in group 2 had a median age of 50.1 years, median BMI of 35.4 kg/m2, and an average pain level of 6.06 ± 1.6 (Table 2).

A total of 8 patients were lost to follow-up. Five were lost in group 1 and 3 were lost in group 2. Our results showed that patients in group 1 who received only thermal RFA at 80°C for 90 seconds reported pain levels of 4.43 ± 2.9 on Day 1 AM and 4.80 ± 3.2 on Day 1 PM, followed by 3.86 ± 2.8 on Day 2 AM and 3.90 ± 2.7 on day 2 PM. Group 2 patients whom received PDRF lesioning at 42°C for 120 seconds followed by thermal RFA at 80°C for 90 seconds had pain levels of 2.38 ± 2.4 on Day 1 AM and 3.08 ± 2.8 on Day 1 PM, followed by levels of 2.31 ± 2.7 on Day 2 AM and 2.60 ± 2.4 on Day 2 PM.

Patients in Group 2 demonstrated statistically significantly lower pain scores on Day 1 AM, with a P-value of 0.01 (Fig. 2). The differences between group 1 and group 2 at Day 1 PM, Day 2 AM, and Day 2 PM were slightly outside of statistical significance with P-values of 0.06, 0.06, and 0.09, respectively (Table 3). The analysis of variance score for Day 1 AM was 0.41, and for Day 2 PM was 0.59. For Day 2 AM the analysis of variance score was 0.80, and for Day 2 PM was 0.59.

In group 1, 38% of the patients reported the use of pain medication after the procedure, while in group 2 only 15% of the patients reported the use of pain medication after the procedure, with a *P*-value of 0.1 (Fig. 3). These pain medications included tramadol, ibuprofen, acetaminophen, naproxen, oxycodone, and/or aspirin.

Table 2. *Demographics*.

| Demographics (n subjects = 55) | | |
|---|---|---|
| | Group 1 (standard) | Group 2 investigation) |
| Gender (% female) | 77% | 75% |
| Age (years) | 52.4 ± 8.5 | 50.1 ± 12.1 |
| BMI (kg/m3) | 36.6 ± 11.2 | 35.4 ± 9 |
| BMI> 30 | 62% | 69% |
| Baseline pain score | 6.96 ± 2 | 6.06 ±1.6 |



Fig. 2. *Reported pain levels on post-procedural Day 1 and Day 2.*
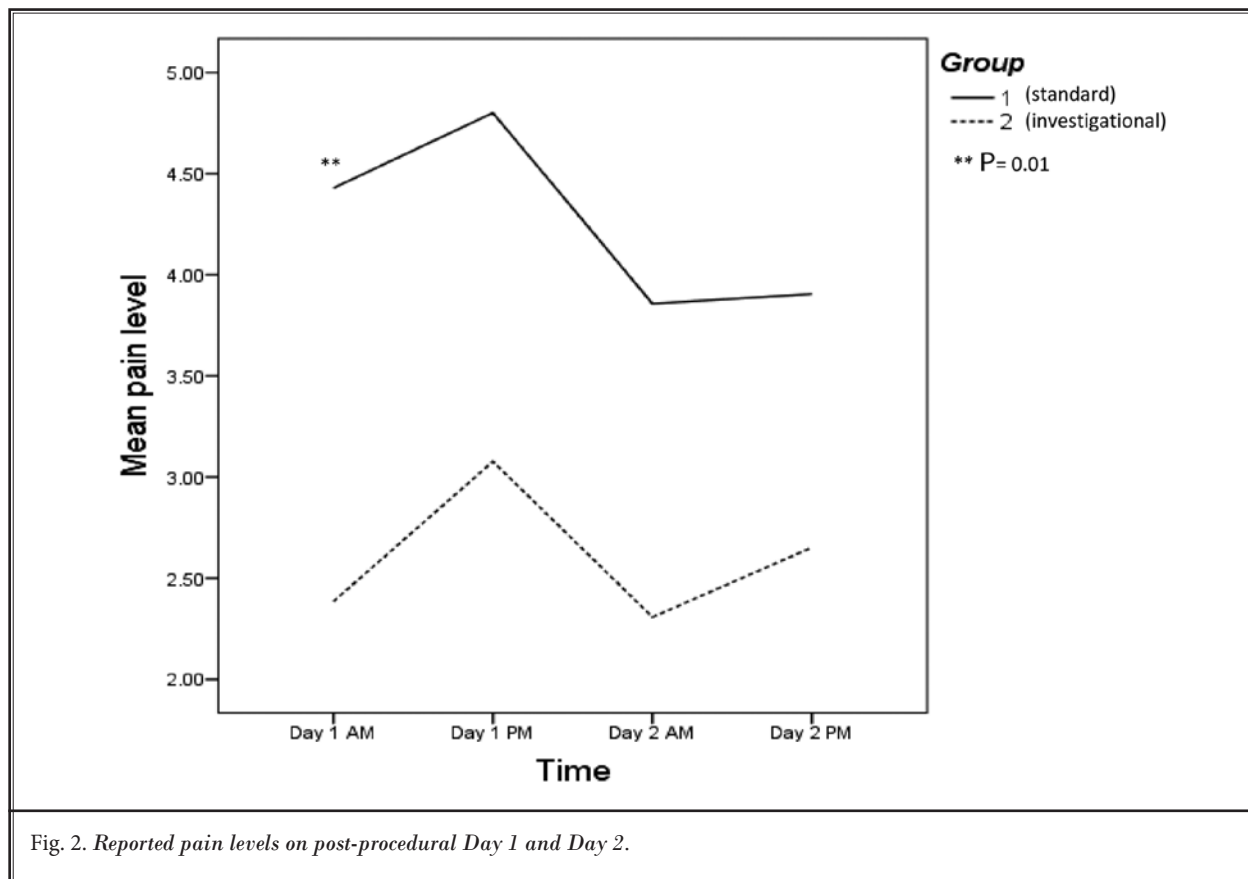
## Discussion

RFA treatments have been used for over 30 years for a variety of pain syndromes: cervicogenic headaches, whiplash injury, intercostal neuralgia, mechanical low back pain due to zygapophyseal joint dysfunction, discogenic pain, and pain associated with the sacroiliac joint (SIJ) (10,11). PDRF procedure on a lumbar dorsal root ganglion was first introduced in 1996 (10,12,13). Since the late 1990s, PDRF has been used for the treatment of many pain conditions, including cervical and lumbar radicular pain, trigeminal neuralgia, SIJ pain, zygapophyseal joints dysfunction, shoulder pain, and groin pain (11,14-16,18)

There are 2 types of RF procedures that are generally accepted. The first category consists of procedures where thermal RF is the standard of care, such as for thermo-coagulation of the medial branch of the dorsal ramus. The second category consists of PDRF treatment for peripheral neuropathies, arthrogenic pain, painful trigger points, and of the dorsal root ganglion in patients with chronic neuropathy or radiculopathy (15).

It has been generally accepted that thermal RF stimulation generates heat lesions of neural substrates above 45°C, resulting in nonselective destruction of both myelinated and nonmyelinated nerve fibers (18). PDRF is believed to have a different mechanism of action, offering other neurobiological effects (19). PDRF induces physiologic changes at the neurologic level. Recording of c-Fos activation, a marker for neuronal activity in the rat dorsal horn, has been found as soon as 3 hours following PDRF and up to 7 days following treatment (20,21). The inhibition of excitatory C-fiber responses due to electrical stimulation has previously been attributed to lead to an increased duration of Fos-like immunoreactivity (17). The biological effect of PDRF is not due to neurological thermal damage, but its selectivity for targeting small-diameter C- fibers and $A\delta$ nociceptive fibers (16).

Research has been aimed at developing RF treatments that limit complications, such as neuritis and chronic neuralgia. Although some reviews have demonstrated conflicting outcomes and evidence on PDRF, it is well accepted that PDRF has demonstrated a decrease in complications during the treatment of peripheral neuropathies (12,13,15,17-21). PDRF has not demonstrated an improvement in long-term outcomes, but has the potential to reduce acute post-procedural pain due to its effect on C-fibers and $A\delta$ nociceptive fibers (16,17).

The purpose of our study was to determine if the use of PDRF, immediately prior to thermal RFA, would reduce acute post-procedural pain and/or reduce the amount of analgesic medication used in the post-procedural period. To the best of our knowledge, there has not been a prospective, double-blinded, randomized, controlled study comparing post-procedural pain levels in the first 48 hours after thermal RFA and thermal RFA preceded by PDRF. The major finding of this study is that patients who received PDRF prior to RFA

Table 3. *Pain levels on post-procedural Day 1 and Day 2.*

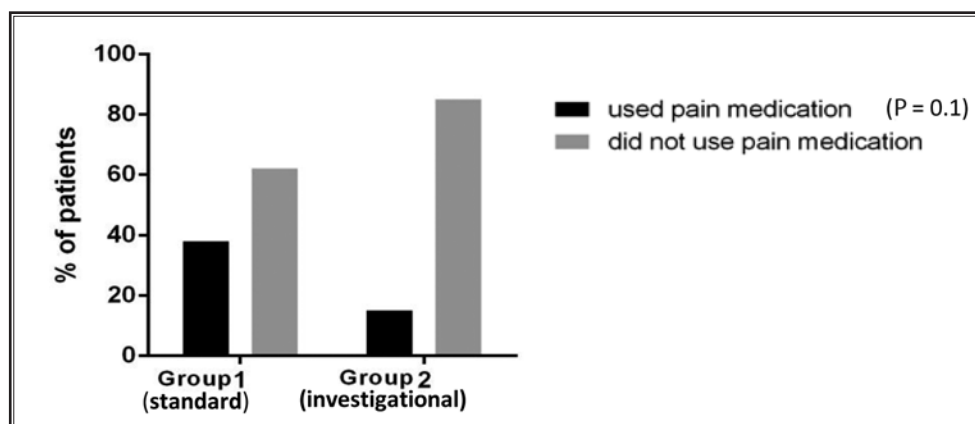| Time | Pain level (μ ± SD) | | Test of variance | *P* value |
|---|---|---|---|---|
| | Group 1 (n = 212) | Group 2 (n = 26) | | |
| Day 1 AM | 4.43 ± 2.9 | 2.38 ± 2.4 | .041 | 0.01 |
| Day 1 PM | 4.80 ± 3.2 | 3.08 ± 2.8 | 0.59 | 0.06 |
| Day 2 AM | 3.86 ± 2.8 | 2.31 ± 2.7 | 0.8 | 0.06 |
| Day 2 PM | 3.90 ± 2.7 | 2.60 ± 2.4 | 0.59 | 0.09 |



Fig. 3. *Percentage of post-op pain medication use in each group.*

reported statistically significantly less pain in the first 24 hours following the procedure. This is the first study to present data demonstrating a potential advantage to adding PDRF immediately prior to thermal RFA. This is due to the biological effect of PDRF on small-diameter C and A$\delta$ nociceptive fibers (17).

Furthermore, group 2 patients used 39.5% less analgesic medication post-procedurally than group 1 patients that underwent RFA alone. Although the *P*-value exceeded the cutoff for significance ($P = 0.1$), a reduction in post-procedural analgesic medication usage is an important clinical finding as these medications, including opioids, have a large adverse effect profile, particularly at high doses. These data support our hypothesis that the addition of PDRF to the thermal RFA reduces the usage of post-procedural analgesic medication, especially within the first 24 – 48 hours.

Combining PDRF and thermal RFA current did not delay the procedure time. It is common practice among pain physicians to allow 45 – 120 seconds before starting RF lesioning after infiltration of local anesthetic to the vicinity of medial branch of the dorsal rami. This time was utilized by proceeding with the PDRF current immediately following local anesthetic infiltration. During PDRF there is application of a full pulse at full amplitude for a specified number of pulses. In our study the PDRF mode was set at 42°C for 240 pulses at 2 Hz. This required between 90 – 120 seconds. On average, there was no significant prolongation of the procedure time. Although the level of pain during the procedure was not assessed, the authors were never made aware of any increase in pain during the PDRF.

A limitation to the generalizability of this study was that it was performed by one board accredited pain physician at one center. To minimize the effects of these factors, the pain physician strictly followed SIS guidelines. Future studies to further validate these findings may include studies with a similar design conducted at multiple centers by multiple pain physicians. It is not implausible that patients undergoing ablation of multiple levels may have experienced increased pain during the study time period. Accordingly, another limitation is that the study was not designed to directly consider the number of levels of ablation the study's participants had undergone in the comparison of pre- and post-procedural pain levels and post-procedural analgesic use. Other limitations of this study included that the procedures were exclusively performed using a Neuro-Therm© radiofrequency generator at a setting for the tip of the electrode at 42°C, and the lesion occurred for 240 pulses. Future studies may examine different pulse doses, frequencies, and other manufacturers' settings.

Future studies into the application and benefits of PDRF may include a larger sample size and long-term follow-up; however, using the SAS protocol, a study size of 55 patients did provide statistically significant data which could be applicable to the larger population.

## Conclusions

In conclusion, this study has demonstrated that the addition of PDRF to thermal RFA of the medial branches of the dorsal rami significantly reduces pain within the first 24 hours following the procedure. The addition of PDRF did not prolong the procedure, as it was performed during the typically allotted time for local anesthetic action. Finally, the addition of PDRF clinically demonstrated a reduced amount of post-procedural analgesic medication used during the initial time period.

### Resolution of Conflicts

There were no conflicts of interest to report in regards to this study. The authors alone were responsible for the content of this article. They have no relation, nor received any compensation, from any companies associated with the procedures or study.

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