Pulsed Shortwave Electromagnetic Field Therapy Increases Passive Range of Motion and Reduces Chronic Pain Due to Osteoarthritis in Canines

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Abstract

Osteoarthritis (OA) is one of the main causes of canine morbidity, chronic pain and limb dysfunction. Existing pharmacological interventions not only need veterinary prescription but are often expensive with known short and long-term side effects. Having alternative ways of treating this disease is a priority for veterinarians and owners of dogs alike. One possible approach is a non-invasive, non-drug, intervention based on pulsed electromagnetic fields (PEMF). This study investigates the efficacy of a FDA-cleared and commercially available medical device which operates at much higher frequencies and much lower magnetic field intensities than the typical PEMF devices used by dog owners and found in veterinary offices. These devices are often referred to as providing pulsed shortwave therapy (PSWT) and multiple studies using PSWT have shown the devices reduce pain, improve physical functionality, and reduce the need for pharmacotherapy in the treatment of human OA. This study looks into the possibility of using such a device to successfully address canine OA. Using a randomized, double-blind, placebo-controlled design, this study investigates the degree to which a PSWT 088 device, ®, reduces pain levels and increases passive range of motion (PROM) over 14-days compared to a placebo group on a sample of 49 dogs, all of whom had a veterinary diagnosis of OA prior to the study. PROM measures of the affected joints were taken at the beginning and conclusion of the 14-day trial using a digital goniometer. The owners recorded their dog's chronic pain daily, using the recognized BEAP Pain Score. The medical device was secured to the dog's collar near the cervical region of the spine where the nerves from the front limb enter the spinal cord. No side effects were reported. Average pain scores for the treatment group were reduced by 45% compared to the placebo group and average PROM scores increased by 5.51 degrees relative to the placebo group. In all, 65% of the treatment group were found to successfully reduce pain and 96% of this group showed either increased PROM or pain reduction or both. Most of the pain changes occurred within the first 8 days of treatment.

Keywords: Canine Osteoarthritis, Pulsed Shortwave Therapy, Pain Reduction, Passive Range of Motion, Mechanism of Action, Central Sensitization

1. Introduction

Osteoarthritis (OA) is one of the main causes of canine morbidity, chronic pain, and limb dysfunction. It is estimated that about 20% of dogs under the age of one year suffer from OA, while over 80% of dogs over the age of eight have chronic maladaptive pain associated with OA (1). This pain often results in changes in the dog's behavior and mobility. It also can limit the ability of the pet from having good interactions with the owner, thereby degrading the bond between owner and pet. Currently, there is no effective treatment for the underlying causes(s) of OA (2).

The most prevalent treatments for canine OA are directed towards pain relief and are pharmacological, often in the form of non-steroidal anti-inflammatory drugs (NSAIDs). Such treatments often need veterinary prescription, are expensive, and have known short and long-term side effects. Recently, a new monoclonal antibody therapy, Bedinvetmab, has offered owners an alternative treatment regimen. A recent randomized, placebo-controlled study showed that after 28 days the treatment group showed success 43% of the time compared to 17% for the placebo group where success was defined as reducing pain by one or more points and reducing negative pain-related behavior by two or more points, with both measures reported on an 11-point scale (3). Dogs using this treatment modality need to visit the veterinarian once a month for a shot and treatment costs can be expensive (often over $100).

Even though there are a number of possible treatments for canine OA, there remains a need for an alternative therapy which is inexpensive, effective and safe (4). One possible approach is a non-invasive, non-drug, intervention based on pulsed electromagnetic fields (PEMF) (5). PEMF interventions affect biologic tissues by inducing electric fields into the patient's tissue through exposure to a time changing magnetic field. Currently, most PEMF devices used to treat canines operate at pulse frequencies in the range of 1Hz to 105Hz (6). Some of these devices are being used in veterinary offices, while others are available for home use, often in the form of a mat or a large loop.

In addition to PEMF devices, there are commercially available electromagnetic field devices which operate at much higher frequencies and much lower magnetic field intensities. These devices are referred to as pulsed shortwave therapy (PSWT) devices. This therapy is also non-invasive and relies on tissue exposure to high-frequency, non-thermal electromagnetic energy (7). A number of studies have shown one of these PSWT devices provides relief for both acute postoperative (8, 9) and chronic pain (10-16) in humans and has received clearance for both conditions from the FDA. Two of these studies specifically looked at osteoarthritis and showed PSWT reduces pain, improves physical functionality, and reduces the need for pharmacotherapy (10, 16). In addition, one prospective six-month study showed these effects are long lasting for subjects who reported initial pain reduction within the first 7 days of use (17). These positive results and the lack of adverse effects makes PSWT especially attractive for possible use as a first-line treatment for OA in canines.

The mechanism by which PSWT relieves chronic pain is still under investigation. Chronic pain is associated with central sensitization, a condition where the nervous system shifts into a persistent state of high reactivity. It is believed that the stimulus from the pulsing electromagnetic

energy influences afferent nerve activity. The application of PSWT at the pain site serves to gradually reduce this over-sensitization; the theory being that the high frequency of electromagnetic energy pulses stochastically increases afferent nerve activity at the site of pain. Over time, the central nervous system (CNS), "learns" to tune out this stochastic noise. In this way the heightened sensitization is reduced through a habituation-like process. As a result, the pain threshold level gradually increases leading to the brain being less likely to perceive non-noxious stimuli as pain (18).

The goal of this randomized, placebo controlled, double-blind study was to investigate the efficacy of one such commercially available PSWT device for the treatment of canine OA. In addition to assessing changes in passive range of motion (PROM) and perceived pain for a broad set of breeds and ages of canines, this study also provides insights into the mechanism of action associated with this treatment modality.

2. Methods and Materials

2.1 Study Design

The experimental protocol was designed according to the guidelines of the current European and UK laws on the protection of animals used for scientific purposes (Directive 2010/63/EU,) and was approved by the Research Ethical Committee of Plumpton College. Prior to enrolment, each owner was briefed about the aims of the study. This briefing included answering questions to assess suitability for enrolment and ensuring that safety measures were explicitly communicated to the owner. Owners were then asked to sign a consent form.

The selected treatment duration was 14 days, consistent with previous studies on humans that found those who reported pain relief usually reported this to occur within 7 days. Treatment duration of 24 hours per day for each dog was selected. PROM measurements were taken at the start of the study and at the end of the study by the lead researcher for each of the joints where there was confirmed OA. Measured joints included carpus, elbow, shoulder, tarsal, and hip. Pain scores, as measured in terms of the animal's behavior, were recorded daily by the owner.

2.2 Animal recruitment

Dogs were recruited from established hydrotherapy, veterinary physiotherapy, and veterinarian facilities as well as local dog walking groups and via advertising, using posters deployed at various dog walking parks across the UK.

The inclusion criterion was the owner's primary veterinarian confirming that the dog had OA in one or more of the animal's joints. All dogs had veterinary permission to be a subject in the research study. No dogs were excluded by breed, gender (entire or neutered), age, size, hair type or color, body weight or severity or duration of the condition. All conditions but severity and duration were recorded.

Exclusion criteria were pregnancy, cancer and/or infections, contraindications associated with the focal PSWT device.

2.3 Treatment Device

The PSWT 088 device used in this study by (Bioelectronics Corporation, Frederick, MD, USA), an over-the-counter (OTC) product cleared by the United States FDA. (Figure 1). This device uses a loop antenna (magnetic dipole) of about 110 cm^2 and produces a pulsed, radio frequency magnetic field with the following signal characteristics: (1) carrier frequency of 27.12MHz; (2) pulse width of 100 µsec; and (3) pulse repetition frequency of 1 KHz. This configuration results in a peak incident power density of 73 $\mu W/cm^2$ which translates into a specific absorption rate (SAR) of approximately 0.35 microwatts/cm^3. This SAR is extremely low; for example, about three orders of magnitude lower than the FDA approved exposure levels for cell phones. This means that although the Actipatch device provides a safe, non-thermal intervention, any effects of the device will be slow to develop. The manufacturer suggests the device be worn at least 12 hours/day and the expected time until the subject experiences results can be 4 days or more.

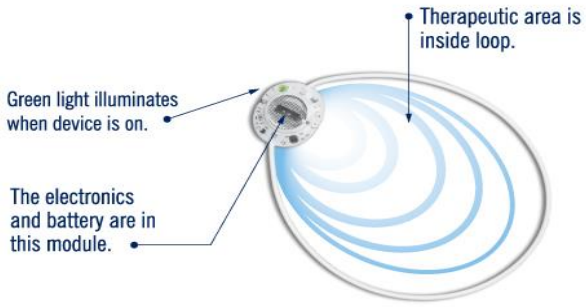

Figure 1 PSWT device showing the area of therapeutic value and the location of the battery

BioElectronics Corporation, upon request from the lead researcher, supplied 60 of their medical devices, 30 of which were placebo and 30 active. The placebo devices were identical to the active units, other than when the device was turned on, no current flowed through the antenna and thus there was no magnetic field generated. Since even the active device is sensation-free from the pulsing magnetic field, it was not possible for the user to determine if the device was active or non-active without conducting sophisticated electronic tests. The codes to the device identity were not released to the lead researcher until the conclusion of the study and recording of the data, resulting in both the lead researcher and owners being blinded to the treatment assignment.

2.4 Placement of the Device

The manufacturer's current recommendation is for the device to be placed over the area of pain in order to stimulate the afferent nerve activity at the site of the perceived pain. However, such placement is impractical for dogs, especially if the dog has OA in multiple joints. Given that the proposed mechanism of action involves gradually increasing the pain threshold by altering nerve activity in the spinal column, the decision was made to place the device on the neck of the dog and in particular near the cervical region of the spine where the nerves from the front limb enter the spinal cord.

The device was taped using clear medical tape to the dog's collar and placed on the back of the dog's neck (Figure 2). Dogs were given 20 minutes to acclimatize to the lead researcher's presence, while a briefing took place informing the owners how to correctly re-tape the device back onto the collar in case it became unsecure.

Figure 2 *Typical attachment of PSWT device to the dogs collar in order to expose the cervical region of the spine to the magnetic field therapy*

2.4 PROM Measures

The dogs' passive range of motion (PROM) angles were measured in degrees using a digital *EasyAngle* Goniometer following the suggested manufacturer's guidelines (Gait and Motion Technology Ltd, Bury St. Edmunds, UK, 2021). This device has been shown to yield highly reliable measurements with an Inter-rater Correlation Coefficient (ICC) between assessors of .994 and a Standard Error of Mean (differences) (SEM) of between 1.15 and 1.48 degrees (19).

Measurements were obtained either in lateral recumbence or in a standing position. However, to insure consistency for a given dog, measurements in both the initial and the 14-day follow-up appointment used the same procedure and were taken by the same person, i.e., the PI. Owner interjection was not permitted when these measurements were taken. Only restricted joint movement (along with the contralateral side of that limb, whether restricted or not) was measured. Carpus, elbow and tarsus were measured in flexion, while shoulder and hip were measured in extension.

Change in PROM over the trial period was measured at the joint level and also averaged over all of the focal joints. Joint level change was determined by first averaging the two readings for a given joint for a given point in time and then subtracting these two joint averages, i.e., one for baseline and the other for the final measure. In the case for extension, the baseline was subtracted from the final reading, leading to a positive value if the dog's extension improved. For flexion, the final reading was subtracted from the baseline, again yielding a positive value for improvement in flexion. These differences were also averaged over all of the measured joints to obtain a measure of average change (in degrees) for the dog.

2.5 Pain Measures

Pain scores were obtained using a multi-measurement instrument, the BEAP Pain Scale, sometimes referred to as the BEAAAAPP scale (Breathing, Eyes, Ambulation, Activity, Appetite, Attitude, Posture, Palpation) created by veterinarian Shea Cox (20). This measurement instrument taps eight different areas of possible change and produces a six-level score with the designations, no pain, mild pain, moderate pain, moderate to severe pain, severe pain and worst pain. In order to make a scale easily comparable to the often used 11 point VAS pain scale found in human studies and many canine studies, we assigned the following scores to the six different pain levels: no pain=0, mild pain=2, moderate pain=4, moderate to severe pain=6, severe pain=8 and worst pain=10 Although this scaling makes translation between the two pain measures easier, it should be noted that there still is a major difference between the commonly used VAS pain score and the BEAP score, in that the VAS measure is subjectively rated directly by the (human) patient while the BEAP score is indirect, using behavioral and physiological assessments (e.g., the dog looks uncomfortable when resting, may whimper or cry, pants intermittently, frequently loses appetite, etc.) and is rated by the dog's owner.

This pain measurement instrument was initially completed as a baseline by the lead researcher and owner together and then every subsequent day by the owner. At the conclusion of the trial the lead researcher collected these daily evaluations and tabulated the individual measures to arrive at the final daily pain score. In a few instances the owner checked some behaviors in one category and the remaining behaviors in another category. In these instances, the score assigned was the average of two categories.

Change in pain level was calculated relative to baseline pain. Pain reduction success was defined as a decrease of at least 2 pain units on the BEAP scale. This success measure is analogous to Corral et al. 2021 (3) definition of success of a two-point reduction in their PIS measure. Success determination was done for day 7 and day 14.

2.6 Statistical Analysis Plan

A statistical power calculation was performed using the G* Power program (21) assuming an effective effect size of .25 (based on human trials) and repeated measures. The needed sample size was determined to be 36. We therefore planned on a sample size of 60 to allow for a 30% drop-out rate. The programming language Python was used to obtain Wilcoxon ranked sum tests to non-parametrically test for differences, if any, between the two group's distributions of starting conditions, e.g., demographics, pain scores and PROM scores, both at the joint level and the aggregate level.

Excel was used to obtain the primary measures of daily percent change in baseline pain and the percent of patients successfully showing a decrease of at least one pain category (two pain level points) from baseline within 7 and 14 days.

Excel was also used to obtain the secondary measures of change in PROM with respect to the initial PROM measures, both with respect to a specific joint and also the patient's average improvement in degrees over the focal joints. Increases in PROM for a given dog were defined

as successful if the increase in the measure was greater than three SEM's of the measurement instrument as determined in (19). Changes over time, in distribution, but within a group, for a given measure were analyzed using Wilcoxon signed rank tests and determined using Python.

In addition, the overall effect of the medical device on the difference in the time paths of pain for each group was investigated by a regression model using a SAS PROC MIXED (SAS Institute, Inc. Cary, NC, USA), which uses iterative optimization methods that maximize the likelihood function. Individual time dummies were interacted with treatment and the effect was measured via these interaction terms. Subjects were included in the time path model as a random effect to allow consideration of both within and between group variances. The effects of the medical device on the aggregate PROM measure was also investigated using a regression model and the SAS PROC MIXED procedure. Significance levels for all tests were set to be a two-tailed test at .05.

3. Results

Sixty client-owned dogs, aged between one and 18 years of age (average 9.9) were enrolled into the study from five locations around the UK. This intent-to-treat sample size of 60 was evenly divided between treatment and placebo. During the 14-day period, 11 dogs chewed and destroyed the medical device, seven in the placebo group and four in the treatment group, leaving an effective sample size of 49, 26 in the treatment group (15M; 11F) and 23 (15M; 8F) in the placebo group, well above the previously derived needed sample of 36. All but seven of the animals had been neutered. Thirty-eight of the dogs had the original tape for the duration of the trial. The remaining eleven had the owners re-tape the device at some point in the study, using such methods as Sellotape or parcel tape. Five dogs were on a course of Librela and so were timetabled between their treatments to ensure the effects of Librela would not influence the trial.

The sample group represented a diversity of possible breeds and sizes and was comprised of: 1 Alsatian, 1 Beagle, 1 Belgium Shepherd, 7 Black Labradors, 1 Blue Merle, 3 Border Collies, 1 Chinchilla Pug, 2 Chinchilla Cross Jack Terriers', 1 Cockapoo, 2 Collie Cross's, 1 Collie Cross Terrier, 1 Curly coated Retriever Cross Labrador, 1 Golden Labrador, 1 Golden Retriever, 1 Husky, 1 Jack Russell, 1 Jack Russel Cross, 1 King Charles Spaniel, 1 Labradoodle, 2 Mixed Collie Old Sheepdog Cross, 1 Old English Bulldog, 1 Podenco, 2 Pointers, 2 Pugs, 1 Ridgeback, 1 Rottweiler Cross, 2 Siberian Husky's, 1 Staffordshire Bull Terrier Cross, 1 Labrador Cross Collie; 1 Standard Poodle, 1 Terrier Labrador Cross, 1 Tibetan Terrier, 2 Whippets, 1 Whippet Cross, 1 Miniature Schnauzer Cross Tibetan Terrier.

The 49 dogs completing the study came from five different parts of the UK. Sixteen were assessed in Brecon, two in Devon, 18 in Hereford, four in the Isle of Wight and nine in London. Each dog was either visited at their home address or a familiar clinic (hydrotherapy center or physiotherapy clinic). The body condition score (BCS) was scored by the lead researcher and the average over the sample was 3.21 ranging from 2.5 to 4.75. Thirty-nine dogs had two joint locations with OA (and thus 4 readings per time period, since measures were taken for both sides), five had only one joint location with OA, while five had 3 or 4 joint locations measured.

Table 1 shows the assignment by mean age, BCS and gender, the initial average pain level and average measured degrees of motion by joint along with the standard deviations. Individual Wilcoxon tests on differences in group distributions across all the measures shown in Table 1 yielded null results, i.e., there were no significant initial group differences in age, BCS, gender, the 5 individual joint PROM measures or pain scores.

	Placebo	Treatment	Typical PROM (24)
Sample size	23	26	
Age in years	8.91 (3.23)	10.7 (3.40)	
BCS	3.12 (.58)	3.29 (.75)	
Percent Female	38%	35%	
Average BEAP pain level 0-10 scale	4.26 (2.38)	4.23 (2.49)	
PROM Carpus (flexion) in degrees	82.6 (29.5)	87.6 (40.9)	29
PROM Elbow (flexion) in degrees	49.1 (14.4)	53.7 (16.3)	30
PROM Shoulder (extension) in degrees	101.4 (31.5)	110.7 (27.2)	163
PROM Tarsus (flexion) in degrees	72.1 (10.3)	82.5 (13.8)	34
PROM Hip (extension) in degrees	85.9 (29.3)	91.8 (28.3)	158

Table 1 Means and standard deviations for initial measurements by group along with the typical PROM in degrees for a healthy canine.

Initial pain levels ranged from 2 to 8 for both the active and placebo groups. Initial average pain level for the active group was 4.23 (2.48) and for the placebo group was 4.26 (2.38), indicating moderate average levels of pain in both groups. All of the dogs were recorded at the start of the trial as showing at least mild pain and the highest pain levels were rated as severe. The two groups had similar distributions of PROM scores for each of the measured joints. In addition, typical PROM measures for dogs without OA are provided in the rightmost column to allow comparison of the degree to which the dogs' joints lacked range of motion.

Daily average pain levels are plotted in Figure 3. Average pain levels for the placebo group remained essentially constant at 4.2 (only one dog was recorded as having any change in pain

levels over the course of the study although a few dogs reported variation in pain level across the 14 days). In contrast the average pain levels for the treatment group decreased over time from 4.26 to 2.31, representing an average reduction of 45% from initial levels. The GLM regression results find the time*treatment effect is highly significant ($p<.001$) and the individual contrasts between the treatment and placebo were significant after day 8. This difference in the time path of pain levels was also found when comparing the percent of patients who showed at least a one pain category level of pain reduction, (e.g. at least two pain points) calculated at day 7 and 14. For the treatment group the figures were 27% and 65% respectively, compared to 9% and 4% respectively for the placebo group.

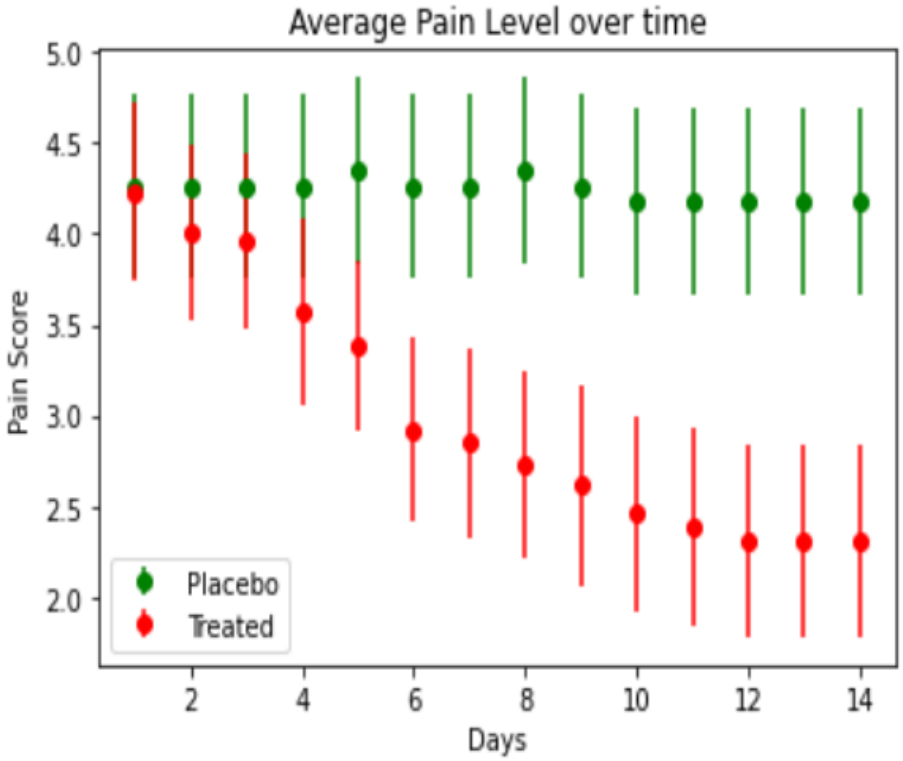

Figure 3. Average pain levels over time for placebo (green) and treatment (red) along with lines for one standard deviation.

Table 2 provides more detail on the reduction in pain over the 14 days and the amount of reduction conditional by the dog's initial pain level. For example, there were five dogs that initially were scored to have moderate pain. Of that group, three were reported as having no pain by the end of the trail, one was reported to have mild pain and one was reported to experience no change in pain level. In total, nine treatment dogs (35%) showed no change in pain, 11 (42%) dogs were reported to have experienced one category level decrease, and 6 (23%) were reported to have two or more levels of improvement. Sixty-nine percent of the treatment dogs by the end of the study were reported to have no or only mild pain level compared to 46% of the dogs having mild pain at the start of the study. In comparison only one placebo dog (4%) was found to have reduced pain over the trial.

End of study / **Start of Study**	No Pain	Mild Pain	Moderate Pain	Moderate to Severe Pain	Severe Pain	Row Totals
No Pain						
Mild Pain	7	5				12
Moderate pain	3	1	1			5
Moderate. To Severe Pain	0	1	2	0		3
Severe Pain	1		1	1	3	6
Total end of trial	11	7	4	1	3	26

Table 2 Pain category at the end of the trial, conditional on baseline pain category for the 26 dogs in the treatment group. Dogs along the diagonal (shown in red) were reported to show no pain reduction. All others were reported to reduce pain at least by one level.

Individual Wilcoxon tests for comparing the before and after distributions of PROM for all 5 joints found that the treatment group had significant improvement for all the joints except the tarsal where the sample size was three. One significant difference was found in the placebo group, this being for shoulder extension. Tests comparing the distribution of average changes in PROM for the focal joints between the two groups was highly significant ($p < .0001$) with the treatment group averaging a 5.66 (1.80) degree increase compared to .050 (1.56) degree increase for the placebo group. The GLM regression results where the dependent value was the average PROM improvement in degrees yielded the treatment effect significant at the .0001 level. When age was added as a covariate, almost an identical level of significance was observed for the treatment variable and the included covariate was found to be insignificant. The coefficient for the treatment variable was 5.51(.46), indicating that the treatment group enjoyed an increase of 5.51 degrees relative to the placebo group. As a robustness check, a GLM model was run with final average PROM measure as the dependent variable and the initial average PROM measure along with the treatment dummy and their interaction as the independent variables. The treatment dummy was highly significant ($p=0.002$), the coefficient on the initial PROM measure was 1.01 (.01) and highly significant. The intercept was insignificant, indicating no significant increase for the placebo group. Likewise, the interaction term was insignificant. Taken together the results imply no shift over time in the PROM levels for the placebo group and that the relationship between the initial PROM measure and the final PROM measure was the same for both groups. Importantly, the relevant measure is the change in degrees in PROM and the relevant comparison is the average difference in this measure across the two groups. In this analysis the coefficient for treatment was 5.83, very similar to the above reported improvement of 5.51

We conducted three post-hoc analyses. The first was to compare the improvements for the front and hind limb joints separately. The average improvement for the front joints was 6.84 (3.40) degrees for the treatment group and .02 (1.77) degrees for the placebo group. The figures for the hind limb joints were 3.56 (2.65) and .22 (1.37) respectively. The second analysis determined the correlation between percent pain reduction and degrees of improvement for PROM within the treatment group, the only group to show any improvement. We found that these two measures were almost independent. Thus, we then calculated the percent of subjects who experienced success in either PROM or pain or both at 7 days and 14 days. For the treatment group these percentages were 92% and 96% respectively and for the placebo group they were 4% and 4%.

4. Discussion

The study findings are encouraging in that we observe a robust effect of PSWT intervention on peripheral OA pain and range of motion when applying the PSWT therapy at the cervical spine region for the treated dogs. Nonetheless, the results also raise a number of interesting questions.

The highly significant reduction in pain and the increase in flexibility as measured by PROM compare favorably to those found in the recent clinical trial for Bedinvetmab. In that trial 45% of the treatment group reported having at least a 2 scale-point reduction on their 11-point pain scale within 14 days (3) The current study shows a two-point reduction in our 11-point pain scale for 65% for the treatment group, also in just 14 days. We note that this 65% figure is close to the response reported by Staelin et al. (17), in a human study which found about 62% of the users of the device indicated getting at least a 2-point reduction on the standard 11-point VAS scale after 7 days. Also encouraging was the finding that over 95% of the treatment group experienced success in reducing pain or improvement in PROM or both and all of this occurred within 14 days.

With that said, in a human study of cervical spine pain utilizing the same therapeutic technology (16), relatively small effect sizes were observed (0.6-0.8; using Cohen's-d test), although in that study the control was the use of prescription strength level NSAIDs. In the current study, we observe a Cohen's-d effect size of 1.64 (utilizing the average standard deviation of change in pain levels for two groups), a remarkably robust effect given that the PSWT therapy was being applied remotely from the pain site. As the proposed explanation of PSWT mechanism of action is central desensitization through modulation of afferent nerve activity at the pain site, these results, if replicated, would seem to indicate that there may be an alternative mechanism of action of the PSWT taking place, at least in dogs.

Another interesting observation is the lack of a placebo response, both in terms of improvement in PROM and pain reduction. Specifically, average decrease in pain for the placebo group was only 2%. While one might not expect the dogs to be aware they were being treated, in this protocol the owners were well aware that their pets might have been given an active device and this knowledge might be expected to influence their BEAP assessments. In the Corral et al. (3) study, for example, the placebo pain effect was roughly 40% of the magnitude of the treatment effect. We, therefore, expected a significant placebo effect in our study, but one was not observed. With this noted, we also found very little variance in the PROM measures for the placebo group over time, a measurement that might be less susceptible to a placebo effect as the assessments were

performed by the PI who was blind to the assignment of dogs. Moreover, when we calculated the variance in the difference between the before and after measures for each of the 10 joints in this placebo group, we find the average of observed variances to be only 1.81 degrees, a figure that is comparable to the SEM measures reported by (19) which were obtained at one point in time. Still, it remains unclear why the data do not exhibit some placebo effect.

Closely related to the question of lack of placebo response was the lack of variability in the placebo data. All but one dog in the placebo group ended the two- week study with the exact same reported pain level as at the start of the study (the one exception dropped from 4 to 2). In pain studies it is not uncommon to see both random recovery and worsening of the pain condition over the course of an experiment. Perhaps the short time course of this experiment prevented observation of such natural variation. Given that we were dealing with animals with chronic pain this might be a reasonable explanation, yet environmental changes commonly result in OA symptoms increasing or decreasing in humans from day to day (22) and even within a single day (23), but we did not observe any such effect in the collected data. Another explanation might be the coarseness of our BEAP measurement instrument that relied on behavioral indicators to infer the dog's pain level. Dog owners were asked to score their dogs daily on eight behavioral measures that could vary from hour to hour depending on the dog's activities. Owners, in all likelihood integrated over the day to come up with average assessments which are less likely to change. Viewed this way, the observed reduction in pain for the treatment group was more impressive.

The drop-out rate was somewhat lower than anticipated, which was encouraging. The fact that 18% of the units "failed" due to the dog removing and/or destroyed the device, should be an easy issue to address for future trials. One could envision a small pouch into which the device could be placed, or embedding the device in a waterproof "bandana" with an easy way to attach it to the collar. Both approaches could greatly reduce this failure rate.

A limitation of this study includes the length of the trial being only 14 days. However, a six-month prospective study in humans found that users who reported getting pain relief within the first 7 day reported maintaining or reducing the pain level with continued use of the device over the remainder of the six month trial (17). Thus, there is some supporting evidence that continued use of the device should keep the pain in abeyance or even result in greater pain relief and range of motion. This possibility could be readily tested as the device utilized in this study has a 30-day life with 24 hour/day use.

Another limitation is that the pain levels for these animals was relatively low, averaging only moderate pain (4.2 on an 11-point scale). However, post-hoc analysis of the 35% of animals with initial pain levels 6 or greater (moderate to severe pain and severe pain), find almost the same improvement in PROM and pain found in the group with lower pain levels. Thus, we find no indication that success is tied to initial conditions.

An important difference of this study to prior studies using this medical device was that we were not able to use the PSWT device according to the manufacturer's recommendation, that is, to place the device at the site of the pain in order to influence afferent nerve activity. Instead, we placed the device over the cervical spine region, and this may explain the slower response time. Prior use of the device on humans found that the vast majority of users report getting pain relieve

within 4 to 5 days. We found that it took about 8 days for the results to show statistically significant differences between the two groups. This could be due to the fact that the pain scores were inferred from the dog's behavior instead of being directly reported by the patient. It is possible that the delay was a result of the owner not being able to quickly determine behavioral changes. Alternatively, the slow response may be due to the placement of the device and that the mechanism of action varied with the different placement and thus the difference in reaction time.

This conjecture is in accordance with the finding that the PROM changes differed by almost 100% between the front and hind limb joints. The placement of the device over the cervical spine would imply that this difference in improvement might be associated with how close the device was to spinal cord entry point of the front and back limb afferent nerve fibers. This raises the issue of how exactly the pets experienced improvements in the hind limb joints. Was this due to more flexibility and less pain in the front joints, allowing more movement in the hind quarters, or was it due to the effects of central sensation and habituation?

A final unanswered observation is why wasn't there more association between pain reduction and increased range of motion? Did the increased flexibility lead the dog to be more active and increase the noxious stimulation, thereby negating pain reduction? More research will be needed to better explicate this finding.

With these caveats and questions noted, we believe that this initial (small and short duration) study promotes the intriguing possibility that PSWT may have the potential to significantly improve pain and functioning for dogs with OA and possibly for other small domestic animals.

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Author Contributions

TS initiated the project, was involved in the study design, collected and coded all the raw data and read the paper for accuracy. KM edited the paper and was involved in the data analysis. RS was involved in the study design, was primarily responsible for analyzing the data, wrote the initial drafts of the paper, and participated in the editing.

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Conflict of Interest

TS declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as her having a potential conflict of interest. KM is a consultant for BioElectronics Corporation. RS is an investor and on the Board of Directors of BioElectronics Corporation

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