A RANDOMIZED, SHAM CONTROLLED, DOUBLE-BLIND STUDY TO EVALUATE THE EFFECTIVENESS OF ENERGEX THERAPY IN THE TREATMENT OF TMJ ARTHALGIA

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1.1 Materials and Methods

Badawi, Mehta, and colleagues at Tufts University School of Dental Medicine, Boston, MA, conducted a randomized, sham-controlled, double-blinded study to evaluate the effectiveness of pulsed radiofrequency energy (PRFE) treatment in patients with temporomandibular joint (TMJ) arthralgia. Forty subjects were enrolled in the study, ranging in age from 22 years to 55 years. The diagnosis of TMJ arthralgia was confirmed according to the Research Diagnostic Criteria for Temporomandibular Joint Disorders. Subjects were randomly assigned into two equal groups: (1) the experimental group received PRFE using the Energex device, and (2) the control group received a sham treatment with a specially modified Energex device.

1.2 Study Procedures and Evaluations

All subjects participating in the study presented for six treatment visits over a two-week period. During each of the six treatment visits, each patient, whether assigned to PRFE treatment or sham treatment, received six treatment units to the affected TMJ. A treatment unit is defined as a 15 second burst of energy. Patients remained blinded to treatment assignment because the sham device was designed to look and sound identical to the active Energex device, and to operate in a manner such that the patient could not tell that the device did not deliver PRFE.

Patient self-assessments of TMJ pain and investigator assessment of mandibular range of motion were recorded immediately before and immediately after each treatment. Before and after each treatment, TMJ pain was measured by a Numerical Rating Scale (NRS) from 0.00 to 10.00 and mandibular range of motion was measured by three parameters: mouth opening, and right and left lateral movement. Patients also returned for follow up at one week and two weeks following the final treatment.

1.3 Findings and Effectiveness

1.3.1 TMJ Pain

In the PRFE treatment group, baseline scores for TMJ pain ranged from a minimum of 4.0 to a maximum of 9.0, mean 6.13 ±1.59, median 6.00. At 2 weeks following the sixth treatment, the mean pain score was 3.05 ±2.76, median 2.50; on average, patients receiving PRFE treatment improved 56% over baseline.

Twelve of the 20 patients (60%) had achieved at least a 50% improvement in pain over baseline, and an additional 2 patients improved at least 33% over baseline. Only two patients (10%) showed no improvement whatsoever. Of note is the observation that all seven patients who had enrolled in the study with a baseline pain score of 4.0 to 5.0 were pain free at the 2 week follow up visit.

In the sham treatment group, baseline scores for TMJ pain ranged from a minimum of 2.5 to a maximum of 8.5, mean 5.35 ±1.59, median 5.00. At 2 weeks following the sixth treatment, the mean pain score was 4.20 ±1.88, median 4.00; on average, patients receiving sham treatment improved 19% over baseline.

Only 3 patients (15%) achieved at least a 50% improvement in pain over baseline following sham treatment. One patient improved 40% over baseline, and the remaining 16 patients (80%) failed to improve at least 33%. One of the sham treatment group patients was pain free at the 2-week follow up visit, compared to a baseline score of 6.00.

TMJ Pain: Comparison of PRFE Treatment to Sham Treatment

	Minimum Change in Pain Score	Maximum Change in Pain Score	Mean Change In Pain Score	Median Change In Pain Score	Total improved ≥50%
PRFE Group	+12.50%	-100.00%	-55.53%	-63.33%	12 (60%)
Sham Group	+60.00%	-100.00%	-18.70%	-18.82%	3 (15%)

TMJ Pain: PRFE Treatment Group

	Baseline	1Wk	2Wk	Raw Change	% Change
Min	4.00	0.00	0.00	+1.00	+12.50%
Max	9.00	8.00	9.00	-6.00	-100.00%
Mean	6.13	2.74	3.05	-3.08	-55.53%
Median	6.00	2.00	2.50	-3.00	-63.33%
StDev	1.59	2.32	2.76	2.05	37.23%

TMJ Pain: PRFE Treatment Group

	1pre	1post	2pre	2post	3pre	3post	4pre	4post	5pre	5post	6pre	6post	1Wk	2Wk
Min	4.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Max	9.00	8.00	8.00	8.00	6.50	6.00	8.00	7.00	8.00	6.00	8.00	6.50	8.00	9.00
Mean	6.13	3.75	4.90	3.73	4.10	2.93	3.68	2.95	2.95	2.03	3.45	2.38	2.74	3.05
Median	6.00	4.00	5.50	4.00	4.00	3.00	4.00	2.50	2.50	2.00	3.50	2.00	2.00	2.50
StDev	1.59	2.44	2.25	2.39	2.00	2.12	2.43	2.46	2.28	1.85	2.36	2.32	2.32	2.76

TMJ Pain: Sham Control Group

	Baseline	1Wk	2Wk	Raw Change	% Change
Min	2.50	0.00	0.00	1.50	60.00%
Max	8.50	7.00	7.00	-6.00	-100.00%
Mean	5.35	3.96	4.20	-1.15	-18.70%
Median	5.00	3.63	4.00	-1.00	-18.82%
StDev	1.59	2.04	1.88	1.67	33.08%

TMJ Pain: Sham Control Group

	1pre	1post	2pre	2post	3pre	3post	4pre	4post	5pre	5post	6pre	6post	1Wk	2Wk
Min	2.50	2.50	2.00	1.00	2.00	2.00	2.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Max	8.50	8.00	7.00	7.00	8.00	6.00	8.00	8.00	8.00	7.00	7.00	7.00	7.00	7.00
Mean	5.35	5.03	4.60	4.08	4.53	4.10	4.35	4.08	4.25	3.88	3.93	3.68	3.96	4.20
Median	5.00	5.00	5.00	4.50	4.00	4.00	4.00	4.00	4.75	3.75	4.00	3.75	3.63	4.00
StDev	1.59	1.53	1.58	1.78	1.64	1.68	2.26	2.31	2.31	2.22	1.98	2.07	2.04	1.88

1.3.2 Range of Motion

Mandibular range of motion was measured according to 3 parameters: mouth opening, right lateral movement, and left lateral movement.

Mouth Opening: In the PRFE treatment group, baseline measurement for mouth opening ranged from a minimum of 25.0 to a maximum of 51.0, mean 34.95 ±6.69, median 34.50. At 2 weeks following the sixth treatment, the mean measurement was 41.70 ±6.51, median 42.0; on average, patients receiving PRFE treatment achieved a 22% increase in this measurement over baseline.

Baseline measurement for mouth opening in the sham control group ranged from a minimum of 30.0 to a maximum of 50.0, mean 38.50 ±5.57, median 38.50. At 2 weeks following the sixth treatment, the mean measurement was 39.65, ±6.51, median 41.50; an average, patients receiving sham treatment achieved a 3% increase in this measurement over baseline.

Range of Motion – Mouth Opening: Comparison of PRFE Treatment to Sham Treatment

	Minimum Change	Maximum Change	Mean Change	Median Change
PRFE Group	-2.17%	120.00%	22.20%	16.32%
Sham Group	12.50%	19.44%	3.45%	3.18%

Range of Motion – Mouth Opening: PRFE Treatment Group

	Baseline	1Wk	2Wk	Raw Change	% Change
Min	25.00	30.00	30.00	-1.00	-2.17%
Max	51.00	55.00	55.00	30.00	120.00%
Mean	34.95	41.80	41.70	6.75	22.20%
Median	34.50	42.50	42.00	6.00	16.32%
StDev	6.69	6.42	6.51	6.96	27.27%

Range of Motion – Mouth Opening: PRFE Treatment Group

	1pre	1post	2pre	2post	3pre	3post	4pre	4post	5pre	5post	6pre	6post	1Wk	2Wk
Min	25.00	27.00	25.00	25.00	29.00	23.00	28.00	28.00	30.00	30.50	30.00	30.00	30.00	30.00

Max	51.00	50.00	50.00	54.00	51.00	52.00	52.00	53.00	54.00	54.00	56.00	56.00	55.00	55.00
Mean	34.95	36.90	36.45	38.90	37.55	38.70	39.10	39.70	39.35	41.68	40.55	41.60	41.80	41.70
Median	34.50	36.00	36.50	38.50	38.50	39.00	38.50	40.50	42.00	43.50	40.50	42.00	42.50	42.00
StDev	6.69	6.84	6.44	6.83	5.65	6.82	5.42	6.06	10.07	6.17	6.39	6.35	6.42	6.51

Range of Motion – Mouth Opening: Sham Control Group

	Baseline	1Wk	2Wk	Raw Change	% Change
Min	30.00	28.00	28.00	-5.00	-12.50%
Max	50.00	47.00	47.00	7.00	19.44%
Mean	38.50	39.65	39.65	1.15	3.45%
Median	38.50	41.50	41.50	1.00	3.18%
StDev	5.57	5.20	5.14	3.33	8.85%

Range of Motion – Mouth Opening: Sham Control Group

	1pre	1post	2pre	2post	3pre	3post	4pre	4post	5pre	5post	6pre	6post	1Wk	2Wk
Min	30.00	30.00	30.00	30.00	30.00	30.00	30.00	30.00	30.00	31.00	31.00	31.00	28.00	28.00
Max	50.00	50.00	50.00	50.00	50.00	50.00	50.00	49.00	49.00	49.00	47.00	47.00	47.00	47.00
Mean	38.50	38.75	38.80	39.35	39.90	40.10	40.15	39.95	39.75	39.95	39.75	39.95	39.65	39.65
Median	38.50	39.50	39.00	40.00	40.00	40.00	40.50	40.50	40.50	40.50	40.50	41.00	41.50	41.50
StDev	5.57	5.76	5.02	4.99	5.60	5.58	5.85	5.38	5.31	5.41	4.74	4.71	5.20	5.14

Right lateral movement: In the PRFE treatment group, baseline measurement for right lateral movement ranged from a minimum of 3.0 to a maximum of 12.0, mean 7.85 ±2.85, median 8.00. At 2 weeks following the sixth treatment, the mean measurement was 10.80 ±2.67, median 11.0; on average, patients receiving PRFE treatment achieved a 38% increase in this measurement over baseline.

Range of Motion – Right Lateral Movement:
Comparison of PRFE Treatment to Sham Treatment

	Minimum Change	Maximum Change	Mean Change	Median Change
PRFE Group	-25.00%	366.67%	59.31%	37.50%
Sham Group	-30.00%	75.00%	7.71%	5.56%

In the sham control group, baseline measurement for right lateral movement ranged from a minimum of 4.0 to a maximum of 12.0, mean 8.6 ±2.39, median 8.50. At 2 weeks following the sixth treatment, the mean measurement was 8.75 ±1.25, median 9.0; on average, patients receiving sham treatment achieved a 7.71% increase in this measurement over baseline.

Range of Motion – Right Lateral Movement: PRFE Treatment Group

	Baseline	1Wk	2Wk	Raw Change	% Change
Min	3.00	5.00	5.00	-2.00	-25.00%
Max	12.00	14.00	14.00	11.00	367.67%
Mean	7.85	10.75	10.80	2.95	59.31%
Median	8.00	11.00	11.00	3.00	37.50%
StDev	2.85	2.51	2.67	3.09	91.02%

Range of Motion – Right Lateral Movement: PRFE Treatment Group

	1pre	1post	2pre	2post	3pre	3post	4pre	4post	5pre	5post	6pre	6post	1Wk	2Wk
Min	3.00	4.00	4.00	5.00	5.00	5.00	5.00	5.00	4.00	5.00	5.00	5.00	5.00	5.00
Max	12.00	13.00	14.00	14.00	13.00	15.00	14.00	14.00	14.00	14.00	14.00	14.00	14.00	14.00
Mean	7.85	8.90	8.80	9.75	9.20	10.00	9.45	9.80	9.55	10.15	10.00	10.25	10.75	10.80
Median	8.00	8.00	9.00	10.00	9.50	10.00	9.50	10.00	9.50	10.00	10.00	10.00	11.00	11.00
StDev	2.85	2.63	2.71	2.61	2.24	2.60	2.46	2.28	2.35	2.48	2.38	2.36	2.51	2.67

Range of Motion – Right Lateral Movement: Sham Control Group

	Baseline	1Wk	2Wk	Raw Change	% Change
Min	4.00	6.00	6.00	-3.00	-30.00%
Max	12.00	10.00	10.00	3.00	75.00%
Mean	8.60	8.75	8.75	0.15	7.71%
Median	8.50	9.00	9.00	0.50	5.56%
StDev	2.39	1.25	1.25	1.87	25.75%

Range of Motion – Right Lateral Movement: Sham Control Group

	1pre	1post	2pre	2post	3pre	3post	4pre	4post	5pre	5post	6pre	6post	1Wk	2Wk
Min	4.00	4.00	4.00	4.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	6.00	6.00
Max	12.00	12.00	13.00	13.00	11.00	11.00	10.00	10.00	11.00	11.00	10.00	10.00	10.00	10.00
Mean	8.60	8.55	8.60	8.65	8.35	8.35	8.35	8.60	8.55	8.60	8.50	8.60	8.75	8.75
Median	8.50	8.50	9.00	9.50	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00
StDev	2.39	2.33	2.23	2.37	1.90	1.90	1.79	1.76	1.79	1.76	1.57	1.47	1.25	1.25

Left lateral movement: In the PRFE treatment group, baseline measurement for left lateral movement ranged from a minimum of 4.0 to a maximum of 14.0, mean 7.63 ±2.50, median 7.00. At 2 weeks following the sixth treatment, the mean measurement was 11.05 ±2.09, median 10.0; on average, patients receiving PRFE treatment achieved a 50.3% increase in this measurement over baseline.

In the sham control group, baseline measurement for left lateral movement ranged from a minimum of 5.0 to a maximum of 12.0, mean 8.5 ±2.31, median 9.00. At 2 weeks following the sixth treatment, the mean measurement was 8.80 ±1.79, median 9.0; on average, patients receiving sham treatment achieved a 6.77% increase in this measurement over baseline.

Range of Motion – Left Lateral Movement: Comparison of PRFE Treatment to Sham Treatment

	Minimum Change	Maximum Change	Mean Change	Median Change
PRFE Group	-12.50%	150.00%	50.30%	46.43%
Sham Group	-25.00%	66.67%	6.77%	0.00%

Range of Motion – Left Lateral Movement: PRFE Treatment Group

	Baseline	1Wk	2Wk	Raw Change	% Change
Min	4.00	8.00	8.00	-1.00	-12.50%
Max	14.00	15.00	15.00	6.00	150.00%
Mean	7.63	11.00	11.05	3.20	50.30%
Median	7.00	10.00	10.00	3.00	46.43%
StDev	2.50	1.91	2.09	2.19	40.39%

Range of Motion – Left Lateral Movement: PRFE Treatment Group

	1pre	1post	2pre	2post	3pre	3post	4pre	4post	5pre	5post	6pre	6post	1Wk	2Wk
Min	4.00	5.00	4.00	6.00	5.00	4.00	5.00	5.00	4.00	6.00	1.00	7.00	8.00	8.00
Max	14.00	13.00	14.00	14.00	14.00	15.00	15.00	15.00	14.00	15.00	15.00	15.00	15.00	15.00
Mean	7.63	9.32	8.68	9.53	8.63	9.37	9.47	10.05	10.21	10.68	10.26	11.11	11.00	11.05
Median	7.00	9.00	9.00	10.00	9.00	10.00	9.00	10.00	10.00	10.00	10.00	11.00	10.00	10.00
StDev	2.50	2.29	2.63	2.63	2.56	3.24	2.61	2.80	2.37	2.16	3.30	2.26	1.91	2.09

Range of Motion – Left Lateral Movement: Sham Control Group

	Baseline	1Wk	2Wk	Raw Change	% Change
Min	5.00	5.00	5.00	-3.00	-25.00%
Max	12.00	12.00	12.00	4.00	66.67%
Mean	8.50	8.80	8.80	0.30	6.77%
Median	9.00	9.00	9.00	0.00	0.00%
StDev	2.31	1.79	1.79	1.63	20.39%

Range of Motion – Left Lateral Movement: Sham Control Group

	1pre	1post	2pre	2post	3pre	3post	4pre	4post	5pre	5post	6pre	6post	1Wk	2Wk
Min	5.00	4.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00

Max	12.00	12.00	13.00	13.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00
Mean	8.50	8.35	8.55	8.75	8.55	8.65	8.60	8.90	8.75	8.85	8.80	8.75	8.80	8.80
Median	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.50	9.00	9.00	9.00	9.00	9.00	9.00
StDev	2.31	2.28	2.26	2.27	1.99	1.93	1.82	1.77	1.74	1.76	1.61	1.68	1.79	1.79

1.4 Statistical Analysis

The results in NRS pain scores, mouth opening, and lateral movement were summarized descriptively. The percent change from baseline was presented for the change between the 2-week follow-up visit and the baseline visit (pre1). Inferential statistics were used to evaluate treatment differences pre- and post-procedures. T-tests were used for each measure and treatment group to evaluate the null hypothesis that the mean change from baseline to 2-week follow-up visit was equal to zero. T-tests were used to evaluate the null hypothesis that the mean change from baseline was the same for both groups and allowed for unequal variances. Baseline values were compared using a T-test to evaluate the null hypothesis that the two groups had the same mean score at baseline.

There were no significant differences in the comparison of baseline means for NRS Scores, mouth opening, right lateral movement, or left lateral movement for the PRFE treatment group and the sham control group. The t-test evaluating the baseline means of mouth opening was marginally significant (p=0.076) with the sham group having a somewhat higher mean value 38.5 mm versus 35.0 mm.

The difference in mean change from baseline in NRS scores between the PRFE group and the sham group was highly statistically significant (p=0.003). A mean difference of –1.93 was observed, indicating nearly a two-point difference in pain score reduction in the PRFE group. Both groups had statistically significant mean change from baseline: the mean change for the NRS pain score in the PRFE group was –3.08+/-2.05 (p<0.001) and the mean change for the sham group was –1.15+/-1.67 (p=0.006).

A difference in mean change from baseline between PRFE and the sham groups in change in mouth opening was 5.60 mm (p=0.003). The PRFE group had 6.75 mm change from baseline and it was highly statistically difference (p<0.001). The sham group mean change from baseline was not significantly different from zero.

Right and left lateral movement had significantly greater mean change from baselines in the PRFE group relative to the sham group. The mean for the PRFE for the right lateral movement was 2.80 mm (p=0.002) greater than for the sham group, and the mean difference for the left lateral movement was 2.90 mm (p=<0.001) greater. The mean change from baseline for the PRFE group was 2.95 mm for right lateral movement (p<0.001) and 3.20 for left lateral movement (p<0.001). The sham group had no significant changes in right or left lateral movement.

Summary of Efficacy Evaluations

Variable	Group	Mean Change: Baseline to 2 Week Follow UP	P-Value[1,2]
TMJ Pain	**Control**	-1.15	0.006
	PRFE	-3.08	<0.001
	Difference	-1.93	0.003
Mouth Opening	**Control**	1.15	0.140
	PRFE	6.75	<0.001
	Difference	5.60	0.003
Right Lateral Movement	**Control**	0.15	0.724
	PRFE	2.95	<0.001
	Difference	2.80	0.002
Left Lateral Movement	**Control**	0.30	0.419
	PRFE	3.20	<0.001
	Difference	2.90	<0.001

(1). For the change from baseline, a t-test was used to evaluate whether the mean change from baseline was equal to zero.

(2). For the difference in mean change from baseline a t-test was performed allowing for unequal variances in the two treatment groups.

This study provides strong evidence that there was a positive treatment effect in the PRFE group. In all measures of efficacy, the PRFE group demonstrated statistically significant improvements in mean change from baseline compared to the sham group. In addition, the percent changes from baseline were consistently larger in the PRFE group. For TMJ pain, 60% of PRFE patients had at least a 50% decrease in NRS pain scores relative to baseline, compared to only 15% of sham patients. In short, PRFE performed well in all four efficacy measures.

1.5 Findings – Safety

No side effects or complications occurred in either the PRFE treatment group or the sham control group. There were no reports of redness or any other localized reactions to the PRFE or sham treatments.

1.6 Conclusions

This randomized, double blinded study showed that PRFE with the Energex device provided clinically and statistically significant relief of pain and improved range of motion in patients with TMJ arthralgia, compared to sham treatment. At 2 weeks follow up after a total of six treatments, 60% of the patients treated with PRFE improved at least 50% over baseline in the NRS pain score. Mandibular range of motion measurements, including mouth opening, right lateral movement, and left lateral movement, corresponded to the findings for pain scores: patients assigned to PRFE treatment had greater improvements in these range of motion measurements than did patients assigned to sham treatment. There were no complications or adverse events in either the PRFE or sham control group. Therefore, it was concluded that, in this patient series, the Energex device was safe and effective for the treatment of TMJ arthralgia.