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ORIGINAL ARTICLE

Twelve-Month Follow-Up of a Randomized Trial Assessing Cooled Radiofrequency Denervation as a Treatment for Sacroiliac Region Pain

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■ Abstract

Objective: The objective of this study was to report the long-term outcomes of cooled radiofrequency (CRF) lateral branch neurotomy (LBN) as a treatment for sacroiliac (SI) region pain. Whereas the 1-, 3-, 6-, and 9-month outcomes of this procedure compared to sham treatment were previously reported, this current report shows the 12-month outcomes of CRF/LBN treatment for SI region pain.

Design: This study originally included 51 subjects who were randomized 2:1 to receive CRF/LBN treatment or a sham intervention, respectively, for SI region pain. Subjects and assessors were blinded for 3 months. At that time, sham participants were permitted to receive CRF/LBN, designated as "crossover" study subjects, and followed for 6 additional months. For the purpose of this evaluation, the original CRF/LBN-treated study subjects were followed for a total of 12 months. Study participants were 18 to 88 years of age and had chronic (symptomatic for >6 months) axial back pain. All subjects were qualified for study inclusion following positive

responses to dual lateral branch blocks. Lateral branch neurotomy was performed by CRF to ablate the S1 to S3 lateral branches and the L5 dorsal ramus. Pain was measured by a numerical rating scale (NRS) and Short Form 36-bodily pain (SF36-BP) scores. The Oswestry disability index and Short Form 36-physical functioning (SF36-PF) assessment each served to evaluate subject disability. Treatment successes ("responders") in the originally treated CRF/LBN group at 12 months, and in the crossover group at 6 months, were also determined.

Results: In the original CRF/LBN treatment group, 12-month outcomes compared to baseline were favorable, with a mean 2.7 point drop in the NRS score, a 13.9 decrease in the ODI, and a 15.8 increase in SF-36BP. In the crossover study group, 6-month outcomes were also favorable, with a mean NRS score decrease of 2.5 points, a reduction in ODI of 8.8, and an increase in SF36-BP of 11.9.

Conclusions: These favorable 12-month results illustrate the durability of effective CRF/LBN-mediated treatment of SI region pain for selected patients. Furthermore, successful CRF/LBN treatments in unblinded crossover study subjects demonstrate the unlikelihood that such positive outcomes are attributable to a "placebo" effect, and suggest that CRF/LBN is an effective therapeutic option for alleviating pain, and improving physical function and quality of life, with few complications. ■

Key Words: radiofrequency ablation, lower back pain, cooled radiofrequency ablation, sacroiliac pain, sacroiliitis, randomized clinical trial

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INTRODUCTION

Sacroiliac (SI) region pain accounts for up to 20% of all chronic axial low back pain.^{1,2} Increasing evidence has emerged to indicate that SI region-derived chronic low back pain is real^{3,4} and increases in frequency with age.⁴ Presently, there is no reliably effective cure for SI region pain. In randomized studies evaluating peri- and intra-articular corticosteroid injections in patients suspected of having SI region pain, inconsistent results are available as to whether or not they offer any long-term benefit.⁵⁻⁷ Studies evaluating conservative therapies are marred by the lack of controlled studies and adequate pretreatment diagnostic work-ups.⁸ Current management of SI region pain generally involves medications, physical therapy, lifestyle changes, and surgical fusion with varying degrees of success.^{1,9}

In the past several years, radiofrequency (RF) denervation has emerged as a promising treatment alternative for refractory cases of SI region pain.^{3,10} Despite the variability in outcomes, there seems to be relevancy to thermal treatment of the SI region. Possible causes of variable outcomes may be related to inconsistency in anatomical landscape, difficulty in device placement, patient selection, operator dependency, and lack of effective heating ability of utilized tools. The variable innervation courses of the SI region by the purported culprit nervous bundles, namely the S1 to S3 lateral branches and the L5 dorsal ramus, present a potentially broad anatomical target field that may not be lesioned by standard RF probes. Standard (monopolar) RF-mediated delivery of thermal energy is subject to heat-associated impedance and tissue charring, thus limiting the affected area of RF application and accentuating the need for precision of device placement. In contrast, device cooling enables RF technology to reduce such potential limitations, while enabling energy transfer to relatively large fields to enhance the likelihood that pain-generating afferent innervation to the SI region is compromised.

Cooled radiofrequency (CRF) technology is designed to create a larger, more efficient heating profile by eliminating excessive heating and cumbersome placement issues associated with previous treatments. A growing body of literature supports the use of CRF denervation as a treatment option offering long-term relief from pain.¹⁰⁻¹³ For example, in a temperature monitoring study, Wright et al.¹⁴ investigated CRF in a clinical setting to evaluate safety and effectiveness and to determine treatment parameters. The investigators

determined that the relatively large area of neurodestruction afforded by CRF made it likely that pain transmission could be eliminated. This study also determined that CRF provides appropriate temperatures for neuroablation in the region lateral to the sacral foramina, while temperatures in the region of the spinal nerve remain safe. Furthermore, a pilot study involving 15 patients who were treated with CRF for SI region pain showed clear clinical and statistically significant pain dissipation and functional capacity improvement within 4 weeks of treatment.¹⁵ Ten of 15 patients had their pain reduced by more than half, and this pain reduction was sustained for the duration of the 6-month study.¹⁵ Although these outcomes support CRF to effectively treat SI region pain, there were no sham-treated populations included to consider the impact of a potential “placebo effect” on the study end points.

To distinguish between the effects of CRF treatment and placebo on relevant outcomes related to SI region pain, Cohen performed the first randomized-controlled trial utilizing CRF.¹⁰ In this study at 3 months following procedures, the CRF-treated group had a pain score decrease of 3.7 compared to a reduction of 0.6 for the sham group, establishing CRF neurotomy as a nonplacebo, viable clinical option to treat refractory SI region pain.

A second randomized, placebo-controlled study to evaluate the effectiveness of CRF-mediated lateral branch neurotomy (LBN) to treat SI region pain was conducted by Patel and colleagues.¹⁶ Fifty-one subjects were randomized on a 2:1 basis to CRF/LBN and sham groups, in which the latter experienced the same procedures as the treatment group, except that RF energy was not delivered after CRF probe placement. Study outcomes, including pain, disability, physical function, quality of life, and, as defined by the study protocol, treatment success, were evaluated at 1, 3, 6, and 9 months following interventions and reported.¹⁶ Subjects and coordinators were blinded to randomization until 3 months, and sham group participants were allowed to crossover to CRF/LBN after that time. The original CRF/LBN treatment group showed significant improvements in all outcomes, compared to the sham group, while the crossover group also showed evidence of CRF/LBN effectiveness.

To demonstrate the durability of CRF/LBN treatment for SI region pain, this current report displays 12-month outcomes for the original CRF/LBN group from the study conducted by Patel et al.¹⁶ Additionally, detailed analyses of CRF/LBN effectiveness assessments

6 months post-treatment are shown for the crossover group. This approach to data presentation does not set a precedent in the field of pain management, as Kemler and colleagues previously published their initial and longer follow-up results concerning spinal cord stimulation for complex regional pain syndrome at two different times in two different journals.^{17,18}

METHODS

Approval for this study was obtained from the Patient Advocacy Council Institutional Review Board (Mobile, AL, U.S.A.), and all patients provided written informed consent prior to study entry.

Full explanations of the general methods and characteristics of patients included in this randomized study were provided in a previous publication that described the 1-, 3-, 6-, and 9-month outcomes of the original CFR/LBN group and some outcomes of the crossover group.¹⁶ Highlights of those study details as applicable to this 12-month follow-up report concerning the original CFR/LBN treatment group, and of the crossover study subjects 6 months after CFR/LBN, are provided below. This study was conducted in a private practice pain management department of an ambulatory center.

Study Design

Fifty-one individuals with SI region-derived (see below) chronic (symptomatic >6 months) low back pain participated in this study. From the beginning of the study, 34 subjects were placed in the CRF/LBN treatment group and 17 in a comparative sham group. Three months after sham or CFR/LBN treatments, sham study subjects were offered the option to receive CRF/LBN treatment. Those who opted for such treatments were referred to as “crossover” study subjects and were followed for 1, 3, and 6 months. While no prescribed co-interventions (eg, analgesic medications) were indicated for either the subject group originally treated by CRF/LBN or the crossover subjects, CRF/LBN acted as a rescue option for the latter group. This report shows outcome assessment results at 12 and 6 months after CRF/LBN treatment for originally treated and crossover study subjects, respectively.

Recruitment and Screening

No financial inducements were provided for participation in the study. The inclusion criteria were as follows:

predominantly axial pain below the L5 vertebrae; axial pain lasting longer than 6 months; 3-day average numerical rating scale (NRS) score^{19–21} between 4 and 8; age greater than 18 years; failure to achieve adequate improvement with comprehensive nonoperative treatments, including, but not limited to, activity alteration, nonsteroidal anti-inflammatory, physical and/or manual therapy, and fluoroscopically guided injections of steroids into the SI region; other possible sources of low back pain reasonably excluded (by means of physical exam, medical history, and magnetic resonance imaging/computed tomography/X-ray as required), including but not limited to bone fractures, the hip joint, symptomatic spondylolisthesis, tumor, and other regional soft tissue structures. Patients with history of potentially confounding intervertebral disk disease or zygapophysial joint pain were excluded, but discography and/or medial branch blocks were not uniformly used to screen for these conditions.

The exclusion criteria were as follows: a Beck’s Depression Inventory score of greater than 20; irreversible psychological barriers to recovery (ie, individuals considered to be mentally incapacitated such that delivery of reliable subjective feedback to fulfill study end points was deemed not possible); spinal pathology that may impede recovery such as spondylolisthesis at L5/S1, or scoliosis; symptomatic moderate or severe foraminal or central canal stenosis; systemic infection or localized infection at anticipated introducer entry site; concomitant cervical or thoracic pain >2/10 on a NRS scale; uncontrolled or acute illness; chronic severe conditions such as rheumatoid/inflammatory arthritis; pregnancy; active radicular pain; immunosuppression (eg, acquired immunodeficiency syndrome, cancer, diabetes, surgery <3 months ago); worker’s compensation, injury litigation, or disability remuneration; allergy to injectates or medications used in the procedure; high narcotics use (>30 mg morphine daily or equivalent); active smokers (termination for at least 6 months with no smoking during follow-up period were acceptable with caution); subject unwillingness to consent to the study.

Subjects meeting all of the aforementioned criteria were then screened with 2 sets of multisite, multidepth anesthetic blocks by injections with bupivacaine on the symptomatic side.²² Patients with bilateral symptoms were blocked bilaterally. The lateral branches of S1 to S3 were blocked using C-arm fluoroscopy, and the dorsal ramus of L5 was subsequently blocked, as described in the International Spine Intervention Society

(ISIS) practice guidelines.²³ Total volumes of bupivacaine did not exceed 2 mL for unilateral injections and 4 mL for bilateral injections. At each injection site, 0.3 mL of bupivacaine was expressed. Corticosteroids were not administered, and sedation was not recommended around the time of the diagnostic blocks. Subjects were required to have greater or equal to 75% relief of their index pain for at least 4 hours following diagnostic injections,²⁴ to be considered as having a positive response to the block. This blocking protocol was repeated on a separate day, after a return to baseline pain. Subjects achieving 75% relief of their index pain after both blocks were required to return to baseline pain before entry into the study.

Treatment Procedure

Detailed descriptions of navigation to the anatomical targets subjected to CRF/LBN treatment are provided in the “Randomization and Primary Treatment” section of the publication¹⁶ that presented the earlier outcomes of this study. Additionally, a diagram comparing the thermal lesion fields between conventional (noncooled) and cooled RF for ablating the target lateral branch nerves is shown in the previous report¹⁶ concerning this study.

Treatment procedures were performed in a fluoroscopy suite equipped with a C-arm. Preceding CRF/LBN treatment, study subjects received local anesthetic and moderate sedation. The generator operator controlled RF application to each subject. The L5 dorsal ramus was lesioned with a CRF SInergy probe (Kimberly-Clark Health Care, Roswell, GA, U.S.A.). Once accurate electrode placement was confirmed, 0.5 mL of 2% lidocaine and 0.5 mL of 0.75% bupivacaine were injected through the introducer to reduce discomfort. Radiofrequency energy was then applied for 150 seconds at a set temperature of 60°C using a Pain Management Radiofrequency Generator (Kimberly-Clark Health Care). The 60°C RF generator setting adjusts the probe surface to this temperature accordingly, while the lesioned tissue may reach temperatures between 75 and 80°C as a result. After coagulation of the L5 dorsal ramus, the sacral lateral branches of S1, S2, and S3 were serially targeted by RF energy for 150 seconds at 60°C. Subjects requiring bilateral treatment received contralateral RF treatment during the same procedural session.

Postlesioning, 1 mL of a 1:1 mixture of 2% lidocaine and 0.75% bupivacaine was given at each intervention-

targeted spinal level to control pain in the immediate postoperative period. Subjects were prescribed analgesics for postoperative pain. Activity was avoided the day of the procedure, and excessive activity was avoided for 1 to 3 days following the procedure.

Outcome Measures and Follow-Up

Outcome measurements were determined by several instruments, including the NRS^{19–21} and Short Form (version 1) 36-Bodily Pain (SF36-BP) assessment for pain,^{25–27} the Oswestry disability index (ODI)^{28,29} and Short Form 36-physical functioning (SF36-PF) assessment for disability,^{25–27} and the Assessment of Quality of Life (AQoL) for quality of life evaluation.³⁰ These end points as well as treatment success or “responder” rates were calculated for 12- and 6-month follow-ups for the original CRF/LBN and crossover treatment groups, respectively. Treatment successes or “responders” were defined per the protocol of this study as those study subjects who experienced a drop in the NRS score $\geq 50\%$, and at least one of the following: (1) at least a 10-point increase (improvement) in SF36-BP or (2) at least a 10-point decrease in the ODI. Clinically relevant treatment successes or “responders” were those individuals who had a drop in the NRS score ≥ 2.5 ,³¹ or a reduction in the ODI score of 10 or greater.³² Positive score changes in SF36-PF and AQoL each indicated CRF/LBN treatment-related improvements in the study subjects.

Statistical Measures and Origin of Data

Means and standard deviations were calculated for continuous variables that described outcomes for originally treated patients at baseline, 3 and 12 months. Crossover patients were calculated at baseline and 6 months and were compared by performing a one-way analysis of variance (ANOVA) (statistical significance: $P \leq 0.05$) followed by the Bonferroni correction method (statistical significance: $P \leq 0.017$ (ie, $P \leq 0.05/3$ groups) (Tables 1 and 2) or Student’s paired *t*-test ($P \leq 0.05$; Table 3). Results for proportions are reported as percentages, followed by confidence intervals calculated at the 95% level.

Unlike the previous article that reported results for this study,¹⁶ the last observation carried forward (LOCF) method of data imputation was *not* used to calculate subsequent results. Outcomes for this report were considered only from those study subjects who fully completed the study, which included 25 of 34

Table 1. Assessments of Originally Treated Study Subjects 12 Months Following CRF/LBN: Pain, Disability, Physical Functioning, and Quality of Life

Outcome*	Mean Baseline Value (SD)	Mean 12-Month Value (SD)	Statistically Significant Difference?***	12-Month Change from Baseline (SD)	Clinically Relevant Change?***
NRS (25)	5.9 (1.2)	3.2 (2.6)	Yes ($P < 0.0001$)	-2.7 (2.6)	Yes
ODI (24)	35.2 (13.8)	21.3 (18.6)	Yes ($P = 0.0003$)	-13.9 (20.8)	Yes
SF36-BP (23)	43 (16)	58.8 (26.4)	Yes ($P = 0.006$)	15.8 (30.5)	N/A
SF36-PF (23)	50.9 (19.3)	68.3 (23.3)	Yes ($P < 0.0001$)	17.4 (22)	N/A
AQoL (24)	0.62 (0.19)	0.69 (0.24)	No ($P = 0.021$)	0.07 (0.15)	N/A

SD, standard deviation; N/A, not applicable.

*Outcome measurements were products of various instruments: NRS, numerical rating scale; ODI, Oswestry disability index; SF36-BP, Short Form 36-bodily pain; SF36-PF, Short Form 36-physical functioning; AQoL, assessment of quality of life. Parenthetical value next to each outcome indicates number of applicable study subjects (N). Results of one-way ANOVA F -tests produced values of $P \leq 0.05$ when means for each measured parameter at baseline and 12 months were simultaneously compared.

**Based on Bonferroni's correction at $P \leq 0.017$.

***Based on NRS³⁰ and ODI.³¹ See text for meaning of "clinically relevant change."

Table 2. Comparisons of 3-Month to 12-Month Assessments of Originally Treated Study Subjects Following CRF/LBN: Pain, Disability, Physical Functioning, and Quality of Life

Outcome*	Mean Score at Three Months (SD)	Mean Score at 12 Months (SD)	Statistically Significant Difference?***
NRS (25)	3 (2.8)	3.26 (2.6)	No ($P = 0.62$)
ODI (24)	22.4 (16.4)	21.3 (18.6)	No ($P = 0.75$)
SF36-BP (23)	61.74 (26.7)	58.8 (26.4)	No ($P = 0.60$)
SF36-PF (23)	68.3 (22.9)	68.3 (23.3)	No ($P = 1$)
AQoL (24)	0.72 (0.224)	0.69 (0.24)	No ($P = 0.24$)

SD, standard deviation.

*Outcome measurements were products of various instruments: NRS, numerical rating scale; ODI, Oswestry disability index; SF36-BP, Short Form 36-bodily pain; SF36-PF, Short Form 36-physical functioning; AQoL, assessment of quality of life. Parenthetical value next to each outcome indicates number of applicable study subjects (N). Results of one-way ANOVA F -tests produced values of $P \leq 0.05$ when means for each measured parameter at 3 and 12 months were simultaneously compared.

**Based on Bonferroni's correction at $P \leq 0.017$.

Table 3. Assessments of Crossover Study Subjects 6 Months Following CRF/LBN: Pain, Disability, Physical Functioning, and Quality of Life

Outcome*	Mean Baseline Value (SD)	Mean Six-Month Value (SD)	Statistically Significant Difference?***	Six-Month Change from Baseline (SD)	Clinically Relevant Change?***
NRS (16)	5.8 (1.3)	3.3 (2.1)	Yes ($P = 0.0003$)	-2.5 (2.2)	Yes
ODI (14)	34.4 (10.6)	25.6 (13)	Yes ($P = 0.05$)	-8.84 (15.5)	No
SF36-BP (15)	42.9 (10.2)	54.8 (18.6)	Yes ($P = 0.05$)	11.9 (21.4)	N/A
SF36-PF (15)	47.5 (25.2)	58.8 (29)	Yes ($P = 0.04$)	11.3 (19.7)	N/A
AQoL (13)	0.52 (0.14)	0.63 (0.23)	No ($P = 0.07$)	0.11 (0.19)	N/A

SD, standard deviation; N/A, not applicable.

*Outcome measurements were products of various instruments: NRS, numerical rating scale; ODI, Oswestry disability index; SF36-BP, Short Form 36-bodily pain; SF36-PF, Short Form 36-physical functioning; AQoL, assessment of quality of life. Parenthetical value next to each outcome indicates number of applicable study subjects (N).

**Based on Student's paired t -test at $P \leq 0.05$.

***Based on NRS³⁰ and ODI.³¹ See text for meaning of "clinically relevant change."

originally treated subjects by CRF/LBN. These 25 study "completers" attended *all* follow-up visits out to 12 months (previous follow-ups were 1, 3, 6, and 9 months post-treatment). Use of 12-month outcomes of the "completers" was considered to be best to evaluate the durability of the CRF/LBN treatment and was not diluted by earlier study outcomes (ie, 3 or 6 months) derived from those who terminated the study early. The latter data could have been included by LOCF imputation, but would not have most accurately represented outcomes specifically at 12 months. The 9 subjects who terminated participation in the study

prematurely did so because of treatment failures ($n = 4$; ie, voluntary self-withdrawal from study to, in some cases, seek other treatment options), concomitant procedures ($n = 3$; analgesic use, treatment for another illness, and spinal decompression), investigator-initiated discharge from study ($n = 1$; due to another illness), and an enrollment violation ($n = 1$). Regarding crossover subjects, 16 of 17 original sham members elected to have the CRF/LBN procedure. These 16 crossover subjects completed *all* follow-up visits out to 6 months (crossover "completers"; previous follow-ups were at 1 and 3 months post-treatment). For the purposes of data

analysis, the baseline values in the crossover group are the values prior to the sham, not the values at 3 months after sham initiation.

Subjects who did not complete a baseline questionnaire for a particular outcome tool were excluded from consideration for the respective outcome. As such, outcome assessment values for the originally treated CRF/LBN group were based on variable numbers of study subjects as follows: NRS = 25, ODI = 24, SF36-BP = 23, SF36-PF = 23, and AQoL = 24. The study subject totals for crossover data determinations were as follows: NRS = 16, ODI = 14, SF36-BP = 15, SF36-PF = 15, and AQoL = 13. The crossover group was not compared to the original CRF/LBN treatment group, because these groups received CRF/LBN treatments in unblinded and blinded manners, respectively. These different treatment contexts also precluded the combination of data from the treatment and crossover groups.

RESULTS

Origins and Objectives of Current Report

Originally, 304 patients were screened for consideration as subjects in this study. Following screening, 253 patients were excluded, leaving 51 patients to be consented, and randomized by a paper-based exercise on a 2:1 basis into CRF/LBN and sham groups, respectively. The 1-, 3-, 6-, and 9-month pain, disability, physical functioning, quality of life, and overall success rate (1-month rate not provided) results following CRF/LBN or sham treatment were previously made available.¹⁶ The primary end point of this study was the comparison of the NRS between CRF/LBN and sham groups, 3 months following these respective treatments. At this point in the study, all subjects were unblinded, and sham subjects were permitted to receive CRF/LBN treatment. Those sham group individuals that chose to receive CRF/LBN treatment ($n = 16$) are herein referred to as “crossover” study subjects.

This report presents: (1) 12-month follow-up outcomes of pain, disability, physical functioning, quality of life, and treatment success rate for the originally treated CRF/LBN group, and (2) more detail concerning pain, disability, physical functioning, and treatment success rate compared to what was previously presented for crossover subjects at 6 months post-CRF/LBN treatment.¹⁶ Figure 1 displays a summary of the history

of this 12-month CRF/LBN randomized assessment study and a perspective of this current publication in that context.

Pain, Disability, Physical Functioning, and Quality of Life

Evaluations 12 Months following LBN Treatment. Assessment values for outcomes of this study at 12 months following CRF/LBN treatment, and their comparisons to respective outcome values at baseline, are shown in Table 1. Pain evaluation scores at 12 months were significantly improved from baseline values, with a mean NRS score change of -2.7 points, while the mean SF36-BP increased by nearly 16 points. The average ODI score for the CRF/LBN group overall at 12 months was significantly less than at baseline (mean score change = -13.9). The SF36-PF score for the CRF/LBN group at 12 months was statistically greater than it was at baseline (mean score change = 17.4), but the AQoL score was not (mean score change = 0.07).

Treatment Successes or “Responders”. According to the study protocol, “responders” to CRF/LBN treatment were synonymous with being “treatment successes.” Treatment success designations were made based on the protocol of this study, as described in “Methods.”

Forty percent of subjects who received CRF/LBN were considered treatment successes 12 months after treatment, based on NRS+ODI scores. Figure 2 shows detailed analyses according to per protocol treatment success criteria, including that 52% of CRF/LBN subjects met the criterion of experiencing at least a 50% reduction in the NRS score (Figure 2A). Figure 2B shows the NRS scores for each individual in the study at 12 months following treatment. Each study subject score for the ODI and SF36-PF, the other 2 components for determining per protocol treatment success, is demonstrated in Figure 2C, D, respectively. The score combinations of these outcome assessments, namely NRS+ODI or NRS+SF36-BP, that determined whether CRF/LBN group members were considered treatment successes, are provided in Table 4. More subjects were “responders” due to qualifying combinations of NRS+ODI scores than to qualifying combinations of NRS+SF36-BP scores.

Based on the NRS scores, the majority of CRF/LBN study subjects (56%) experienced clinically meaningful

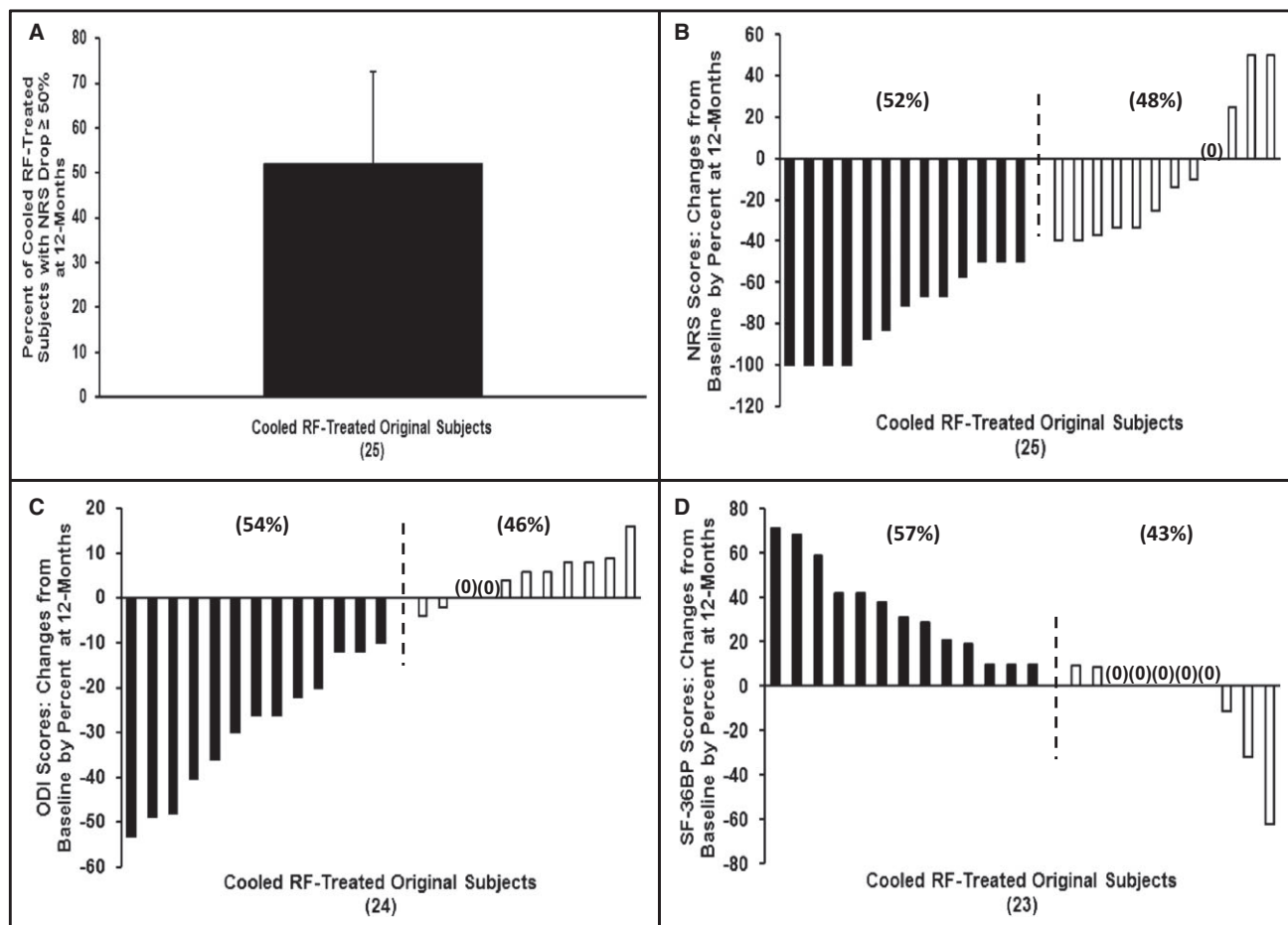


Figure 2. Results of assessment tools used to determine per study protocol treatment success or “responder” are shown. In (A), the proportion of the originally treated CRF/LBN study group “completers,” or those who completed every study follow-up, that recorded a drop in the NRS score $\geq 50\%$ 12 months post-treatment, is illustrated. In (B), the percent change in NRS score for each “completer” at 12 months compared to baseline is shown, while in (C) and (D), the ODI and SF36-BP score changes from baseline to 12 months are shown for each “completer.” In (A), the box indicates mean value, and whisker denotes the 95% confidence interval within which the mean is found. In (B–D), the parenthetical numerical percentage values indicate the proportions of study subjects whose outcome assessment score changes met (left of dotted line) or did not meet (right of dotted line) per protocol requirements for contributing to an individual being considered a “treatment success.” The “(0)” notation indicates the applicable score of a study subject. The parenthetical numerical values indicate the number of subjects from which data were determined.

mean score changes occurred with respect to the NRS (change = -2.5), ODI (change = -8.8), SF36-BP (change = 11.9), and SF36-PF (change = 11.3). Although the mean score change for AQL was in a favorable direction (change = 0.11), the change was not statistically significant.

Treatment Successes or “Responders” Within the Crossover Group

Per the study protocol, 44% of crossover study subjects were considered “responders” to CRF-mediated LBN 6 months after treatment. Detailed presentations of “responder” outcome assessment criteria are provided

in Figure 4, with 56% (A), 50% (B), and 40% (C) of this population having favorable scores changes in the NRS, ODI, and SF36-BP, respectively. Inspections of outcome assessment score changes and their combinations for defining “responders” revealed that 38% and 31% of crossover subjects qualified as being CRF/LBN “responders,” based on the NRS+ODI or the NRS+SF36-BP scores, respectively (Table 5).

Crossover subject clinically meaningful treatment “responders” 6 months after CRF/LBN included 50% of this population, based on a NRS drop that was ≥ 2.5 (Figure 5A). Figure 5B shows these results for each crossover group member. Fifty percent of the crossover group qualified as treatment successes, based on the ODI

Table 4. Identifications and Descriptions of Treatment Successes of Originally Treated Study Subjects after 12 Months

Subject	NRS Score	ODI Score	SF-36BP Score	Treatment Successes: NRS + ODI*	Treatment Successes: NRS +SF-36BP*
1	-100	-48.9	70.8	X	X
2	-83.3	16	9.6		
3	-50	0	0		
4	-33.3	-2	10		
5	50	8.9	-62		
6	0	No Data	No Data		
7	-40	4	9		
8	-50	6	-11		
9	-66.7	-20	0	X	
10	-33.3	6	0		
11	-100	-53.3	68	X	X
12	50	-4	No Data		
13	-37.5	0	29		
14	-100	-26	59	X	X
15	-100	-12	38	X	X
16	-40	8	0		
17	-10	-12	0		
18	-71.4	-36	42	X	X
19	-87.5	-48	42	X	X
20	-50	-30	19	X	X
21	25	8	-32		
22	-14.3	-10	10		
23	-25	-26	10		
24	-66.7	-40.4	31	X	X
25	-57.1	-22	21	X	X
N	25	24	23	10	9
			Success Rate:	10/25 (100) = 40%	9/25 (100) = 36%

NRS, numerical rating scale; ODI, Oswestry disability index; SF36-BP, Short Form 36-bodily pain.

*"X" marks qualifications of success, as indicated.

*Per protocol of this study.

score changes 6 months following CRF/LBN treatment (Figure 4C).

DISCUSSION

It has been established that large lesion RF neurotomy is superior to placebo in 2 explanatory studies comparing CRF to sham at 3 months with no dropouts in either study at the 3-month interval.^{10,16} This particular 12-month follow-up study establishes the durability of CRF for the treatment of SI region pain. The 12-month data express that CRF/LBN treatments in this study are both statistically significant and clinically relevant.

At least 3 pieces of evidence noted in this report support CRF/LBN as a treatment having relatively long-term beneficial effects. First, compared to baseline values, the 12-month outcome assessment values for pain, disability, and physical function were each statistically significantly favorable regarding CRF/LBN treatment. Considering that SI region pain increases with age,⁴ elderly patients would benefit from these treatments. Relief of SI joint pain may mitigate the need for physical therapy, medications, intra-articular injections, and surgery, which are all modalities currently offered, but not rigorously studied.

This study supports “real-world” use of CRF for patients afflicted with SI region pain. Unlike acute pain, where a 3.5 to 4.7 point decrease in pain is required to be clinically meaningful,³¹ an 18 to 19 mm decrease in visual analog scale (VAS)-based pain scores or a 10-point improvement in the ODI is considered clinically relevant in the chronic pain setting.³² Indeed, the International Spine Intervention Society (ISIS) Evidentiary Table assessing Individual Studies of Therapeutic Effectiveness [User Guide V1.0] specifically states “we recommend that the reviewers take the above figures into consideration when analyzing studies of treatment for spine pain, and regard outcome of <2/10 reduction in NRS or 2/100 in VAS as not clinically important.” Fifty-six percent and 54% of the treated study population met the requirements for treatment success at 12 months, according to reductions in the NRS³¹ and ODI³² scores, respectively.

Those individuals designated as “crossovers” formerly consisted of the sham control group until month three of the study. At that point, unblinding occurred, and patients were offered treatment in accordance with the IRB-approved protocol. Ninety-four percent (16/17) of sham subjects opted to receive CRF/LBN treatment after 3 months of the study had passed.

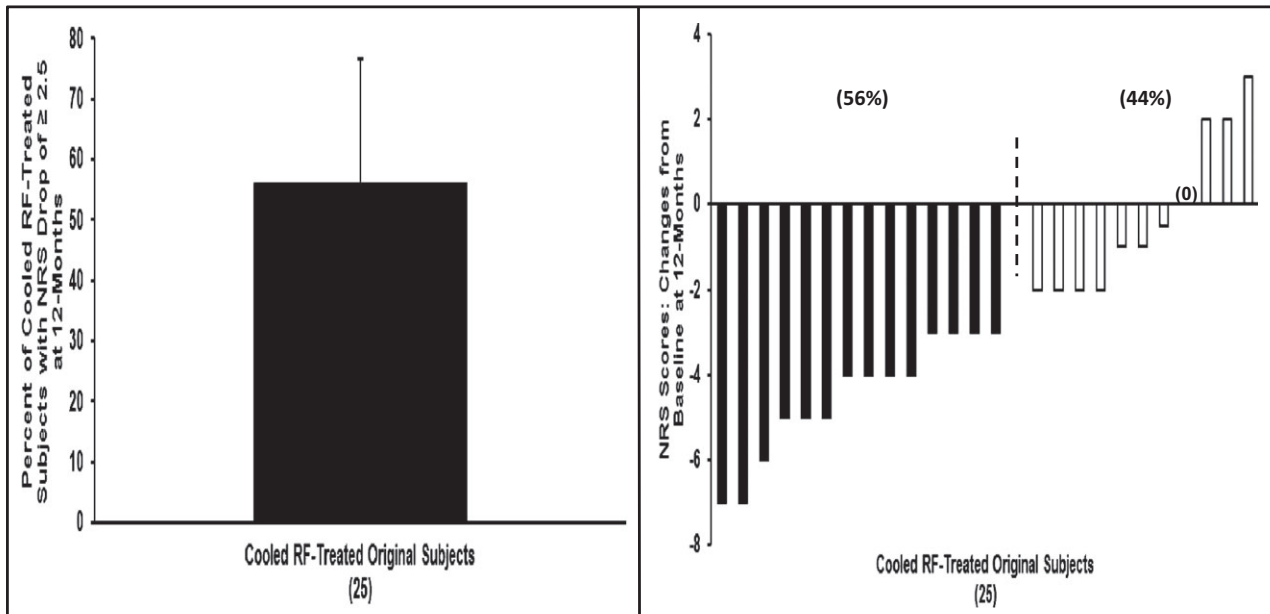


Figure 3. The proportion of the originally treated CRF/LBN study group “completers,” or those who completed every study follow-up, that recorded a NRS decrease ≥ 2.5 points 12 months after treatment is demonstrated (A). In (B), the absolute values of score changes from baseline to 12 months are shown for each “completer.” In (A), the box indicates mean value, and whisker denotes the 95% confidence interval within which the mean is found. In (B), the parenthetical numerical percentage values indicate proportions of study subjects whose NRS score changes met (left of dotted line) or did not meet (right of dotted line) requirements to be considered clinically meaningful “treatment successes.” The “(0)” notation indicates the applicable score of a study subject. The parenthetical numerical values indicate the number of subjects from which data were determined.

The CRF/LBN treatment produced favorable outcomes in this group, with score changes in outcome assessment values for the NRS, ODI, SF36-BP, and SF36-PF that were statistically significant from baseline at 6 months.

Chronic low back pain originating from the SI region is real.^{3,4} Thus, effective, long-lasting treatment is warranted to primarily treat the pain, which should facilitate bodily function and improve quality of life. It is in the best interest of the patient to reduce SI region pain and to maintain that result for as long as possible. Whereas former reports^{10,16} showed that CRF/LBN treatment effectiveness can last for up to 6 months and particular emphasis is given to this current report, given that it shows that CRF/LBN treatment effectiveness can last for up to 12 months. The complicated and variable afferent nociceptive nerve tracks from the SI region present significant challenges for therapeutic strategies that depend upon mechanically mediated nerve ablation. Dreyfuss and colleagues have recognized that the posterior nerve course leading to the SI region is highly variable and requires a multisite, multiddepth approach for blocks to be effective.²² Whereas this report discusses targeting of the L5 dorsal

ramus and S1-S3 lateral branches to enable relief of SI joint-derived pain, others¹⁰ relied on evidence indicating that the SI joint is frequently innervated from S4³³ to deliver RF-mediated pain relief. Given such anatomical uncertainties associated with treating SI region pain by ablation, it is advantageous to produce wide-ranging ablative lesions that will effectively compromise nervous transmission.¹⁴ It should be emphasized that it is the “cooling” aspect of the CRF technology used in this study that is responsible for producing a large-volume lesion, which minimizes the chances of missing the nerves targeted for neurotomy. The previous report concerning this study¹⁶ illustrated that CRF produces a lesion size that is approximately double in diameter compared to that generated by noncooled (conventional) RF. Thus, the probability of success for treating SI region pain appears greater with CRF compared to monopolar RF, as also hinted by Cohen et al.³⁴

In summary, 12-month outcome assessments associated with CRF/LBN treatment for chronic SI region pain have revealed that this can be an effective therapeutic strategy, with long-lasting effectiveness. Roughly 40% to 50% of individuals that undergo this

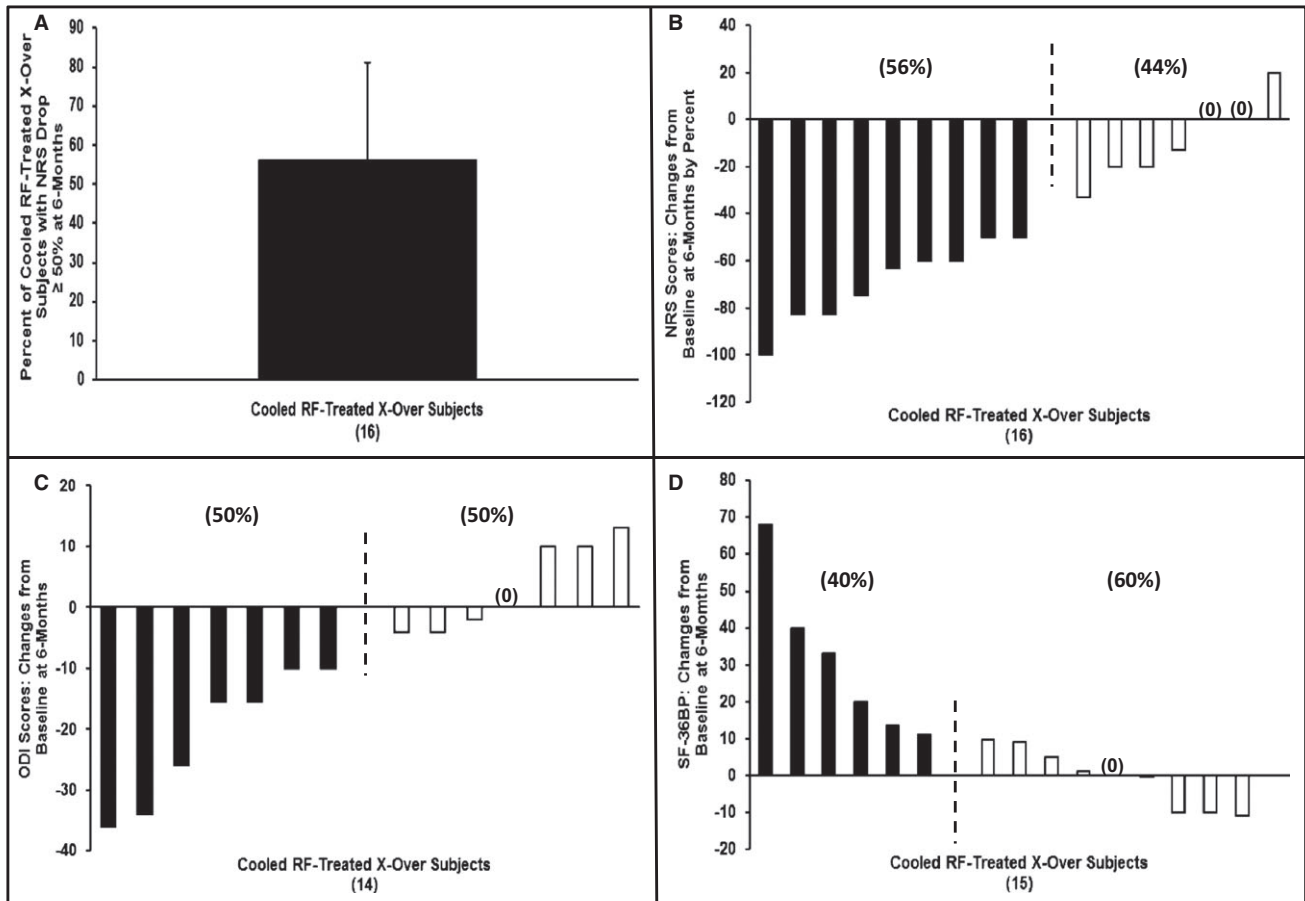


Figure 4. Results of assessment tools used to determine per study protocol treatment success or “responder” are shown. In (A), the proportion of the crossover CRF/LBN study group “completers,” or those who completed every study follow-up, that recorded a drop in the NRS score $\geq 50\%$ 6 months post-treatment, is illustrated. In (B), the percent change in NRS score for each “completer” at 6 months compared to baseline is shown, while in (C) and (D), the ODI and SF36-BP score changes from baseline to 6 months are shown for each “completer.” In (A), the box indicates mean value, and whisker denotes the 95% confidence interval within which the mean is found. In (B–D), the parenthetical numerical percentage values indicate the proportions of study subjects whose outcome assessment score changes met (left of dotted line) or did not meet (right of dotted line) per protocol requirements for contributing to an individual being considered a “treatment success.” The “X” denotes “crossover,” and “(0)” indicates the applicable score of a study subject. The parenthetical numerical values indicate the number of subjects from which data were determined.

treatment in the “real-world” may respond to it favorably. Expected benefits include pain reduction, enhanced physical functioning, and perhaps, an improved quality of life. The durability of this treatment offers convenience for those afflicted with SI region pain at all ages, but especially those who are limited in mobility, time, or have other medical issues that may compromise the use and effectiveness of analgesics or repetitive injections. It is expected that improvements in patient selection for CRF/LBN treatment coupled with increasingly refined techniques for using the CRF device probe will complement the aforementioned “cooling” improvement of RF-mediated ablative therapy to maximize the number of

patients that can be successfully treated with CRF/LBN for SI region pain.

There is additional scope for improvement of outcomes by better patient selection. Intra-articular SI joint block may not be a criterion for selecting patients for LBN. Dreyfuss showed that the multisite, multidepth lateral blocks can detect pain generators from the posterior ligament joint complex at a rate of 70%,²² but they do not diagnose pain from the SI region. There is anatomical evidence that the intra-articular portion of the SI region is innervated from both ventral and dorsal sources.²² Thus, patients selected for LBN on the basis of intra-articular local anesthetic may not be expected to have good outcomes, and the correct patient for RF

Table 5. Identifications and Descriptions of Treatment Successes of Crossover-Treated Study Subjects after 6 Months

Subject	NRS Score	ODI Score	SF-36BP Score	Treatment Successes: NRS + ODI*	Treatment Successes: NRS + SF-36BP*
1	-50	0	-0.1		
2	20	-2	13		
3	-12.5	13	5		
4	-83	-16	9.6	X	
5	-63	-36	20	X	X
6	-20	No Data	-11		
7	-60	-16	0	X	
8	-75	10	-10		
9	-33	No Data	No Data		
10	0	10	9		
11	-100	-34	68	X	X
12	-20	-4	-10		
13	-50	-10	11	X	X
14	-83	-26	40	X	X
15	-60	-4	33		X
16	0	-10	1		
N	16	14	15	6	5
			Success Rate:	6/16 (100) = 38%	5/16 (100) = 31%

NRS, numerical rating scale; ODI, Oswestry disability index; SF36-BP, Short Form 36-bodily pain.

*"X" marks qualifications of success, as indicated.

*Per protocol of this study.

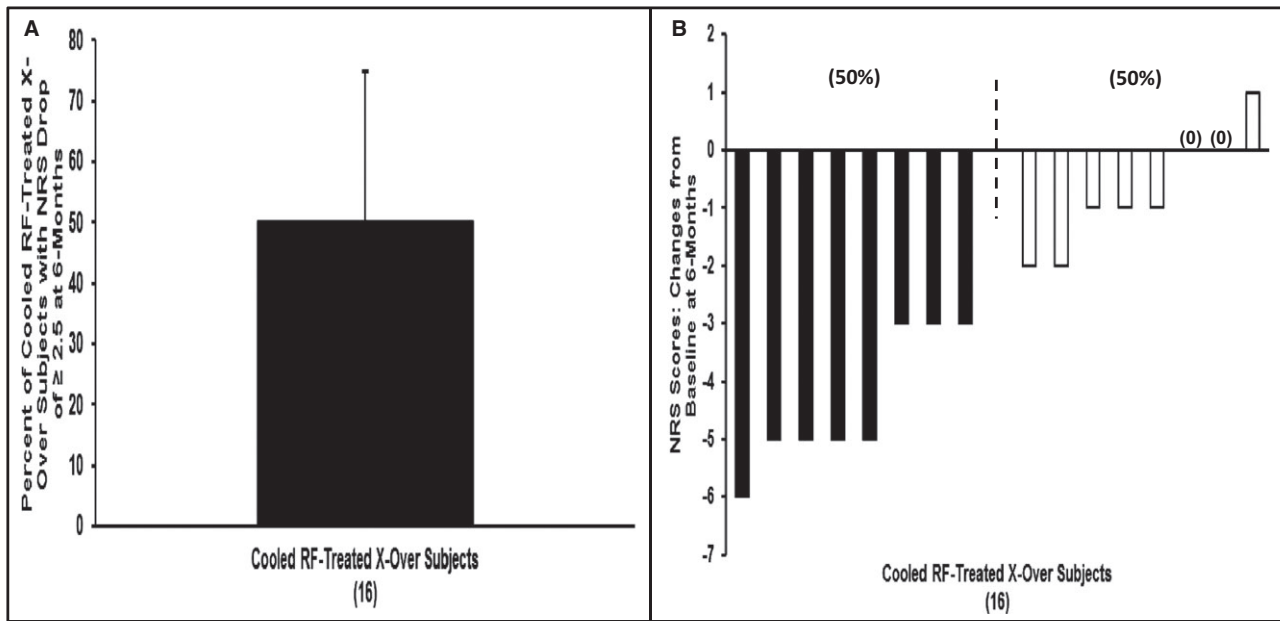


Figure 5. The proportion of the crossover CRF/LBN study group “completers,” or those who completed every study follow-up, that recorded a NRS decrease ≥ 2.5 points 6 months after treatment is demonstrated (A). In (B), the absolute values of score changes from baseline to 6 months are shown for each “completer.” In (A), the box indicates mean value, and whisker denotes the 95% confidence interval within which the mean is found. In (B), the parenthetical numerical percentage values indicate proportions of study subjects whose NRS score changes met (left of dotted line) or did not meet (right of dotted line) requirements to be considered clinically meaningful “treatment successes.” The “X” denotes “crossover,” and “(0)” indicates the applicable score of a study subject. The parenthetical numerical values indicate the number of subjects from which data were determined.

neurotomy is likely the one who has excellent temporary relief with the comparative anesthetic (multisite, multi-depth lateral branch) blocks.³⁵ This double block paradigm has been effective in identifying patients for RF neurotomies.³⁶⁻³⁹

Limitations

This study was not conducted at multiple sites and was without a sham control group past 3 months after CRF/LBN treatment. The latter is due to an ethical concern in

that it was not in the best interest of the study for patients to continue to feel pain, but instead of paramount importance for patients in the sham group to exploit the CRF/LBN therapy as soon as possible to experience pain relief.

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