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Significantly Reduced Pain and Improved Function Following Short-Term Use of the BioWaveHOME High Frequency Neurostimulation System for Conservative Pain Management

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White Paper

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ABSTRACT

Introduction: To date, more than 750,000 people in the United States alone have died from a drug overdose, with two out of every three overdose deaths in 2018 involving the use of opioids. In 2019 alone, the estimated cost of the opioid epidemic was reported at $179.4 billion, with $72.6 billion attributed to overdose deaths and $60.4 billion attributed to related healthcare costs [1]. Veterans, who are more likely to suffer from chronic pain and post-traumatic stress disorder (PTSD) than civilians, are twice as likely to die from an opioid addiction. With opioids as one of the most commonly utilized methods of pain management, it is not surprising that opioid addiction and overdose among Veteran populations has increased in recent years, creating a dire need for non-pharmacological, non-invasive, and non-addictive conservative treatment alternatives. The BioWaveHOME system provides an alternative to opioid pain management through electrical field generation inside the body, potentially addressing this unmet medical need.

Methods: From the period of February 2019 through July 2020, 6,245 subjects received a BioWaveHOME for at-home pain management on an as-needed basis for a minimum of two weeks, with some subjects receiving in-facility prior treatment with the BioWavePRO system. With the BioWaveHOME, subjects were provided with a mail-in survey to record pre-and post-treatment pain (Numeric Rating Pain Scale (NRS)), change in activities of daily living (ADL Scale) following treatment with the BioWaveHOME system, and other subject-reported outcomes, including satisfaction and quality of life, following two weeks of use. Also evaluated was change in pain and ADL based on anatomic region.

Results: Following two weeks of BioWaveHOME use, four hundred sixty three (463) subjects provided responses via returned surveys. The BioWaveHOME device provided subjects with statistically and clinically significant reductions in pain, with an average reduction in pain score of 3 points. Most subjects that initially reported pain localized to the back (n=257) reported an improvement in pain score of 3, with patients reporting pain localized to the hip (n=39), knee (n=57), and shoulder, (n=91) reporting an improvement in pain score of ~3.5 points. Further, the majority of subjects (87.7%) reported that using the BioWaveHOME improved their quality of life. With regard to activities of daily living, subjects reported significant improvement following use of the BioWaveHOME, with an improvement of 1.8 points. Analysis by anatomy revealed that all anatomies fared similarly with regard to improvement in ADL, with all reporting an improvement of around 1.8 to 2 points. With most subjects reporting daily use of the system, the average period of relief provided after each use was reported as eight (8) hours. Importantly, more than half (51.8%) of subjects reported either eliminating or reducing pain medication consumption while using the BioWaveHOME system. Patient satisfaction was particularly high, with the majority of subjects (97%) reporting being satisfied with the BioWaveHOME system with an expressed desire to continue using the system. All subjects were reported to have continued use of the BioWaveHOME device after the two-week recording period. Overall, use of the BioWaveHOME for two weeks on an as-needed basis resulted in substantial improvement in quality of life and reduction in pain for patients suffering from chronic and acute pain.

INTRODUCTION

According to the most recent dataset from the Center for Disease Control (CDC), approximately 50 million adults in the United States suffered from some form of chronic pain in 2018, up from 20 million adults in 2016 [2]. Further, greater than 19.6 million chronic pain sufferers categorize their pain as "high impact," defined as physically-limiting, debilitating pain lasting for greater than six months. Chronic pain has been reported as one of the most common reasons adults seek medical care, linked to restrictions in mobility and activities of daily living, substance abuse, anxiety, and depression.

A higher prevalence of chronic pain has been observed in older populations, correlated to advancing age and the female gender [2]. Former military personnel have also been linked to high rates of chronic pain, with a recent study conducted by the Veterans Health Administration reporting that 47-78% of Veterans presenting to VA clinics for care were seeking treatment for some form of persistent pain [3].

While there is currently no definitive "gold standard" treatment for chronic pain, prescription opioids are one of the most commonly utilized methods of care. While satisfactory in the short-term, the prolonged use needed to allay chronic pain has devolved into an epidemic of widespread misuse and a 2017 public health emergency declaration by the Department of Health and Human Services. In 2018, it was reported that an estimated 10.3 million Americans were misusing opioids, with two million of these adults actively seeking treatment for opioid use disorder. The National Institute for Drug Abuse estimated that opioid overdose takes the lives of 130 people each day, further underscoring the significance of this epidemic [4]. The predominance of chronic pain among Veteran populations is particularly concerning, as studies have demonstrated former military personnel are ten times more likely to become addicted to opioids and two times more likely to succumb to opioid addiction than the general population due to an increased rate of psychiatric comorbidities, such as PTSD [5].

With an aging population and prevalence of chronic pain on the rise, the public health burden of pain and opioid addiction is becoming exponentially more costly. In 2019 alone, opioid addiction cost the United States $179.4 billion, with $72.6 billion attributed to overdose deaths and $60.4 billion attributed to healthcare costs [1]. To combat this, alternative treatments are being actively sought while physicians attempt to decrease the number of opioid prescriptions written. From 2009 to 2011, 50% of chronic non-cancer pain Veterans treated within the VA health system received an opioid prescription. In 2016, the number of opioid prescriptions within the VA health system decreased by 25% [6]. While encouraging, non-prescription opioid use is largely unregulated and, as such, long-term use of opioids still remains an issue with the general and veteran population.

One promising treatment avenue that presents a non-addictive, non-pharmacological therapy to pain sufferers is the use of transcutaneous electrical nerve stimulation therapies, commonly referred to as TENs units. The technology is such that low-dose, non-invasive electrical current stimulates vibration receptors in the area treated for pain, reducing the transmission of painful stimuli to the brain. Repeat use results in the release of endogenous endorphin, contributing to the reduction in pain [7]. TENs technology works to mask the pain, providing short-term relief. The limitation of TENs technology is that the pain signals are not blocked, only masked. Using a novel patented electrical signal technology, BioWave Corporation has developed the BioWavePRO and BioWaveHOME neurostimulation systems for in-office and in-home pain relief, respectively. Both systems have been cleared by the FDA for use, with BioWavePRO cleared for physician use in 2005 and BioWaveHOME cleared for in-home use in 2015.[1]

A 2017 white paper reviewing the use of the BioWavePRO and BioWaveHOME systems in 66 surveyed veterans over the course of 18-months reported that 84.8% of all subjects experienced a reduction in pain, increased range of motion, and improved participation in activities of daily life. Of note, 58.7% of the surveyed veterans reported eliminating or reducing consumption of prescription pain medication since beginning treatment with the BioWaveHOME [8]. To further understand the impact of BioWaveHOME as a pain relief intervention and its impact on a patient's activity of daily living, additional patients should be evaluated.

PURPOSE

The objective of this study is to evaluate the use of the BioWaveHOME system in 463 surveyed subjects, including both Veterans and members of the general population, suffering from chronic or acute pain. The outcomes collected from returned surveys include pre- and post-treatment pain and activity, frequency of use, change in concomitant pain medications, satisfaction with the treatment, and other subject-reported quality of life outcomes.

MATERIALS/METHODS

Eligible subjects were provided with the BioWaveHOME System for pain management

[1] BioWavePRO – K052289; BioWaveHOME – K152437

following treatment at either a VA Medical Center, pain clinic, or orthopedic clinic. Some patients were treated previously with BioWavePRO during in-facility visits while others were only provided the BioWaveHOME system for in-home use. Accompanying the unit was an optional survey to complete following two weeks of continued use. Of the 6,245 subjects provided with the BioWaveHOME device, 463 provided fully or partially answered surveys back to BioWave, Inc. (7.4% response rate). Survey responses were mostly received following two weeks of use of the BiowaveHOME, though some responses were submitted to BioWave later. The dataset includes surveys returned from February 2019 through July 2020.

The survey was intended to capture responses after two weeks of BioWaveHOME use. Subjects were asked to record the following:

- **Description of Pain**: *Subjects were asked to detail their pain, inclusive of anatomic area.*
- **Type of Pain**: *Subjects were asked to check a box correlated to type of pain: chronic, acute, neuropathic, and/or nociceptive in nature.*
- **Pre-Treatment and Post-Treatment Pain Evaluation**: *Subjects were asked to circle a number on an NRS scale of 0 (no pain) to 10 (worst pain), correlated to the Wong-Baker Faces scale.*
- **Pre-Treatment and Post-Treatment Activities of daily living Evaluation**: *Subjects were asked to circle a number on an activities of daily life (ADL) scale of 0 (normal) to 10 (I need help), correlated to the Wong-Baker Faces scale.*
- **How is your satisfaction with BioWave?** *Subjects were asked to circle a number on a scale of 0 (poor) to 10 (excellent).*

The following questions were included on the survey:

- **BioWave helped me**: *Subjects were asked to check a box indicating if they were experiencing the following: "walk farther, stand longer, sit longer, sleep better, improved mood, and/or lift more," with an additional "Other" line for written responses.*
- **Effect of BioWave on pain medication consumption**: *Subjects were asked to check a box correlated to one of the following: "eliminated, reduced, or stayed the same."*
- **How often do you use BioWave?** *Subject were asked to check a box correlated to one of the following: "multiple times a day, daily, weekly, or monthly."*
- **Approximately how many hours of Pain Relief are you experiencing?** *Subjects were asked to provide a written response.*
- **Has BioWave improved your quality of life?** *Subjects were asked to provide a written response.*
- **Would you like to continue using BioWave?** *Subjects were asked to provide a written response.*

Information was captured using a Salesforce database. No formal hypothesis testing was performed. For survey study, descriptive statistics including number of patients (n), standard deviation (SD), median, minimum maximum, and 95% confidence intervals (CI) are utilized for all continuous variables. For categorical variables, per category, the absolute counts (n), and percentages (%) are created and summarized. Based on survey responses to anatomic region of pain, patients were grouped and mean change in pain and activities of daily living from baseline were compared. Within the survey, patients could write-in the anatomic area(s) where they were experiencing pain. As such, grouping was done in a manner where patients were not duplicatively represented based on variations within the written responses.

Treatment Device

The BioWaveHOME neurostimulator is a non-pharmacologic, non-narcotic, non-addictive, non-invasive treatment for pain **(Figure 1).**

Figure 1: BioWaveHOME Unit

The device works by delivering a back and forth summation of two high frequency sinusoidal alternating current signals at 3,858hz and 3,980hz. Current travels

between two electrodes. Electrodes are placed directly over one or two locations of pain. The mechanism of action that results from the electrical field generated from BioWave devices is similar to chemical anesthetics and is based on Frequency Conduction Block Theory. This technology is in contrast to TENS devices, which are based on Gate Control Theory. The sensation created by the TENS device can create a noxious sensation at the skin surface, acting as a distraction to pain but not blocking the pain signal itself.

The BioWave electrodes through which the high frequency signals are delivered consist either of a B-set or E-Set electrodes (**Figure 2**).

Figure 2: B-Set (Left) and E-Set (Right) Electrodes

B-set: Two 2.0" diameter round electrodes for (i) treating two distinct locations of pain, (ii) the origin of pain and most proximal location of pain to the origin (for example in the case of a radiculopathy) or (iii) one large area of pain (the electrodes are placed one inch apart from one another).

E-set: One 1.375" diameter round electrode placed directly over a single location of pain and one 2" x 4" rectangular dispersive electrode placed over a bony prominence which is a comfortable location to receive stimulation.

Endpoints

Primary endpoints include changes in pain and function as measured by the NRS Pain Scale and ADL Scale, respectively. Secondary endpoints include quality of life outcomes, including time of pain relief provided, the effect on pain med consumption, satisfaction and desire to continue to use the BioWaveHOME, and if the BioWaveHOME device use improved walking distance, ability to stand or sit for extended periods of time, sleep and mood quality, and ability to lift greater weight. As an exploratory evaluation, improvement in pain and function by anatomic pain location was assessed.

RESULTS

Demographics

Of the 463 subjects with submitted surveys, 374 subjects were male (80.3%) and 91 (19.7%) were women. Mean age was reported as 57 years (Minimum age 37, Maximum age 66). Four-hundred twenty-three subjects were Veterans, 39 subjects were treated at pain or orthopedic clinics.

With regard to type of pain recorded on the survey, 93.3% of subjects responded. Of these responders, 84.9% reported having chronic pain and 19.4% reported having acute pain. Neuropathic pain was reported in 22% of subjects and nociceptive pain was reported in 2.6% of subjects. Subjects could select multiple pain types (e.g. acute, chronic) so overlap exists between these types of pain. In response to how often subjects used the BioWaveHOME device, the majority subjects reported using the device daily (51.0%) or multiple times per day (30.0%).

Effectiveness

As described previously, pain was captured using a 10-point numeric rating scale. Following two weeks of treatment, a significant reduction in pain was reported, with a mean decrease in pain score of 3 points (**Table 1**). The upper bound of the 95% confidence interval is below zero, indicating subjects saw a statistically relevant reduction in pain ($p<0.001$). It can be concluded with 95% confidence that the pain reduction is at least 2.9 for subjects. Plots mapping change in pain are presented in **Figure 3**.

Table 1: Pain Scores

						95% CI	
	Mean	**SD**	**Med**	**Min**	**Max**	**LB**	**UB**
Pre	7.3	1.7	8.0	1.0	10.0	7.2	7.4
Post	4.2	2.0	4.0	0.0	10.0	4.1	4.5
Δ	**-3.0**	**2.0**	**-3.0**	**-10.0**	**6.0**	**-3.2**	**-2.9**

Similarly, a significant improvement in activities of daily living was reported. Note, a reduction in ADL score in the survey indicated an increase in ADL function with the best possible score being 0 ('I feel Great'). Subjects experienced a mean reduction in ADL score of 1.8 points (**Table 2**). The upper bound of the 95% confidence interval is below zero, indicating subjects saw a statistically relevant increase in ADL function ($p<0.001$). It can be concluded with 95% confidence that the ADL function

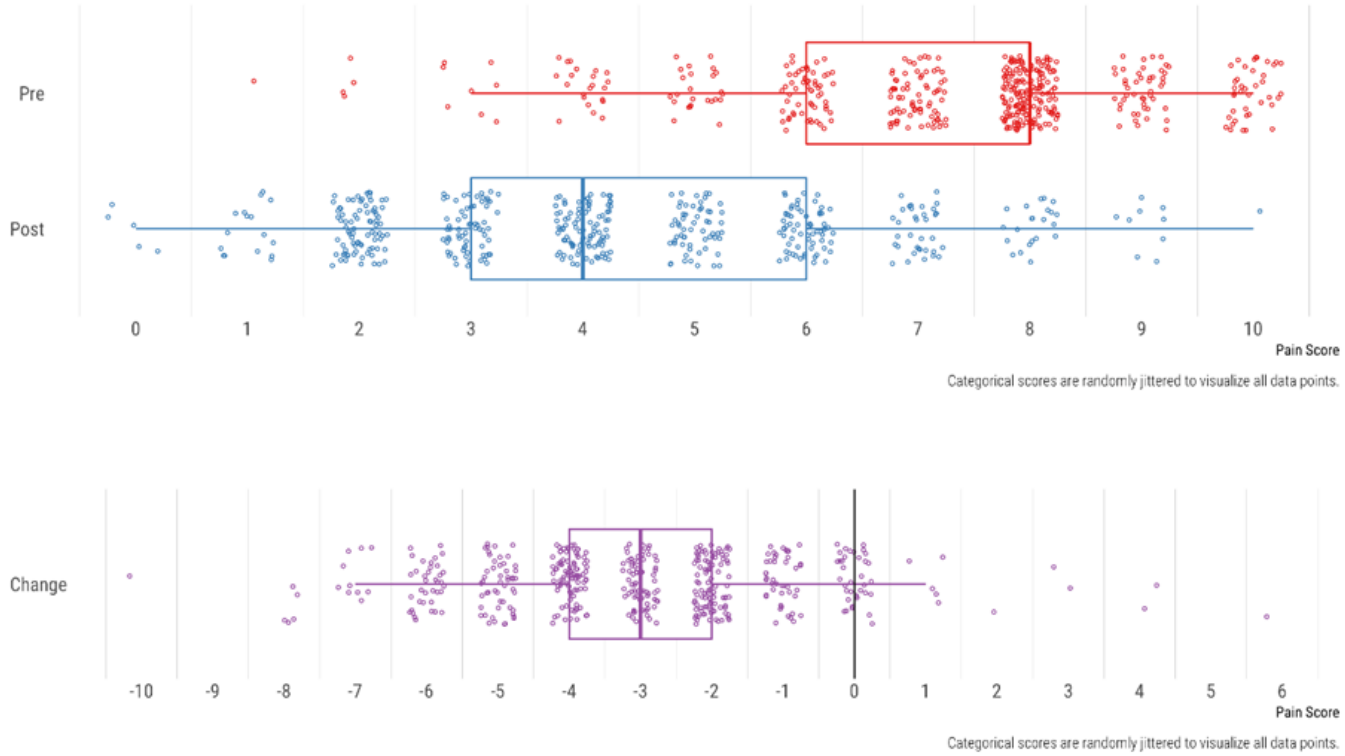

Figure 3: Boxplot indicating Pre- and Post-Treatment Pain Scores (Top) and Change in Pain Scores (Bottom)

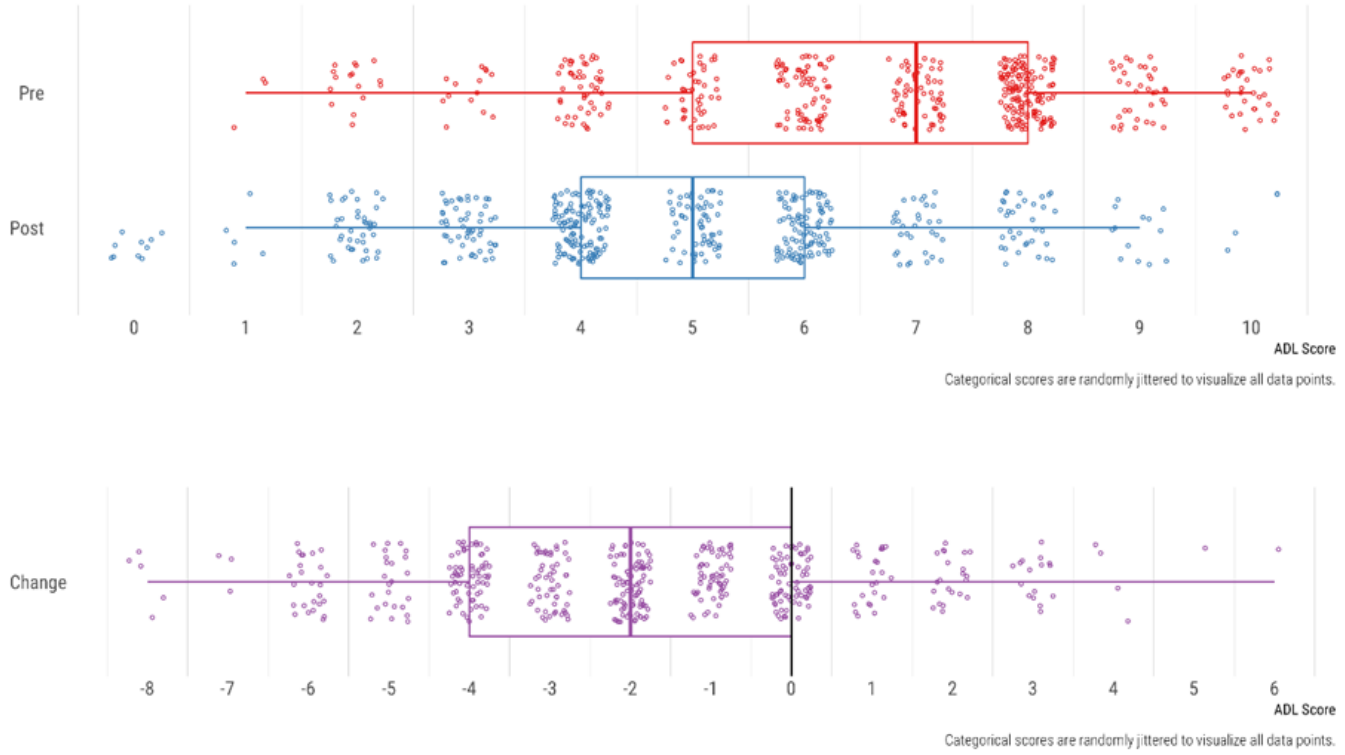

Figure 4: Boxplot indicating Pre- and Post-Treatment ADL Scores (Top) and Change in ADL Scores (Bottom)

increased by at least 1.6 for subjects. Plots mapping change in pain are presented in **Figure 4**.

Table 2: ADL Scores

						95% CI	
	Mean	**SD**	**Med**	**Min**	**Max**	**LB**	**UB**
Pre	6.7	2.0	7.0	1.0	10.0	6.5	6.9
Post	4.8	2.0	5.0	0.0	10.0	4.7	5.0
Δ	**-1.8**	**2.4**	**-2.0**	**-8.0**	**6.0**	**-2.0**	**-1.6**

As demonstrated, two-week treatment with the BioWaveHOME resulted in significant reduction in pain and significant improvement in function as measured by activities of daily living.

As an exploratory analysis, improvement in pain and ADL by anatomic pain location reported on the returned patient survey was evaluated. Grouping patients by area of pain, most patients reported some form of back pain (n=257), with the second most reported area being followed by shoulder pain (n=91). A total of 98 patients did not report a specific region for their pain.

In comparing the different anatomies with regard to change in pain score from baseline, it is clear that no anatomy performed significantly worse than the mean reported improvement (3 points), with most reporting improvements in-line with the overall mean improvement (**Figure 5**). Patients reporting back pain, which encompasses most of the overall patient population, had a mean improvement of ~3 points. Excluding patients that did not report a specific region of pain, the second most reported area of pain was the shoulder (n=91), which reported a mean improvement of ~3.5 points. While numerically higher, this improvement is not significantly different from the overall mean improvement. Similarly, improvement in ADL by anatomy revealed a near identical improvement from baseline for all anatomies, ~1.8 points (**Figure 6**).

When asked how many hours of pain relief was provided by BioWaveHOME, mean time of relief was reported as eight (8) hours, with relief times ranging from 30 minutes to up to 73 hours after each use. With regard to pain medication, over half (51.8%) of subjects reported either reducing or eliminating use of medications for pain during the two-week treatment period.

When asked if BioWaveHOME has improved the subject's quality of life, 69.8% of subjects reported "very much" or "yes." Satisfaction with the BioWaveHOME system was high, with subjects reporting a mean 8.1 points on the 10-point scale used to evaluate treatment satisfaction. Additionally, 97% of subjects reported a desire to continue using the BioWaveHOME system.

With regard to the aspect of life improved by incorporation of the BioWaveHOME system into the subjects' pain management routine, subjects reported being able to walk further, stand longer, sit longer, sleep better, lift more, and be in a better mood during the two-week period where the BioWaveHOME was being used.

Safety

There were no reports of any burns, or any electro-thermal injury or any other adverse events.

DISCUSSION

This study sought to evaluate the effectiveness of the BioWaveHOME system, an in-home, non-pharmacological, non-invasive pain management device. The current study is the second investigation conducted evaluating the effectiveness of the device in subjects with chronic pain. The first study, a survey of 66 Veterans using the BioWaveHOME for long-term use (6-18 months), reported that 90% of subjects described a significant decrease in pain, increased range of motion, or an increased ability to participate in activities of daily life after incorporating the device into an existing pain management routine [8]. Of the study participants, 58.7% reported reducing or eliminating use of prescription opioids while using the BioWaveHOME. While the results from this initial evaluation were encouraging, additional investigations were necessary to evaluate use of the BioWaveHOME in a larger patient population with validated, subject-reported outcome measures. Additionally, the effect of short-term BioWaveHOME use was also important to investigate, as an effective, easy-to-use, in-home alternative to prescription opioids that provides immediate and sustained relief could potentially have a significant impact on how treating physicians view pain management.

This study, inclusive of 463 survey responders, demonstrates that the BioWaveHOME is an effective non-pharmacological, non-invasive, non-addictive pain treatment solution for chronic and acute pain sufferers. Pain, as measured by this evaluation using a numeric rating scale within the provided survey, was found to

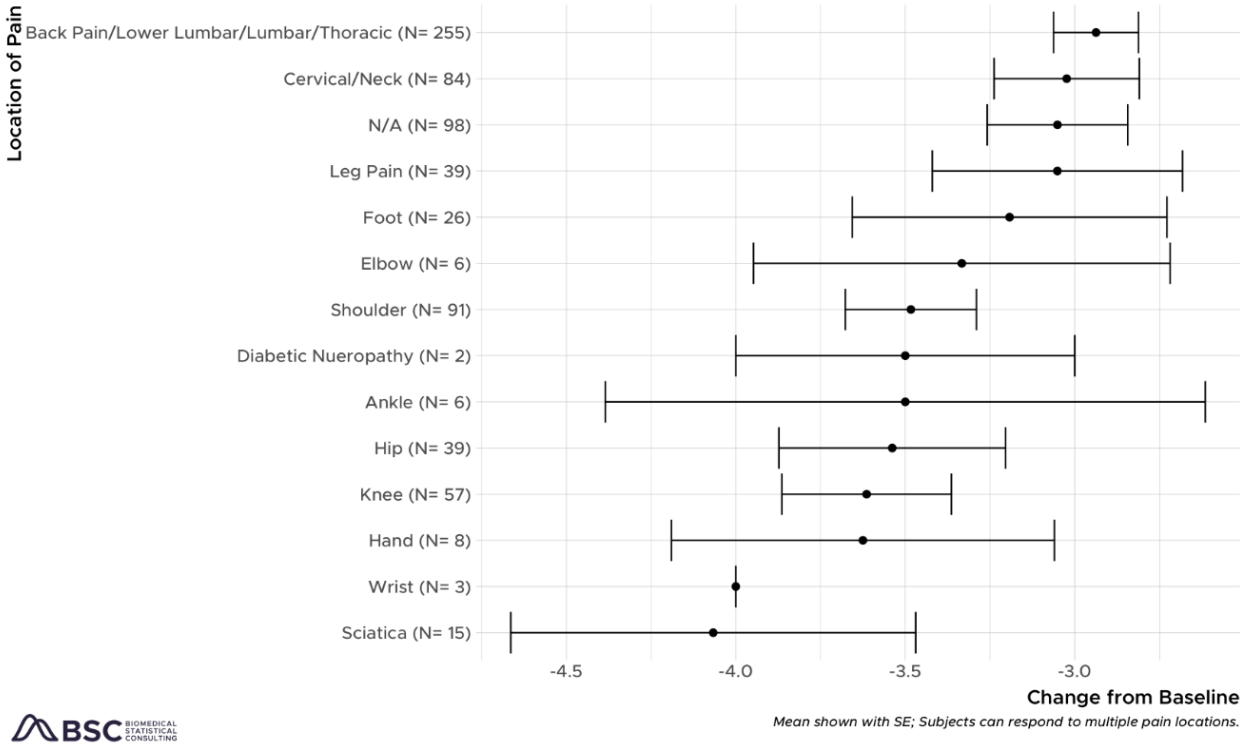

Figure 5: Change in Pain Score from Baseline by Anatomy

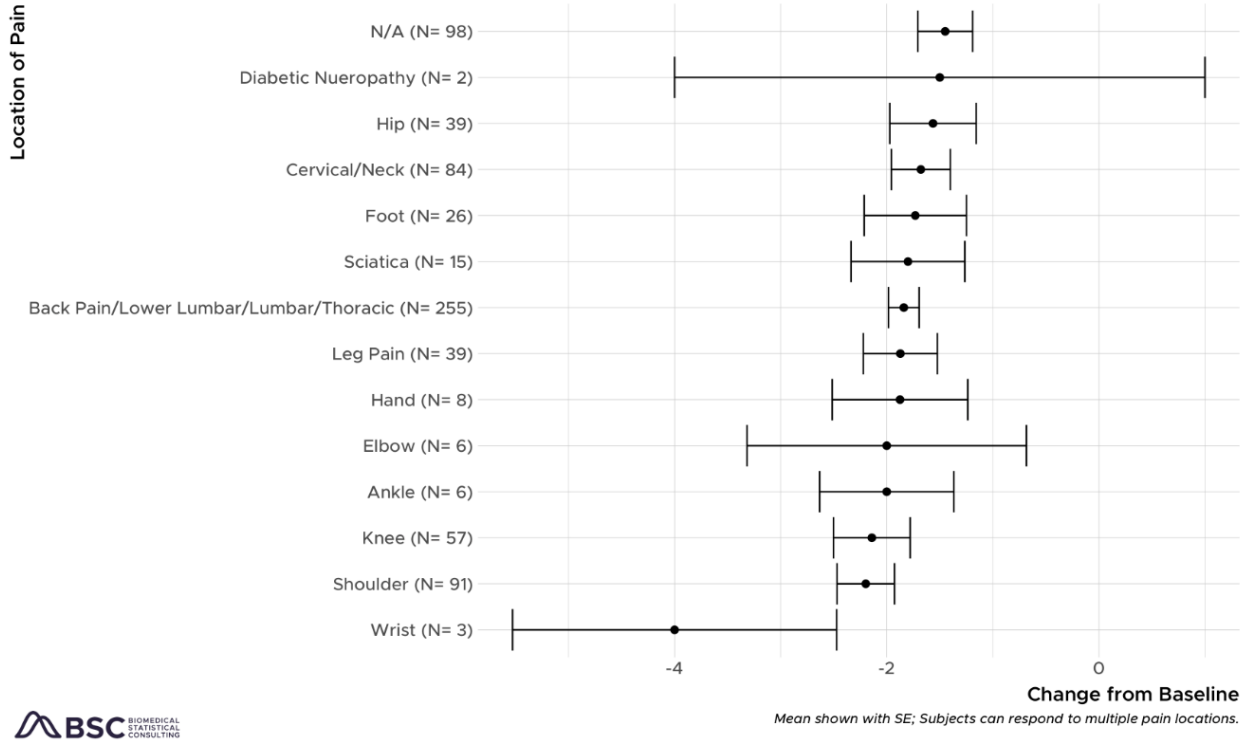

Figure 6: Change in ADL Score from Baseline by Anatomy

significantly decrease following use of the BioWaveHOME. Subjects in the study reported a mean decrease in pain of three (3) points, which is a greater improvement than what is considered to be the minimal clinically important difference (MCID) for general chronic pain (1.7-points) and chronic musculoskeletal pain (1-point) [9]. Within the survey, the pain scale was correlated to the Wong-Baker Faces rating scale, which has been reported to have an MCID of two to three points on a numerical scale [10]. Considering both pain scales, subjects within this study experienced a clinically significant reduction in pain after incorporating the BioWaveHOME device into their pain management routine for two weeks. Importantly, 51.8% reported completely eliminating or reducing pain medication during the two-week treatment period, further supporting the significant relief experienced by subjects when using the BioWaveHOME. Subjects reported an average of eight hours of relief following use of the device, which likely contributed to the subjects being able to reduce pain medication intake or eliminate use completely. Subjects in the study reported a significant improvement in activities of daily living following use of the BioWaveHOME for two-weeks per the patient-reported 10-point scale included within the survey. Pre-treatment, subjects recorded an average of 6.7 points out of 10 on the scale, where increasing numbers correlate to increased disability. Following two-weeks of BioWaveHOME use, subjects reported a mean improvement of 1.8 points, with a post-treatment mean of 4.8 points. Related, the majority of the subjects in the study reported that the BioWaveHOME improved their quality of life, with 87.7% reporting at least some degree of improvement. With these improvements, subjects reported being able to walk farther, stand longer, sit longer, sleep better, and reported having an improved mood while using the BioWaveHOME. Considering both the improvement in pain and reduced disability, the BioWaveHOME was found to considerably improve subject quality of life after just two-weeks of use. Additionally, evaluating pain and ADL improvement by anatomy revealed an important conclusion: significant improvement in pain and function are not exclusive to specific anatomies, all treated areas in the study benefited from treatment with the BiowaveHOME device. While no specific anatomy reported a mean improvement significantly different from the mean pain and ADL improvement, it is encouraging to see the various anatomies reported responding equally to the treatment. One of the most pressing concerns with prescription opioids in chronic pain sufferers is the need to continue medicinal treatment to have continued relief. Long-term opioid use can result in tolerance, which requires more of the drug to create the same level of relief, commonly resulting in opioid misuse, addiction, and, regrettably, overdose. With opioid misuse, users are likely to seek out non-prescription alternatives as these are often less costly and easier to obtain than prescription opioids. A recent survey of active heroin users reported that 80% of users surveyed switch to heroin following opioid misuse [11]. Within this study, over half of the surveyed BioWaveHOME users reported being able to eliminate or reduce pain medication use and reported having an average of eight hours of sustained relief following each use of the device. As a non-opioid, non-addictive simple-to-use treatment device that can be used in-home, this study supports that the BioWaveHOME system could provide a viable alternative to prescription pain medication that is effective and sustained.

Non-opioid alternatives to pain management are not novel. TENs units are non-pharmacologic, non-addictive, non-invasive devices that can be incorporated into existing pain management routines. The main limitation of the TENs technology is that it is based on the "gate control theory" of pain, which focuses primarily on masking pain signals. By masking pain signals, relief is only short-term. The technology behind the BioWaveHOME, alternatively, is based on the "frequency conduction block theory," which blocks pain signals by preventing the sodium-potassium ion exchange across the membrane of nociceptive pain fibers. Through this pathway, the action potential does not move through the pain fibers, stopping the pain signal. The BioWave technology is able to provide long-term relief by blocking the pain signal, as evidenced by the long periods of relief reported by the subjects within this study.

Considering the increasing public health burden and healthcare costs of the opioid epidemic in both the general and Veteran populations and the current lack of effective commercially available alternatives, this study demonstrates that the BioWaveHOME has the potential to meet an unmet healthcare need: an easy-to-use, non-addictive alternative to pain management that has been shown to be effective in providing immediate pain reduction and improving quality of life. Almost all of the surveyed subjects reported wanting to continue using the device, with 73.2% of subjects reporting a satisfaction of 8, 9, or 10 on a 10-point scale of increasing treatment satisfaction. Overall, the

BioWaveHOME was effective at significantly reducing pain and improving function in the surveyed group and provides a viable alternative to prescription drug pain management.

CONCLUSIONS

In conclusion, the BioWaveHOME was found to effectively and significantly reduce pain and improve quality of life following two-weeks of as-needed use. In addition, the majority of study subjects reported great satisfaction with the treatment, with most reporting reducing or eliminating prescription pain medication use and expressing a desire to continue using the device.

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