

Does Anodyne Light Therapy Improve Peripheral Neuropathy in Diabetes?

A double-blind, sham-controlled, randomized trial to evaluate monochromatic infrared photoenergy

LAWRENCE A. LAVERY, DPM, MPH
DOUGLAS P. MURDOCH, MD

JAYME WILLIAMS, MD
DAVID C. LAVERY, MD

OBJECTIVE — The purpose of this study was to determine the efficacy of anodyne monochromatic infrared photo energy (MIRE) in-home treatments over a 90-day period to improve peripheral sensation and self-reported quality of life in individuals with diabetes.

RESEARCH DESIGN AND METHODS — This was a double-blind, randomized, sham-controlled clinical trial. We randomly assigned 69 individuals with diabetes and a vibration perception threshold (VPT) between 20 and 45 V to two treatment groups: active or sham treatment. Sixty patients (120 limbs) completed the study. Anodyne units were used at home every day for 40 min for 90 days. We evaluated nerve conduction velocities, VPT, Semmes-Weinstein monofilaments (SWM) (4-, 10-, 26-, and 60-g monofilaments), the Michigan Neuropathy Screening Instrument (MNSI), a 10-cm visual analog pain scale, and a neuropathy-specific quality of life instrument. We used a nested repeated-measures multiple ANOVA design. Two sites (great toe and fifth metatarsal) were tested on both the left and right feet of each patient, so two feet were nested within each patient and two sites were nested within each foot. To analyze the ordinal SWM scores, we used a nonparametric factorial analysis for longitudinal data.

RESULTS — There were no significant differences in measures for quality of life, MNSI, VPT, SWM, or nerve conduction velocities in active or sham treatment groups ($P > 0.05$).

CONCLUSIONS — Anodyne MIRE therapy was no more effective than sham therapy in the treatment of sensory neuropathy in individuals with diabetes.

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Monochromatic infrared energy (MIRE) has been suggested to improve diabetic sensory neuropathy and even to prevent foot ulcers (1–7). However, the results of clinical studies are mixed. In a randomized clinical trial (RCT) by Clift et al. (8), MIRE did not provide improvement in peripheral sensation compared with sham treatment. In contrast, RCTs by Leonard et al. (4) and Arnall et al. (6) reported a significant improvement in peripheral sensation with MIRE. In all three studies one foot was

randomly assigned to receive active therapy and one to receive sham therapy. In all three studies Semmes-Weinstein monofilament (SWM) testing was used to evaluate the primary clinical outcomes. Leonard et al. (4) randomly assigned extremities of 27 patients to receive active or sham MIRE in a 2-week study. Leonard et al. reported significant improvements in peripheral sensation with SWMs, the Michigan Neuropathy Screening Instrument (MNSI), pain, and self-reported balance impairment in a subset of patients

with “less severe” neuropathy, whereas patients with severe neuropathy did not improve. Arnall et al. (6) used a similar approach and randomly assigned extremities of 22 patients to active or sham therapy for 8 weeks. Arnall et al. reported improved sensation with SWMs but not with vibration perception threshold (VPT) testing.

We planned a randomized clinical study to determine the efficacy of anodyne MIRE therapy in improving diabetic peripheral sensory neuropathy. Our hypothesis was that MIRE therapy would improve measures of peripheral sensation compared with sham therapy.

RESEARCH DESIGN AND METHODS

This study was conducted as a double-blind, sham-controlled RCT to determine the efficacy of treatments using anodyne MIRE therapy. The study was approved by the hospital institutional review board, and informed consent was obtained before enrollment. We randomly assigned 69 subjects of whom 60 (120 limbs) completed the 3-month evaluation period: 33 active therapy patients and 27 sham control subjects. We collected patient information regarding age, sex, duration of diabetes, and glycated hemoglobin at baseline and at the conclusion of the study.

Inclusion criteria for the study were as follows: subjects with diabetes who were mentally competent and able to understand and comply with the study, had a VPT ≥ 20 and ≤ 45 V, and were able to complete the required study visits and record treatment activity in the study log book. Subjects were excluded if they met the following criteria: had uncontrolled hypertension of >180 mmHg systolic or >110 mmHg diastolic; were pregnant or breast-feeding or likely to become pregnant during the study; had active malignancy on the lower extremities; had nerve damage as a result of prior reconstructive or replacement knee surgery, back surgery, spinal stenosis, spinal compression, or radiculopathy; were nonambulatory; had a history of neuromuscular disease,

From the Department of Surgery, Texas A&M University Health and Science Center College of Medicine, Scott and White Hospital, Temple, Texas.

Address correspondence and reprint requests to Lawrence A. Lavery, 703 Highland Spring Ln., Georgetown, TX 78633. E-mail: lklaavery@yahoo.com.

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Abbreviations: MIRE, monochromatic infrared energy; MNSI, Michigan Neuropathy Screening Instrument; NeuroQoL, neuropathy-specific quality of life instrument; RCT, randomized clinical trial; SWM, Semmes-Weinstein monofilament; VPT, vibration perception threshold.

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Table 1—Results for demographics and repeated-measures statistical analysis

	Demographics		P
	Anodyne group	Sham group	
<i>n</i>	33	27	
Age (years)	65.7 ± 1.9	64.2 ± 2.0	0.59
Sex (% male)	35	0.2	
Duration of diabetes (years)	13.4 ± 2.0	13.4 ± 2.1	0.99
Diabetes medication (counts of patients)		0.34	
Oral	22	21	
Insulin	7	2	
Combination	3	4	
Diet	1	0	

	Repeated-measures general linear model statistical results				P value
	Anodyne group		Sham group		
	Start	End	Start	End	
Glycated hemoglobin	7.6 ± 0.22	7.6 ± 0.21	7.7 ± 0.26	7.7 ± 0.24	0.70
VPT great toe (V)					
Right	33.5 ± 1.1	34.8 ± 3.0	30.4 ± 1.2	36.1 ± 3.3	0.33
Left	34.2 ± 1.2	36.8 ± 2.9	30.5 ± 1.3	32.7 ± 3.1	0.92
VPT fifth metatarsal (V)					
Right	33.1 ± 1.3	38.2 ± 3.1	29.3 ± 1.4	34.2 ± 3.4	0.97
Left	32.7 ± 1.3	37.7 ± 1.3	32.5 ± 1.5	36.2 ± 1.4	0.77
Visual analog scale pain score	62.6 ± 5.9	59.6 ± 6.1	64.1 ± 6.6	55.5 ± 6.8	0.85
MNSI	7.5 ± 0.42	7.4 ± 0.46	6.8 ± 0.46	7.1 ± 0.51	0.42
NeuroQoL unsteadiness walking	9.4 ± 1.01	10.0 ± 0.96	8.2 ± 1.09	9.6 ± 1.04	0.46
NeuroQoL unsteadiness standing	8.1 ± 0.76	8.5 ± 0.82	6.5 ± 0.85	8.5 ± 0.91	
Difference (start–end)		0.4		2.0*	0.5*
Nerve conduction velocity					
Distal motor latency peroneal nerve	4.1 ± 0.16	4.2 ± 0.24	4.3 ± 0.19	4.5 ± 0.28	0.55
Amplitude peroneal nerve	2.3 ± 0.33	2.1 ± 0.32	2.2 ± 0.38	1.8 ± 0.37	0.15
Mean peroneal nerve	61.6 ± 1.44	60.6 ± 1.38	58.9 ± 1.70	58.0 ± 1.63	0.90
Distal motor latency tibial nerve	4.6 ± 0.20	4.4 ± 0.12	4.5 ± 0.22	4.4 ± 0.13	0.79
Amplitude tibial nerve	1.9 ± 0.36	1.7 ± 0.35	2.3 ± 0.41	2.4 ± 0.40	0.12
Mean tibial nerve	62.8 ± 1.41	60.9 ± 1.48	59.2 ± 1.61	59.1 ± 1.69	0.20

Data are means ± SD, except for the information on medications. Medication is presented as the counts of subjects under a specific medication regimen. The significance or *P* value for the demographics data represents the difference by treatment. For the repeated-measures analysis the significance (*P* value) is for the treatment-time interaction in a repeated-measures ANOVA. *Significant sham result. NCV, nerve conduction velocity.

leprosy, chronic alcoholism, or sarcoidosis; or had foot ulcerations or transmetatarsal or higher amputation.

Monochromatic infrared photoenergy therapy

We used the Anodyne Therapy Professional System 480 (Anodyne Therapy, Tampa, FL) for application of the near-infrared light therapy treatments. The device consists of a base power unit and therapy pads containing 60 near-infrared (890 nm) gallium aluminum arsenide diodes used to increase circulation by dilating arteries and veins. Active units provided $1.3 \text{ J} \cdot \text{cm}^{-2} \cdot \text{min}^{-1}$ of photoenergy. Sham devices were created with the identical appearance of active units and

acquired from the same factory. In the sham units, the diodes were inactivated so that no near-infrared photoenergy was emitted, and heaters were added and preset at 37°C to provide local warmth. Neither investigators nor subjects could discriminate active from sham devices either visually or by temperature. Active versus inactive therapy pads were identified by serial number. The serial numbers were provided to the investigators in a sealed package to be open at the conclusion of the study. Active and sham units were sent by the manufacturers and randomly selected from inventory. Four anodyne therapy pads were placed in the following locations on each lower limb: two on the plantar aspect of the foot in a T

formation and one pad on the medial and lateral side of the calf for 40 min daily using a preset and locked power setting. Subjects were instructed to use the device 7 days a week for 90 days and to keep a daily treatment log to document the time and length of therapy. Subjects received written and verbal instructions on how to use the anodyne device at the time of enrollment, and they returned after 2 weeks of therapy to review the protocol.

Sensory evaluation

Sensory function was evaluated with SWMs (Touch-Test Sensory Evaluator; North Coast Medical, Morgan Hill, CA), VPT testing (VPT meter; Xilas Medical, San Antonio, TX), nerve conduction ve-

locity (NC-Stat; NeuroMetrix, Inc., Waltham, MA), the MNSI, and a 10-cm visual analog scale. We used 4-, 10-, 26-, and 60-g SWMs (sizes 4.56, 5.07, 5.46, and 5.88) to evaluate pressure sensation at 10 sites on each foot. The 10 sites tested included the plantar aspect of the first, third, and fifth digits; the plantar aspect of the first, third, and fifth metatarsal heads; the medial and lateral plantar midfoot; the plantar heel; and the dorsal midfoot. The filaments were applied until they began to bend and were held in place for ~1.5 s. Each site was tested randomly during the sensory evaluations. We recorded the lowest monofilament recognized accurately by patients at each anatomic site. The outcomes of the SWM testing were considered to be on an ordinal scale. If the lowest perceived SWM was a 4-g monofilament, the measure at the site was scored a 1, if the lowest perceived SWM was a 10-g monofilament, the measure at the site was scored a 2, and so forth (4 g = 1, 10 g = 2, 26 g = 3, 60 g = 4, and >60 g = 5). We replaced monofilaments after evaluating every 10 patients.

We evaluated VPT with the VPT testing instrument as described by Lavery and Young and colleagues (9,10). Measurements were taken at the distal aspect of the great toe and the fifth metatarsal head. The amplitude of vibration was read as a continuous variable in volts on a 0–100 scale. Both monofilament testing and VPT testing were performed with subjects in a reclined sitting position. Both tests were demonstrated on the upper extremity, and the subjects were allowed to visualize the testing process. The subjects were then asked to close their eyes for the lower extremity testing procedures. The subjects responded by saying “yes” when they felt the monofilament and then were asked to correctly identify the site at which they felt the monofilament. If the patient could not identify the site correctly, the test was recorded as a negative response. We evaluated nerve conduction velocities in the tibial nerve and superficial peroneal nerve of each subject with the NC-Stat nerve conduction system on the right foot only (11). Subjects were not included in the analysis if they had unobtainable tibial or peroneal nerve responses.

Neuropathy quality of life instrument

Subjects completed the MNSI (12) and a neuropathy-specific quality of life instrument (NeuroQoL) (13) at each visit. The

NeuroQoL consists of a 35-item survey organized as a hierarchical scale, and it assesses patients’ subjective evaluation of their ability to function and their quality of life in six domains. Each domain is assessed with questions designed to measure pain and paresthesias, symptoms of loss of sensation, sensory motor symptoms, limitations in daily activities, interpersonal problems, and emotional burden. It has been validated and has a high degree of internal consistence (Cronbach’s $\alpha = 0.94$) and robust test-retest reliability ($r = 0.85$) (13).

Statistical analysis

In the statistical analysis of the data, we performed an “efficacy analysis” in which we only included subjects who completed the entire 90-day treatment period. Our rationale for using this approach was to evaluate the efficacy of this therapy under ideal treatment parameters.

Initially, descriptive statistics were generated for all variables. To test whether the treatment groups were statistically similar, age and duration of diabetes were compared by treatment, sex, and medication regimen using a multiple ANOVA statistical framework. In addition, a cross-tabulation of the counts of patients by sex, medication, and treatment was analyzed using a log-linear model. The VPT scores, continuous variables measured on at least a ratio scale, were analyzed using a nested repeated-measures design via the MIXED procedure in SPSS (version 14; SPSS, Chicago, IL). Two sites (great toe and fifth metatarsal) were tested on both the left and right feet of each patient, so for the experimental design, the two feet were nested within each patient and two sites were nested within each foot. Other variables that were or could be feasibly treated as continuous variables, including glycosylated hemoglobin, nerve conduction velocities (several measures for both peroneal and tibial nerves), visual analog scale pain scores, MNSI scores, and NeuroQoL scores, were evaluated using repeated-measures ANOVA via the SPSS GLM procedure. Initially, repeated-measures tests were run with treatment group as a factor and also with continuous covariates (age and duration of diabetes) and categorical factors (sex and medication type). However, because none of these added factors were significant, a single-factor repeated-measures design was used with just one factor: treatment group. The four monofilaments provided at most a five-level

ranking of neuropathy. To analyze the ordinal SWM scores, a nonparametric factorial analysis for longitudinal data was used (14,15). The NeuroQoL survey has pairs of related questions: one on a five-point scale for degree or severity and one on a three-point scale of importance. These five- and three-point scale values were multiplied together, forming a composite score. The paired questions were grouped into five categories (Table 2), and each category had a question on the overall importance of that category. A composite category score was created by multiplying the sum of individual category scores by the category importance score, providing an approximately continuous measure that could be analyzed by repeated-measures ANOVA.

In all of the statistical tests, the main focus was to examine whether there was a treatment-time interaction. The treatment-time interaction looks at four effect sizes: treatment at baseline, treatment after 3 months, sham at baseline, and sham after 3 months. It tests whether there is a change in the effects of the treatment group over time compared with the sham group over time. If there was a significant treatment-time interaction, differences in the baseline and ending marginal effects were examined to determine whether the sham or anodyne treatments were associated with the result.

RESULTS— We screened 174 subjects. Sixty-nine subjects met the inclusion and exclusion criteria and were randomly assigned in the study. Sixty subjects (120 limbs) completed the 90-day evaluation period. There were 33 completers in the anodyne MIRE treatment arm and 27 in the sham treatment arm. One study-related adverse event was reported: one subject developed a small wound on his lower leg that healed without incident. Of the nine noncompleters, one had a myocardial infarction, one could not attend visits because of work, and the remainder withdrew without any additional comment.

Demographics were similar among the active and sham groups at baseline (Table 1). There were no statistically significant changes in SWM, VPT, nerve conduction velocity, MNSI, visual analog scale pain (Table 1), or NeuroQoL scores (Table 2) for active compared with sham therapy. The ordinal results for the SWM tests were analyzed using a nonparametric factorial design for longitudinal data (Table 3). The effect size is based on an

Table 2—Results for the NeuroQoL

Aggregated results and treatment	Time	Mean ± SE	95% CI	Difference	Treatment-time interaction P value	
Painful symptoms	MIRE	Start	222.8 ± 26.6	169.1–276.6	70.5	0.67
		End	293.4 ± 32.6	227.5–359.3		
	Sham	Start	172.3 ± 29.9	111.9–232.7	86.9	
		End	259.2 ± 36.7	185.2–333.3		
Loss of feeling	MIRE	Start	65.04 ± 11.7	41.6–88.5	30.8	0.53
		End	95.8 ± 13.9	67.8–123.7		
	Sham	Start	80.8 ± 12.6	55.5–106.2	41.3	
		End	122.2 ± 15.0	912.0–152.4		
Sensory motor symptoms	MIRE	Start	105.6 ± 13.8	77.8–133.4	12.1	0.14
		End	117.7 ± 13.7	90.0–145.4		
	Sham	Start	85.1 ± 15.3	54.2–116.1	32.9	
		End	118.0 ± 15.3	87.2–148.9		
Limited home and leisure activities	MIRE	Start	59.2 ± 7.0	45.2–73.2	4.6	0.05
		End	63.8 ± 7.9	47.9–79.7		
	Sham	Start	26.3 ± 8.2	9.8–42.8	26.4	
		End	52.7 ± 9.3	34.0–71.4		
Emotional burden	MIRE	Start	348.4 ± 47.1	252.9–444.0	113.6	0.85
		End	462.0 ± 60.7	338.8–585.2		
	Sham	Start	356.5 ± 47.1	260.9–452.0	123.2	
		End	479.6 ± 60.7	356.4–602.8		
Overall rating	MIRE	Start	6.0 ± 0.21	5.6–6.4	0.03	0.27
		End	6.0 ± 0.22	5.6–6.5		
	Sham	Start	5.8 ± 0.23	5.3–6.2	0.37	
		End	6.1 ± 0.24	5.7–6.6		

These data are results for aggregated scores for social-psychological categories evaluated by the survey.

integral of the product of functions derived from empirical distribution functions of the overall or marginal distributions of the ordinal data (14,15). Overall, there was no statistical evidence that the anodyne treatment was effective in improving sensory perception compared with the sham treatment. Not only was there no clear benefit from the treatment, but there also was a large placebo effect in which sham therapy showed double the number of improvements in effect size compared with the anodyne treatment.

We used the NeuroQoL to evaluate self-reported functional status (Table 2). For each category the sham results showed a larger increase than that for the anodyne treatment. There was one statistically significant treatment-time interaction, “Limited home and leisure activities,” but it was significant because the sham group improvement was much greater than that for the anodyne group.

To assess balance we used two questions from the NeuroQoL that evaluate unsteadiness when standing and walking (Table 1). There was a significant improvement in self-reported unsteadiness with walking in the sham treatment group ($P = 0.05$). To evaluate pain we used a 10-cm visual analog pain scale and the NeuroQoL (Table 2). Neither demonstrated any significant change during the treatment period.

CONCLUSIONS— The results of this study demonstrate that anodyne MIRE therapy provided no more improvement in peripheral sensation, balance, pain, or quality of life than sham therapy. In our study the daily treatment was more frequent and the 90-day evaluation period was longer than those in previous studies. We used several objective and subjective measures of sensory neu-

ropathy, and none of them showed a significant improvement after 90 days of therapy compared with sham treatment. Our results are similar to the RCT reported by Clift et al. (8).

An evaluation of the data from Leonard et al. (6) and Arnall et al. (4) suggests that there was probably not an overall improvement in sensory neuropathy despite their stated conclusions. There were several classic errors in analysis. First, Leonard et al. did not perform an ITT analysis, as the data from the entire study population were not included in the analysis or reported in the article. Instead, they separately evaluated subgroups with moderate and severe neuropathy. It seems very likely that there would not be a significant effect if the entire patient population had been included in the analysis. Second, the analysis used was not appropriate in the studies of Arnall et al. and Leonard et al. The Semmes Weinstein data are count data, and the authors used

Table 3—Results for nonparametric factorial analysis of SWM data

Site	Treatment effect size						Interaction P value	
	Left side			Right side			Left	Right
	Start	End	Difference	Start	End	Difference		
Dorsum foot								
MIRE	0.556	0.489	−0.067	0.560	0.477	−0.083	0.056	0.18
Sham	0.451	0.493	0.042*	0.489	0.576	0.086		
Great toe								
MIRE	0.519	0.473	−0.046	0.526	0.477	−0.048	0.57	0.11
Sham	0.523	0.468	−0.055	0.489	0.517	0.028		
Third toe								
MIRE	0.554	0.436	−0.118	0.531	0.488	−0.044	0.004*	0.19
Sham	0.488	0.523	0.036*	0.492	0.496	0.004		
Fifth toe								
MIRE	0.508	0.520	0.012	0.562	0.483	−0.079	0.24	0.031*
Sham	0.458	0.507	0.049	0.458	0.497	0.039*		
Fifth metatarsal								
MIRE	0.537	0.520	−0.017	0.557	0.520	−0.037	0.40	0.31
Sham	0.464	0.467	0.003	0.456	0.447	−0.009		
Third metatarsal								
MIRE	0.496	0.509	0.013	0.519	0.561	0.042†	0.35	0.014†
Sham	0.479	0.514	0.035	0.497	0.411	−0.086		
Lateral midfoot								
MIRE	0.564	0.477	−0.087	0.490	0.572	0.082†	0.34	0.041†
Sham	0.503	0.446	−0.056	0.481	0.458	−0.023		
First metatarsal								
MIRE	0.543	0.504	−0.040	0.526	0.522	−0.003	0.057	0.50
Sham	0.444	0.498	0.054*	0.473	0.470	−0.003		
Medial midfoot								
MIRE	0.533	0.518	−0.016	0.530	0.517	−0.013	0.42	0.21
Sham	0.470	0.468	−0.002	0.452	0.486	0.034		
Heel								
MIRE	0.484	0.527	0.043	0.494	0.530	0.035	0.20	0.21
Sham	0.498	0.489	−0.009	0.490	0.477	−0.013		

Treatment effects are shown for the start and end of the study. Seventeen positive differences (shown in bold) indicate improvement over time. Of these, four treatment-time interactions, two for the sham and two for the anodyne treatment, were significant at the 5% level (last two columns). Although the positive differences in effect size are not all statistically significant, 11 of 17 times there was an improvement of the sham treatment, whereas there were only six positive differences for the anodyne treatment. *Significant sham result. †Significant anodyne result.

tests for continuous data in their analysis. Third, both Arnall et al. and Leonard et al. failed to provide analysis comparing the interaction of how patients' conditions changed over time for sham and active therapy. An examination of the data suggests that whereas there was a significant marginal improvement, there was not a significant change over time between the active and sham treatments. Both studies separately compared means at the beginning and end of the study via a *t* test for the active and sham treatments and then compared the *P* values from these separate tests. This results in what is called a Simpson's paradox: whereas one of the marginal results is significant, comparisons of treatment differences over time are not.

Placebo effect

Surprisingly, there was a strong placebo effect in our study and in previous RCTs. Clift et al. (8), Arnall et al. (4), and Leonard et al. (6) demonstrated improved sensation with SWMs in the sham group. Arnall et al. were the only investigators who evaluated VPT. No data were provided in the text, but the authors indicated that VPT did not improve. In fact, in the study of Leonard et al., there was a significant improvement with the MNSI in both active and sham groups with moderate neuropathy. If these studies had failed to include a sham therapy arm, MIRE would appear to provide a significant improvement in peripheral sensation because of the placebo effect. This effect may help to explain the observations in

uncontrolled studies showing that MIRE was effective (1–3,5). On the basis of these observations, the majority of the existing work that supports MIRE therapy for pain, sensory improvement, or wound healing is problematic.

One of the main limitations in evaluating neuropathy is the accuracy and reliability of the tools for longitudinal testing. The SWM was the primary instrument used to assess neuropathy in the RCTs of Leonard et al. (6), Arnall et al. (4), and Clift et al. (8) and in several uncontrolled studies. Even new monofilaments have considerable variation in accuracy and durability with significant reduction of loading force after repetitive loading (16–19). Our study as well as the study by Clift et al. used several "levels" of SWMs.

In the RCT of Clift et al., a new set of SWMs from North Coast Medical was used at the beginning of the study (8). However, in the study by Leonard et al. no information was provided about the manufacturer, previous use, or replacement of SWMs. We used 4-, 10-, 26-, and 60-g monofilaments and replaced them after evaluating every 10 patients in an effort to reduce SWM wear and increase reproducibility of results. In addition, our study and that of Arnall et al. used VPT testing. VPT is a well-accepted device for quantitative sensory testing (20); however, large coefficients of variation have been identified in several studies when individuals with diabetes and elderly individuals were tested (21,22).

In addition, our study may have been underpowered to determine subtle changes in neuropathy with therapy. However, previous studies reported positive results with fewer subjects who received fewer treatments with shorter evaluation periods than in our RCT. We did not see any strong trends that MIRE was different from sham therapy, and, in fact, there were instances in which sham therapy was superior to MIRE therapy.

Pain and balance

Evaluation of pain and balance were not the primary objectives in our study or in other RCTs. We included them because they were outcomes used in a previous study (4). One of the problems in previous work was that "pain" and "balance" were not separately evaluated in legs treated with sham and active therapy. There was no distinction based on therapy, so it was not possible to determine whether the reported "improvement" was due to the effect of MIRE or the strong placebo effect observed in all of the RCTs with MIRE. We did not enroll subjects on the basis of symptoms of painful neuropathy or balance impairment, so many of our study subjects did not have severe symptoms. Our results did not identify any difference in pain or balance in patients treated with MIRE or sham therapy. However, we probably did not enroll the optimal study population to evaluate these outcomes.

The result of this study should be generalizable to individuals with diabetes with "loss of protective sensation." In normal practice MIRE therapy is initially provided three times a week in a clinical setting. Many patients, will subsequently use the device at

home, so our daily "dosing" regimen and period of evaluation reflects long-term use patterns. At present there is no compelling evidence that MIRE can improve loss of protective sensation such that high-risk people with diabetes have a decreased risk of foot complications. Our results did not show a change in self-reported balance, pain, quality of life, electrodiagnostic studies, or clinical sensory measures. MIRE is no more effective than placebo or sham therapy in improving peripheral sensation, balance, and pain in individuals with diabetes.

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