MULTI RADIANCE® MEDICAL

MR5™ ACTIV PRO LaserShower

NCT04322812

A double-blind, placebo-controlled randomized evaluation of the effect of the MR5™ ACTIV PRO LaserShower for the temporary relief of pain associated with fibromyalgia.
Version 1.4, May 30, 2018

PROTOCOL IDENTIFICATION NUMBER - ***DeNovo01 Version 1.0***

CLINICAL STUDY RESULTS

August 9, 2020

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6. PURPOSE OF STUDY

The purpose of this clinical study was to determine the effectiveness of the Multi Radiance® Medical MR5™ ACTIV PRO LaserShower, manufactured by Multi Radiance® Medical (the Company), for the temporary relief of pain associated with fibromyalgia.

7. INDICATION FOR USE

The indication (claim) being sought through support of the results of this clinical study is:

“The Multi Radiance® Medical MR5™ ACTIV PRO LaserShower is indicated for temporary pain relief associated with fibromyalgia.”

SECTION II: DEVICE INFORMATION: MULTI RADIANCE® MEDICAL MR5™ ACTIV PRO LASERSHOWER

1. DEVICE DESCRIPTION AND DETAILS

The MR5™ ACTIV PRO LaserShower is a cordless, ultra-portable laser therapy system employing synchronous use of Super Pulsed Laser (GaAs 905 nm), and ultra-bright infrared, red and blue LEDs (850 nm, 630 nm and 470 nm) to optimize the biological effects of the entire phototherapeutic window to accelerate healing and reduce pain.

The Super Pulsed Laser (905 nm) produces high powered light in billionth-of-a-second pulses that deliver photons, or light energy, deep into the target tissue without any harmful effects; that is, it produces high photon density without hazardous thermal impact to tissue. It enables unique control of depth/power of laser energy delivering controlled light energy deep into tissue more effectively than Continuous Wave and pulsed-modulated lasers while preserving the overlying epidermis. In addition, multiple radiances of pulsed red light (660nm) and pulsed broadband infrared emitting diodes (850 nm) penetrate shallower tissue depths than the laser but provide a broader spectrum of coverage.

NOTE: The MR5™ ACTIV PRO LaserShower used in this clinical study **DID NOT EMPLOY THE BLUE LIGHTS.** The final product available for market after clearance will not include software to enable activation of the blue light output.

Additional information and details regarding the MR5™ ACTIV PRO LaserShower device are contained under the section titled: 'DEVICE INFORMATION: MR5™ ACTIV PRO LASERSHOWER of the accompanying clinical study protocol.

2. REGULATORY HISTORY

The MR4™ Multi Radiance Therapy system and its various emitters and accessories have received the following 510(k) clearances from the United States Food and Drug Administration (FDA):

- K080102
- K071445
- K061614
- K043055

Additional information and details regarding the device regulatory history are contained under the section titled: 'REGULATORY HISTORY: MR5™ ACTIV PRO LASERSHOWER of the accompanying clinical study protocol.

SECTION III: STUDY AND SAMPLE DESIGN

1. STUDY DESIGN

The study was a placebo-controlled, randomized, double-blind, parallel group, multi-center design.

2. SAMPLE DESIGN

2.1. SAMPLE POPULATION

Subjects were females aged 25 to 60 years with a diagnosis of fibromyalgia as per the current American College of Rheumatology (ACR) criteria and symptoms present for greater than 3 months.

All subjects who qualified as eligible for participation in this clinical study satisfied each of the inclusion criteria and none of the exclusion criteria as contained in full in the STUDY QUALIFICATION section of the accompanying clinical study protocol.

2.2. SAMPLE SIZE

Ninety (90) individuals were enrolled in the study. All 90 enrolled subjects completed study participation according to protocol.

Of the 90 participating subjects, 45 were randomized to the active treatment group and 45 were randomized to the placebo treatment group.

2.3. RECRUITMENT AND COMPENSATION

All qualifying study subjects were recruited from among the investigators' normal pool of patients who voluntarily came to their offices seeking treatment for fibromyalgia and from among individuals who responded to recruitment flyers and print ads.

Qualifying subjects received financial compensation of $550 for completed study participation.

3. STUDY TREATMENT ADMINISTRATION

Each subject received nine total treatment administrations with the MR5™ ACTIV PRO LaserShower device (active or sham) across a consecutive three-week period: three procedures per week, each procedure two or three days apart.

Exposure time to the MR5™ ACTIV PRO LaserShower device per each of the nine treatment administration sessions was 2 minutes per subject-reported tender point, with a minimum of 3 tender points and a maximum of 18 tender points treated, for a total possible range of treatment time from 6 to 36 minutes per session.

Each treatment administration session took place at the investigator's test site.

SECTION IV: STUDY PROCEDURES AND EVALUATIONS

1. STUDY PROCEDURES

The study comprised the three following successive phases.

1.1 PRE-PROCEDURE PHASE

The pre-procedure phase comprised:

(i) Study Qualification Evaluation
(ii) Pain Management Stabilization Phase

The Pain Management Stabilization Phase occurred during the one-week (7 day) period immediately preceding commencement of the procedure phase. During the stabilization phase, the subject was required to employ only the medication(s) and treatment(s)/ therap(ies) specified in her individualized pain management regimen as determined by the study investigator at commencement of the stabilization phase, for management of her fibromyalgia symptoms as needed.

The individualized pain management regimen was determined for each subject based on the medication(s) and treatment(s)/therap(ies) that she was using at the time of study entry to manage her fibromyalgia symptoms as needed. The individualized pain management regimen was therefore customized and different for each subject. The specific medication(s), treatment(s), therap(ies) and associated dosage/usage directions as per the subject's individualized pain management regimen was recorded by the investigator at commencement of the stabilization phase. Subjects recorded each incidence of use of the permissible medication(s), treatment(s) and therap(ies), as applicable, in the Subject Daily Diary on each day of the one-week stabilization phase.

At completion of the one-week pain management stabilization phase, the investigator reviewed the content of the Subject Diary to ensure there were no deviations in medication/ treatment/therapy use significant enough to warrant withdrawal of the subject from the study at that time. The subject then progressed to the Procedure Phase.

Additional information and details regarding the pre-procedure phase are contained under the section titled: 'PRE-PROCEDURE ASSESSMENT PHASE' of the accompanying clinical study protocol.

1.2 PROCEDURE PHASE

Each subject received nine total treatment administrations at the test site with the MR5™ ACTIV PRO LaserShower device (active or sham) across a consecutive three-week period: three procedures per week, each procedure two or three days apart, with total treatment administration time per individual session varying from 3 to 36 minutes depending on the number of subject-reported tender points, as explained in the STUDY TREATMENT ADMINISTRATION section above.

Additional information and details regarding the Procedure Phase, including the step-by-step treatment administration protocol, are contained under the section titled: 'PROCEDURE PHASE' of the accompanying clinical study protocol.

1.3 POST-PROCEDURE PHASE

There were two post-procedure evaluation visits following completion of the procedure phase:

(i) At completion of the last procedure administration: STUDY ENDPOINT EVALUATION.
(ii) Four (4) weeks following completion of the last treatment administration: FOLLOW-UP EVALUATION.

2. STUDY EVALUATIONS

The following outcome measures were recorded in this study at the applicable visits.

(i) Tender Point Count
(ii) Fibromyalgia Impact Questionnaire (FIQ)
(iii) Pain Rating on the 0-100 Visual Analog Scale (VAS)
(iv) Subject Satisfaction Rating on the Likert Scale
(v) Blinding Efficacy Evaluation
(vi) Adverse Events
(vii) Daily Subject Diary

Additional information and details regarding the Study Evaluations are contained in the accompanying clinical study protocol.

SECTION V: RESULTS SUMMARY AND CONCLUSION

BACKGROUND: The purpose of this clinical study was to determine the effectiveness of the Multi Radiance® Medical MR5™ ACTIV PRO LaserShower, manufactured by Multi Radiance® Medical (the Company), for the temporary relief of pain associated with fibromyalgia.

STUDY DESIGN: The study was a placebo-controlled, randomized, double-blind, parallel group, multi-center design.

SUBJECTS: Ninety (90) subjects completed the study: 45 randomized to the active procedure group and 45 randomized to the placebo group. Subjects were females aged 25 to 60 years with a diagnosis of fibromyalgia as per the current American College of Rheumatology (ACR) criteria and symptoms present for greater than 3 months. Average subject age was 45.24 years. Subjects were predominantly Caucasian (43%) and Hispanic (44.44%).

At study entry, subject average tender point count was 15.25, average Visual Analog Scale (VAS) pain rating was 77.76, and average Total Fibromyalgia Impact Questionnaire (FIQ) score was 78.61.

STUDY PROCEDURES: Subjects received nine treatment administrations with the MR5™ ACTIV PRO LaserShower (active or sham) to self-identified tender points region across a three-week period: three treatments per week, each procedure two to three days apart.

Subjects agreed to use only the medication(s), treatment(s) and therap(ies) determined during the individualized medication stabilization phase of the study to relieve any fibromyalgia pain, as needed, throughout study participation duration.

STUDY RESULTS

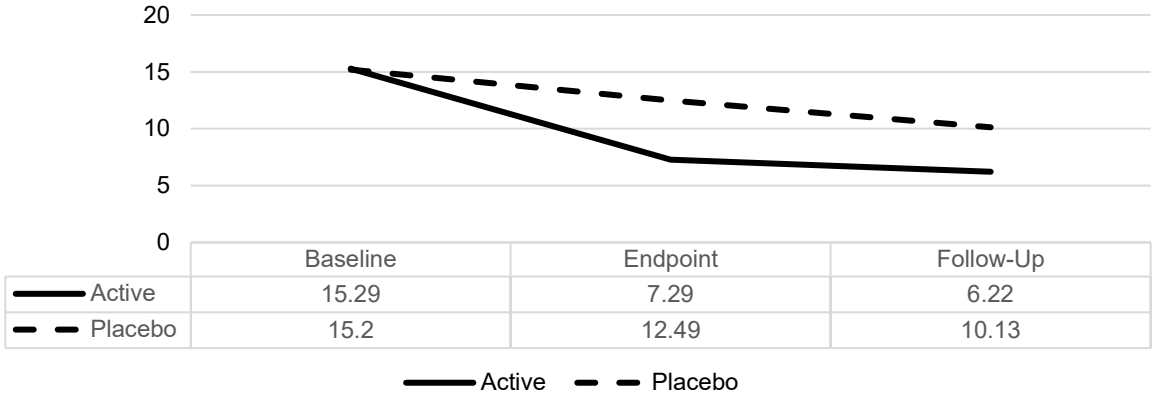
Primary efficacy outcome measure was predefined as the difference in the proportion of subjects between active and control groups who attained a decrease in tender point count of 20% or greater at study endpoint relative to baseline. Overall study success was predefined as at least a 30% difference in the proportion of individual subject successes between procedure groups.

86.67% of subjects who received the active procedures with the MR5™ ACTIV PRO LaserShower met the individual subject success criteria compared with 48.89% of placebo group subjects. Fischer's Exact Test for two independent proportions found the 37.78% difference to be statistically significant at $p<0.0005$.

Chart 1 below show the mean change in Tender Point Count across study duration.

While there was a slight progressive placebo effect across study duration, the treatment effect was substantially larger for the active procedure group that prevailed through to the 4-week follow-up evaluation.

Chart 1: Tender Point Count Across Study Duration



	Baseline	Endpoint	Follow-Up
Active	15.29	7.29	6.22
Placebo	15.2	12.49	10.13

The treatment effect as supported by mean VAS Ratings was substantially greater from baseline to 4-weeks follow-up evaluation for active group subjects versus placebo group subjects: a 46.17-point decrease compared with a 25.31-point decrease - a 20.86-point difference.

The treatment effect as supported by mean Total FIQ scores was substantially greater from baseline to 4-weeks follow-up evaluation for active group subjects versus placebo group subjects: a 38.04-point decrease compared with a 24.93-point decrease - a 13.11-point difference.

ADVERSE EVENTS: Adverse event incidence was minimal, and each was determined to be mild and either unrelated or potentially related to the study treatment. No adverse event required any intervention nor resulted in a subject withdrawing or being withdrawn from the study. Each adverse event fully and satisfactorily resolved by study completion.

CONCLUSION: These study results demonstrate that the MR5™ ACTIV PRO LaserShower is an effective tool for reducing fibromyalgia pain over a 3-week period.

SECTION VI: STUDY OUTCOME STATISTICAL ANALYSIS: RESULTS AND REPORT

1. SAMPLE DEMOGRAPHICS

The following sample demographics were recorded at Baseline evaluation.

1.1. GENDER

All 90 study subjects were female, as per the study inclusion criteria.

1.2. AGE

Table 1 below shows the mean, standard deviation (SD), and range of subject age in years for active and placebo group subjects.

Table 1: Age by Procedure Group

Age (years)	**Active (n=45)**	**Placebo (n=45)**
Mean	45.53	46.96
Standard deviation	7.95	8.11
Range	30 - 57	28 - 58

A **t-test for independent samples** revealed the 1.43 years difference in age between active and placebo group subjects to be not statistically significant: t=0.84; df=88; p(two-tailed) = 0.403 (p>0.05).

1.3. ETHNICITY

Table 2 below shows ethnicity breakdown for active and placebo group subjects.

Table 2: Ethnicity by Procedure Group

Ethnicity	**Active (n=45)**	**Placebo (n=45)**
Caucasian	16 (36%)	23 (51%)
Hispanic	21 (47%)	19 (42%)
African American	8 (17%)	2 (5%)
Asian	0 (0%)	1 (2%)

Subject ethnicity was predominantly and comparably Caucasian and Hispanic in each of the active and placebo subject groups.

1.4. WEIGHT

Table 3 below shows mean, standard deviation and range of weight in pounds for active and placebo group subjects.

Table 3: Weight by Procedure Group

Weight (lbs)	Active (n=45)	Placebo (n=45)
Mean	154.57	154.61
Standard Deviation	21.21	25.40
Range	130.07 – 187.34	130.07 – 191.80

A **t-test for independent samples** revealed the 0.04-pound difference in weight between active and placebo group subjects to be not statistically significant: t=0.010; df=88; p(two-tailed) = 0.992 (p>0.05).

1.5. HEIGHT

Table 4 below shows mean, standard deviation and range of height in inches for active and placebo group subjects.

Table 4: Height by Procedure Group

Height (ins)	Active (n=45)	Placebo (n=45)
Mean	63.15	64.09
Standard Deviation	2.60	2.30
Range	59.06 – 68.90	59.06 – 68.11

A **t-test for independent samples** revealed the 0.94-inch difference in height between active and placebo group subjects to be not statistically significant: t=1.83; df=88; p(two-tailed) = 0.071 (p>0.05).

1.6. FITZPATRICK SKIN TYPE

Table 5 below shows Fitzpatrick Skin Type for active and placebo group subjects.

Table 5: Fitzpatrick Skin Type by Procedure Group

Fitzpatrick Skin Type	Active (n=45)	Placebo (n=45)
I	5 (11%)	6 (13%)
II	9 (20%)	8 (18%)
III	19 (42%)	21 (47%)
IV	7 (16%)	8 (18%)
V	4 (9%)	2 (4%)
VI	1 (2%)	0 (0%)

Across both procedure groups, most subjects fell comparably within the range of Fitzpatrick Skin Types I through IV. Fitzpatrick Skin Type III was the most prevalent, followed by Types II, IV and I, respectively.

2. PRE-PROCEDURE MEASURES

The following pre-procedure measures were recorded at Baseline evaluation.

2.1. TENDER POINT COUNT

Table 6 below shows the mean and standard deviation of subject-reported tender point count at pre-procedure evaluation for active and placebo group subjects.

Table 6: Tender Point Count by Procedure Group

Tender Point Count	Active (n=45)	Placebo (n=45)
Mean	15.29	15.20
Standard Deviation	3.08	2.69

A **t-test for independent samples** revealed the 0.09 difference in tender point counts between active and placebo group subjects to be not statistically significant: t=0.15; df=88; p(two-tailed) = 0.88 (p>0.05).

2.2. VISUAL ANALOG SCALE (VAS) PAIN RATINGS

Table 7 below shows the mean and standard deviation of subject-recorded VAS pain ratings at pre-procedure evaluation for active and placebo group subjects.

Table 7: Visual Analog Scale (VAS) Pain Ratings by Procedure Group

VAS Pain Rating	Active (n=45)	Placebo (n=45)
Mean	80.64	74.89
Standard Deviation	13.99	13.54

A **t-test for independent samples** revealed the 5.75 difference in VAS pain ratings between active and placebo group subjects to be not statistically significant: t=1.98; df=88; p(two-tailed) = 0.051 (p>0.05).

2.3. FIBROMYALGIA IMPACT QUESTIONNAIRE (FIQ)

Table 8 below shows the mean and standard deviation of total FIQ scores at pre-procedure evaluation for active and placebo group subjects.

Table 8: FIQ Total Score by Procedure Group

FIQ Total Score	Active (n=45)	Placebo (n=45)
Mean	79.68	77.54
Standard Deviation	11.05	11.57

A **t-test for independent samples** revealed the 2.14 difference in FIQ Total Scores between active and placebo group subjects to be not statistically significant: t=0.908; df=88; p(two-tailed) = 0.37 (p>0.05).

In conclusion, at baseline, there were no statistically significant differences found between subjects randomized to the two procedure groups (active and placebo) for any of the recorded sample demographics and pre-procedure measures. Therefore, none of these variables is considered a potential covariate in impacting study outcome.

3. PRIMARY EFFICACY OUTCOME ANALYSIS

3.1. PRIMARY STUDY SUCCESS EVALUATION

The aim of this study was to determine if the treatment effect of the MR5™ ACTIV PRO LaserShower for the active procedure group is greater than that for the placebo procedure group.

The study was predetermined to be considered a success if, using the Intent-To-Treat (ITT)) analysis, the primary endpoint was statistically significant at the 0.05 level.

Primary efficacy outcome measure was predefined as the difference in the proportion of subjects between active and control groups who achieved a clinically meaningful and statistically significant decrease in tender point count of 20% or greater at study endpoint (end of procedure administration phase) relative to baseline (pre-procedure).

Overall study success was predefined as at least a 30% difference in the proportion of individual subject successes between procedure groups. It was anticipated that about 60% of subjects in the test group would meet the individual success criteria and about 30% of subjects in the placebo group would meet the individual success criteria.

Study success endpoint evaluation was pre-determined as following completion of the 3-week procedure administration phase.

Rationale and justification for the study primary outcome measure and related success evaluation is contained in the 'STATISTICAL ANALYSIS PLAN' section of the accompanying clinical study protocol document.

Populations Examined
It was intended that the primary outcome measure be evaluated for the following two subject populations:

(i) *Intent-to-Treat (ITT) Population*

Primary efficacy analysis was predetermined to be performed per the intent to treat (ITT) principle; wherein subjects are included in the analysis if they were randomized to study procedure group and had a valid baseline (pre-procedure) visit. Dropouts, terminated subjects, and so forth were to be handled by either the Last Observation Carried Forward (LOCF) method, Tipping Point Analysis, or Multiple Imputation Analysis.

(ii) Per-Protocol Population

Per-protocol analysis was intended to corroborate the conclusions drawn from the analysis based on the ITT population. The per-protocol analysis would exclude subjects with major protocol deviations and incompletes (drop-outs, non-compliant subjects, disqualified subjects, etc.).

As every enrolled randomized subject in this clinical study completed all study visits and procedures and had all study measurements recorded through to study endpoint evaluation, only the ITT analysis was performed for primary outcome study success evaluation, with no need to employ missing data methodology.

3.2. PROPORTION OF SUCCESSES

Table 9 below shows the number and percentage of active and placebo group subjects who met the study **individual subject success criteria** of a 20% or greater decrease in Tender Point Count from baseline to endpoint evaluation.

Table 9: Individual Success Criteria Met by Procedure Group

	Active Subjects	**Placebo Subjects**
n	45	45
n meeting success criteria	39	22
% meeting success criteria	**86.67%**	**48.89%**

There is a difference of 37.78% in the proportion of subjects who met the individual success criteria between procedure groups, such that 37.78% more active group than placebo group subjects evidenced a decrease in Tender Point Count of 20% or greater from baseline to study endpoint, exceeding the pre-established target of a 30% difference between procedure groups by +7.78%, indicative of **superior treatment effect of the MR5™ ACTIV PRO LaserShower over placebo**.

A **Fischer's Exact Test** for two independent proportions was conducted to compare the statistical significance of the proportion of successes between procedure groups.

The results are as follows:

2 X 2 Table	**Success Met**	**Success Not Met**	
Test Group	39	6	45
Placebo Group	22	23	45
	61	29	90

- p(two-tailed) = 0.00023; p<0.0005

The difference in the proportion of study successes between procedure groups was found to be **statistically significant at p<0.0005,** meaning that the two procedure groups gave significantly different results, such that the greater treatment effect observed for the study primary outcome measure of change in Tender Point Count from baseline to study endpoint for subjects in the active group relative to subjects in the placebo group is statistically significant and can be attributed to the **efficacy of the application of the MR5™ ACTIV PRO LaserShower over a placebo device.**

Therefore, study success as per the primary outcome evaluation of study success according to the predefined criteria has been attained.

3.3. CHANGE IN TENDER POINT COUNT

Table 10 below shows the mean, standard deviation, and magnitude of the change in Tender Point Count from baseline to study endpoint evaluation for active versus placebo group subjects.

Table 10: Baseline and Endpoint Tender Point Count by Procedure Group

	Active Group (n=45)		Placebo Group (n=45)	
	Mean	**SD**	**Mean**	**SD**
Baseline	15.29	3.08	15.20	2.69
Endpoint	7.29	3.99	12.49	3.92
# Change	*-8.00*	*4.72*	*-2.71*	*3.67*

The 8.00-point mean decrease in Tender Point Count from study Baseline to Endpoint for active group subjects is about 3 times greater than the relative 2.71-point mean decrease in Tender Point Count attained for placebo group subjects. A **t-test for independent samples** found the 5.29 difference in mean change in Tender Point Count between active and placebo group subjects to be statistically significant ($p<0.0001$).

Change scores were additionally evaluated by **Analysis of Covariance (ANCOVA),** with change from Baseline to Endpoint in Tender Point Count as the dependent variable, pre-procedure (Baseline) Tender Point Count as the covariate and procedure group (active or placebo) as the main effect.

Table 11 below shows the observed and adjusted means for the absolute change in Tender Point Count from baseline to study endpoint, adjusting for baseline Tender Point Count.

Table 11: Change in Tender Point Counts Adjusting for Baseline Tender Point Count

Tender Point Count	**Active Subjects (n=45)**	**Placebo Subjects (n=45)**
Observed mean	-8.00	-2.71
Adjusted mean	-7.97	-2.74

- $F=41.9$; $p<0.0001$

In consideration of baseline Tender Point Count as a covariate, $F=41.9$ is statistically significant at $p<0.0001$, such that if the individual differences in baseline Tender Point Count are removed, the two adjusted means significantly differ to the degree of $p<0.0001$.

These results indicate that the actual (active) MR5™ ACTIV PRO LaserShower is more effective than the placebo device in treating fibromyalgia pain, and that this statistically significant treatment effect is independent of the baseline Tender Point Count.

1. SUPPORTIVE SECONDARY OUTCOME ANALYSIS

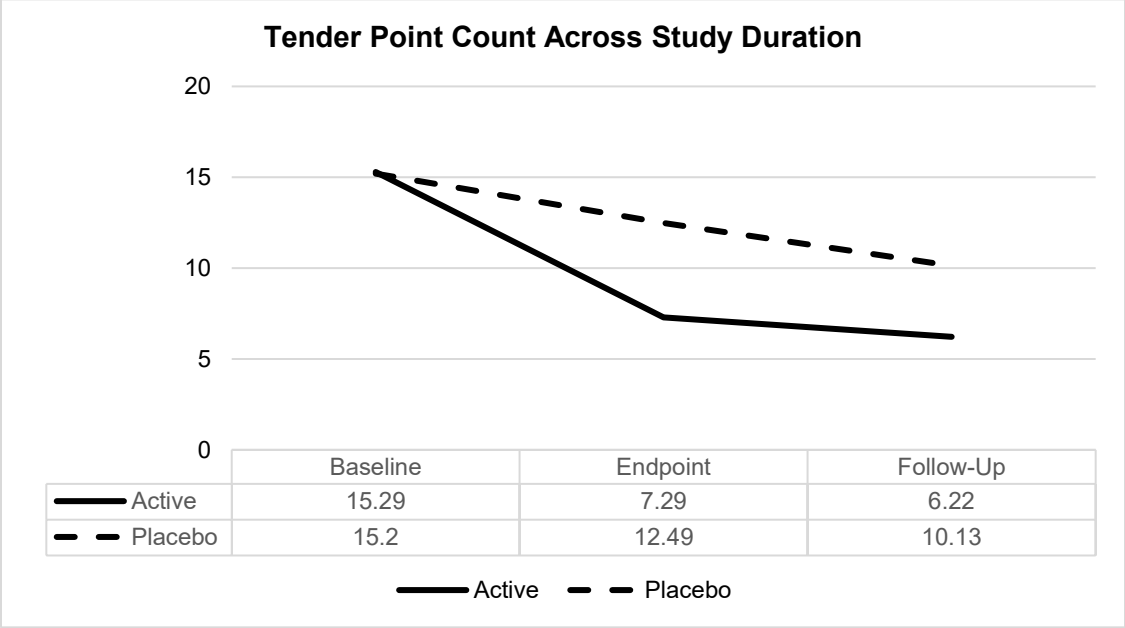
4.1 CHANGE IN TENDER POINT COUNT ACROSS STUDY DURATION

Table 12 and Chart 1 below show the mean and standard deviation of tender point count across study duration, encompassing baseline, endpoint and 4-week follow-up evaluations, for active versus placebo group subjects.

Table 12: Tender Point Count Across Study Duration by Procedure Group

	Active Group (n=45)		Placebo Group (n=45)	
	Mean	**SD**	**Mean**	**SD**
Baseline	15.29	3.08	15.20	2.69
Endpoint	7.29	3.99	12.49	3.92
Follow-Up	6.22	4.25	10.13	4.66

Chart 1: Tender Point Count Across Study Duration by Procedure Group



From Table 12 and Chart 1, it is observed that while there was a slight progressive placebo effect across study duration, the treatment effect was substantially larger, and as demonstrated previously statistically significantly greater and prevailed through to the 4-week follow-up evaluation.

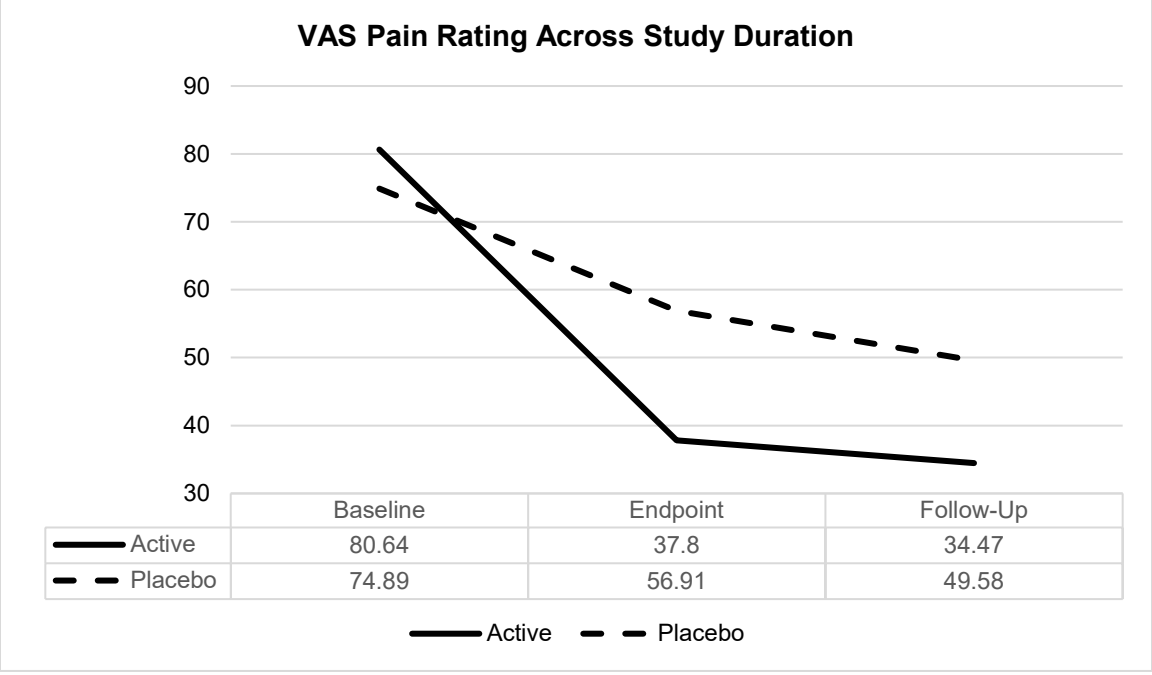
4.2 CHANGE IN VISUAL ANALOG SCALE (VAS) PAIN RATINGS ACROSS STUDY DURATION

Table 13 and Chart 2 below show the mean and standard deviation of VAS pain scores on the 0 to 100 Visual Analog Scale (VAS) across study duration, encompassing baseline, endpoint and 4-week follow-up evaluations, for active versus placebo group subjects.

Table 13: VAS Pain Rating Across Study Duration by Procedure Group

	Active Group (n=45)		Placebo Group (n=45)	
	Mean	**SD**	**Mean**	**SD**
Baseline	80.64	13.99	74.89	13.54
Endpoint	37.80	23.31	56.91	20.31
Follow-Up	34.47	26.34	49.58	26.21

Chart 2: VAS Pain Rating Across Study Duration by Procedure Group



From Table 13 and Chart 2, it is observed that as with Tender Point Count, while there was a progressive placebo effect across study duration for VAS Pain Ratings, the treatment effect was substantially larger – a 46.17-point decrease in mean VAS ratings for active group subjects from baseline to follow-up evaluation compared with a 25.31-point decrease in mean VAS ratings for placebo group subjects, a 20.86-point difference in the change between treatment groups, in favor of the active treatment group.

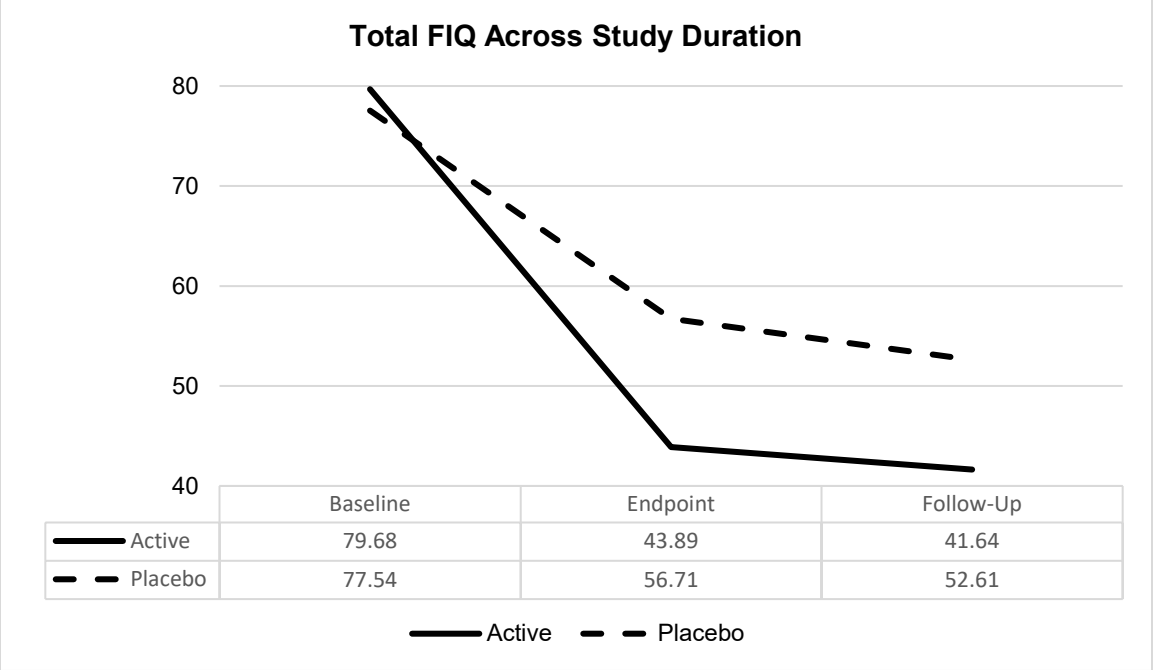
4.3 CHANGE IN TOTAL FIBROMYALGIA IMPACT QUESTIONNAIRE (FIQ) ACROSS STUDY DURATION

Table 14 and Chart 3 below show the mean and standard deviation of Total FIQ scores across study duration, encompassing baseline, endpoint and 4-week follow-up evaluations, for active versus placebo group subjects.

Table 14: Total FIQ Across Study Duration by Procedure Group

	Active Group (n=45)		Placebo Group (n=45)	
	Mean	**SD**	**Mean**	**SD**
Baseline	79.68	11.05	77.54	11.57
Endpoint	43.89	22.34	56.71	18.63
Follow-Up	41.64	25.86	52.61	21.57

Chart 3: Total FIQ Across Study Duration by Procedure Group



From Table 14 and Chart 3, it is observed that as with Tender Point Count and VAS Pain Ratings, while there was a progressive placebo effect across study duration for the Total FIQ Score, the treatment effect was substantially larger – a 38.04-point decrease in Total FIQ Score for active group subjects from baseline to follow-up evaluation compared with a 24.93-point decrease in mean Total FIQ Scores for placebo group subjects, a 13.11-point difference in the change between treatment groups, in favor of the active treatment group.

4.4. STUDY OUTCOME SATISFACTION RATINGS

The subject was asked to rate how satisfied she was with the treatment outcome at study endpoint and at study follow-up evaluations, by selecting the most applicable response from the following 5-point Likert scale.

- Very Satisfied
- Somewhat Satisfied
- Neither Satisfied nor Dissatisfied
- Not Very Satisfied
- Not at All Satisfied

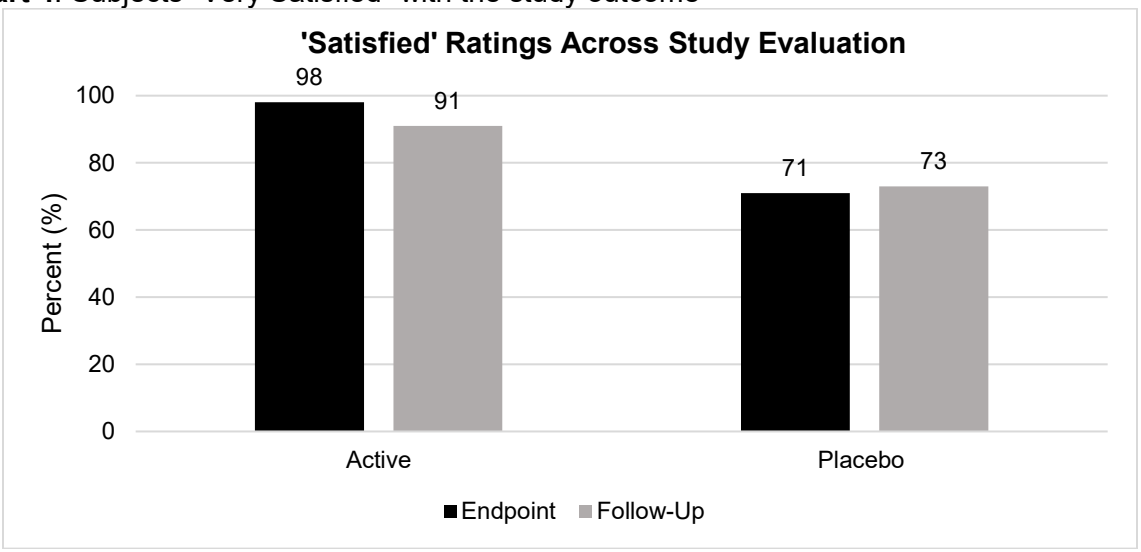
Table 15 below shows the number of subjects who reported each level of satisfaction/ dissatisfaction by procedure group at each of the two evaluations.

Table 15: Study Outcome Satisfaction

	Endpoint		Follow-Up	
	Active (n=45)	Placebo (n=45)	Active (n=45)	Placebo (n=45)
	n (%)	n (%)	n (%)	n (%)
Very satisfied	36 (80%)	23 (51%)	34 (76%)	26 (58%)
Somewhat satisfied	8 (18%)	9 (20%)	7 (15%)	7 (15%)
Neither satisfied nor dissatisfied	-	7 (15%)	4 (9%)	6 (13%)
Not very satisfied	1 (2%)	3 (7%)	-	3 (7%)
Not at all satisfied	-	3 (7%)	-	3 (7%)

Chart 4 below shows the number of subjects who were 'Very Satisfied' with the study outcome following procedure administration week #8, by procedure group.

Chart 4: Subjects "Very Satisfied" with the study outcome



Fischer's Exact Test for two independent proportions was conducted to compare the statistical significance of the proportion of successes between procedure groups at each evaluation.

The results are as follows:

Endpoint	**'Satisfied'**	**'Neither' / 'Not Satisfied**	
Active Group	44	1	45
Placebo Group	32	13	45
	76	14	90

- p(two-tailed) = 0.00076; p<0.001

Follow-Up	**'Satisfied'**	**'Neither' / 'Not Satisfied**	
Active Group	41	4	45
Placebo Group	33	12	45
	74	16	90

- p(two-tailed) = 0.051; p>0.05

The difference in the proportion of subjects who reported being 'Satisfied' with the treatment outcome was statistically significant at p<0.001 at endpoint evaluation, but not statistically significant at follow-up evaluation (p>0.05).

2. POTENTIAL CONFOUNDING STUDY FACTORS

Potential confounding factors were evaluated and determined to not have had an impact on study outcome, as presented below.

5.1. TREATMENT TIMES

Treatment time with the MR5™ ACTIV PRO LaserShower device per administration session had a possible range of 6 to 36 minutes: 2 minutes per subject-reported tender point, with a minimum of 3 tender points and a maximum of 18 tender points treated. The impact of the variation in treatment times on treatment outcome was evaluated.

Table 16 below shows the mean, standard deviation (SD), and range of treatment times in minutes for active and placebo group subjects.

Table 16: Treatment Time by Procedure Group

Treatment Time (mins.)	**Active (n=45)**	**Placebo (n=45)**
Mean	21.12	22.87
Standard deviation	5.68	6.35
Range	9.78 - 36	11.87 - 36

A **t-test for independent samples** revealed the 1.75-minute difference in treatment times between active and placebo group subjects to be not statistically significant: t=-1.38; df=88; p(two-tailed) = 0.17 (p>0.05).

The impact of treatment time variations was additionally evaluated by **ANCOVA** with change from Baseline to Endpoint in Tender Point Count as the dependent variable, treatment time as the covariate, and procedure group (active, placebo) as the main effect.

Table 17 below shows the observed and adjusted means for the absolute change in Tender Point Count from baseline to study endpoint, adjusting for treatment time.

Table 17: Change in Tender Point Count Adjusting for Treatment Time

Tender Point Count	**Active (n=45)**	**Placebo (n=45)**
Observed mean	-8.00	-2.71
Adjusted mean	-8.03	-2.68

- F=35.07; p<0.0001

In consideration of treatment time as a covariate, F=35.07 is statistically significant at p<0.0001, such that if the individual differences in treatment times are removed, the two adjusted means significantly differ to the degree of p<0.0001.

This result indicates that the actual (active) MR5™ ACTIV PRO LaserShower is more effective than the placebo device in treating fibromyalgia pain, and that this statistically significant treatment effect is independent of the total treatment time.

5.2. MEDICATION AND THERAPY USE

The control methodology for non-study pain medication and therapy use across study duration was the implementation of individualized pain management regimens. The individualized pain management regimen was determined for each subject based on the medication(s) and treatment(s)/therap(ies) that she was using at the time of study entry to manage her fibromyalgia symptoms as needed. The individualized pain management regimen was therefore customized and different for each subject. The specific medication(s), treatment(s), therap(ies) and associated dosage/usage directions as per the subject's individualized pain management regimen was recorded by the investigator at commencement of the stabilization phase. Subjects recorded each incidence of use of the permissible medication(s), treatment(s) and therap(ies), as applicable, in the Subject Daily Diary on each day of her study participation.

Implementation of the subject's individualized pain management regimen commenced with a one-week (7 day) Pain Management Stabilization Phase that occurred immediately preceding commencement of the procedure phase. At completion of the one-week pain management stabilization phase, the investigator reviewed the content of the Subject Diary to ensure there were no deviations in medication/treatment/therapy use significant enough to warrant withdrawal of the subject from the study at that time. The subject then progressed to the Procedure Phase and then the Post-Procedure Phase.

There were no deviations in medication/treatment/therapy use significant enough to warrant withdrawal of any subject from the study following completion of the Stabilization Phase.

5.2.1. Medication Use

5.2.1.1. First Day Medication Use by Study Period

Subjects recorded on which day of each of the Stabilization, Procedure, and Follow-Up evaluation study phases they took their first dose of a medication listed in their Individualized Pain Management Regimen.

Table 18 below shows the number and percentage of subjects who did not take any medications listed in their Individualized Pain Management Regimen across each of the respective study phases, by procedure group

Table 18: Incidence of No Medication Use Across Study Period by Procedure Group

Study Phase	**Active Group (n=45)**	**Placebo Group (n=45)**
Stabilization	10 / 22%	6 / 14%
Procedure	9 / 20%	6 / 14%
Follow-Up	12 / 27%	7 / 16%

The number of subjects who did not take any authorized pain medication during each of the study phases was consistent between active and placebo procedure groups and across the respective study phases.

Table 19 below shows the frequency of first day authorized pain medication use by subjects across Stabilization, Procedure, and Follow-Up evaluation study phases for each of active and placebo group subjects.

Table 19: Frequency of First Day Medication Use Across Study Period by Procedure Group

	Active Group (n=45)			**Placebo Group (n=45)**		
First Day	**Stabilization**	**Procedure**	**Follow-Up**	**Stabilization**	**Procedure**	**Follow-Up**
1	26 (58%)	24 (53%)	20 (45%)	31 (68%)	26 (58%)	20 (45%)
2	4 (10%)	4 (10%)	1 (2%)	3 (6%)	3 (6%)	-
3	2 (4%)	5 (11%)	2 (4%)	3 (6%)	2 (4%)	6 (13%)
5	1 (2%)	-	1 (2%)	1 (2%)	-	2 (4%)
6	1 (2%)	-	1 (2%)	1 (2%)	3 (7%)	1 (2%)
7	1 (2%)	1 (2%)	2 (4%)	-	2 (4%)	2 (4%)
8+	-	2 (4%)	6 (14%)	-	3 (7%)	7 (16%)

Most subjects (about one-half overall) who used authorized pain medication(s) during the respective study phases did so on the first day of each phase consistently across each of the three respective study phases and across active and placebo procedure groups.

5.2.1.2. Total Medication Dosage by Study Period

Table 20 below shows the mean and standard deviation of the number of authorized doses of medication subjects took to manage their pain across Stabilization, Procedure, and Follow-Up evaluation study phases for each of active and placebo group subjects.

Table 20: Total Medication Doses Across Study Period by Procedure Group

	Active Group (n=45)			Placebo Group (n=45)		
First Day	**Stabilization**	**Procedure**	**Follow-Up**	**Stabilization**	**Procedure**	**Follow-Up**
Mean	4.93	9.91	18.89	6.58	17.42	27.64
SD	6.94	12.53	31.55	8.18	25.33	45.78

One-Way ANOVA for correlated samples was performed to assess the change in total medication doses taken between each of the three successive study phases by procedure group.

(i) *Active Group*: Statistically significant differences in total medication doses taken across successive study phases were detected for active group subjects: F=9.65; p=0.000162 (p<0.0005).

Subsequent **Tukey HSD Analysis** revealed those statistically significant differences to occur between the following study phases:

- Stabilization to Follow-Up: p<0.01
- Procedure to Follow-Up: p<0.05

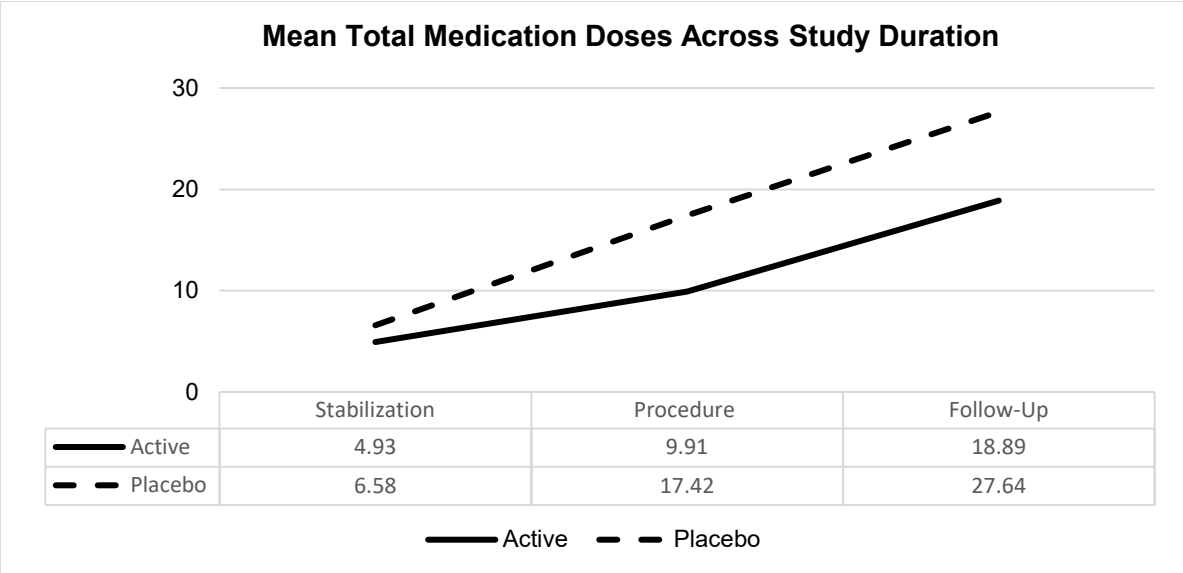
(ii) *Placebo Group:* Statistically significant differences in total medication doses taken across successive study phases were detected for placebo group subjects: F=9.68; p=0.000162 (p<0.0005).

Subsequent **Tukey HSD Analysis** revealed those statistically significant differences to occur between the following study phases:

- Stabilization to Follow-Up: p<0.01

Chart 5 below shows the mean total medication doses taken by subjects across the three successive study phases by procedure group.

Chart 5: Mean Total Medication Doses Across Study Phases by Procedure Group



From Chart 5, it is observed that total mean authorized medication doses taken during the stabilization study phase were comparable, indicating that prior to entering the study procedure phase, subjects' pain medication use was consistent across procedure groups (t-test for independent samples: t=-1.03, p=0.306, p<0.05).

It is also observed that total mean authorized medication doses taken increased progressively across the three successive study phases for both subject groups, but the increase was notably greater for placebo group subjects at both the procedure and follow-up evaluation phases.

5.2.2. Specific Medications

Table 21 below lists the number of active group subjects who took the individual authorized medications by category across study phases.

Table 21: Authorized Medication Use Across Study Phases for Active Group Subjects

Component	Medicine	Stabilization	Procedure	Follow-Up
NSAIDS (Non-Steroidal Anti-Inflammatory Drugs)	Ibuprofen	2	4	2
	Amitriptyline	3	4	1
	Cyclobenzaprine	3	5	3
	Advil	2	1	2
	Neosaldine	0	3	0
	Torsilax	0	1	1
	Infralax	1	2	1
	PACO	1	2	0
	Neolefrin	0	0	0
	Fluoxetine	2	1	3
	Naproxen	1	1	1
	Gabapentin	2	1	2
	Voltaren	0	2	0
	Decadron	0	2	0
	Mionevrix	0	1	1
NNA (Non-Narcotic Analgesics)	Profenid	0	2	1
	Dorflex	7	9	9
	Dipyrone	5	10	11
PST (Psychotropics)	Lyser	0	0	1
	Tylex	0	1	0
	Musculare	1	1	1
	Buprovil	1	0	0
	Tramadol	3	0	1
	Miosan	4	4	4
	Nimesulide	0	1	0
	Pregbalin	3	2	2
	Myorilax	1	0	1
	Neuralgex	1	0	0

	Clonazepam	0	0	1
	Vimovo	0	0	1
	Paracetamol	2	1	0
	Tramal	3	2	3
	Benziflex	0	0	1
	Novalgina	1	1	0
	Anador	0	1	0
	Diprospam	1	0	0
	Naproxen	0	1	0
	Revange	0	1	0
	Diclofenac	0	1	1
	Vescaten	0	1	0
	Piroxican	0	0	1
	Prebictal	0	0	1
	Corticoid	0	0	1
	Toragesic	0	0	2
	Lyrica	0	0	2
	Amitriptyline	1	0	0
	Deocil	2	0	0
	Hydrochloride	0	0	1
	Duloxetine	1	1	2
	Codeine	1	3	3
	Velija	4	4	4
	Topirmate	1	1	1
	Stilnox	1	0	1
	Quetiapine	0	1	1
	Sertraline Hydrochloride	1	0	0
	Nortriptyline Hydrochloride	1	0	1
	Rivotril	1	1	1
	Pamelor	1	0	0
Sleeping Pill	Glucosan	0	1	0
Diabetic Medication	Glifage	1	1	0
Herbals Medicines and Supplements	Folic Acid	1	1	1
	Calcium	1	1	0
	Magnesium	1	0	1
	Folic Acid	1	0	0
	Vitamin D	0	0	1
	Vitamin E	0	0	1

Table 22 below lists the number of placebo group subjects who took the individual authorized medications by category across study phases.

Table 22: Authorized Medication Use Across Study Phases for Placebo Group Subjects

Component	Medication	Stabilization	Procedure	Follow-Up
NSAIDS	Chondroylin	0	1	0
	Ibuprofen	3	4	2
	Amitriptyline	4	4	4
	Oxotron	1	1	1
	Cyclobenzaprine	6	4	9
	Advil	3	2	3
	Neosaldine	1	0	2
	Ketoprofen	1	1	3
	Torsilax	2	3	1
	Flanax	1	2	3
	Lizax	1	0	0
	Infralax	2	1	2
	PACO	1	1	0
	Meloxicam	2	2	3
	Tandrilax	1	2	4
	Neolefrin	0	1	0
	Opradol	0	0	1
	Profenid	0	0	1
NNA	Dorflex	7	8	5
	Dipyrone	7	2	1
	Lyser	1	2	2
	Tylex	2	1	0
	Musculare	0	0	1
	Tramadol	1	1	2
	Buscopan	1	1	0
	Atrosil	1	0	0
	Dual	1	1	1
	Miosan	2	1	2
	Nimesulide	1	1	1
	Pregbalin	2	7	5
	Nortriptyline	1	1	0
	Myorilax	1	0	0
	Neuralgex	1	1	0
	Trilax	1	0	1
	Clonazepam	2	2	3
	Argador	1	0	0
	Vimovo	1	0	0

	Paracetamol	1	1	2
	Tramal	2	2	2
	Proclimax	1	2	1
	Cannabidiol	1	2	1
	Tylenol	0	2	2
	Benziflex	0	1	0
	Tiflex	0	1	0
	Hemal	0	1	0
	Novalgina	0	1	0
	Miralax	0	1	0
	Anador	0	1	0
	Melatonin	0	1	1
	Dolamin Flex	0	0	1
	Toragesic	0	0	1
BETA BLOCKER	Fronal	0	0	1
	Diacerein	0	0	1
	Tecnomet	0	0	1
SUPPLMEMENT	Vitamin D	2	2	1
	Vitamin B1	0	2	0
	Vitamin B6	0	2	0
	Vitamin B12	0	2	0
	Saffron	1	1	0
	Magnesium Dimalate	1	2	2
PST	Amitriptyline	1	0	0
	Elifore	1	1	1
	Dorene	1	1	0
	Anafranil	1	1	1
	Enalapril	2	1	0
	Lyrica	2	0	1
	Duloxetine	0	1	0
	Hydrochloride	2	2	0
	Prefiss	1	1	0
	Miosan	0	2	0
	Duloxetine	1	0	0
	Donaren	1	0	0
	Agomelatine	1	0	0
	Carisprodal	1	0	1
	Prednisolone	1	1	1
	Codeine	1	1	2
	Velija	0	1	1
	Abretia	0	1	1

	Seretid	0	1	0
	AMI	0	0	1
	Doril	0	0	1
	Quetiapine	0	0	0
	Rivotril	0	1	2
	Trazodone Hydrochloride	0	0	1
DIURETIC	Hydrochlorithazide	1	0	0
HERBAL MEDS	Ginkgo Biloba	1	0	0
	Methotrexate	1	1	0
CORTICOSTEROID	Pantoprazol	1	0	1
PROTON INHIBITOR	Pantoprazol	1	0	1
	Glucosan	0	0	1
ANTI DIABETIC	Ibuflex	0	0	1
ANTI DEPRESSANT	Flouxetine	0	0	0

5.2.2. Treatment/Therapy Use

5.2.2.1. First Day Treatment/Therapy Use by Study Period

Subjects recorded on which day of each of the Stabilization, Procedure, and Follow-Up evaluation study phases they first engaged in a treatment/therapy listed in their Individualized Pain Management Regimen.

Table 23 below shows the number and percentage of subjects who did not partake in any treatment(s)/therap(ies) listed in their Individualized Pain Management Regimen across each of the respective study phases, by procedure group.

Table 23: Incidence of No Treatment/Therapy Use Across Study Period by Procedure Group

Study Phase	**Active Group (n=45)**	**Placebo Group (n=45)**
Stabilization	26 / 58%	22 / 49%
Procedure	27 / 60%	18 / 40%
Follow-Up	22 / 71%	27 / 60%

The number of subjects who did not partake in any authorized treatment/therapy use during the study was slightly greater for active than placebo group subjects during the procedure and follow-up evaluation phases, indicative of a decreased need for alternative means of pain control outside of the study treatment administration, indicative of a greater treatment effect for the active device compared with sham.

Table 24 below shows the frequency of first day authorized pain medication use by subjects across Stabilization, Procedure, and Follow-Up evaluation study phases for each of active and placebo group subjects.

Table 24: Frequency of First Day Medication Use Across Study Period by Procedure Group

	Active Group (n=45)			Placebo Group (n=45)		
First Day	**Stabilization**	**Procedure**	**Follow-Up**	**Stabilization**	**Procedure**	**Follow-Up**
1	7 (16%)	8 (18%)	2 (4%)	11 (24%)	7 (16%)	3 (7%)
2	5 (11%)	1 (2%)	-	5 (11%)	3 (7%)	1 (2%)
3	2 (4%)	1 (2%)	3 (7%)	2 (4%)	5 (11%)	2 (4%)
4	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)	2 (4%)
5	-	1 (2%)	1 (2%)	2 (4%)	3 (7%)	4 (9%)
6	4 (9%)	1 (2%)	-	1 (2%)	-	-
7	-	1 (2%)	-	1 (2%)	-	-
8 +	-	4 (9%)	6 (14%)	-	8 (18%)	6 (14%)

Most subjects (about one-half overall) who used authorized pain medication(s) during the respective study phases did so on the first day of each phase consistently across each of the three respective study phases and across active and placebo procedure groups.

5.2.2.2. Specific Treatment/Therapies

Table 25 below lists the number of active group subjects who partook in any of the individual authorized treatments/therapies across study phases.

Table 25: Treatment/Therapy Use by Active Group Subjects Across Study Duration

Treatment/Therapy	Stabilization	Procedure	Post-Procedure
Massage	9	10	6
Gel (Vecasten, Salonpas)	3	4	3
Water Sports	1	0	1
Pilates	1	1	1
Hot Water	1	1	0
Acupuncture	3	2	3
Hydrotherapy	1	0	0
Corticosteroid Ointment	1	1	1
Physiotherapy	1	2	3
Ice	0	1	0
Stretching	0	1	1
Meditation	0	1	0
Thermal Cushion	0	1	0
Walk/Run	0	0	1

Table 26 below lists the number of placebo group subjects who partook in any of the individual authorized treatments/therapies across study phases.

Table 26: Treatment/Therapy Use by Placebo Group Subjects Across Study Duration

Treatment/Therapy	Stabilization	Procedure	Post-Procedure
Hot Water	4	4	3
Massage	11	14	6
Dorflex	2	0	0
Propanol	1	0	0
Dramin	1	0	0
Frontal	1	0	0
Dance	1	1	1
Drainage	2	3	1
Stretching	4	4	2
Ice bag	1	1	1
Pilates	2	3	2
Accupuncture	7	3	1
Walk/Run	1	1	2
Water Sports	1	1	1
lian Gong	1	0	0
Gel Cream	0	3	5
Exercise Ball	0	1	0
Hemotherapy	0	1	0
Laser	0	1	0
Auriculotherapy	0	1	0
Physiotherapy	0	1	3
Fluoxetine	0	1	0
Cataflan Spray	0	0	2
Compress	0	0	1
TENS	0	0	1

3. BLINDING EFFICACY EVALUATION

Blinding efficacy evaluation was conducted through analysis of Subject and Assessment Investigator Perceived Subject Group Allocations and Rationale responses, recorded at study endpoint and again at the 4 weeks post-procedure evaluation.

6.1. SUBJECT PERCEIVED GROUP ALLOCATIONS

The number and percentage of subjects who accurately determined her group allocation (active or placebo laser) at each of study endpoint and 4-week follow-up evaluations is as follows:

Study Endpoint

- ✓ 39 of the 45 (86.67%) active group subjects accurately determined they had been assigned to the active procedure group.
- ✓ 14 of the 45 (31.1%) placebo group subjects accurately determined they had been assigned to the placebo procedure group.

4 Weeks Follow-Up

- ✓ 38 of the 45 (84.44%) active group subjects accurately determined they had been assigned to the active procedure group.
- ✓ 14 of the 45 (31.1%) placebo group subjects accurately determined they had been assigned to the placebo procedure group.

Fischer's Exact Test for two independent proportions was conducted to compare the statistical significance of the proportion of successes between procedure groups at each evaluation.

The results are as follows:

Endpoint	**Active Group Allocation**	**Placebo Group Allocation**	
Active Group	39	6	45
Placebo Group	31	14	45
	70	20	90

- p(two-tailed) = 0.0743; p>0.05

Follow-Up	**Active Group Allocation**	**Placebo Group Allocation**	
Active Group	38	7	45
Placebo Group	31	14	45
	69	21	90

- p(two-tailed) = 0.134; p>0.05

6.1.1. Subject Perceived Group Allocation Rationales

Subjects provided the following verbatim reasons for their perceived determination of group allocation at completion of the procedure administration phase.

(i) Study Endpoint: Active Group Subjects: Active Procedure Group Allocation Determination

Because of decreasing pain.
Because I haven't had any more seizures of fibromyalgia pain.
Because the pain decreased a lot and at some points was solved.
Because I got improvements in tiredness, sleep, pains.
For after the sessions, I often felt an improvement in the intensity of pain.
Because it went straight to the point of pain and decreased.
It worked for me.
I feel it was real because it decreased by 60% of the pain.
Because there was a reduction in pain and willingness.
Because pain has decreased a lot in this period.
They helped me a lot with the pains.
Because I felt a little improvement.
Because you softened the pain.
Feeling better.
Because I found treatment very professional and I improved a lot until my high esteem. I look great.
Because after the applications, I felt very good.
It was real because it slowed down a lot and gave me more courage.
Because the treatment worked!! Sometimes it can be even psychological.
Because I felt good.
Right after the first session, I felt the pain sits or decreased.
Heating of the region, reactions after treatment. Some moments I questioned if the laser was applied (placebo) because i did not feel what I mentioned above.
I think it was real because my pains have subsided a lot.
Because I felt improvement, come out relieved after the treatments.
Because I felt in my body and I believe.
The pains disappeared.
Because I feel so good.
I think I was in the real because my pain subsided, tiredness decreased, mood improved.
Because I don't feel pain.
I think it's real because it did very well.

Because I felt improvement in many areas, I don't think it's psychological.
Because I felt less pain and started sleeping well, which happened before.
I felt an improvement in my pains and quality of life, I was able to perform my activities better
My pains are real and diffuse by changes several times a day.
Today I no longer feel the pains that were almost constant.
In 2 sessions I noticed improvement, but very little, so for that reason I think falls into the real group (active).
I felt good after the session at the pain site!
Pain soothed.
I felt some relief within a few days.
Today I feel great.

(ii) 4 Weeks Follow-Up: Active Group Subjects: Active Procedure Group Allocation Determination

Because they lessened the pain.
I relieved some of the severe pain I had.
Pain slowed greatly and in some cases was remedied.
Because I felt a difference in disposition, days without feeling weight in the body and severe pain.
For a few days I felt better.
I slept well and relieved of low back pain.
Because it was great, and I'm feeling very well.
I believe it was the real because I had a lot of improvement, even in the days that the psychological wasn't so well, I felt laser improvement.
Because it reduced the pain picture.
Especially from what I felt in the morning when I got up. I felt significant improvement.
When doing the treatment, I felt better, painless, and when doing the treatment was without medication.
I had a little improvement.
Because after I finished the treatment, I felt less pain.
Because you softened the pain.
For feeling better.
because I presented improvement even after.
I think, I don't think I'm sure it's real because of the improvement I've had.
Because I had a great relief in pain.
Because I felt good.
Because right after the first session I felt good and saw results.

Because I felt heating during application, reduced pain, and improved sleep.
I think it was true because I've improved my pains. I felt better when I did my day-to-day tasks.
The reason is a lot of pain.
Because I felt reactions to treatment.
Because I got better with my pain, I'm great.
Because I felt a lot of pain to the point of crying, the second day of treatment was already decreasing the pains. Today I say I'm fine.
Because in the first week, I've already started to feel better.
Because I felt improved (lesser) pain.
It was real because it's been a lot less pain.
I had no pain after treatment for three weeks, and after a death in the family, the pain started again.
The treatment was so real and effective – it changed my life.
Since I started the treatment, I have been able to perform my activities better, with more willingness and with better quality.
I felt a difference in fatigue from 10 to 8 improvement in motivation to treat and hope to take this treatment in a popular way.
Because the pain slowed greatly after.
I believe I was inserted into the real group because at least two sessions I feel a little improvement (little) but I felt it.
Improved pain at applied site.
For feeling relief in pain.
It was real because I felt much better about the pain.

(iii) Study Endpoint: Active Group Subjects: Placebo Procedure Group Allocation Determination

Some points solved and others did not.
Because I get out of the house, come get something to improve and knowing that stress makes me in more pain.
The temperature of the appliance, the same did not always make noise.
I didn't feel any improvement or reaction.
For the permanence of pain.
I got better! But with doubts, joint pains.

(iv) 4 Weeks Follow-Up: Active Group Subjects: Placebo Procedure Group Allocation Determination

By doing the treatment I felt less pain, I think due to the fact that I had the hope of an improvement it made me less stressed and helped me to have more positive thoughts
I think that because of the speed of treatment in the stitches and because I feel no reaction as to the laser applied on site (hot or cold type)
Because I had days where I felt nothing happened.
Didn't feel any improvement or worsening.
For the reason that I continue with severe pain in the body.
I think it had a psychological effect.
I didn't feel much difference.

(v) Endpoint: Placebo Group Subjects Placebo Procedure Group Allocation Determination

Because I didn't see such an expected result.
Because it wasn't right for me, I didn't feel any effect.
I didn't get any pain relief.
Because I didn't feel any significant improvement. In the first week I slept better, but I think it was because of the change in routine.
I could have improved more, because there was a day of improvement and a difficult day, I don't know if it's in my head "I want to improve" I want to end the pain completely.
Because I didn't see a significant result regarding pain relief.
Because it improves now and then. Sometimes it was fine and sometimes it wasn't. Even because I don't know if for my pain, the number of times applied was sufficient.
For the little I know about the laser and the conversation I had with the other girls who had a significant improvement, I could not feel all this improvement. I expected more improvement.
The pains disappeared and came back during treatment.
Because there was no improvement.
For the reason of not having passed the pain.
I didn't feel any improvement.
I have chronic pain in the shoulder blade at point 14 and I have not improved with the treatment. That pain was the compass.
Despite seeing a "light" on the device, I did not feel much result in my pain.

(vi) 4-Week Follow-Up: Active Group Subjects: Placebo Procedure Group Allocation Determination

I didn't feel any improvement.
Some points were good, others were not.
I feel pain in the same way as before.
Regarding the pains, I didn't feel so much difference.
The pains continued.
Because I didn't feel any significant improvement, and I continued with the pain.

I had an expectation of pain improvement.
What I felt before remained. So I didn’t feel any effective improvement, which makes me believe I received a placebo.
I believe that there would be a greater improvement in relation to pain, for not having a 100% improvement, I believe that the group I was in was the placebo.
During that one month, after the treatment, I had two strong crises. I showed a little improvement that in my opinion was due to the temperature change (in the cold I feel better).
One day I felt better, others didn't.
Because I felt nothing, no improvement.
Because I felt no difference in pain, especially in the shoulder blade and hips (most painful points).
Because I expected improvement during the treatment, and I didn't feel it.

(vii) Endpoint: Placebo Group Subjects Active Procedure Group Allocation Determination

By improving pain and sleep, even though I have to move more to attend.
Because it took my pain away.
Because it decreased pain, improved anxiety, and muscle tension.
The treatment is real, but my problem still hasn't resolved 100%, but 50% has, and I realized that with a lot of effort it hurts more.
Because it improved a little.
Change in sleep, I slept for more hours.
I believe it to be real, because my body reacted in some way with the application of the laser, either positive or negative hours.
Because I felt an improvement in pain after application.
Because the pains were remedied after treatment.
I believe it is the real one because I felt a difference in pain, and it changed the pain points and decreased them.
I believe it was the real laser because during the day I felt positive points and positive changes in daily activities.
Daily provision.
Because I felt really good during the 3 weeks of treatment.
I believe I was treated for feeling a great relaxation on the days that the laser was applied, especially on Mondays, perhaps for being Saturday and Sunday without treatment, too much sleep, too relaxed, with many hours of sleep between 10 and 14 hours.
I believe I am being treated in the real group because I had satisfactory results with the pain. If it was not the device, I had a miracle because I feel pain free.
Because I felt improvement, mainly in the legs.
Because the pain improved.
Pain reduction.
Improved quality of life.

Because it's cold, and I'm out of medicine, and I'm not in pain.
Because I didn't feel much pain / I was able to do my tasks without pain.
By having peaks of improvement in pain.
Despite everything, I feel much better than before.
It was real because I had a little improvement.
Because I felt better.
I think it was real, I was fine in the first week because of a tragic news I couldn't improve until then.
Because I felt so much better.
I noticed improvement.
My right hand's stiffness improved a lot.
I believe that during those 30 days, I saw my improvement in fibromyalgia pain.
Improvement of acute pain.

(viii) 4 Weeks Follow-Up: Placebo Group Subjects Active Procedure Group Allocation Determination

Due to the decrease in pain during the procedures and a progressive increase after a few days without treatment.
Because I'm without pain.
Because it lessened the pain and anxiety.
Because I leave here relaxed.
Because I improved a little.
Before going through this treatment, I didn't have any latent pain at the points of fibromyalgia, and after the first application, I started to have more pain than I had without the laser application.
Because the pains got better.
Our mind wants everything right. Sometimes grass tea makes you beautiful. So: difficult because our mind lies.
I felt improvement withn the treatment.
I believe that as there are other types of laser treatment, this one also had a positive effect due to the sharpness of my improvement. I don't believe that fibromyalgia can be just emotional.
For being more willing to day to day.
Because I'm very well.
Yes, because it also received chrome.
It was real due to the change in the body, mind is fine, pain free.
Because my pains have lessened. I think you should include your feet at the points.
Because it tingled the legs.
Improvement in pain at the points of the fibro.

I believe that my treatment was real due to body changes, the pain decreased 50% in the places that hurt the most. I improved my self-esteem.
Because I am pain free and very happy
Because my pains passed, I felt great relief.
Because there was an improvement and a decrease in medications.
Because in the third week I felt him heating up.
because my pains have improved a lot. The quality of life, my night's sleep has also improved.
I had a little improvement.
Because I did not feel pain in the stitches.
Decreased pain.
Because I felt better during the applications.
I had pain reduction.
One day my hand was stiff and in pain later without realizing it the same day it improved.
Because I felt 100% improvement in fibromyalgia.
Because I felt improvement in local pain after using the device.

6.2. THERAPIST PERCEIVED GROUP ALLOCATIONS

The number and percentage of accurate determinations of subjects' group allocation (active or placebo laser) made by the study Therapist at each of study endpoint and 4-week follow-up evaluations is as follows:

Study Endpoint

- ✓ 36 of the 45 (80%) active group subjects were accurately determined by the Therapist to have been assigned to the active procedure group.
- ✓ 20 of the 45 (44.44%) placebo group subjects were accurately determined by the Therapist to have been assigned to the placebo procedure group.

4 Weeks Follow-Up

- ✓ 32 of the 45 (71.11%) active group subjects were accurately determined by the Therapist to have been assigned to the active procedure group.
- ✓ 19 of the 45 (42.22%) placebo group subjects were accurately determined by the Therapist to have been assigned to the placebo procedure group.

Fischer's Exact Test for two independent proportions was conducted to compare the statistical significance of the proportion of accurate subject group allocation determinations made by the study Therapist between procedure groups at each evaluation.

The results are as follows:

Endpoint	**Active Group Allocation**	**Placebo Group Allocation**	
Active Group	36	9	45
Placebo Group	25	20	45
	61	29	90

- p(two-tailed) = 0.023; p<0.05

Follow-Up	**Active Group Allocation**	**Placebo Group Allocation**	
Active Group	32	13	45
Placebo Group	26	19	45
	58	32	90

- p(two-tailed) = 0.271; p>0.05

6.2.1. Study Therapist Perceived Group Allocation Rationales

The rationales provided by the study Therapist for their perceived subject group allocations are provided verbatim below.

(i) Endpoint: Therapist Determination of Active Group Subjects as Being Allocated to the Active Procedure Group

Because the patient reported improved pain.
Because the patient reports pain lessening.
Patient reported immediate improvement in pain.
Because the patient showed improvement in pain in the first week.
Because the patient showed improvement in the second week.
Because the patient showed improvement in pain.
Because the patient achieved pain improvement.
Patient reports being better.
Because the patient achieved pain improvement.
Because the patient got better in the first week.
Why patient reports improvement of pain.
Because the patient achieved pain improvement.
Because the patient presented improvement and disposition.
Because the patient improved.
Patient stabilized pain points.
Because it got better in the second week.

Patient has postponed pain points.
Because patient reported improved pain.
Because the patient reported improvement
Because the patient reported improvement
Because reported improved pain during all treatment
Because the patient felt pain improvement
Because the patient reported improvement
Because it reports pain improvement
Because it showed improvement
Patient reported improvement
Patient reported improvement in pain and disposition
Patient claims to have improved
Because it reported improved pain
Because patient reported relief from pain.
Because the patient reports improvement
because the pain subsided
Because the patient claims to have improved
Because the patient claims to have decreased her degree of pain
Patient reports improvement of pain
Patient reports improvement of pains

(ii) 4 Weeks Follow-Up: Therapist Determination of Active Group Subjects as Being Allocated to the Active Procedure Group

Because the patient is still pain free.
Because the patient is still pain free.
Because the patient continued with improved pain.
Because the patient finished treatment painlessly.
Because the patient finished treatment with some points of pain.
Because the patient finished treatment without pain.
Because the patient continued with improved pain.
Because the patient finished treatment with significant improvement of pain.
Because the patient finished the treatment pain free.
Because you finished treatment painlessly.
Because the patient reports that pain decreased.
Because the stabilized pain treatment ended.
Because the patient improved.

Because the patient finished treatment painlessly.
Patient finished treatment with fewer pain points and decreased pain.
Because the patient finished treatment with fewer pain points.
Because the patient finished treatment without pain.
Because patient remained painless.
Because the patient observed improvement.
Because the patient says she greatly decreased her pain.
Because patient reports decreased pain.
Because reported improvement.
Patient says she has improved.
Patient claims to have improved.
Patient goes on without pain.
Patient reports better.
Because patient remained painless.
Because patient reported improved pain after treatment.
Because patient reports pain improvement.
Because patient reports pain improvement.
Because patient reports pain improvement.
Because it (the treatment) improved pain.
Because patient reports pain improvement.
Patient reports improvement.
Patient reports pain improvement.
Patient reports having improved.

(iii) Endpoint: Study Therapist Determination of Active Group Subjects as Being Allocated to the Placebo Procedure Group

Because the patient didn't have much pain improvement.
Because the patient reported indifference.
Because the patient continues without improvement.
Because the patient had no improvement.
Because the patient had no evolution.
Because the patient is still in pain.
Had no improvement.
Showed no improvement.
Didn't show so much improvement

(iv) 4 Weeks Follow-Up: Study Therapist Determination of Active Group Subjects as Being Allocated to the Placebo Procedure Group

Because the patient did not present significant improvement in pain.
Because the patient reports that it has improved little.
Because the patient reports having pain.
Because the patient finished treatment without evolution.
Because treatment did not achieve significant results.
Because the patient still reports pain.
Because patient reports that the pains have returned.
Because patient still have pain.
Because patient still in pain.

(v) Endpoint: Study Therapist Determination of Placebo Group Subjects as Being Allocated to the Placebo Procedure Group

Because the patient did not feel any improvement.
Patient showed no improvement.
Patient showed no improvement.
Because there was no improvement in pain.
Because the patient had no pain improvement.
Because the patient showed no improvement.
Because the patient did not improve.
Because the patient does not reduce the pain.
Because the patient showed instant improvement.
Because patient did not report pain improvement.
Because patient did not see improvement.
Because the pains are not completely gone.
Because patient still reports pain.
Because the patient had no pain relief.
Because patient did not report pain improvement.
Because the patient has not seen improvement.
Reported no improvement.
Because there was no improvement.
Pains don't stop completely.
Patient reported improvement but not as significant.

(vi) 4-Weeks Follow-Up: Study Therapist Determination of Placebo Group Subjects as Being Allocated to the Placebo Procedure Group

Because the patient still reports pain.
Patient had no pain improvement
Because the patient finished treatment without any improvement.

Because the patient finished treatment without improvement.
Because the patient finished treatment without any improvement.
Because the patient did not have an improvement in pain points.
Because the patient finished treatment without improving pain.
Because the patient finished treatment with pain.
Because the patient finished treatment with little improvement.
Because patients reported that the pains ran to the head (headaches).
Because there was little improvement observed.
Because patient did not report improvement.
Because the patient still reports having pain.
Because patient did not report improvement.
Because the reported that she had no significant improvement.
There was little improvement in pain.
Dd not report improvement.
Because it (the treatment) didn't significantly decrease the pain.
Hasn't improved so much.

(vii) Endpoint: Study Therapist Determination of Placebo Group Subjects as Being Allocated to the Active Procedure Group

Because the patient reports not feeling pain.
Because the patient improved (reduced) pain.
Reported to have decreased pain.
Because the patient got better in the second week.
Because the patient got an improvement in pain and fatigue.
Because it improved a little.
Because the patient improved in the second week of treatment.
Because the patient reduced the pain.
Because the patient improved in the second week.
Because there was a small improvement.
Because the patient improved in the second week.
Because the patient got better in the second week.
Because patient reported improvement in pain.
Because patient reported improvement in pain.
Because there was observed improvement.
Because patient reported improvement in pain.
Because it reports decreased pain.
Because the patient reports pain improvement.
Patient felt improvement.

Patient felt improvement.
Because the patient reports pain improvement.
Because patient reported improvement in pain.
Because patient reported improvement in pain.
Because it showed improvement in pain.
Because it lessened the pain.

(viii) Endpoint: Study Therapist Determination of Placebo Group Subjects as Being Allocated to the Active Procedure Group

Because the patient reports no more pain.
Because the patient reported improved pain.
Because the patient decreased pain and pain points.
Because the patient ended without pain the treatment.
Because the patient finished treatment with pain improvement
Because the patient greatly improved pain and decreased pain points.
Because the patient finished treatment without pain and pain-free points.
Patient showed significant improvement.
Because it achieved significant improvement.
Because the treatment ended without pain and decreased pain points.
Because the patient finished the treatment with significant improvement in pain points and pain.
Because despite the emotional shock, the pain was still controlled.
Because patient reports it (the treatment) controlled pain.
Because patient obtained observed improvement.
Because the patient reports improvement of pain at fibromyalgia points.
Because the patient reports pain improvement.
Because the patient reports pain improves.
Because the patient reported improved pain.
Because reported improved pain.
Because account improves pain.
Claims to have reduced pain.
Patient felt improvement.
Because it showed improvement.
Reported improvement in pain.
Patient felt improvement.
Because patient reports improvement

6.3. ASSESSOR PERCEIVED GROUP ALLOCATIONS

The number and percentage of accurate determinations of subjects' group allocation (active or placebo laser) made by the study Assessor at each of study endpoint and 4-week follow-up evaluations is as follows:

Study Endpoint

- ✓ 29 of the 45 (64.44%) active group subjects were accurately determined by the Assessor to have been assigned to the active procedure group.
- ✓ 28 of the 45 (62.22%) placebo group subjects were accurately determined by the Assessor to have been assigned to the placebo procedure group.

4 Weeks Follow-Up

- ✓ 32 of the 45 (71.11%) active group subjects were accurately determined by the Assessor to have been assigned to the active procedure group.
- ✓ 21 of the 45 (46.67%) placebo group subjects were accurately determined by the Assessor to have been assigned to the placebo procedure group.

Fischer's Exact Test for two independent proportions was conducted to compare the statistical significance of the proportion of accurate subject group allocation determinations made by the study Assessor between procedure groups at each evaluation.

The results are as follows:

Endpoint	**Active Group Allocation**	**Placebo Group Allocation**	
Active Group	29	16	45
Placebo Group	17	28	45
	46	44	90

- p(two-tailed) = 0.0199; $p<0.05$

Follow-Up	**Active Group Allocation**	**Placebo Group Allocation**	
Active Group	32	13	45
Placebo Group	24	21	45
	56	34	90

- p(two-tailed) = 0.127; $p>0.05$

6.3.1. Study Assessor Perceived Group Allocation Rationales

The rationales provided by the study Assessor for their perceived subject group allocations are provided verbatim below.

(i) Endpoint: Assessor Determination of Active Group Subjects as Being Allocated to the Active Procedure Group

Because patient reported better of (reduced) pain.
For patient reported improved pain and decreased number of points.
Because the patient reported that pain decreased in some points and came to run out of pain at points that were quite intense as that of glutes/lumbar.
Because the patient reports improvement at the time of evaluation.
Because the patient reports that pain has improved and is feeling better.
Because the patient reports pain improvement by more than 60% and decrease the feeling of fatigue.
Because the patient reports that pain has improved and is feeling better.
Because the patient reports that pain has improved and is feeling better.
Because the patient reported improvement.
Because the patient improved the pain.
Because the patient greatly improved the pains.
Because the patient reported much improvement in pain and fatigue.
Because the patient reported improved pain.
Patient reports improvement.
Because patient improved pain.
Patient greatly improved pain.
Because patient can improve pain in evaluation.
Because the patient presents improvement of pain.
Patient reports a lot of improvement with treatment.
Because patient reported pain relief.
Because patient reports pain improvement.
Because patient reports pain improvement.
Because the patient presented mild decrease in pain.
Because patient reports improvement.
Improved pain and fatigue.
Because the patient reported improvement.
Because the patient reported improvement.
Because the patient reported improved pain.
Because the patient reports a lot of improvement.

(ii) 4 Weeks Follow-Up: Assessor Determination of Active Group Subjects as Being Allocated to the Active Procedure Group

Because the patient presents improvement in pain and fatigue.
Because the patient reported that she is not in pain.
Because the patient feels much better and almost pain-free.
Patient reports pain improvement.
For patient reported decreased pain.
Because patient reported much improvement in pain.
Because the patient has reported much improvement and no longer feels severe pain or discouragement.
Because the patient reports improvement of pain last week by death in the family and fell ill.
Because the patient appears to be better and almost pain-free.
Because the patient reports improvement of pain and quality of life.
Because the patient reported improvement.
Because the patient reported that after the end of treatment, she had improvement in pain.
Because the patient reports that she feels better.
Because the patient reported improvement of pain even after 1 month of treatment.
Because the patient reported that she has very little pain, pain only on the shoulders.
Because patient reported fatigue relief.
Because the patient is still pain-free.
Because patient reported improved pain.
Because patient reports that pain has decreased.
Because patient improved pain.
Because patient reported improvement of pain.
Because she reports minimal pain.
Because patient is a little better.
Because patient reports improvement.
Because patient reports a lot of improvement.
Because the patient reports being painless.
Because the patient reported improvement.
Because the patient presents improvement in pain.
Because the patient improved the pain.
Because patient has diminished pain.
Patient goes on without pain.
Because patient improved pain.

(iii) Endpoint: Assessor Determination of Active Group Subjects as Being Allocated to the Placebo Procedure Group

Because patient said he stabilized the pain but didn't improve.
Because the patient reported pain last week.
Because the patient stressed that pain just didn't get worse, in her hands she decreased.
Because the patient reported that pain continues at some points.
Because the patient felt little improvement.
Because the patient still has pain.
Because patient still has pain.
Because the patient reports only little improvement.
Because the patient reports on the evaluation still a lot of pain.
Because patient still reports pain.
Still reports pain.
Because patient reported little improvement.
Because patient still has pain.
Patient continues with pain.
Because the patient still has pain.
Because patient reported little improvement.

(iv) 4 Weeks Follow-Up: Assessor Determination of Active Group Subjects as Being Allocated to the Placebo Procedure Group

Because the patient reported that the pains returned.
Because patient reports having pain this past week.
Because the patient reports that she feels pain still.
Because the patient did not feel pain improvement.
Because patient did not report improvement.
Because patient does not report any improvement.
Because patient still in pain.
Because patient has pain.
Because the patient reports that only improved half the pain.
Still in pain.
Patient continues with pain.
Patient says he still has pain.
Patient continues with pain.

(v) Endpoint: Assessor Determination of Placebo Group Subjects as Being Allocated to the Placebo Procedure Group

Because the patient still reports pain at all points.
Because the patient reported that only improved pain after massaging and not with the use of phototherapy.

For the patient reported that the pain continued.
Because the patient reported that pain comes back when he makes effort.
For patient reported that there was a small improvement only of a few points.
Because the patient still reports pain and behavior of depression.
Because the patient reported that the pain continued.
Because the patient reported that the pain continued.
For the patient reported worsening of pain and exhaustion.
Because the patient reports that he still continues with the pain.
Because the patient did not improve pain.
Because the patient has pain.
Because the patient improved very little.
Because the patient still has many pain points.
Because the patient reported little improvement.
Because the patient still reports having pain.
Because the patient still has pain.
Because patient still continues with pain.
Because the patient reports little improvement in pain
Because patient reports little improvement.
Still has pain.
Because the patient reported that she still feels a lot of pain.
Did not report improvement.
Because patient still has a lot of pain.
Because patient still in pain.
Because patient reported little improvement.
Because you didn't feel any better.
Patient improved little.

(vi) 4 Weeks Follow-Up: Assessor Determination of Placebo Group Subjects as Being Allocated to the Placebo Procedure Group

Because patient still reports pain.
Because the patient reported that he still has pain.
Because the patient just improved the pain a little.
Because the patient still reports a lot of pain.
Because the patient still reports a lot of pain.
Because the patient still reports a lot of pain.
Because the patient reports that there was no improvement in pain.
Because the patient reported no improvement.

Because the patient still feels a lot of pain
Because the patient is in pain, it started/ it hurt again in the last week.
Because the patient reports that she still has a lot of pain.
Because the patient reports that she still has pain.
Because patient reports pain after treatment.
Because patient did not report improvement of pain.
Because the patient has little better.
Because reported no improvement.
Because the patient has little better.
Because patient still reports pain.
Because patient still continues with pain.
Because the patient still has pain.
Patient did not report much improvement.

(vii) Endpoint: Assessor Determination of Placebo Group Subjects as Being Allocated to the Active Procedure Group

Because the patient reported improvement in pain and stitches.
Because patient reports improvement in pain.
For the patient reports that he immediately felt improvement.
Because the patient reported improvement of some symptoms such as tiredness.
Because the patient showed improvement in pain.
Because the patient improved.
Because reported improved pain.
Because the patient reported improvement.
Because patient improved pain.
Because the patient reports that she feels better.
Why patient felt relief from pain.
Because the patient improved.
Because patient reports decrease in pain points.
Because the patient improved.
Patient reported improvement.
Because patient reported improvement.
Because in the end patient reported improvement.

(viii) 4 Weeks Follow-Up: Assessor Determination of Placebo Group Subjects as Being Allocated to the Active Procedure Group

Patient reports that soon after treatment noticed pain improvement more than half, but one month after the end of treatment pain returned.
Because the patient reports that she no longer has pain.
Because the patient reported much improvement in pain.
Because some points have decreased.

Because the patient reports improvement in pain
Because the patient reported improved pain and tiredness, having more disposition and less anxiety.
Because patient reports improvement of pain even after end of treatment.
Because the patient reports much improvement of pain.
Because the patient reports pain improvement.
Because the patient felt improvement in the legs.
Because the patient reports improved (reduced) pain.
because patient reports decreased pain.
Because the patient reports improved (reduced) pain.
There was a little improvement in pain.
Because the patient improved (reduced) the pain.
Because the patient reports that he greatly improved the pains.
Because patient reports improvement.
Because the patient reports improvement.
Because the patient reports improved pain.
Because the patient reports pain improvement.
Because the patient greatly improved the pain.
Because patient has improved a lot.
Because patient reports much improvement in pain.
Because it shows decreased pain.

6.4. BLINDING EFFICACY EVALUATION SUMMARY OF FINDINGS

Most subjects, Therapists and Assessors accurately determined active subject procedure group allocation as active at each of the study endpoint and 4-week follow-up evaluations. The results were a little more mixed for the placebo group subject group allocation determinations, which is not unexpected due to the nature of fibromyalgia.

Rationales provided by subjects, Therapists and Assessors in support and justification of why they made the subject group determinations that they did, whether those group allocation determinations were accurate or not, were based on the subject's reports of changes in pain levels and other fibromyalgia variables such as fatigue and were NOT based on detectable clues arising from the device itself (such as noise, heat, light, sensation output, etc., emitted from the device during procedure administration), or from any other factors such as overhearing that a subject was receiving a test/placebo device procedure, making group assignment records available, etc., as applicable

Therefore, these findings positively indicate that **study blinding was successfully executed and maintained throughout the course of study duration**.

4. ADVERSE EVENTS EVALUATION

Table 27 below shows the number and percentage of study subjects who did not experience an adverse event throughout each of the study endpoint and 4-week follow-up evaluations for each of active and placebo group subjects.

Table 27: Incidence of No Adverse Events Across Study Period by Procedure Group

Evaluation Period	**Active Group (n=45)**	**Placebo Group (n=45)**
Endpoint	37 / 82.22%	39 / 86.67%
Follow-Up	24 / 93.33 %	42 / 93.33%

Table 28 below shows the adverse events reported to have been experienced by study subjects throughout each of the study endpoint and 4-week follow-up evaluations for each of active and placebo group subjects.

Table 28: Reported Adverse Events Across Study Period by Procedure Group

	Active Group (n=45)		**Placebo Group (n=45)**	
Adverse Event	**Endpoint**	**Follow-Up**	**Endpoint**	**Follow-Up**
Increased pain/tension	3	-	4	1
Itching	1	1	-	-
Spasms	1	-	-	-
Redness at treatment sites	1	1	-	-
Drowsiness/ somnolence	1	1	-	-
Headache	1	-	-	-
Blurred vision	1	-	-	-
Warm sensation	-	-	1	1
Palpations and anxiety	-	-	1	1
Weight loss	-	-	1	-
Scratch	1	-	-	-
TOTAL AEs	**10**	**3**	**7**	**3**

Most subjects, regardless of procedure group assignment, did not report experiencing an adverse event throughout study participation. The low number of adverse events reported were determined to be mild and either unrelated or potentially related to the study treatment. No adverse event required any intervention nor resulted in a subject withdrawing or being withdrawn from the study, and each fully and satisfactorily resolved by study completion.

APPENDIX A:

CLINICAL STUDY RESULTS BY INDIVIDUAL TEST SITES

Test Site #1: Laboratory of Phototherapy and Innovative Technologies in Health

Test Site #2: HM Nishioka Institute

Test Site #3: Vila Maria Outpatient Clinic

1. STUDY SUBJECT POPULATION

There were three individual test sites in this clinical study, as follows.

- **Test Site #1:** Laboratory of Phototherapy and Innovative Technologies in Health
- **Test Site #2:** HM Nishioka Institute
- **Test Site #3:** Vila Maria Outpatient Clinic

The following site by site analysis shows that the study demographics and outcome measures are comparable across the three individual test sites and comparable to the respective values attained for the subject group summed across all test sites. Therefore, pooling of data across the three test sites for the overall study analysis is justified.

1.1. SUBJECT SAMPLE

Table 1 below shows subject sample size breakdown between test sites by procedure group.

Table 1: Sample size breakdown between test sites by procedure group

Test Site	Active Group (n=45)	Placebo Group (n=45)
Test Site #1	24	29
Test Site #2	8	9
Test Site #3	13	11

The distribution of active and placebo group subjects was even and comparable across the three test sites.

1.2. SAMPLE DEMOGRAPHICS

1.2.1. Age

Mean and standard deviation of age in years for active and placebo group subjects by test site is shown in Table 2 below.

Table 2: Age (years) by procedure group by test site

Test Site #1	Active (n=24)	Placebo (n=25)
Mean	45.25	48.04
Standard Deviation	7.78	7.92
Test Site #2	**Active (n=8)**	**Placebo (n=9)**
Mean	50.00	46.67
Standard Deviation	2.98	8.69
Test Site #3	**Active (n=14)**	**Placebo (n=11)**
Mean	43.31	44.73
Standard Deviation	9.60	8.38

Mean subject age was comparable across test sites, between procedure group, and compared to the combined subject sample.

1.1.2 Ethnicity

Subject ethnicity breakdown for active and placebo group subjects by test site is shown in Table 3 below.

Table 3: Subject Ethnicity by Procedure Group by Test Site

	Active Group (n=45)			Placebo Group (n=45)		
Ethnicity	**Test Site #1 (n=24)**	**Test Site #2 (n=8)**	**Test Site #3 (n=13)**	**Test Site #1 (n=25)**	**Test Site #2 (n=9)**	**Test Site #3 (n=11)**
Caucasian	10	3	3	14	6	2
Hispanic	10	4	7	9	3	7
African American	4	1	3	2	0	1

1.1.3. Fitzpatrick Skin Type

Subject Fitzpatrick Skin Type breakdown for active and placebo group subjects by test site is shown in Table 4 below.

Table 4: Fitzpatrick Skin Type by Procedure Group by Test Site

	Active Group (n=45)			Placebo Group (n=45)		
FST	**Test Site #1 (n=24)**	**Test Site #2 (n=8)**	**Test Site #3 (n=13)**	**Test Site #1 (n=25)**	**Test Site #2 (n=9)**	**Test Site #3 (n=11)**
I	3	1	1	4	2	-
II	7	2	-	4	2	2
III	8	3	8	8	4	9
IV	3	2	2	7	1	-
V	2	-	2	2	-	-
VI	1	-	-	-	-	-

2. STUDY OUTCOME ANALYSIS: TENDER POINT COUNT

2.1. PROPORTION OF PRIMARY SUCCESSES

Table 5 below shows the number and percentage of test and placebo group subjects who met the study **individual subject success criteria** of a 20% or greater decrease in Tender Point Count from baseline to endpoint evaluation at each test site.

Table 5: Individual Success Criteria met by Procedure Group by Test Site

Test Site #1	**Active Group**	**Placebo Group**
n	24	25
n meeting success criteria	21	12
% meeting success criteria	**87.5%**	**48%**

Test Site #2	**Active Group**	**Placebo Group**
n	8	9
n meeting success criteria	8	8
% meeting success criteria	**100%**	**88.89%**
Test Site #3	**Active Group**	**Placebo Group**
n	13	11
n meeting success criteria	10	2
% meeting success criteria	**76.92%**	**18.18%**

The difference in the proportion of individual subject success between procedure groups exceeded the pre-established minimum of 30% at Test Site #1 (39.5%) and at Test Site #3 (58.74%) in favor of the active procedure group. The lesser difference in proportion of successes at Test Site #2 is due to the small sample size at this site.

2.2. TENDER POINT COUNT CHANGE SCORES

Table 6 below shows the mean, standard deviation, and magnitude of the change in Tender Point Count from baseline to study endpoint evaluation for active versus placebo group subjects at each of the three individual test sites.

Table 6: Change in Tender Point Counts by Procedure Group by Test Site

Test Site #1	**Active (n=24)**		**Placebo (n=25)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	14.92	3.39	14.48	2.76
Endpoint	5.92	2.96	11.68	3.64
Change	*-9.00*	*4.63*	*-2.80*	*3.91*
Test Site #2	**Active (n=8)**		**Placebo (n=9)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	16.13	2.42	16.11	2.71
Endpoint	7.38	4.00	11.11	4.23
Change	*-8.75*	*3.49*	*-5.00*	*2.29*
Test Site #3	**Active (n=13)**		**Placebo (n=11)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	15.46	2.93	16.09	2.21
Endpoint	9.77	4.68	15.45	2.94
Change	*-5.69*	*5.06*	*-0.64*	*2.98*

Mean baseline Tender Point Count was comparable across treatment sites and to that for the combined subject sample. At each of the three test sites, the mean change with respect to decrease in the mean number of Tender Point Count from baseline to endpoint evaluation was greater for active group subjects than for placebo group subjects, consistent with the findings for the combined subject population.

2.3. TENDER POINT COUNT SCORES ACROSS STUDY DURATION

Table 7 below shows the mean and standard deviation Tender Point Count across study duration (baseline, endpoint, follow-up) for active versus placebo group subjects at each of the three individual test sites.

Table 7: Tender Point Count Across Study Duration by Procedure Group by Test Site

Test Site #1	**Active (n=24)**		**Placebo (n=25)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	14.92	3.39	14.48	2.76
Endpoint	5.92	2.96	11.68	3.64
Follow-Up	6.71	4.45	11.12	4.26
Test Site #2	**Active (n=8)**		**Placebo (n=9)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	16.13	2.42	16.11	2.71
Endpoint	7.38	4.00	11.11	4.23
Follow-Up	3.38	2.28	7.67	3.77
Test Site #3	**Active (n=13)**		**Placebo (n=11)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	15.46	2.93	16.09	2.21
Endpoint	9.77	4.68	15.45	2.94
Follow-Up	7.08	4.11	9.91	5.74

Individual subject results for Tender point Count across study duration, by procedure group and by test site are contained in the 'INDIVIDUAL SUBJECT RESULTS' section below.

2.4. VAS PAIN RATING SCORES ACROSS STUDY DURATION

Table 8 below shows the mean and standard deviation VAS Pain Ratings across study duration (baseline, endpoint, follow-up) for active versus placebo group subjects at each of the three individual test sites.

Table 8: VAS Pain Rating Across Study Duration by Procedure Group by Test Site

Test Site #1	**Active (n=24)**		**Placebo (n=25)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	80.21	14.81	72.72	14.01
Endpoint	33.71	19.91	53.92	19.49
Follow-Up	33.83	28.41	50.32	26.57
Test Site #2	**Active (n=8)**		**Placebo (n=9)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	84.38	12.27	78.89	10.69
Endpoint	33.88	29.04	53.33	17.38
Follow-Up	26.00	29.69	51.33	21.66

Test Site #3	**Active (n=13)**		**Placebo (n=11)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	79.15	14.03	76.55	14.67
Endpoint	47.77	24.29	66.64	22.89
Follow-Up	40.85	19.74	46.45	30.81

2.5. VAS PAIN RATING SCORES ACROSS STUDY DURATION

Table 9 below shows the mean and standard deviation Total FIQ Scores across study duration (baseline, endpoint, follow-up) for active versus placebo group subjects at each of the three individual test sites.

Table 9: Total FIQ Scores Across Study Duration by Procedure Group by Test Site

Test Site #1	**Active (n=24)**		**Placebo (n=25)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	76.68	11.31	76.12	10.31
Endpoint	40.71	19.26	55.28	18.25
Follow-Up	36.95	24.79	54.93	21.18
Test Site #2	**Active (n=8)**		**Placebo (n=9)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	86.29	8.97	85.61	10.09
Endpoint	29.29	19.18	45.24	15.49
Follow-Up	38.42	24.82	41.54	20.06
Test Site #3	**Active (n=13)**		**Placebo (n=11)**	
	Mean	**SD**	**Mean**	**SD**
Baseline	81.16	10.29	74.16	13.26
Endpoint	58.74	22.44	69.33	15.39
Follow-Up	52.28	27.22	56.40	22.56

APPENDIX B:

INDIVIDUAL SUBJECT RESULTS

The following tables contain the individual subject data for the
Primary Outcome Measure of Tender Point Count
recorded across all study evaluation points
by procedure group and by individual test site

INDIVIDUAL SUBJECT TENDER POINT COUNT ACROSS STUDY DURATION

The table below shows the total Tender Point Count for active and placebo group subjects at each of the three test sites across each of the three study evaluations at Baseline, Study Endpoint, and 4-Weeks Follow-Up

SUBJECT #	GROUP	TEST SITE	BASELINE	ENDPOINT	FOLLOW-UP
1	Active	1	11	6	7
3	Active	1	6	5	2
7	Active	1	16	11	3
9	Active	1	10	1	11
10	Active	1	12	10	8
17	Active	1	18	7	1
19	Active	1	18	8	7
20	Active	1	18	8	12
23	Active	1	15	6	8
24	Active	1	18	1	3
25	Active	1	13	8	7
27	Active	1	14	10	4
32	Active	1	12	10	6
33	Active	1	15	7	7
35	Active	1	18	7	16
38	Active	1	18	6	9
39	Active	1	18	4	8
41	Active	1	10	4	0
44	Active	1	16	6	2
46	Active	1	18	5	7
48	Active	1	14	6	14
49	Active	1	14	3	5
51	Active	1	18	3	0
58	Active	1	18	0	14
61	Active	2	18	10	0
66	Active	2	14	6	4
67	Active	2	14	7	8
68	Active	2	12	2	1
69	Active	2	18	8	4
74	Active	2	18	11	4
76	Active	2	18	2	0
77	Active	2	17	13	6
80	Active	3	14	11	5
83	Active	3	14	18	18
85	Active	3	14	13	3
88	Active	3	18	8	7
89	Active	3	18	18	4

90	Active	3	18	7	5
92	Active	3	18	7	6
93	Active	3	11	2	4
94	Active	3	13	9	9
97	Active	3	17	10	8
98	Active	3	10	7	7
101	Active	3	18	12	12
102	Active	3	18	5	4
2	Placebo	1	16	18	18
4	Placebo	1	9	11	8
5	Placebo	1	7	8	15
6	Placebo	1	16	10	6
8	Placebo	1	13	16	16
12	Placebo	1	14	10	5
13	Placebo	1	10	14	6
14	Placebo	1	17	15	16
21	Placebo	1	12	13	10
22	Placebo	1	15	14	12
28	Placebo	1	15	11	9
29	Placebo	1	15	11	15
30	Placebo	1	14	11	14
31	Placebo	1	16	13	13
36	Placebo	1	16	12	18
37	Placebo	1	14	12	9
40	Placebo	1	18	18	6
42	Placebo	1	18	16	11
43	Placebo	1	17	12	9
47	Placebo	1	18	10	14
50	Placebo	1	15	7	5
52	Placebo	1	15	14	16
53	Placebo	1	13	6	8
54	Placebo	1	13	6	13
56	Placebo	1	16	4	6
59	Placebo	2	15	12	7
60	Placebo	2	14	4	6
63	Placebo	2	18	12	10
64	Placebo	2	18	13	11
65	Placebo	2	17	13	10
70	Placebo	2	17	12	11
71	Placebo	2	10	4	4
72	Placebo	2	18	16	0
75	Placebo	2	18	14	10
78	Placebo	3	14	18	17

79	Placebo	3	12	13	6
81	Placebo	3	18	18	18
82	Placebo	3	18	15	7
84	Placebo	3	16	17	12
87	Placebo	3	16	11	4
91	Placebo	3	18	18	18
96	Placebo	3	18	18	5
99	Placebo	3	18	17	12
100	Placebo	3	16	10	3
103	Placebo	3	13	15	7

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