A Clinical Study of the Efficacy of the Biowave Device for Reducing Pain and Increasing Range of Motion Over 24 Hours Following a 20-Minute Treatment of Shoulder, Knee, Hip and/or Extremity Pain.

This study was performed at the Coren Clinic in Norwalk, CT. The primary objective of the investigation was to evaluate the efficacy of the Biowave device for the relief of symptomatic shoulder, hip, knee or extremity pain. Efficacy was determined by comparing a patient's pre-treatment baseline pain score, utilizing the Visual Analog Scale (VAS), to his/her VAS pain score immediately following discontinuation of treatment, and at 6 and 24 hours following discontinuation of treatment.

The secondary objectives of the study were to demonstrate whether the Biowave device has a residual and/or cumulative effect in preventing the perception of pain and in providing an increase in Range of Motion (ROM) and to determine optimal pad size and pad placements for different treatment locations on the body.

The study was conducted on 22 patients and a total of 36 treatments were completed. The number of treatments received by each patient was randomized so that the patient was supposed to receive either three (3) treatments or one (1) treatment. Six (6) patients received a total of three (3) treatments each, two (2) patients received two (2) treatments each and fourteen (14) patients received 1 treatment each. Each treatment was separated by a minimum of 48 hours, but not by more than one (1) week. Feed Signal frequency settings were preset to 8.00 kHz and 8.122 kHz for all treatments. The beat frequency developed in the body was 122 Hz for all treatments. Patients were instructed to increase the power level on the device until they felt a strong and comfortable pressure sensation at the Pain Site Pad. Total treatment time was 20 minutes. Patients completed visual analog scale (VAS) and categorical pain assessments at baseline (before treatment), after 20 minutes of treatment (after the device was turned off and pads removed), and at 6 hours and 24 hours following the end of the treatment. Active range-of-motion (ROM) assessments were completed at baseline and after 20 minutes of treatment (after the device was turned off and pads removed).

All patients, 21 years of age or older, presenting to the clinic for symptomatic relief of shoulder, hip, knee or extremity pain were potential study candidates. Patients were selected without bias to gender, and must have been willing to comply with follow-up and post-treatment procedures. Patients were screened and who fulfilled all inclusion and no exclusion criteria were offered the opportunity to participate in the study. Those patients who subsequently fulfilled all inclusion criteria and no exclusion criteria and who provide study specific written informed consent were entered into the study. The patients must have had a score of ≥ 40 mm on the VAS pain scale for

their baseline pain score.

Patients were connected to the Biowave device by application of the Feed Pad to a location opposite their pain and a Pain Site Pad to a location directly over the pain site. For example, patients with pain on the front of their shoulder would have a Pain Site Pad placed on the front of their shoulder directly over the location from which the pain emanates. A Feed Pad would be placed on the back of the shoulder blade directly on the other side of the body (opposite) from the location of the Pain Site Pad. Feed Signal frequency settings were preset to 8.00 kHz and 8.122 kHz for all treatments. Beat Frequency settings were 122 Hz for all treatments. Patients were instructed to increase the power level on the device until they felt a strong and comfortable pressure sensation at the Pain Site Pad. If the sensation subsided slightly, patients were instructed to increase the power level until the strong and comfortable sensation returned. Patients made incremental increases in signal amplitude until they reached a steady state strong and comfortable pressure/tingling sensation that did not fade at the Pain Site electrode. Total treatment time was 20 minutes. Patients completed visual analog scale (VAS) and categorical pain assessments at baseline (before treatment), after 20 minutes of treatment (after the device was turned off and pads removed), and at 6 hours and 24 hours following the end of the treatment. Active range-of-motion (ROM) assessments were completed at baseline and after 20 minutes of treatment (after the device was turned off and pads removed). Vital signs were taken before and after each treatment session.

Results were analyzed for each treatment location on the body. The percentage of pain reduction was calculated by subtracting the post treatment VAS measurement from the baseline (before treatment) VAS measurement and dividing that result by the baseline VAS measurement. Range of motion (ROM) for flexion, extension, lateral movement, adduction and abduction was measured in degrees using a goniometer before and after the 20 minute treatment, and the percent increase in ROM was calculated.

The results are shown in Table 1 below and were evaluated as the follows:

- Median percent pain reduction for each location on the body and overall pain reduction immediately following the treatment, at 6 hours and at 24 hours post treatment
- Percent of Patients that achieved 50% or greater pain reduction immediately following the treatment, at 6 hours and at 24 hours post treatment.
- Median Percent increase in Range of Motion for each location on the body immediately following the treatment.

Table 1. Median Percent Reduction in VAS Scores Immediately Following Treatment and at 6 Hours and 24 Hours Post Treatment

Location	# of Treatments	# of Patients	% Pain Reduction 0 hours After Treatment	% Pain Reduction 6 hours After Treatment	% Pain Reduction 24 hours After Treatment
Elbow	4	2	65.9%	97.7%	94.1%
Foot	2	2	34.6%	37.0%	9.3%
Hip	5	3	65.1%	70.6%	56.8%
Knee	8	5	74.3%	62.6%	70.7%
Neck	3	1	52.2%	39.2%	38.5%
Shoulder	14	9	65.4%	55.1%	42.2%
TOTAL/MEDIAN	**36**	**22**	**64.7%**	**62.7%**	**56.8%**

Pain Reduction

The data from Table 1 above is also summarized in Figure 1 below. The median percent reduction in VAS pain scores across all treatments and all locations was 64.7% immediately following the 20-minute treatment, 62.7% at 6 hours and 56.8% at 24 hours. The elbow, hip, knee and shoulder treatments had the greatest level of efficacy, with neck treatments still showing positive results, but with not quite as strong a residual effect. As there are only two data points for the foot, no meaningful conclusion can be drawn.

P-values for the shoulder are as follows: vas 0hr $p<0.001$ n=13, vas 6hr $p<0.001$ n=13, vas 24hr $p<0.001$ n=13. P-values for the knee are: vas 0hr $p<0.001$ n=8, vas 6hr $p<0.003$ n=5, vas 24hr $p<0.02$ n=5. For the hip, p-values are: vas 0hr $p<0.01$ n=5. The population of VAS data for the hip at 6 and 24 hours, and for the elbow, foot and neck are too small to calculate meaningful p-values.

In general, initial indications for significant pain relief over 24 hours are positive for most locations on the body as shown below in Figure 1.

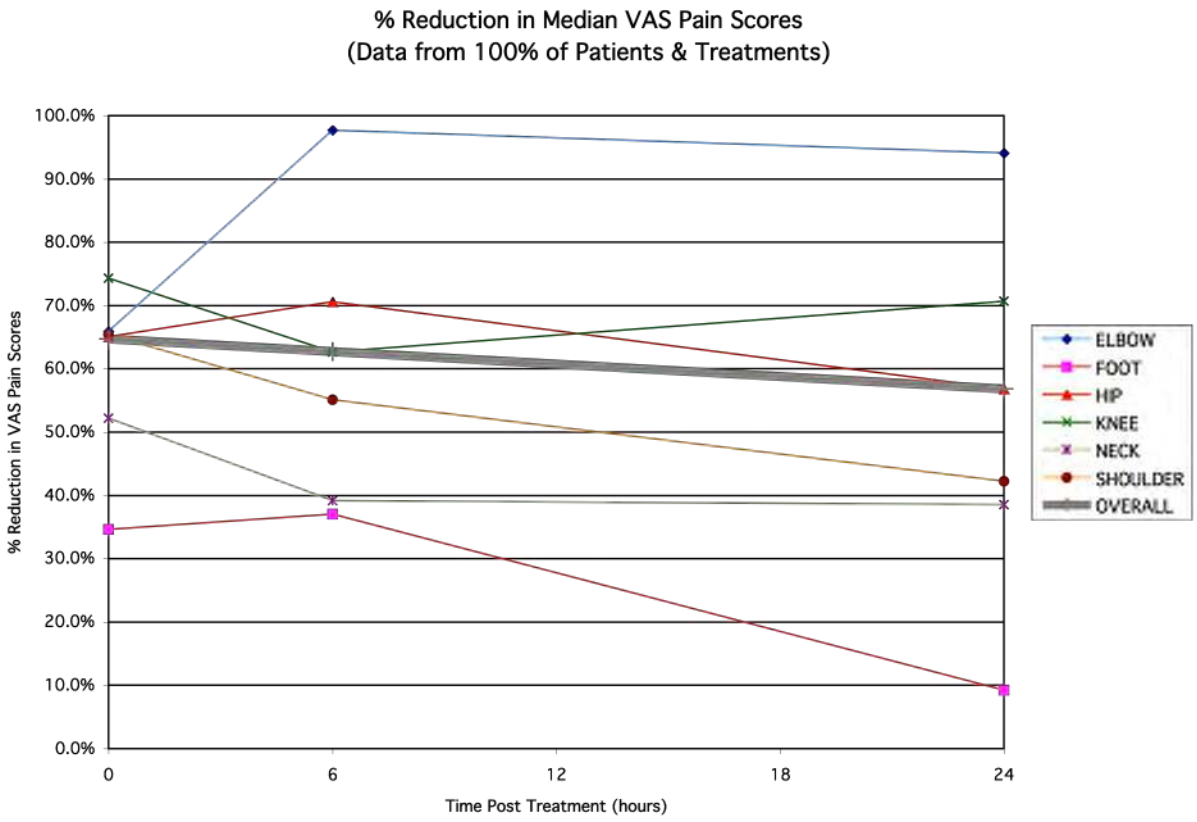

Figure 1. Percent Reduction in Median VAS Pain Scores

Percentage of Patients With Greater Than or Equal to 50% Pain Reduction

Most clinical studies focused on efficacy involving pain management devices rate the efficacy of a device based on the percentage of patients that achieve 50% or more pain relief. In comparing results from published clinical studies for the treatment of pain, Transcutaneous Electronic Nerve Stimulation (TENS) devices typically provide only 50% of the patients with an average 50% reduction in pain, only while the device is on. 50% of the patients receive no relief (less than 10% reduction in pain). The results for the Biowave device can also be seen below in Tables 2, 3 and 4 as well as graphically in Figure 2, which show the percentage of patients with 50% or greater pain reduction at 0 hours, 6 hours and 24 hours post treatment, respectively.

Table 2. Percent of Patients With 50% or Greater Pain Reduction at 0 Hours Post Treatment

Location	TOTAL # of Patients	# of Patients with > 50% Reduction in Pain	% of Patients with > 50% Pain Reduction 0 hours After Treatment
Elbow	4	2	50%
Foot	2	1	50%
Hip	5	4	80%
Knee	8	8	100%
Neck	3	2	67%
Shoulder	14	10	71%
TOTAL/MEDIAN	**36**	**27**	**75%**

Table 3. Percent of Patients With 50% or Greater Pain Reduction at 6 Hours Post Treatment

Location	TOTAL # of Patients	# of Patients with > 50% Reduction in Pain	% of Patients with > 50% Pain Reduction 6 hours After Treatment
Elbow	4	3	75%
Foot	1	-	0%
Hip	4	4	100%
Knee	5	4	80%
Neck	2	1	50%
Shoulder	13	7	54%
TOTAL/MEDIAN	**29***	**19**	**66%**

Table 4. Percent of Patients With 50% or Greater Pain Reduction at 24 Hours Post Treatment

Location	TOTAL # of Patients	# of Patients with > 50% Reduction in Pain	% of Patients with > 50% Pain Reduction 24 hours After Treatment
Elbow	4	4	100%
Foot	1	-	0%
Hip	4	3	75%
Knee	5	3	60%
Neck	2	1	50%
Shoulder	13	4	31%
TOTAL/MEDIAN	**29***	**15**	**52%**

***** Out of 36 Total Patients, 7 patients did not return to the investigator, the Case Report Forms with their VAS pain scores at 6 hours and at 24 hours post treatment. Therefore the Total Number of Patients at 6 hours and at 24 hours post treatment is 29 patients.

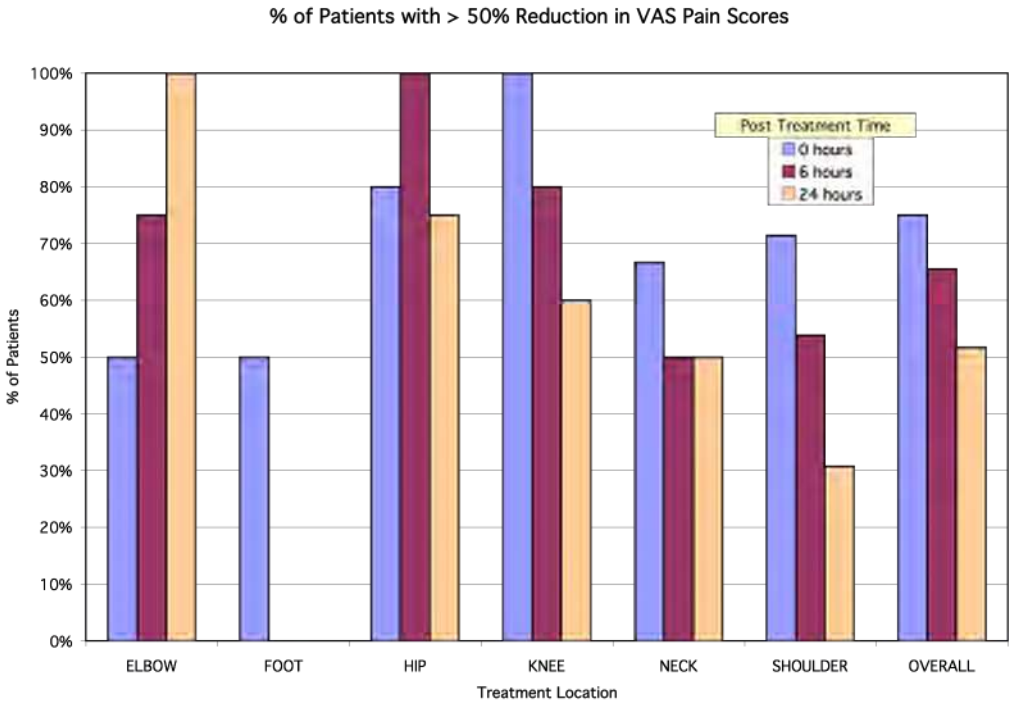

Figure 2. Percentage of Patients with > 50% Reduction in Pain

These results indicate that immediately following the Biowave treatment, the percentage of patients that received 50% or greater pain relief was 75% for all treatment locations (OVERALL) in comparison to TENS studies where typically only 50% of the patients receive a 50% or greater reduction in pain. Overall, at 6 hours post treatment, 66% of the patients still had a 50% or greater reduction in pain and at 24 hours post treatment, 52% of the patients had a 50% or greater reduction in pain. The results of this study show that a 20-minute treatment on the Biowave device provides continued pain relief at 0, 6 and 24 hours post treatment.

Range of Motion

Range of motion (ROM) for flexion, extension, lateral movement, adduction and abduction was measured in degrees using a goniometer before and after the 20 minute Biowave treatment, and the percent increase in ROM was calculated. All five ROM measurements are not applicable for all locations on the body. The types of measurements as well as the median percent increase (or decrease) in Range of Motion for each location on the body are presented in the table below. Median percent increase (or decrease) is derived from comparing a baseline reading immediately before the treatment to a reading immediately following the 20-minute treatment.

Table 5. Median Percent Increase in Range of Motion For Each Location on the Body Immediately Following the Treatment.

Location	# of Treatments	% Increase/ (Decrease) in Flexion	% Increase/ (Decrease) in Extension	% Increase/ (Decrease) Laterally	% Increase/ (Decrease) in Adduction	% Increase/ (Decrease) in Abduction
Elbow	4	35.1%	11.5%			
Foot	2	-10.8%	-9.0%			
Hip	5	29.6%	46.7%	65.4%		
Knee	8	15.4%	5.8%			
Neck	3	30.0%	18.2%	19.0%	12.5%	6.7%
Shoulder	14	5.4%	16.0%	26.4%	34.0%	5.9%

Range of motion (ROM) increase is statistically significant for the shoulder, knee and hip. There were not enough data points from the other locations on the body to draw any meaningful conclusion.

For the shoulder p-values were: flex $p<0.003$ $n=14$; ext $p<0.002$ $n=14$.

For the knee p-values were: flex $p<0.02$ $n=8$; ext $p<0.09$ $n=8$ significance would be much better with a larger sample size.

For the hip, p-values were: flex p=N.S. $n=5$, the sample size is too small; ext $p<0.08$ $n=5$ significance would be much better with a larger sample size.

The following have too small a population of ROM data to report: elbow, foot, neck and shoulder adduction and abduction.

ROM data is also presented in graphical format below in Figure 3 below.

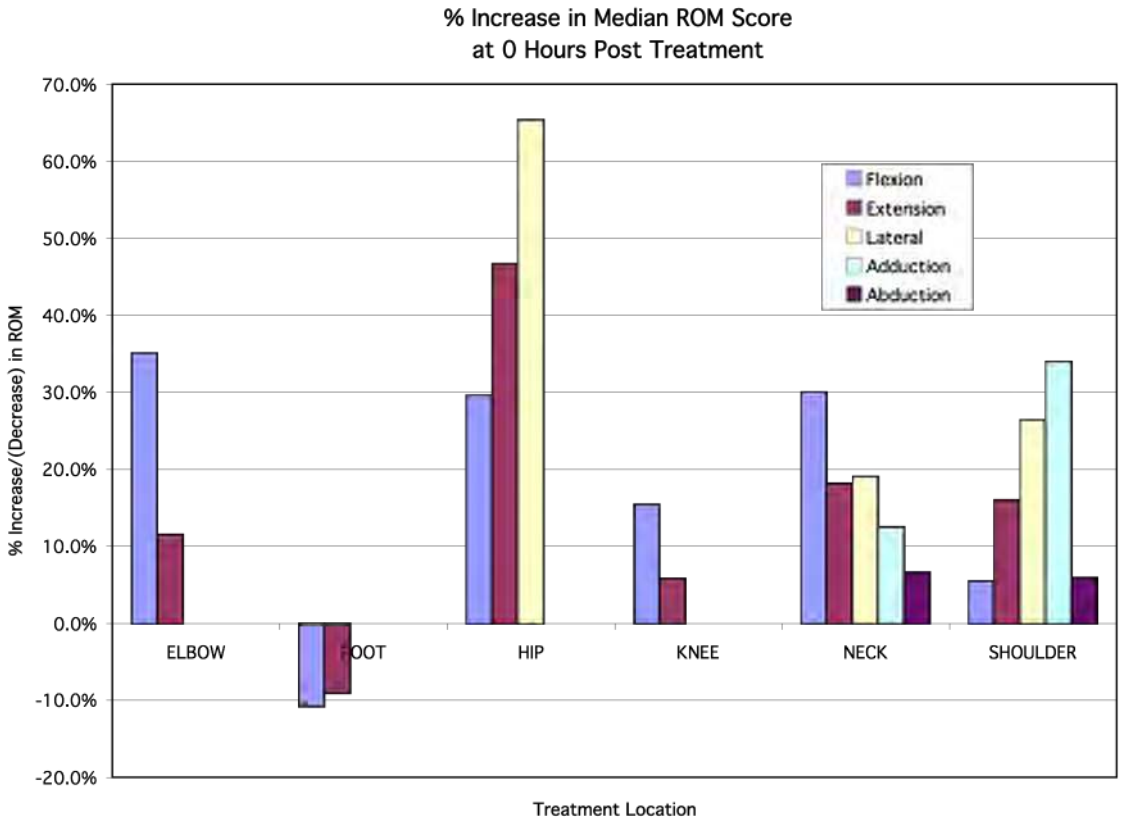

Figure 3. % Increase in Median ROM Score at 0 Hours Post Treatment

Adverse Events

One female patient experienced an extended tingling sensation in her shoulder, following her first treatment, which lasted for about 60 minutes after the device was turned off. One male patient experienced an extended tingling sensation in his hip, following his first treatment, which lasted for about 15 minutes after the device was turned off. Neither patient complained about the tingling and both patients still rated the treatment "excellent". Neither patient had residual tingling from their subsequent treatments. The female patient operated the device at slightly lower signal amplitudes for her second and third treatments. The male patient actually operated the device at higher signal amplitudes for his second and third treatments as compared to his first treatment.

Conclusion

This study shows that the Biowave device is an effective treatment for relieving shoulder, hip, knee, and neck or elbow pain. Median VAS scores, based on all data points, at the end of the 20-minute treatment, and at 6 and 24 hours following the treatment were significantly below the baseline VAS score for all locations tested on the body. The median percent reduction in pain

across all data points following the treatment were 65% at 0 hours, 63% at 6 hours and 57% at 24 hours post treatment.

The study also shows that the percentage of patients that experienced a 50% or greater reduction in pain using the Biowave device is statistically significantly better than published TENS results. Immediately following the Biowave treatment the percentage of patients that received 50% or greater pain relief was 75% which is significantly better than reported TENS studies where typically only 50% of the patients receive 50% or greater reduction in pain. For Biowave at 6 hours post treatment, 66% of the patients still had a 50% or greater reduction in pain and at 24 hours post treatment, 52% of the patients had a 50% or greater reduction in pain. The Biowave device had greater efficacy at 0, 6 and 24 hours post treatment as compared to published TENS results at 0 hours post treatment demonstrating that the Biowave device provides 24 hours of residual pain relief.

The above clinical studies demonstrate that the Biowave device provides pain relief for up to 24 hours post treatment. Since there are very few published studies regarding TENS devices and extended pain relief, Biowave Corporation demonstrated that the Biowave device provided greater extended pain relief in comparison to the TENS device in phase 3 of the Weill Medical College Study at Cornell University/New York Presbyterian Hospital.