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Cooled radiofrequency ablation versus standard medical management for chronic sacroiliac joint pain: a multicenter, randomized comparative effectiveness study

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ABSTRACT

Introduction Low back pain is the leading cause of disability worldwide, with sacroiliac joint pain comprising up to 30% of cases of axial lower back pain. Conservative therapies provide only modest relief. Although placebo-controlled trials show efficacy for sacral lateral branch cooled radiofrequency ablation, there are no comparative effectiveness studies.

Methods In this randomized, multicenter comparative effectiveness study, 210 patients with clinically suspected sacroiliac joint pain who obtained short-term benefit from diagnostic sacroiliac joint injections and prognostic lateral branch blocks were randomly assigned to receive cooled radiofrequency ablation of the L5 dorsal ramus and S1–S3 lateral branches or standard medical management consisting of pharmacotherapy, injections and integrative therapies. The primary outcome measure was mean reduction in low back pain score on a 0–10 Numeric Rating Scale at 3 months. Secondary outcomes included measures of quality of life and function.

Results 3 months post-treatment, the mean Numeric Rating Scale pain score for the cooled radiofrequency ablation group was 3.8±2.4 (mean reduction 2.5±2.5) compared with 5.9±1.7 (mean reduction 0.4±1.7) in the standard medical management group (p<0.0001). 52.3% of subjects in the cooled radiofrequency ablation group experienced ≥2 points or 30% pain relief and were deemed responders versus 4.3% of standard medical management patients (p<0.0001). Comparable improvements favoring cooled radiofrequency ablation were noted in Oswestry Disability Index score (mean 29.7±15.2 vs 41.5+13.6; p<0.0001) and quality of life (mean EuroQoL-5 score 0.68±0.22 vs 0.47±0.29; p<0.0001).

Conclusions In patients with sacroiliac joint pain, cooled radiofrequency ablation provided statistically superior improvements across the spectrum of patient outcomes compared with standard medical management.

Trial registration number NCT03601949.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Cooled radiofrequency ablation is a pain management procedure commonly used across a number of anatomical locations. Evidence suggests it may be particularly well suited for patients with chronic sacroiliac joint pain.

WHAT THIS STUDY ADDS

⇒ This is the first large, prospective, randomized, multicenter study to compare cooled radiofrequency ablation to standard medical management for subjects with chronic sacroiliac joint pain.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study confirms the safety and effectiveness of cooled radiofrequency ablation and its superiority over standard medical management for this patient population.

INTRODUCTION

Low back pain (LBP) is one of the top causes of physician visits and disability in the world, with a lifetime prevalence between 51% and 84%.[1]

Mechanical LBP, which includes degenerative spine changes, accounts for the majority of these visits, with epidemiological studies suggesting up to 30% of cases may originate from the sacroiliac joint (SIJ).[2–4] Identification and isolation of the pain source in patients with LBP and SIJ pain is extremely challenging.[4 5] Diagnostic injections can result in false positives and available treatment options are limited to pharmacotherapy, injections, integrative therapies and, in severe refractory cases, SIJ fusion.[4 5]

The SIJ can be divided into intra-articular and extra-articular components, which are equally likely to be pain generators.[6] Steroids typically provide only short-term to intermediate-term relief and minimally invasive fusion can treat intra-articular SIJ pain characterized by joint degeneration or instability, but has yielded mixed results and is not recommended for extra-articular pathology.[7] In individuals who experience meaningful but temporary relief from SIJ injections, lateral branch radiofrequency ablation (RFA) has demonstrated benefits in numerous randomized controlled trials

(RCT).[8–10] Since the lateral branches innervate the SIJ ligaments and posterior bone but not the fibrous joint capsule, prognostic lateral branch blocks (LBB) are sometimes employed to identify patients with extra-articular pathology, improving selection for RFA.[11 12]

Standard radiofrequency (RF) probes are simple electrodes that deliver thermal energy to targeted nerves through ionic heating.[13] However, the lesion size created by standard RF probes is limited by desiccation and charring at the tissue-tip interface, increasing the risk of failed nerve capture.[14] Cooled RF probes, where water is circulated through the probe tip to regulate temperature at the tissue-tip interface, mitigate tissue charring and create larger thermal lesions with distal projection from the probe tip.[15] Distal projection allows for a simpler and less injurious perpendicular approach for probe introduction and larger spherical lesions may increase capture rate in the context of nerve course variability. In addition to theoretically improving the procedure success rate, preclinical evidence suggests that structural changes produced by cooled radiofrequency ablation (CRFA) outlast those effected by conventional RFA, which may translate to longer clinical benefits.[16]

Society guidelines specifically recommend CRFA technology to maximize the capture rate of SIJ nociceptive input; however, there are no randomized studies that directly compare cooled to other forms of RFA.[17] For CRFA of the lateral branches, two out of three retrospective studies found CRFA to be superior to conventional RFA.[18–20] Large retrospective studies in other anatomical locations with comparable nerve variability also suggest superiority of CRFA.[21 22] Despite several RCTs demonstrating efficacy for SIJ CRFA over sham, there have been no comparative effectiveness studies, which are more generalizable to real-world practice.[8 9] The main objective of this multicenter study is to compare sacral lateral branch CRFA to standard medical management (SMM) in patients with refractory SIJ pain.

METHODS

This randomized clinical study was registered on ClinicalTrials.gov (NCT03601949) on 26 July 2018. All participants were enrolled and treated between 29 June 2018 and 9 August 2021.

Selection criteria

Adult subjects over 21 years old diagnosed with chronic SIJ pain lasting at least 3 months were eligible. Key inclusion criteria were: (1) at least one positive SIJ provocation test (eg, thigh thrust, compression, sacral thrust); (2) ≥50% pain relief lasting at least as long as the expected duration of anesthetic or medication from a therapeutic or diagnostic SIJ injection; (3) ≥50% pain relief lasting at least as long as the duration of action of local anesthetic from LBB performed after the effects of the SIJ injection wore off; (4) Numeric Rating Scale (NRS) low back or buttock pain score ≥4 over the last 7 days; and (5) no other major identifiable source of LBP.

Exclusion criteria included prior RFA of the sacral lateral branches, active hip pathology, lumbosacral radicular pain excluded by history, physical examination and imaging when available, body mass index (BMI) greater than 40 kg/m², secondary gain, prescribed opioid medications totaling ≥90 mg oral morphine equivalents per day, and having an implanted electronic device (ie, pacemaker).

Study sites, randomization and trial design

Study sites included 15 civilian academic, private practice, and military treatment facilities in a variety of urban and suburban settings throughout the USA. Eligible participants were randomized in a 1:1 ratio by computer-generated randomization tables at each site to receive either CRFA (treatment group) or physician-prescribed SMM (control group). CRFA participants received treatment within 30 days of randomization. Blinded outcome assessors conducted all follow-up visits. Although the primary endpoint was 3 months, follow-up was planned through 12 months. An optional crossover-to-treatment design was adopted for participants randomized to SMM after 3 months.

Diagnostic LBBs

Prognostic sacral LBBs were performed using a periforaminal technique with bupivacaine or ropivacaine 0.5% using a total volume ≤2 mL under fluoroscopic guidance in multiple views, according to standard protocols.[9 23] Anesthetic was placed at one to three locations (eg, 2:00 and 4:00 on the face of a clock for right-sided procedures) within 1 cm of the posterior S1–S3 foramina and at the L5 dorsal ramus between the sacral ala and articular process. When S4 was located at or above the inferior margin of the SIJ, lateral branches coalescing at this level were targeted. Subjects with bilateral pain had bilateral blocks performed on the same day. Participants who experienced ≥50% pain relief lasting at least as long as the expected duration of anesthetic proceeded to treatment allocation.

CRFA procedure

CRFA procedures were performed according to standard protocol using fluoroscopic guidance in multiple views.[9 24 25] Nine lesions for each lateral segment were created at locations specified in relation to the S1–S3 sacral foramina and L5 dorsal ramus, with S4 targeted at provider discretion in patients where the foraminal opening was situated at or above the inferior aspect of the SIJ (figure 1). At each level, introducers were inserted until the stylet tip contacted bone at approximately 1:30, 3:30 and 5:30 on the face of a clock for right-sided lesions at S1 and S2, and 1:00 and 3:00 at S3, with mirror image locations used for left-sided lesions. L5 was targeted in the groove lateral to the sacral articular process. After correct positioning was confirmed, stylets were removed and replaced with 17-gauge CRFA probes, ensuring the probe tip was offset 2 mm from bone. The probe was energized for 150 s at a power level regulated to maintain a 60°C temperature on the active tip at each of the nine locations, translating to a tissue temperature >80°C. Subjects with bilateral pain received CRFA treatment on both sides on the same day.

Standard medical management

The control arm consisted of physician-prescribed SMM, including pharmacotherapy, physical and chiropractic therapy, lifestyle changes, acupuncture, yoga, and therapeutic injections into the sacroiliac ligaments or joint cavity. Patients were instructed to continue regular exercise programs and encouraged to resume or engage in physical activities. To control for temporary short-term benefits, no acupuncture or injections were permitted within 4 weeks of follow-up visits. At each study visit, investigators assessed participants' health status and had the option to modify SMM according to clinical judgment. Treatments administered are listed in online supplemental table 1, which included steroid injections, nerve blocks, physical therapy and acupuncture.

Outcome measures and follow-up

Baseline data collected included demographics, medical history and a combination of patient self-reported outcomes, including

Figure 1 Nine target regions for lateral branch blocks and cooled radiofrequency ablation (CRFA) procedures. The nine target regions (orange circles) were situated around the sacral foramina at the S1–S3 levels and in the groove between the sacral ala and articular process, targeting the dorsal ramus of L5. These targets were used for both the lateral branch block and CRFA procedures (ie, the periforaminal technique).

0–10 NRS pain scores, Oswestry Disability Index 2.1 (ODI) which assesses back pain-related disability, 36-Item Short Form Survey (SF-36) physical function domain, and EuroQoL-5 (EQ-5D-5L) which measures quality of life in five dimensions.[26 27] These self-reported outcomes were reassessed at each follow-up visit, which occurred 1 and 3 months post-treatment. Concomitant medications, healthcare utilization, concurrent interventions and adverse events were assessed at each visit, as was patient satisfaction using the Patient Global Impression of Change (PGIC) scale, a 7-point Likert scale in which higher numbers indicate greater improvement.[27] The primary outcome measure was mean reduction in average NRS pain score at 3 months.

Consistent with the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommendations, responders were predefined as participants who had a ≥30% or 2-point decrease in average daily NRS pain score over the past week coupled with a score ≥5 (moderately better) on the PGIC scale at 3 months.[27]

Statistical analyses

All study data were entered into a 21 CFR 11-compliant electronic data capture system that included an electronic case report form, with an independent monitor verifying accuracy. Using conservative literature-based assumptions regarding an anticipated mean NRS reduction from baseline to 3 months for CRFA and SMM of 3.6 (±2.2) and 2.6 (±2.2), respectively, it was determined that a sample size of 168 was required to obtain 90% power to determine superiority at a one-sided significance level of 0.05 and 83% power using a two-sided test. At least 208 subjects were planned for enrollment, accounting for an expected 20% attrition rate.[8 9 28] The lower boundary of a two-sided 95%

CI was calculated for the difference in pain reduction between treatments for the primary endpoint in this intention-to-treat analysis. If the lower bound is greater than 0, superiority of CRFA compared with SMM is established. To further elucidate the impact of baseline variables on the treatment effect, a linear regression model was employed, including prespecified factors: age, sex, duration of diagnosis, BMI, response to blocks and opioid use. All factors were included in the model at one time without applying stepwise removal. No adjustments for multiple testing were performed. Sensitivity analyses to impute missing data, including but not limited to last observation carried forward and multiple imputation, were performed to understand the robustness of primary endpoint results.

Role of funding organization

The sponsor paid for research personnel, equipment, an independent 3rd party statistical analysis, and provided the first drafts of the protocol and consent. The steering committee, with the sponsor's input, designed the study and edited the protocol and consent. The steering committee interpreted the data and drafted the initial version of the manuscript.

RESULTS

Baseline characteristics and screening

A total of 5713 individuals were prescreened for eligibility. Among patients who proceeded to prognostic LBB, 225 out of 236 (95.3%) were positive. Two hundred and fifty-four individuals signed informed consent and progressed to full screening, resulting in 210 subjects randomized, half (n=105) of whom received CRFA and half of whom were treated with SMM (figure 2).

In the SMM group, 26/105 (24.8%) subjects received SIJ injections, 54/105 (51.4%) received non-steroidal anti-inflammatory drugs, 31/105 (30.0%) received adjuvants (antidepressants or membrane stabilizers), 13/105 (12.4%) received muscle relaxants, 26/105 (25.0%) received acetaminophen, 2/105 (1.9%) received additional physical therapy (as nearly all patients previously underwent physical therapy) and 42/105 (40.0%) received opioids (tramadol, n=16, and/or pure mu agonists, n=30).

Baseline demographics across groups were comparable, with no significant differences between groups (table 1). The mean age in the CRFA cohort was 57.8 years±13.6 compared with 55.5±13.8 in the SMM group. The CRFA group had 77.3% female participants compared with 74.3% in the SMM group. Subjects had long-standing back pain, with a mean duration in the CRFA group of 115.0±108.1 months versus 123.9±131.3 months in the SMM group.

Study retention post-treatment at 3 months was 89.5%, with similar proportions between groups. The present study was underway during the COVID-19 pandemic and three subjects (1.5%) reported contracting the virus prior to their 3-month follow-up, with no study visits missed. However, the pandemic drove remote visits in 17 and 14 of the active and control cohorts, respectively.

Primary outcome measure and responder rates

Baseline pain scores in both groups were in the moderate range (mean 6.3, SD 1.4 in both groups) (table 2). At 3 months, the mean NRS pain score for the CRFA group was 3.8±2.4 compared with 5.9±1.7 in the SMM group (p<0.0001). The mean reduction in average NRS pain score was 2.5±2.5 in the CRFA group (38.6% pain reduction from baseline) compared
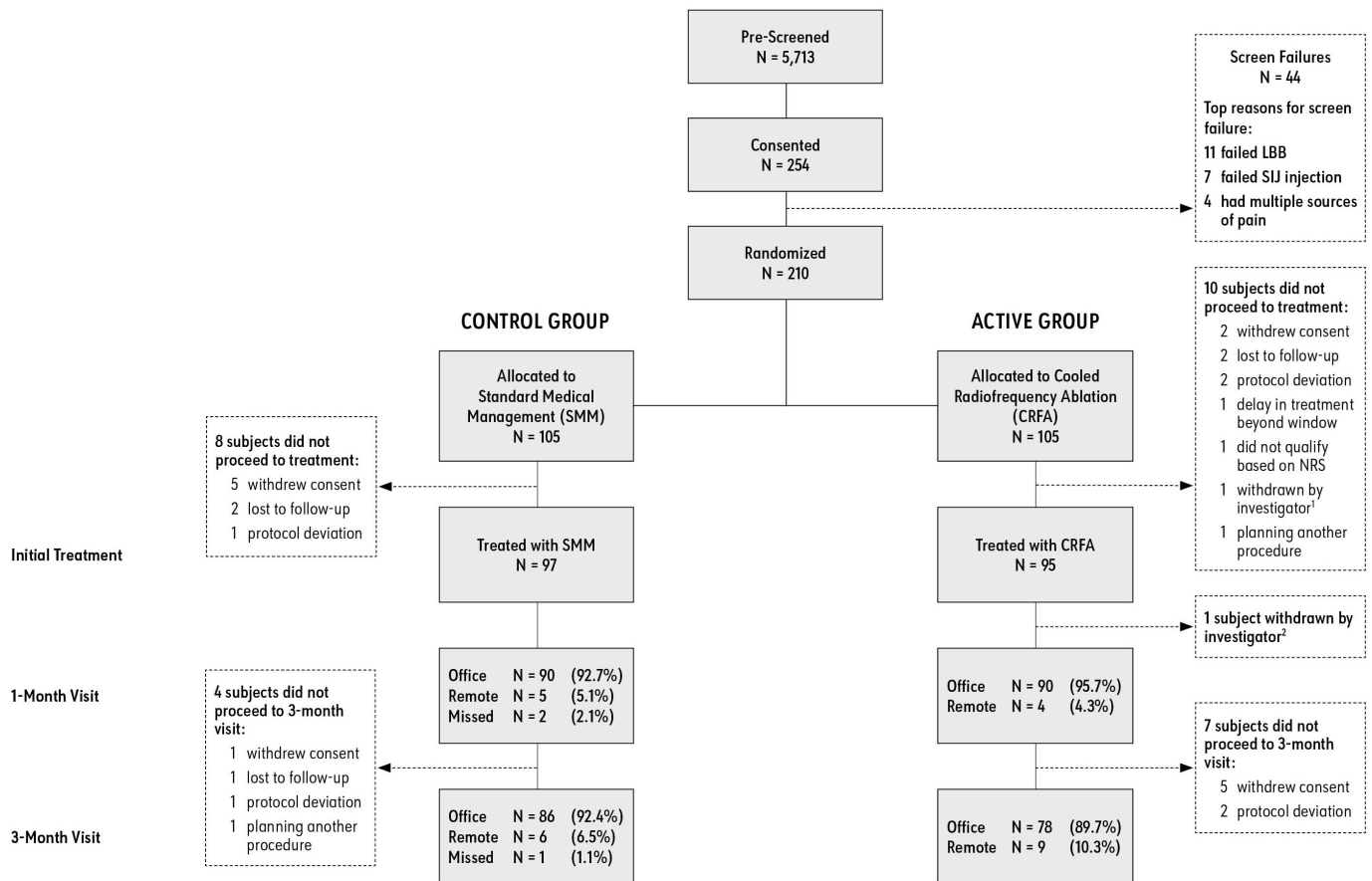
Figure 2 Study design diagram showing the randomization of subjects between CRFA and a control group receiving SMM, and study progress. LBB, lateral branch block; NRS, Numeric Rating Scale; SIJ, sacroiliac joint. Subject 02–053 was randomized to SMM but inadvertently received CRFA treatment. The subject is counted in the SMM group for the purposes of disposition and effectiveness analyses, but in the CRFA group for safety summaries. [1]Subject 04–031 was randomized prematurely and then withdrawn due to block failure. [2]Subject 07–003 was withdrawn due to psychological decompensation preventing ongoing participation.

Table 1 Baseline subject demographic and clinical data

Baseline demographics	CRFA (N=105)	SMM (N=105)
Age (mean±SD)	57.8±13.6	55.5±13.8
Female sex (n/N (%))	77/105 (77.3)	78/105 (74.3)
BMI (kg/m^2) (mean±SD)	28.5±5.2	29.3±5.5
Race/ethnicity (n/N (%))		
Hispanic or Latino	6/105 (5.7)	0/105 (0.0)
Non-Hispanic White	92/105 (87.6)	99/105 (94.3)
Black or African American	4/105 (3.8)	5/105 (4.8)
Asian	3/105 (2.9)	0/105 (0.0)
Other	0/105 (0.0)	1/105 (1.0)
Laterality (n/N (%))		
Unilateral	56/105 (53.3)	54/105 (51.4)
Bilateral	49/105 (46.7)	51/105 (48.6)
Duration of low back pain (months) (mean±SD)	115.0±108.1	123.9±131.3
Analgesic use for low back pain (n/N (%))		
Non-opioid analgesic use	42/105 (40.0)	43/105 (41.0)
Opioid use	41/105 (39.0)	38/105 (36.2)
Lateral branch block		
% Decrease in NRS pain score (mean±SD)	85.7±18.1	84.0±17.7

BMI, body mass index; CRFA, cooled radiofrequency ablation; NRS, Numeric Rating Scale; SMM, standard medical management.

with a 0.4±1.7 reduction (4.9% from baseline) in the control group (p<0.0001).

At 3 months, 52.3% of subjects in the CRFA group were deemed responders per protocol definition, compared with 4.3% in the SMM group (p<0.0001). In the CRFA group, 41.9% of subjects reported ≥50% reduction in NRS pain score, defined as 'substantial improvement', compared with 6.5% in the SMM group (p<0.0001). The superiority of CRFA compared with SMM held true with sensitivity (eg, complete case) analyses.[29]

Secondary outcome measures

At 3 months, the CRFA group had an SF-36 function score of 40.2±9.0 from a baseline of 33.6±7.8, representing a 6.5±9.2 point (24.5%) improvement. In comparison, the 3-month SF-36 score increased to 33.0±6.8 from a baseline of 32.3±6.4 in the SMM group, representing a 4.5% improvement (p<0.0001).

Overall ODI score for the CRFA group improved from a baseline of 40.7±13.8 to 29.7±15.2 at 3 months, which was a significantly greater decrease compared with the control group (p<0.0001). Positive trends in individual ODI categories were seen across the CRFA cohort (figure 3). The percentage of patients with minimal disability increased from a baseline of 6.7% to 34.5% and the percentage of patients with severe disability decreased from a baseline of 39.0% to 24.1% at 3

Table 2 Primary outcome measures and responder rates

Numeric Rating Scale pain score

	Baseline			1-month follow-up			3-month follow-up		
	CRFA (n=105)	SMM (n=105)	P value*	CRFA (n=94)	SMM (n=95)	P value*	CRFA (n=86)	SMM (n=92)	P value*
Usual level of pain									
Mean (SD)	6.3 (±1.4)	6.3 (±1.4)	0.91	4.1 (±2.4)	5.2 (±1.9)	<0.001	3.8 (±2.4)	5.9 (±1.7)	<0.0001
Change from baseline in usual level of pain									
Mean (SD)				2.3 (±2.1)	1.1 (±2.0)	<0.001	2.5 (±2.5)	0.4 (±1.7)	<0.0001
Responder rate (≥30% or 2-point decrease in average NRS pain score+a score ≥5/7 on PGIC) (%)				(41.5)	(14.7)	<0.0001	(52.3)	(4.3)	<0.0001
Subjects reporting ≥50% pain relief (%)				(39.4)	(13.7)	<0.0001	(41.9)	(6.5)	<0.0001

SF-36 Physical Component Summary score

	Baseline			1-month follow-up			3-month follow-up		
	CRFA†	SMM	P value*	CRFA	SMM‡	P value*	CRFA§	SMM	P value*
Mean (SD)	33.6 (±7.8)	32.2 (±6.4)	0.15	38.4 (±9.1)	34.3 (±7.5)	<0.01	40.2 (±9.0)	33.0 (±6.8)	<0.0001

Oswestry Disability Index (ODI)

	Baseline			1-month follow-up			3-month follow-up		
	CRFA	SMM	P value*	CRFA	SMM	P value*	CRFA§	SMM	P value*
Mean (SD)	40.7 (±13.8)	43.7 (±13.9)	0.27	32.0 (±16.7)	38.8 (±14.8)	<0.01	29.7 (±15.2)	41.5 (±13.6)	<0.0001

EQ-5D-5L index score

	Baseline			1-month follow-up			3-month follow-up		
	CRFA¶	SMM	P value*	CRFA	SMM	P value*	CRFA§	SMM	P value*
Mean (SD)	0.48 (±0.27)	0.46 (±0.27)	0.53	0.65 (±0.25)	0.53 (±0.26)	<0.001	0.68 (±0.22)	0.47 (±0.29)	<0.0001

Patient Global Impression of Change (PGIC)

	1-month follow-up		3-month follow-up	
	CRFA**	SMM‡	CRFA§	SMM
Worse pain, no change or almost the same (combined PGIC scores of 1, 2 and 3) (%)	(23.6)	(62.1)	(21.8)	(64.1)
A little better or somewhat better, but change has not made any real difference (PGIC score of 4) (%)	(20.5)	(20.0)	(12.6)	(29.3)
Moderately better, and a slight but noticeable change (PGIC score of 5) (%)	(18.3)	(6.3)	(20.7)	(4.3)
Better and a definite improvement that has made a real and worthwhile difference (PGIC score of 6) (%)	(22.6)	(7.4)	(26.4)	(0.0)
A great deal better and a considerable improvement that has made all the difference (PGIC score of 7) (%)	(15.1)	(4.2)	(18.4)	(2.2)

Patients reporting improved PGIC score (%)**

1-month follow-up			3-month follow-up		
CRFA††	SMM	P value*	CRFA§	SMM	P value*
(55.9)	(17.9)	<0.0001	(65.5)	(6.5)	<0.0001

*P values are reported between groups.
†(n=104).
‡(n=94).
§(n=87).
¶(n=103).
**Improved PGIC score defined as ≥5/7.
††(n=93).
CRFA, cooled radiofrequency ablation; NRS, Numeric Rating Scale; SF-36, 36-Item Short Form Survey; SMM, standard medical management.

months in the CRFA group. Similar trends were not observed in the SMM cohort.

At 3 months, the CRFA cohort reported a mean increase in EQ-5D-5L of 0.19 points, exceeding the established minimal clinically important difference of 0.074 for an individual patient, versus a mean increase of 0.01 points in the SMM cohort.[30]

Factors associated with treatment success

Results of linear regression demonstrated that receipt of CRFA treatment was a predictor of NRS reduction (estimate=2.058, SE=0.335, 95% CI 1.402 to 2.714, p<0.0001) as was age (for every 1-year increase in age, NRS was reduced by 0.026 points, SE=0.013, 95% CI 0.001 to 0.052, p=0.047) (online supplemental table 2). There was a trend for a higher BMI to
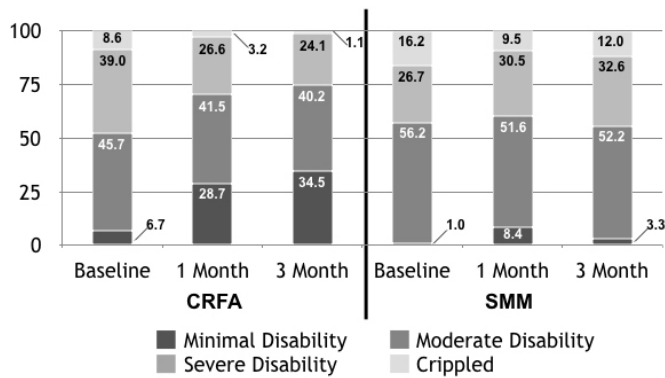
Figure 3 Percentage of subjects in Oswestry Disability Index categories. CRFA, cooled radiofrequency ablation; SMM, standard medical management.

be associated with greater pain reduction (for every 1 kg/m^2 increase in BMI, NRS was reduced by 0.056, SE=0.031, 95% CI −0.005 to 0.117, p=0.07) (table 3). Participants ≥65 years of age also responded more favorably to SMM.

Adverse events
There were a total of 105 adverse events (CRFA: 65 events in 47 of 96 subjects, 49.0%; SMM: 40 events in 28 of 104 subjects, 26.9%). In the CRFA cohort, 16 of these events were deemed related to the procedure, while in the SMM patients, five events were deemed related to procedures. In the SMM cohort, four subjects reported postprocedural pain from an injection, and one reported musculoskeletal pain in the lower back. The majority of CRFA-related adverse events involved worsening pain in the lower back or around the SIJ (11 subjects). In the CRFA cohort, four subjects reported postprocedural pain. There was one report of an unrelated cardiovascular adverse event in the CRFA cohort. There were no reports of serious related adverse events, including nerve injury, in either cohort.

DISCUSSION
Main findings and comparison to other studies
The principal finding in this study is that CRFA resulted in statistically and clinically superior improvements across multiple domains compared with SMM. Fifty-two percent of subjects achieved a positive outcome based on prespecified criteria and 41.9% obtained substantial benefit (≥50% reduction in NRS), which corroborates previously published literature. In two previous RCTs that compared CRFA to sham RFA, 64% and

47% of treatment patients, respectively, experienced a successful binary outcome, defined as ≥50% pain relief.[8] [9] Other studies have shown CRFA can provide durable improvements in pain, quality of life and analgesic usage.[20] [25] [31–33]

The results of this trial can be viewed in the context of another open-label comparative effectiveness study, the highly publicized MINT study, which compared stand-alone RFA of facet joints, SIJ or a combination of the two, to a standardized exercise program plus RFA.[12] Although the authors found no significant difference between groups for the facet joint substudy, the primary outcome measure at the primary endpoint was positive for the SIJ and combination substudies, though there was no significance between group differences after 3 months and the results for secondary outcomes in these substudies were mixed. The MINT studies were criticized in numerous letters and editorials for design, patient selection, procedural technique including small electrodes that create small lesions, and data analysis.[34–38]

One difference in this study compared with previous literature is the conversion rate from screening to enrollment. Our study found a 4% conversion rate from subjects identified with LBP, which is lower than literature suggesting up to 30% of LBP originates from the SIJ.[4] [5] The present study had strict enrollment criteria that sought to isolate extra-articular mediated SIJ pain, thus potentially excluding many potential subjects that would have qualified for other studies. The stringent screening process and selection criteria are supported by our high rate of positive prognostic LBB (95.3%). In contrast to our study, the MINT study reported that a slightly lower 76% of patients who underwent a screening LBB had a positive block.[12] Whereas double LBBs have not been used in any previous RCT, given the high false-positive rate of uncontrolled SIJ injections, requiring a second controlled block would probably have significantly reduced the LBB response rate (ie, the number who were randomized), but may have resulted in a higher RFA success rate. However, this would likely have come at the expense of an increased false-negative rate.[39]

Some,[12] but not most,[8] [9] [40] prior randomized studies have required at least three pain provocation tests as a criterion for enrollment, with all three studies that required none or only one test yielding positive results. Provocation tests may be more likely to reproduce pain from intra-articular (than extra-articular) pathology, which may not be predictive of RFA results as sacral lateral branch denervation targets extra-articular pathology. Moreover, a very recent large prospective study failed to demonstrate that two of the most common provocation tests have predictive value for intermediate-term outcomes after SIJ injections.[41]

In previous randomized studies, a majority of enrolled subjects reported >24 months of pain duration, highlighting the lack of reliable treatments for SIJ pain and limited commercial coverage for SIJ RFA.[9] [10] In the present study, both groups had >115 months of axial back pain. Previous literature has shown that increased pain duration is associated with poorer outcomes following LBP treatment, including facet joint RFA and SIJ injections.[41] The results of this study suggest CRFA is effective in treating refractory patients with long-standing SIJ pain. One explanation for our finding that higher BMI was associated with a positive outcome is that overweight individuals have a greater contribution to their SIJ pain from pathology involving soft tissue (eg, ligaments), which receives innervation by the lateral branches treated.

Table 3 Linear regression for primary effectiveness endpoint of reduction in NRS at 3 months on possible predictors

Source	Estimate	SE	95% CI	P value
Intercept	−3.360	1.594	−6.484 to −0.235	0.04
Treatment group (CRFA)	2.058	0.335	1.402 to 2.714	<0.0001
Age	0.026	0.013	0.001 to 0.052	0.046
Sex (female)	0.474	0.396	−0.302 to 1.251	0.23
Duration of diagnosis	−0.001	0.001	−0.003 to 0.002	0.56
BMI	0.056	0.031	−0.005 to 0.117	0.07
Response to blocks	0.006	0.010	−0.013 to 0.026	0.54
Baseline opioid use (yes)	−0.276	0.347	−0.956 to 0.404	0.43

BMI, body mass index; CRFA, cooled radiofrequency ablation; NRS, Numeric Rating Scale.

Cooled versus conventional RFA

There have been misconceptions and debates over the past several years regarding differences in mechanisms, effectiveness and safety between conventional RFA and CRFA. As noted above, conventional RFA has physical limitations for treating SIJ pain and several procedural strategies have been described to better enable conventional RFA to effectively target the highly variable location of sacral lateral branches.[42] Bipolar RFA has been proposed to increase the capture rate of the lateral sacral branches. However, this technique requires more electrodes and greater precision, and creates greater tissue trauma.[42] In contrast, the distal projection afforded by CRFA allows for a simpler and less injurious perpendicular approach, and larger, spherical lesions may increase capture rate in the context of nerve course variability.

Whereas no prospective trials have been conducted comparing cooled to conventional technologies in the SIJ, several retrospective studies have compared the effectiveness of CRFA to other forms of RFA for SIJ pain. In a study examining factors associated with sacral lateral branch RFA outcomes, Cohen *et al* reported a 65% success rate for CRFA versus a 47% success rate for conventional RFA.[18] Tinnirello *et al* found that CRFA resulted in a significantly greater reduction in mean pain scores at 6 months (5.0 vs 3.4) and 12 months (4.2 vs 2.6) compared with RFA performed using a single long electrode that employs a combination of monopolar and unipolar RFA.[20] In contrast, Cheng *et al* conducted an 88-patient non-randomized study which reported no significant difference between CRFA and conventional RFA.[19]

In a retrospective study evaluating different techniques for RFA of the genicular nerves in 170 patients with knee osteoarthritis, Kapural *et al* reported that CRFA was associated with a greater decrease in pain score and a longer duration of pain relief than conventional RFA.[22] In another large (n=265) study evaluating factors associated with treatment outcome for genicular nerve radiofrequency treatment, Chen *et al* reported a 67.5% success rate for CRFA, which favorably compared to traditional RFA (55.3% success rate) and pulsed RF (42.9%).[21] These findings are consistent with a rodent study demonstrating that CRFA results in greater structural damage to pain-transmitting nerve fibers and a longer duration of effect than conventional RFA.[16]

Limitations

The design of this study did not allow for blinding of participants. Although outcome assessors were ostensibly blinded, blinding was not assessed, and some reviews have found non-blinded studies to be associated with higher success rates.[43] This effect, however, may have been attenuated in this study given the long-standing duration of pain in participants. Second, some patients randomized to SMM may have already tried and failed variants of interventions they received (nearly all had previously undergone physical therapy), such as different non-steroidal anti-inflammatory drugs or adjuvants, or an SIJ injection in a different location (eg, an intra-articular vs extra-articular or combination injection). This, and the fact that coverage issues limit the availability of RFA treatment for this condition, could have led to increased expectations for patients randomized to CRFA, resulting in a higher placebo response rate.[44] In spite of efforts to isolate the SIJ joint as the primary pain generator in this study, this placebo effect could have been mitigated by the complex nature of chronic LBP and the high likelihood of secondary pain sources in this population. Finally, the lack of specific requirements for the control group reflects real-life conditions but could undermine the interpretation of generalizability.

CONCLUSIONS

The findings of this multicenter study demonstrate that CRFA is superior to SMM in managing chronic SIJ pain. The majority of subjects receiving CRFA reported meaningful improvements in pain, function and quality of life, despite reporting a long duration of pain. CRFA may be particularly well suited to treat SIJ pain, as the results of this and other randomized trials demonstrate. More research is needed to optimize neural targets and better identify potential treatment responders, as well as improve access to care.

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