

Prospective Randomized Single-blinded Controlled Clinical Trial of Percutaneous Neuromodulation Pain Therapy Device Versus Sham for the Osteoarthritic Knee: A Pilot Study

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This pilot study presents the initial results for a percutaneous neuromodulation pain therapy device (Deepwave) that is associated with no morbidity, good pain relief, and increased function in patients with knee osteoarthritis.

Osteoarthritic pain can be debilitating and lead to significant and undesirable lifestyle changes. Increased emphasis on addressing pain has been fueled by the recent description of pain as the “5th vital sign” by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO).¹ Despite efforts to develop new technolo-

gies and methods to treat pain, an “analgesic gap” exists.^{2,3}

Currently, the first step in symptomatic relief includes anti-inflammatory agents such as nonsteroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase (COX)-selective drugs in conjunction with lifestyle modifications. Often, these measures are not sufficient to completely alleviate the pain, which pushes patients to seek other alternatives such as depot corticosteroid injections, narcotics, and surgery. However, narcotics are capable of producing adverse effects including respiratory depression, sedation, nausea, vomiting, and even behavioral problems.⁴ Corticosteroid injections are more invasive, can only be re-

peated on a limited basis (ie, up to 3 times each year), and have an associated risk of infection and post-steroid flare-up.⁵ For these reasons, other treatment methods are needed to help close the treatment gap and thus reduce patient morbidity.

In addition to pharmacologic treatments, other nonpharmacologic alternatives have been used including acupuncture, cooling, physical therapy, chiropractic manipulation, and

transcutaneous electrical nerve stimulation is justified by the gate control theory, which states that the brain recognizes a limited amount of neural input from a given point in the body at any given moment. This impulse may be superseded by another more powerful and conducive neural input. Although transcutaneous electrical nerve stimulation has been shown to be useful for superficial tissues, it lacks the

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transcutaneous electrical nerve stimulation. Unfortunately, these alternatives fall short with respect to duration and magnitude of analgesia.

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ability to penetrate into deeper tissue.

A recently developed deep tissue percutaneous neuromodulation pain therapy device, Deepwave (Biowave Corp, Norwalk, Conn), is a viable alternative for narrowing the analgesic gap in treating osteo-

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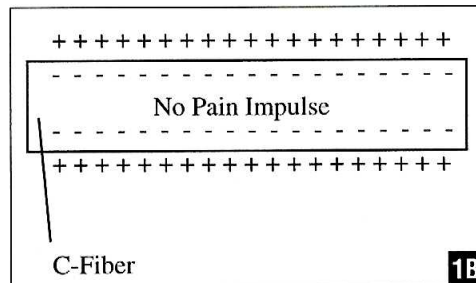
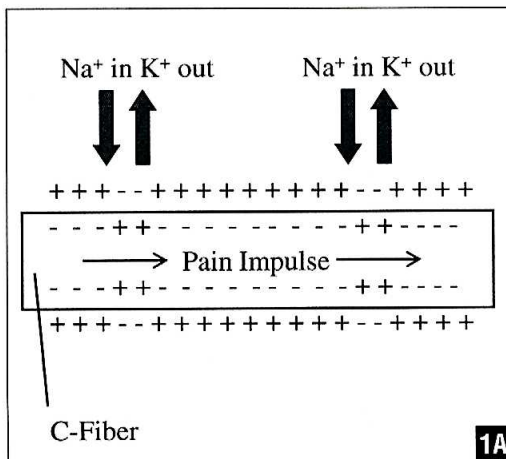


Figure 1: Deepwave (Biowave Corporation, Norwalk, Conn) mechanism of action via frequency conduction block. Normal propagation of pain signal along pain fibers (C-fibers) (A). Deepwave electric field interrupts sodium/potassium ion exchange, thereby inhibiting the cell wall from changing polarity and impeding transmission of pain impulses (B).

arthritic pain. Unlike transcutaneous electrical nerve stimulation, the Deepwave device can deliver a precise electrical signal to a specific volume of tissue in the body that blocks the transmission of pain impulses. The electrical signal created in the body is theorized to have a secondary effect of releasing endorphins and serotonin, and therefore leading to a localized analgesia at the treatment site. This analgesic effect depends on the duration and amplitude of treatment.

The Deepwave device sends a premixed modulated envelope of two high frequency electronic wave forms (“feed

signals”) into deep tissue via a larger feed electrode and a smaller pain site electrode called a percutaneous electrode array. The percutaneous electrode array facilitates delivery of the feed signals into deep tissue by providing a direct conductive pathway for current through the outermost layers of skin.

Percutaneous electrode arrays are comprised of 1014 microneedles, each of which is 0.73 mm in length and housed within a 2.5-inch diameter hydrogel-based electrode. Polarized structures in the body cause an electric field to form with a low frequency compo-

nent equal to the difference in frequency between the two feed signals. Formation of the low frequency field occurs in the form of a modulated electric field envelope with a location dependent on the placement of the two electrodes. The volume of tissue affected is dependent on electrode size and placement as well as the amplitude of the feed signals. With the configuration used in this study, the electric field is believed to form immediately adjacent to and beneath the percutaneous electrode array over the pain site, along the path between the opposing feed electrode and the percutaneous electrode array. The low frequency electric field is believed to demodulate nerve cells, resulting in an altered Na⁺/K⁺ equilibrium. As a result, the membrane potential of the nerve cell is stabilized (hyperpolarized) and is therefore unable to transmit action potentials and thereby pain impulses (Figures 1 and 2).

The use of Deepwave as a single therapy is efficacious and safe in reducing the severity of acute and chronic pain in knee osteoarthritis patients.

This study investigated the efficacy of Deepwave in reducing knee pain experienced by our patient population, and reduction of drug consumption over the 1-week period following the treatment.

MATERIALS AND METHODS

Patients

This is an Institutional Review Board-approved, single-blinded, randomized pilot study of 70 patients over an 8-month period. The study began in March 2005 and the data from the last patient was collected in December 2005. Patients were blinded to either live or sham treatment groups. All patients presented to the clinic with knee pain secondary to osteoarthritis. The diagnosis of knee osteoarthritis was made based on the American College of Rheumatology guidelines, which include knee pain with radiographic changes of osteophyte formation and at least one of the following: patient age >50 years, morning stiffness lasting ≤30 minutes, or crepitus on motion.¹⁵ Informed consent was received on 70 patients. Seven patients were lost to follow-up. Of the 63 completed patients, 28 patients were randomly assigned to the sham group and 35 patients were randomly assigned to the live treatment group. Table 1 presents the demographics for these two groups.

Inclusion criteria consisted of any man or woman who met the following conditions: aged between 18-85 years, diagnosis of osteoarthritis, knee pain secondary to osteoarthritis with a visual analog pain scale

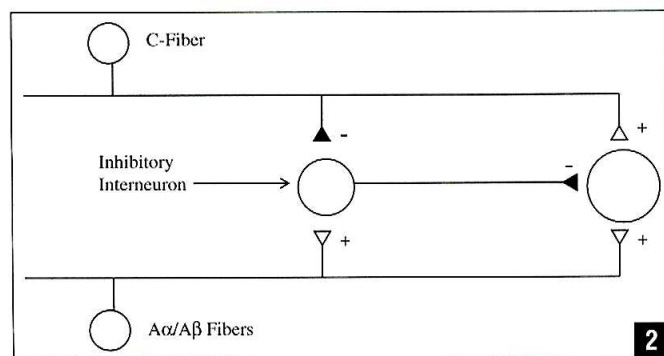


Figure 2: Deepwave (Biowave Corporation, Norwalk, Conn) mechanism of action via the gate control theory. The Deepwave may also activate the Aα/Aβ fiber, which occurs at both the inhibitory interneuron and projection fiber, thus causing a suppression of the pain sensation.

Table 1

Patient Demographics for Live and Sham Groups

	No (%)	
	Live Treatment (N=35)	Sham Treatment (N=28)
Men	11	7
Women	24	21
Mean age (range)	55.3 (34-83)	58.2 (28-80)
Affected side		
Right	15 (43)	10 (36)
Left	20 (57)	18 (64)
Pain location		
Anterior	33 (94)	25 (89)
Posterior	6 (17)	7 (25)
Medial	18 (51)	12 (43)
Lateral	7 (20)	5 (18)

>30 mm, and the ability to understand and willingness to cooperate with the study procedures.

Exclusion criteria excluded any patient with an allergy or intolerance to adhesive materials; surgical intervention or injection of a corticosteroid or viscosupplement within the prior 30 days of the treatment of the painful knee or its underlying etiology; history of any substance abuse or dependence within the past 6 months; history of pacemaker use; existence of implantable electronic devices; any clinical evidence of cardiovascular, pulmonary, renal, psychological, hepatic, neurological, hematologic or endocrine abnormalities; and having received an investigational drug or device in the past 30 days.

Pain Therapy Device

The Biowave deep tissue neuromodulation pain therapy device (Deepwave) was used.

The active percutaneous electrode placed over the pain site was a 1.5-inch diameter round percutaneous electrode array embedded within a 2.5-inch diameter round carbon/silver electrode (Unipatch, Wabash, Minn). The feed electrode placed opposite the pain site was the Classic 2404, 4x2-inch self adhesive electrode (Unipatch).

Visual Analog Pain Scale

A visual analog pain scale was used to determine pre- and post-treatment pain levels (immediate, 6 hours, 24 hours, and 48 hours post-treatment). A 100-mm scale was used to mark the patient's subjective pain. At the far left of the scale was "no pain" and on the far right was "worst pain imaginable." The visual analog pain scale has been proven to be a valid and reliable assessment of pain.¹⁶

Treatment

For all patients, the active percutaneous electrode

Table 2

Comfort and Safety Profile of Live and Sham Groups at 1-week Follow-up

	No (%)		P value
	Live	Sham	
Comfortable			.872
Yes	34 (97)	27 (96)	
No	1 (3)	1 (4)	
Pain/pressure/tingling			.367
Yes	1 (3)	2 (7)	
No	34 (97)	26 (93)	
Skin adverse effects			.427
Yes	1 (3)	0 (0)	
No	34 (97)	28 (100)	

was positioned on their site of maximum knee pain while the feed electrode was placed directly across the joint line (medial and lateral or anterior and posterior). Treatment duration was 30 minutes in both groups. Patients were instructed to sit in a chair with their backs to the Biowave machine. Live treatment group patients were instructed to tell the examiner when they had achieved the highest tolerable intensity. The intensity levels then were reassessed and increased as tolerated by the patient after 5, 10, and 15 minutes from initiation of the treatment session. The mean intensity levels for the live group were 16%, 19%, 21%, and 23% at the 0-, 5-, 10-, and 15-minute time points, respectively.

The sham treatment group was instructed that because the percutaneous electrode has microneedles that penetrate through the outer skin layers, they would not perceive the normal "pins and needles"

usually associated with electrical stimulation. Throughout the entire sham treatment the machine was not turned on although the appropriate intensity buttons were pressed to simulate the live treatment.

Subjective Outcomes

Additionally, the Western Ontario and McMaster Osteoarthritis Index (WOMAC) questionnaire was completed by each patient prior to receiving the treatment and again at 48 hours post-treatment. The WOMAC questionnaire has proven valid in assessing pain, stiffness, and function of the osteoarthritic patient.¹⁷ Posttest data identical to the pretest data was collected immediately post-treatment (0 hours) by the tester. At 6, 24, and 48 hours, post-treatment data were recorded by the patient and all study materials were mailed to the investigator at the completion of the study. A phone call to each patient at the 6-, 24-, and 48-hour time

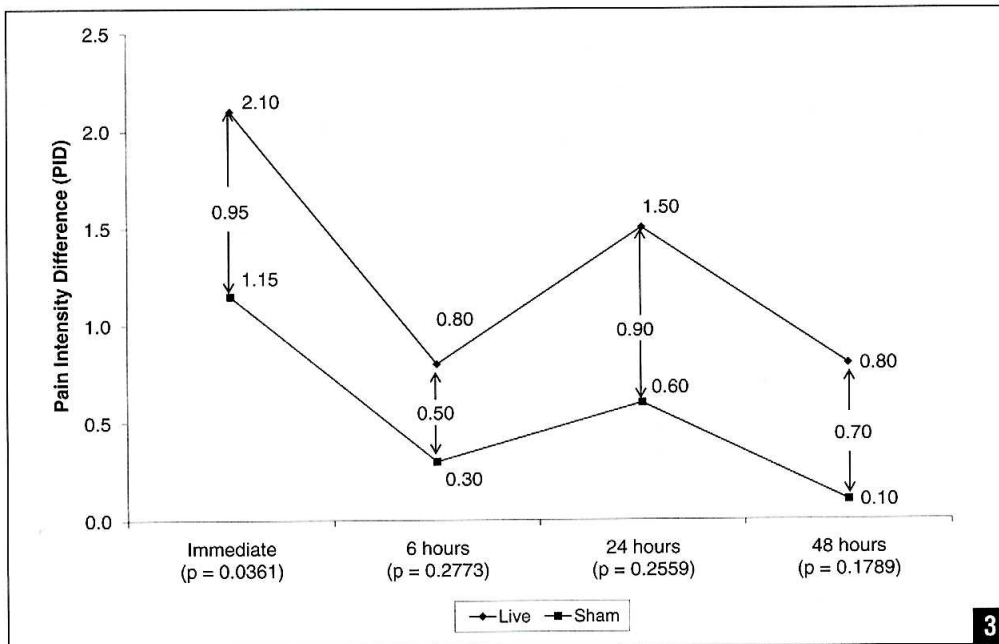


Figure 3: Pain intensity difference (values noted as centimeters on visual analog pain scale) for the live and sham groups.

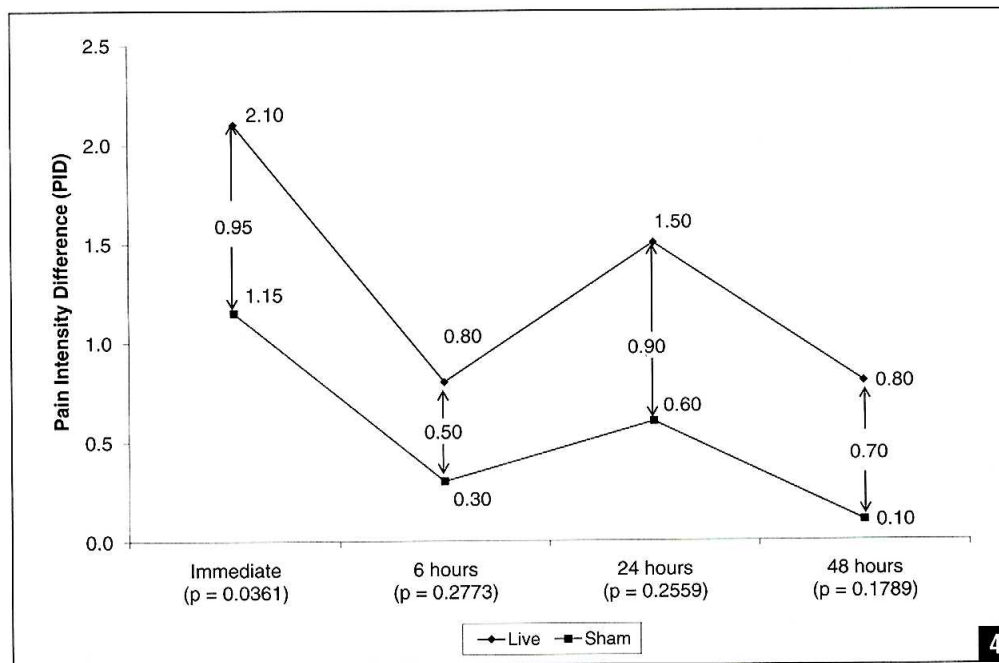


Figure 4: Summed pain intensity difference (values noted as centimeters on visual analog pain scale) for the live and sham groups.

points was performed to enhance patient compliance. The immediate, 6-, and 24-hour post-treatment data consisted of a visual analog pain scale and perceived overall improvement (0%-100%). The 48-hour

data included the visual analog pain scale, perceived improvement, follow-up knee survey, and subjective questions regarding pain control and relief. Finally, a 1-week phone survey was conducted with subjective

questions regarding adverse effects and medication use.

Statistical Analysis

Normally distributed continuous variables were analyzed with an analysis of vari-

ance (ANOVA) model with repeated measurements. Continuous variables that were normally not distributed were analyzed using the Wilcoxon test for pairwise comparisons. Categorical variables were analyzed with a chi-square test. Significance levels were set at $P < .05$.

RESULTS

Comfort and Safety

No serious adverse events were noted in either the live or sham groups. As seen in Table 2, there were no significant differences between live and sham groups with respect to comfort or adverse effects. One patient reported a mild erythematous maculopapular rash where the percutaneous electrode array was placed. This rash had resolved on its own within 24 hours. Three patients (1 live, 2 sham) reported mild tingling that resolved on its own within 6 hours of onset.

Pain Intensity Difference

Pain intensity difference was the primary measure of efficacy. Pain intensity difference is defined as the difference in visual analog pain scale noted at pretreatment (baseline) versus the visual analog pain scale noted at each post-treatment period. In this respect, figure 3 demonstrates that the live group had significantly greater efficacy than the sham group in the immediate post-treatment period ($P = .0361$). The live group's pain intensity difference was greater than the sham group's pain intensity difference by 9.5 mm, 5.0 mm, 9.0 mm, and 7.0 mm for

