



# Overview



**BioElectronics Corporation**  
4539 Metropolitan Court, Frederick, MD 21704 USA  
301-874-4890 | [info@bielcorp.com](mailto:info@bielcorp.com) | [www.bielcorp.com](http://www.bielcorp.com)

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## Company Overview

BioElectronics Corporation, headquartered in Frederick, Maryland, USA, is the leading company in the field on non-invasive electroceutical medical devices. The devices are used to treat acute and chronic pain and promote wound healing. The BioElectronics' technology is a pioneering advancement of pulsed shortwave therapy. Traditional pulsed shortwave therapies are clinically proven, effective, safe and have been used for decades by physicians and physiotherapists but are large devices for hospital or outpatient use. Advances in microelectronics have now made it possible to deliver this therapy in a small, wearable and economical medical device. BioElectronics' devices provide superior extended duration treatments and hospital and home use to help self-management of pain and lower the cost of care. The devices do not produce heat or, a tingling sensation, like a TENS.



## Product Portfolio

 <b>Musculoskeletal Pain Relief</b> 5x better than OTC drugs and 100% safer for relieving musculoskeletal pains.  actipatch.com	 <b>Foot Care Heel Pain Relief</b> Advanced Electro-Pulse technology & comfortable gel insoles providing maximum heel pain relief.  smart-insole.com	 <b>Menstrual Pain Relief</b> Revolutionary, drug-free treatment for pain and discomfort associated with menstruation.  myallay.com	 <b>Postoperative &amp; Wound Care</b> Clinically proven medical therapy for postoperative pain, inflammation and accelerated recovery.  recoveryrx.co
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## Prevalence and Problems of Chronic Musculoskeletal Pain

Recent studies estimate the prevalence of chronic pain in the population to be about **20–40%**, depending on how it is measured. Chronic pain affects more than the number affected by diabetes, heart disease and cancer combined. There is also a new focus on the costs of chronic pain with studies showing the extreme economic burden placed on healthcare systems and individuals<sup>1</sup>.

**Chronic musculoskeletal pain is the cause of 80-85% of all chronic pain.** Osteoarthritis is the cause of 85% of all arthritis. Once it occurs, it is irreversible and progressive with therapy focused on the reductions of symptoms and maintenance of quality of life. Chronic lower back pain, with a prevalence of 23%, is the leading cause of chronic musculoskeletal pain. Only the minority of people with chronic knee and hip pain opt to have a joint replacement to alleviate some of the symptoms. The main causes of pain reported by US citizens include: low back pain (28.1%), neck pain (15.1%), knee pain (19.5%), shoulder pain (9.0%), finger pain (7.6%), and hip pain (7.1%).

**A comprehensive European pain survey showed that 19%<sup>3</sup> of people suffer from moderate to severe chronic pain and the effects of which pervade all aspects of their lives:**

- 66% less able to sleep
- 50% find walking and household chores difficult
- 40% have difficulty with sexual relations
- 33% less able or unable to maintain an independent lifestyle
- 40% feel helpless that they cannot function normally
- 60% less able to work outside the home
- 20% had lost their job due to pain
- 30% who were not retired said their hours or employment status had been effected
- Increased depression and doubles suicide risk

The high prevalence of chronic musculoskeletal pain is clear evidence of the ineffectiveness and inadequacy of the currently available therapeutic options. There are no consistent and dependably effective analgesic treatments. The escalating doses and drug combinations do not provide effective pain relief and result in increasing incidence of adverse effects and serious harm, particularly in an ageing population that are less tolerant of drugs. Many patients are intolerant of non-steroidal anti-inflammatory drugs (NSAIDs) as well as opioids. Recent studies have shown that acetaminophen (paracetamol) is ineffective for relieving chronic musculoskeletal pain<sup>4</sup>. Chronic use of opioids and NSAIDs negatively impact public health, and society<sup>5</sup>.

The stark reality is that for a very significant percentage of the population, suffering from moderate to severe chronic pain no appropriate alternative therapy is available. ActiPatch would provide a valuable new mode of chronic pain therapy and result in substantial public health benefits by reducing the burden of pain, the complications of its treatment, as well as associated healthcare costs.

1. Baker M, Collett B, Fischer A *et al.* Improving the current and future management of chronic pain. A *European Consensus Report* (2010).
2. Gaskin DJ, Richard P. The economic costs of pain in the United States. *J. Pain* 13(8), 715-724 (2012).
3. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D: Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur. J. Pain* 10(4), 287-333 (2006).
4. Machado GC, Maher CG, Ferreira PH *et al.* Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomised placebo controlled trials. *BMJ* 350, h1225 (2015).
5. Momeni M, Katz JD. Mitigating GI risks associated with the use of NSAIDs. *Pain Med.* 14 Suppl 1, S18-22 (2013).

## Superior Safety to Analgesic Drugs

**ActiPatch is completely safe with no risk of heat injury or any other significant adverse events.** Over one million devices have been used and no serious adverse events have been reported.

Drug therapy is the mainstay of chronic musculoskeletal pain treatment and all drugs have wide ranging adverse effects. The major problems and issues of the most commonly used drugs for musculoskeletal pain are set out below:

### Acetaminophen

- Liver failure - In the U.S., acetaminophen toxicity has replaced viral hepatitis as the most common cause of acute hepatic failure, and is the second most common cause of liver failure requiring transplantation
- Kidney Injury
- Gastrointestinal Bleeding

According to the Centers for Disease Control and Prevention, between 2001 and 2010, more than **1,500** people in the U.S. died from **accidental acetaminophen overdoses**. This number is far higher than any other over-the-counter pain reliever.

### NSAIDs

NSAIDs are a leading cause of drug-related morbidity especially in the elderly and patients with co-morbidities. The mechanisms of NSAID toxicity are well understood, but the consequences are largely uncontrolled in

clinical practice. GI ulcers, including bleeding ulcers, may occur in several percent of all chronic unprotected, high-dose NSAID users. Renal side effects may precipitate renal failure resulting in acute dialysis and chronic retention. This includes sodium retention resulting in arterial hypertension, heart failure, and atherosclerotic events. Cardiovascular risk may be tripled by chronic high-dose NSAID use in long-term clinical trials though "real-life studies" that indicate lower risk ratios. Off-target side effects include allergic reactions, drug-induced liver injury, and central nervous system effects.

- Gastrointestinal bleeds-annual risk of serious GI complication is **1.3%** for Rheumatoid Arthritis and **0.73%** for Osteoarthritis
  - **100,000** hospital admissions per year in U.S.
  - **16,000 Deaths per year**
  - Need for co-prescribing proton pump inhibitors
- Kidney Injury
  - Adverse renal events occur in approximately **1-5% all patients using NSAIDs**
  - Because of the large number of patients that take NSAIDs (U.S. estimates of more than 70 million prescriptions and 30 billion over-the-counter doses annually), this translates to upwards of **2.5 million patients experiencing a nephrotoxic event annually.**
- Bleeding
- Heart failure
- Hypertension
- **Increased risk of heart attack, stroke and DVT**
- Drug interaction particularly with anticoagulants and anti-platelet drugs
- Hearing loss

The American College of Rheumatology, and other rheumatologic associations around the world, recommend use of **NSAIDs at the lowest effective dose and for short duration** and they be limited to mainly control flare ups. This leaves many chronic pain sufferers with the dilemma of running the risk of adverse effects from chronic NSAID use, or moving onto opioids with their own inherent and potentially worse problems and risks.

## Opioids

- An analysis by the Centres for Disease Control and Prevention (CDC) found that opioid analgesic sales increased four-fold between 1999 and 2010 and paralleled by an increase in opioid overdose deaths and substance abuse treatment admissions during the same time period. . 1 in 15 people who take non-medical prescription pain relievers will try heroin within 10 years.
- In 2010, 1 in 20 people in the US (age 12 or older) reported using prescription painkillers for nonmedical reasons
- In 2012, there were **16,000 deaths** in the U.S. from using opioids and 6,000 from heroin.
- An estimated **2.1 million** suffered from prescription opioid substance abuse and an estimated 467,000 were addicted to heroin.
- **58% of people dying from prescription opioid overdoses have a history of chronic pain.**

## **Favorable Efficacy**

Recent evidence has demonstrated that acetaminophen has little efficacy in chronic spinal and osteoarthritis pain. Efficacy of long term NSAIDs and opioid use in chronic musculoskeletal conditions of the spine and knee is also limited.

Statistically significant and clinically meaningful pain reduction has been demonstrated in three ActiPatch RCTs, two in chronic and one acute musculoskeletal pain. The consumer data from 4187 respondents, 3,595 with chronic pain, had an average baseline Visual Analogue Scale (VAS) score of 8.02 (scale is 0-10), and demonstrated an average of 41% reduction in chronic knee pain and 37% reduction in chronic back pain. The consumer data has been bias tested and the placebo effects from the ActiPatch RCTs range from 3.9-7.0% so the effect is more than likely to be very real. The consumer data demonstrates a consistent clinically

meaningful effect in chronic musculoskeletal pain from osteoarthritis, rheumatoid arthritis, fibromyalgia, post-surgical, and neuropathic affecting different regions of the body (back, hip, knee, wrist, elbow, and shoulder). The magnitude of the beneficial effect compares very favourably with current analgesic pain medications.

Choice of analgesic is not based solely on efficacy, as safety is very important. The ActiPatch **risk/benefit profile is superior to all analgesic drugs**. Furthermore, in the ActiPatch consumer data, effectiveness was demonstrated in people who on average had very high baseline pain scores and were already on two modes of analgesics therapy without good effect.

## Benefits of ActiPatch/RecoveryRx

The ActiPatch device provides treatment continuously for 720 hours for constant and consistent pain relief.

The ActiPatch mechanism of action provides a **unique analgesic profile** of decreasing local pain sensitivity of the affected region due to an anti-inflammatory effect as well as decreasing central pain perception by a neuromodulation effect;

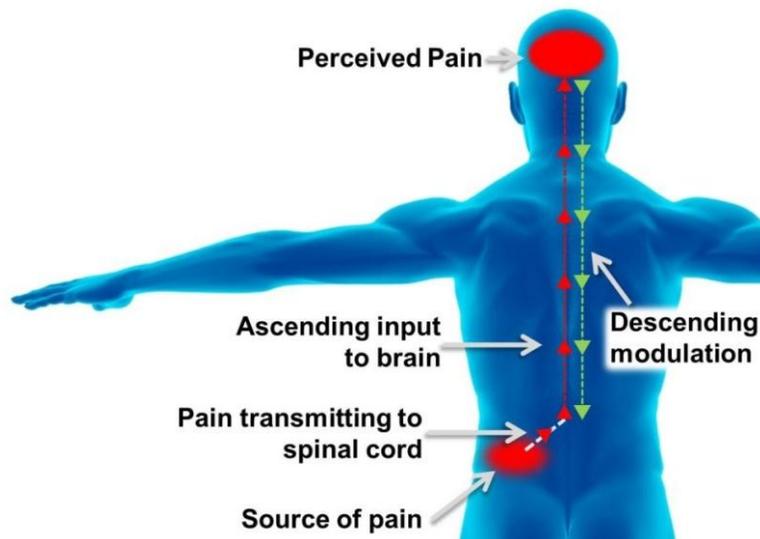
- The new non-drug analgesic modality that provides statistically significant and clinically meaningful pain relief;
- Absolute safety due to novel low power mechanism of action;
- Reduction or avoidance of analgesic drug use and lowering the risk of adverse effects, including death from opioids and NSAIDs;
- Alternative analgesic for those who are intolerant or unwilling to take drugs;
- Reducing potential for harmful drug interactions e.g., NSAIDs and anticoagulants or anti-platelet drugs (both increasingly common in the aging population); and
- Easy to use and cost effective with less need for advanced pain interventions.

## Chronic Pain & Central Sensitization

Chronic pain results from central sensitization, which causes the nervous system to develop a persistent state of high reactivity. This serves to amplify and maintain the pain even after the initial injury has healed.

Therefore, chronic pain is often poorly correlated to the degree of peripheral tissue injury.

ActiPatch's electromagnetic signal pulses 1,000 times per second to stimulate neuromodulation of the afferent nerves to dampen the brain's perception of pain. The pulsed signal rate prevents adaptation to allow long-term use. This extended pain relief improves sleep, physical activity and overall quality of life.



## Clinical Effects

In acute and chronic pain, there is local sensitization of peripheral nerves to painful and non-painful stimuli by a number of inflammatory mediators that bind to the sensory nerve endings. Through its effect on ion channels, the ActiPatch device decreases inflammation within the target tissue and **decreases peripheral sensitization** to pain.

Afferent nerves are sensory nerves that carry nerve impulses from receptors toward the central nervous system. By periodically stimulating afferent nerves from the target tissue, the ActiPatch device increases the non-painful sensory traffic to the brain and decreases central perception of pain from the affected area, a process known as **neuromodulation**.

## Target Populations/Indications for Use:

### ActiPatch

- Chronic musculoskeletal pain affecting joints, muscles and soft tissues
- Acute musculoskeletal pain affecting joints, muscles and soft tissues

### RecoveryRx

- Chronic musculoskeletal pain affecting joints, muscles and soft tissues
- Acute musculoskeletal pain affecting joints and soft tissues
- Post-operative pain and oedema
- Wound healing

### Allay

- Menstrual pain

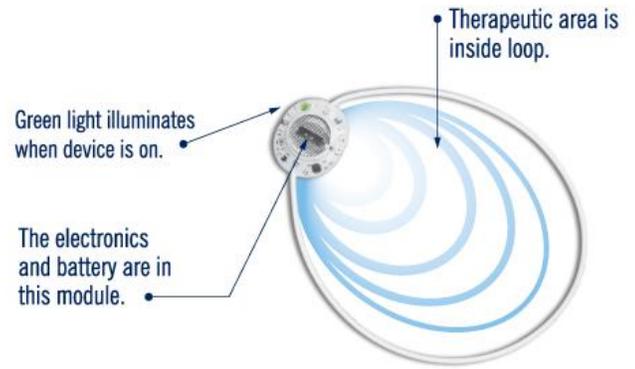
### Smart Insole

- Plantar Fasciitis
- Heel pain

## Device Description

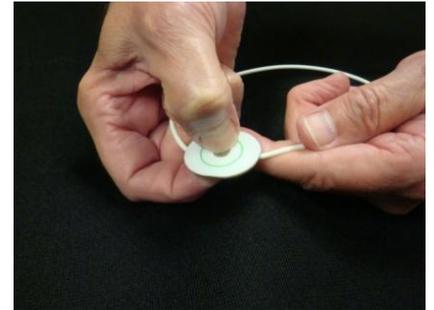
The device is constructed from three main components: an integrated circuit, an antenna and a 3 Volt battery. The circuitry consists of digital/analog electronics that control the timing functions to produce the therapeutic radiofrequency (RF) field at the pre-set pulse frequency. This closed loop system of the antenna, low energy signal generator circuit, and battery power supply, transfers the RF energy to the target tissue as a localized therapy with no far field effects.

ActiPatch delivers a pulsed RF treatment by way of a flexible induction coil that is placed over the area to be treated as illustrated below. The entire unit is wrapped in soft stretchable laminate material.



## Device Activation & Use

- The button switch is depressed for 2-3 seconds and then released. A green light will be illuminated confirming device is on and ready for use.
- To turn off the device, the button switch is again depressed for 2-3 seconds and then released. The green light will turn off confirming that the device is no longer active.
- Last approximately 720 hours = 30 days continuous use
- If the green light no longer illuminates, then the device is no longer operational and should be disposed.



ActiPatch can be applied in several ways:

- Affixed to the skin over the area to be treated with standard medical adhesive strips;
- Used with wraps for the knee and back to hold the device in place over the target area;
- More than one ActiPatch device can be worn as long as they do not overlap.

### • Applications Included:

#### Back Wrap:



#### Knee Wrap:



#### Medical Adhesives:



## Optional Methods:

- Affix to clothing that is in **close proximity** to the body over the target area of treatment
- Applied over medical dressings and plaster casts overlapping.



ActiPatch produces a durable response with no loss of effectiveness over extended durations of usage. In chronic musculoskeletal pain, the device has been shown to provide over 60% benefit within 3 days of continuous use and most of those who respond will do so by day 5. Chronic pain sufferers most likely have had the pain for years. What is important to them is that they experience pain relief rather than an immediate onset of action.

The pathophysiology of acute pain is different to chronic pain allowing ActiPatch to work much more quickly providing an effective non-drug alternative for acute musculoskeletal pain.

## **Precautions & Safety**

- ActiPatch® should not be used by women who are pregnant or think they may be pregnant as no studies have been conducted in pregnancy.
- ActiPatch® is not a sterile device. For post-operative or other wounds, place over sterile dressings.
- ActiPatch® will not interfere with other electronic equipment in use.
- ActiPatch® should not be used by skeletally immature persons (under 16 years of age).
- Do not attempt to modify this device or replace the battery.
- Once the LED light stops coming on the device is no longer operational and can be disposed of.

## Clinical Evidence

Clinical trials play a crucial role in testing new treatments and therapies. BioElectronics has undertaken clinical trials, user studies and compiled patient testimonials to build up the clinical evidence for its unique medical device product range. Many of the trials have been published in high ranking peer reviewed journals. For example, a plantar fasciitis heel pain clinical study was published in the respected journal; *The Journal of Foot and Ankle Surgery*. Although we believe we have combined a considerable amount of high quality clinical evidence, we are undertaking a significant number of new clinical trials to further develop the medical application and bring attention to our products. These clinical trials are being undertaken in respected universities and research hospitals by experienced and well published clinical researchers from around the world.

Significant progress has been made on this front, with clinical trials on three musculoskeletal pain conditions, plantar fasciitis, acute lower back and osteoarthritis of the knee. Two studies are being conducted on postoperative pain, hernia recovery and 3<sup>rd</sup> molar extraction. An independent study is also being conducted on venous stasis ulcer wound healing and pain management.

### Ongoing Clinical Research Studies

Study	Principal Investigator	Primary Outcome Measure	Enrolment	Status
<b>Bilateral Hernia Surgical Recovery</b>	Dr. Frederik Berrevoet University Hospital Ghent, Ghent, Belgium	Analgesic medication use and pain over 7 day recovery.	20 bilateral 60 unilateral	May 2015 (4 bilateral patients to completion)
<b>Dental Implant</b>	Dr. Operti, Dr Tealdo Valle Belbo Implant Center, Italy	Pain and Edema at day 3 and day 5	60	Recruiting Complete Dec 2015
<b>Chronic Back Pain</b>	Prof. Tipu Aziz Oxford University, John Radcliffe Hospital	VAS pain at 10 days	40	Started June 2015
<b>Chronic Back Pain</b>	Prof. Tipu Aziz BackCare UK Charity	VAS pain at 10 days	90	Pending Ethics Approval

### New Studies

**Migraine Pilot** To investigate the effect of ActiPatch in Chronic Migraine. Prof Martelletti Chief of the Headache Centre, Saint Andrea Hospital, Rome, Italy. World name in headaches. Vice President European Headache Federation. Understands neuromodulation and is interested. 60-80 patient study \$60,000-\$100,000.

**Diabetic Foot Neuropathic Pain Pilot** To investigate 3 months foot pain relief on diabetic patients cost for 40 patients \$20,000.

## Articles Published

Study	Journal	Publication Date Estimate	Author	Institution
<b>Blepharoplasty</b>	Aesthetic Plastic Surgery	Published 1982;6(3):169-71	Frederick V. Nicolle, Richard M. Bentall	London, United Kingdom
<b>Soft Tissue Injury</b>	<i>Bioelectrochemistry and Bioenergetics</i>	<i>Published 1986;16, 531–548.</i>	Richard Bentall	Institute of Bioelectrical Research
<b>Postoperative Pain</b>	Aesthetics of Plastic Surgery	Published: 2012 Apr;36(2):458-63	Rawe IM, Lowenstein A, Barcelo CR, Genecov DG	Genecov Plastic Surgery Group Dallas, Texas
<b>Chronic Wound Case Study</b>	International Wound Journal	Published: 2012 Jun;9 (3):253-8	T. Vlahovic, IM Rawe	Temple University Philadelphia, PA
<b>Plantar Fasciitis</b>	Journal of Foot and Ankle Surgery	Published: 2012 May – June;51(3):312-6	Brook J, Dauphinee DM Korpinen J, Rawe IM	Hunts Regional Medical Center Greenville, Texas
<b>Oosteoprogeniter Cell Differentiation Into Bone</b>	Journal of Craniofacial Surgery	Published 2012 Mar;23(2):586-93	Dr. Russell Reid	University of Chicago Medical School
<b>PEMF Review Wound Healing</b>	Wounds International	Published 20012 3(4):32-34	Ian Rawe	BioElectronics
<b>Case for OTC use of shortwave therapy</b>	Pain Management	Published 2014 Jan;4(1):37-43	Ian Rawe	BioElectronics
<b>OA of the Knee</b>	Rheumatology	Published Dec 2015	Dr. G. Bagnato	University Hospital Gaetano Martino, Messina, Italy

## Randomized Controlled Trials

The most important clinical benefit of ActiPatch is reduction of pain; this indication is supported by the three randomized controlled trials (RCT) and significant evidence of a marketed device provided. The RCT's are placebo controlled double blind studies; two are published and the third has been submitted for publication in February 2015.

### A Randomized, Double Blinded, Placebo Controlled, Clinical Trial of Pulsed Shortwave Therapy in Osteoarthritis of the Knee

<https://clinicaltrials.gov/ct2/show/NCT01877278>

Un-sponsored study-independent investigator  
Submitted to *Osteoarthritis and Cartilage* 2/2/2015

#### Method

A double blind randomized controlled trial of ActiPatch® treatment 12 hours a day for 4 weeks in osteoarthritis of the Knee, N=60, (30 Control, 30 ActiPatch). Assessments were compared at baseline and at 4 weeks.

#### Primary Outcome measures:

- Visual analogue pain scores (VAS)
- Functional scores assessed by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), as recommended by the Outcome Measures in Rheumatology Clinical Trials Group. The WOMAC assessment incorporates stiffness, and physical function assessments in addition to pain.

#### Secondary outcome measures:

- Quantity of analgesic medication use;
- Pain pressure threshold (PPT) measured at two distinct locations, the distal interphalangeal joint and the anterior portion of the quadriceps muscle;
- Reduction or disappearance of joint effusion determined by ultrasound; and
- Health survey based on 36 questions (SF36 v2).

#### Results

Statistically significant p value < 0.05 in the following:

- Reduced Pain **25%** VAS v 3% Placebo
- Reduced WOMAC TOTAL **18.3%** v 2.3% Placebo
- No adverse effects

#### Commentary

Osteoarthritis (OA) is a painful chronic joint disease characterized by progressive structural changes to the whole joint, including loss of articular cartilage, development of osteophytes, synovial inflammation, subchondral bone changes, meniscal damage, muscle weakness, and ligamentous laxity. The pathological process of OA is the same in all affected joints; there is no pathological difference in the process that occurs in the knee compared to the hip, shoulder or spine or any other joint affected by OA.

The reduction in knee effusions is indicative decreased synovitis (synovial inflammation causes fluid build up to cause the knee effusion). This finding provides evidence that ActiPatch is directly *decreasing synovial inflammation* as well as pain in the knee.

Pressure pain threshold (PPT) is the amount of pressure that needs to be applied to elicit pain, by increasing the PPT (not of the affected knee), ActiPatch is demonstrating that central pain processing has been decreased or there is less hypersensitivity to pain. In chronic pain states, there can be a lowering of the general pain threshold, not just at the affected site.

## **Pulsed Radiofrequency Electromagnetic Field Therapy: A Potential Novel Treatment of Plantar Fasciitis.**

*The Journal of Foot & Ankle Surgery 51 (2012) 312–316*

### **Method**

A multicentre, prospective, randomized, double-blind, placebo controlled trial. A total of 70 subjects diagnosed with plantar fasciitis were enrolled in the study. The subjects were randomly assigned a placebo (control group) or active ActiPatch device (study group). The subjects wore the ActiPatch or Placebo device overnight, recorded their morning and evening pain using a 0- to 10-point visual analog scale (VAS), and logged any medication use. The primary outcome measure for the present study was morning pain, a hallmark of plantar fasciitis.

### **Results**

- The day 7 morning VAS score was **40%** lower than the day 1 morning VAS score; placebo group a 7% reduction.
- Result statistically significant **p=0.03**
- Medication use in treatment group showed a trend downward but was static in placebo group.
- No adverse events

### **Commentary**

The pain of plantar fasciitis is usually most acute in the morning because the fascia, a thick band of connective tissue, tightens up during the night. Plantar fasciitis is a common cause of chronic heel pain and can take up to 2 years to achieve resolution. Plantar fasciitis is a degenerative process that occurs with or without inflammatory changes. The study demonstrates pain reduction and possibly also benefits in the healing process as excessive stretching of the plantar fascia can result in microtrauma. The loading of the degenerative and healing tissue at the plantar fascia cause the plantar pain. This study showed efficacy and safety for treating a complex and intractable musculoskeletal pain condition.

This published study can be viewed at <http://www.bielcorp.com/biel/wp-content/uploads/2013/03/plantar-study-printed-copy.pdf>

## Control of Postoperative Pain with a Wearable Continuously Operating Pulsed Radiofrequency Energy Device: A Preliminary Study

*Aesth Plast Surg (2012) 36:458–463*

### Method

A double blind randomized placebo controlled trial on submuscular breast augmentation surgery was conducted to assess ActiPatch on acute post-operative surgical muscular pain. The RCT assessed pain using a standard visual analogue scale (0-10) and narcotic analgesic use over the 7 days of postoperative recovery. The devices used were an active ActiPatch device (study group) or an identical placebo device (control) that does not emit an RF field.

### Results

- The study demonstrated that patients in the study group had statistically significantly less pain on six of the seven postoperative days.
- By day 7, the baseline VAS remaining in the study group was 7.9% versus 38% in the placebo group.
- Overall, 50% less pain was experienced in the study group over the 7 day postoperative period.
- The added benefit was that patients in the study group consumed significantly ( $p = 0.002$ ) less narcotic pills in the 7-day recovery period.
- There were no adverse events.

This published study can be viewed at <http://www.bielcorp.com/biel/wp-content/uploads/2013/03/BioElectronics-Postoperative-Pain.pdf>

### Commentary

In submuscular breast augmentation the implants are placed below the pectoralis major muscle. Pain is caused by the trauma of surgery to the *muscle* when creating the pocket for the implant as well as stretching of the muscle by the implant. This study demonstrates reduction of acute muscle pain by ActiPatch.

## Consumer Registry Study Data

### A UK registry study of the effectiveness of a new over-the-counter chronic pain therapy

Pain Manag. 2015 Nov;5(6):413-23

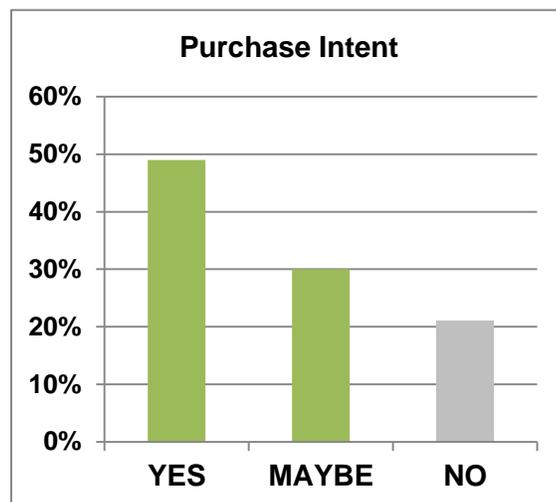
<http://www.futuremedicine.com/doi/full/10.2217/PMT.15.35>

The UK and Ireland trial program consisted of chronic pain sufferers that purchased a continuous use 7-Day Trial ActiPatch device. The commercial ActiPatch® Therapy device lasts for 30-Days with on/off functionality.

After receiving and using the 7-Day trial device, follow up assessments, via email marketing software, were sent to the consumers after 30, 90 and 360 days to evaluate their baseline pain, current use of pain modalities, and the effectiveness of ActiPatch® in reducing pain from different causes, and locations of pain. We collected data on the intent to purchase and recommendations to friends and family.

#### Summary of Surveys:

- The 7-Day single use trial device was sold for £2.95
- 8.02 was the average baseline VAS (Visual Analogue Score) score on the 0-10 scale in the survey respondents indicating severe pain
- 71% of the consumers had an average of 54% reduction in musculoskeletal, arthritic, post-surgery, fibromyalgia and neuropathy pain.
- **80%** of the consumers said they “intended” to or would “maybe” purchase an ActiPatch after using the 7-day trial device
- **80%** did purchase an ActiPatch® device
- 67% of pain medication users, including opioid users, reported a moderate to complete elimination of pain medication use.
- After one year, 86% of the 71% users continue to use ActiPatch and have purchased an average of 2.7 devices.
- 70% reported better sleep
- 74% reported they are more physically active
- 84% reported a moderate to a great deal better quality of life.
- There have been no adverse effects



The medical journal Pain Management is scheduled to publish this month, *A United Kingdom Registry Study of the Effectiveness of a New OTC Chronic Pain Therapy*, our 5,000+-consumer survey.

#### 30-Day Pain Management Assessment

Sample users reported a very high rate of benefit from many of the major causes of chronic pain such as arthritis, fibromyalgia, neuropathy and post-surgical chronic pain. The primary areas of pain reported were the back, knee, shoulder and hip. Overall 71% indicated a pain reduction with ActiPatch® Therapy and of these; the average pain reduction was 54% or a 4.44 VAS reduction. This level of pain reduction is clinically significant.

The high rate of clinical benefit shows a close relationship with the actual purchase of the ActiPatch® device.

## Chronic Pain Causes in 5,000 Registry Study

Results synopsis of the Registry Study reporting effectiveness by cause and location (2 or greater VAS reduction criteria for effective).

Indication	Effective	VAS Score/% Reduction
<b>Musculoskeletal Pain</b>		
<b>Back</b>	65%	4.30 VAS (53%)
<b>Knee</b>	69%	4.52 VAS (55%)
<b>Hip</b>	70%	4.48 VAS (55%)
<b>Shoulder</b>	68%	4.37 VAS (54%)
<b>Arthritis</b>		
<b>Osteoarthritis</b>	66%	4.67 VAS (56%)
<b>Rheumatoid arthritis</b>	71%	4.92 VAS (58%)
<b>Post-surgery pain</b>	65%	4.54 VAS (55%)
<b>Fibromyalgia</b>	68%	4.41 VAS (51%)
<b>Neuropathy</b>	59%	4.64 VAS (58%)

## 90-Day Pain Management Assessment

This survey consisted of chronic pain sufferers who used a 7-day sample device and stated in a previous assessment that they “intended to” or “maybe” would purchase the commercially available 720-hour ActiPatch® device. This follow-up assessment was sent out to 3,300 of which 954 responded, a 28% response rate, approximately 3-5 months after the initial survey to measure:

1. Actual purchases;
2. Determination of the long-term benefits by assessing:
  - Impact on their pain, quality of life, and medication use.

### Actual Purchases

The 764 individuals (80% of the 952 respondents) actual purchase of the 30-day commercial ActiPatch® device was calculated as 1409. Therefore, an average of 1.8 devices had been purchased per individual (approximately 0.60 devices per month) over a 3-month period.

### Number Devices Purchased

	% reporting	Number reporting	Total Number Devices Purchased
<b>One</b>	45%	345	345
<b>Two</b>	36%	277	554
<b>Three or four</b>	17%	133	465
<b>Five or more</b>	1%	9	45
<b>Total</b>			<b>1,409</b>

### Causes & Location of Pain

Arthritis (51%) was the major cause of pain with 35% reporting osteoarthritis and 16% reporting rheumatoid arthritis.

Consumers reported more than one cause of pain.

### Causes of Pain

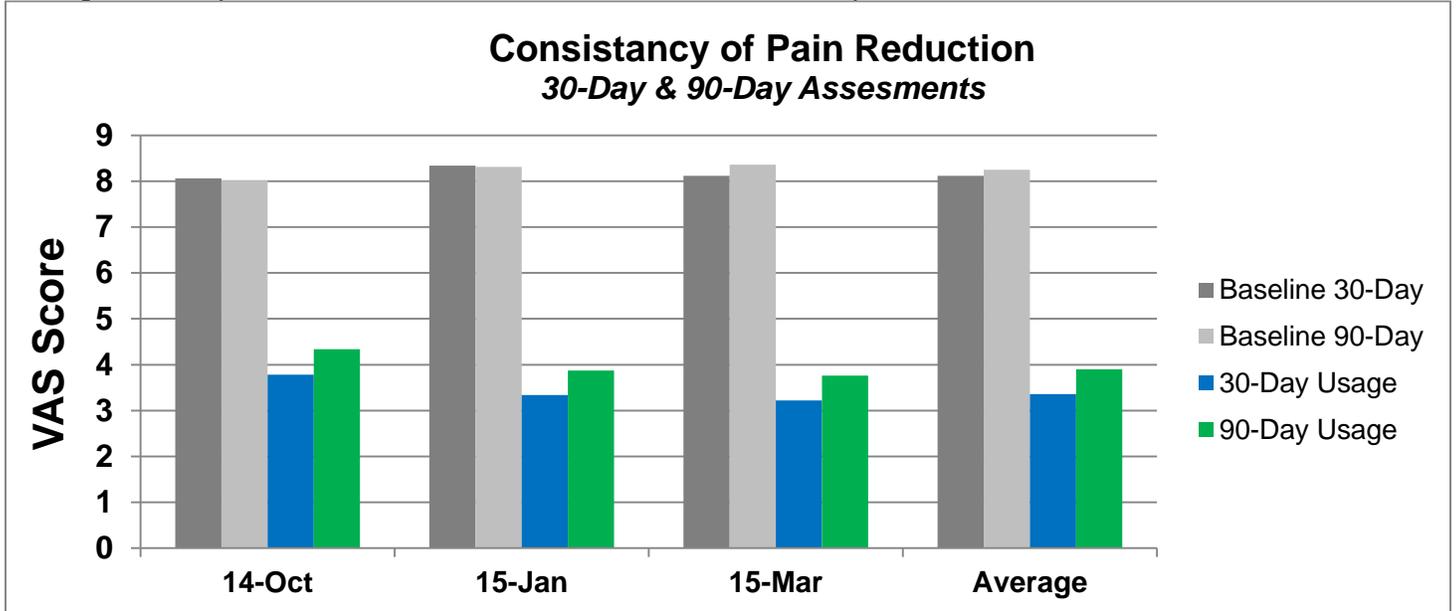
	% reporting
<b>Osteoarthritis</b>	35%
<b>Rheumatoid Arthritis</b>	16%
<b>Fibromyalgia</b>	15%
<b>Sports Injury</b>	8%
<b>Post-Surgery pain</b>	6%
<b>Tendonitis</b>	3%
<b>Neuropathy</b>	5%
<b>Other</b>	29%

### Location of Pain

	Percentage
<b>Back</b>	43%
<b>Knee</b>	24%
<b>Neck</b>	4%
<b>Shoulder</b>	11%
<b>Hip</b>	10%
<b>Other</b>	8%

## Pain Scores

The average VAS pain score during the initial 7-day trial was 8.12 and the 3-month follow up assessment was 8.25. The baseline pain scores are present with two pain therapies being taken prior to ActiPatch therapy. On this follow up survey, the pain relief experienced by ActiPatch users over three months is sustained, with an average of 53% pain reduction and a 50% decrease in the use of pain medications.



## Pain Medications

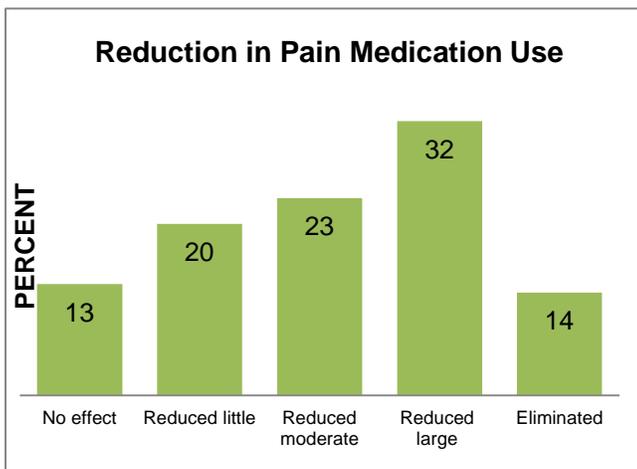
Respondents (95%) reported taking pain medications before using ActiPatch®. The medications consisted of NSAID's, paracetamol, Cox-2 inhibitors, weak opioids, strong opioids and others, with an average of 1.9 pain medications being used per individual.

## Analgesic medications used by the subjects

Analgesic	Percent Using
Paracetamol (acetaminophen)	55%
NSAID's	52%
Cox-2 inhibitors	5%
Weak Opioids	35%
Strong Opioids	32%
other	22%

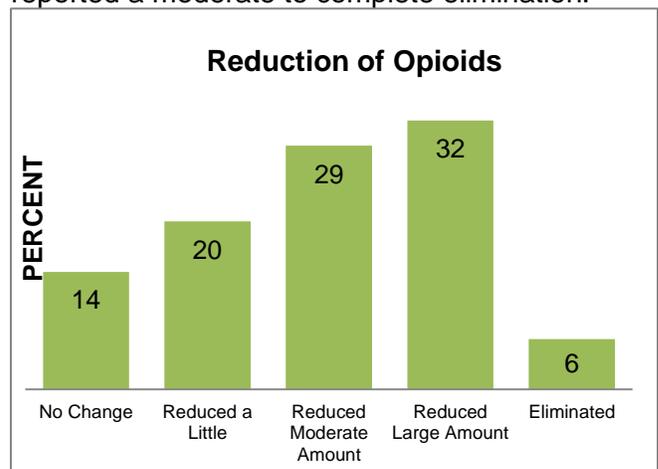
## ActiPatch's Effect on Pain Medication Use

The overall effect on pain medication use was an average of 50% decrease. 67% reported a moderate to complete elimination of pain medication use.



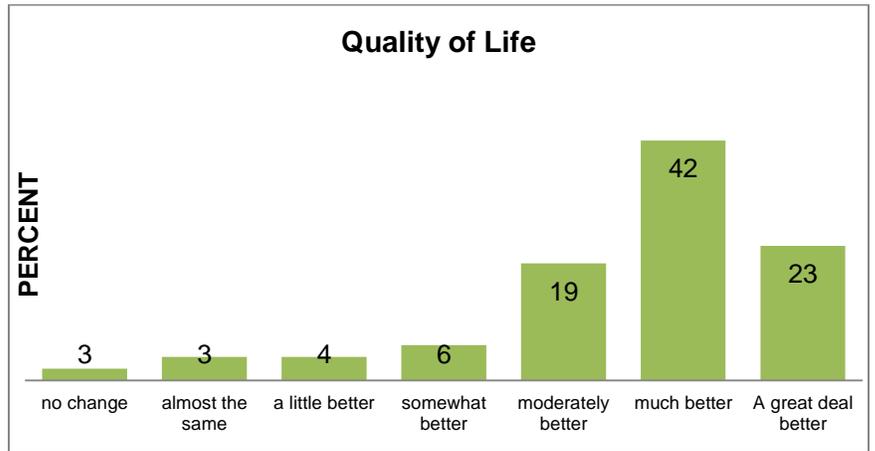
## Reduction of Opioids

Users of opioids or in combination with other analgesics were analyzed separately and 64% reported a moderate to complete elimination. Those who reported only using opioid medications, 67% reported a moderate to complete elimination.



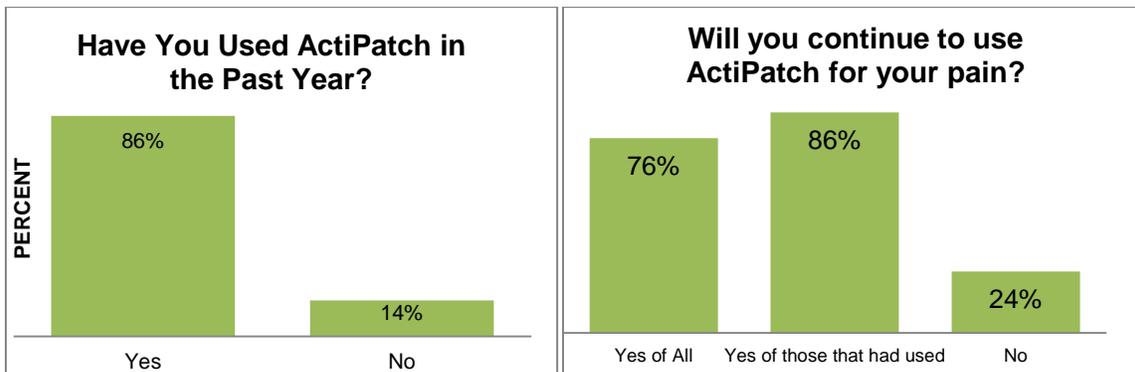
## Quality of Life (QOL)

A total of 84% of the respondents marked a moderately better to great improvement in QOL. 65% indicated that using the device made their life much better or a great deal better. This data, demonstrates that ActiPatch improves quality of life for the majority of long-term users.



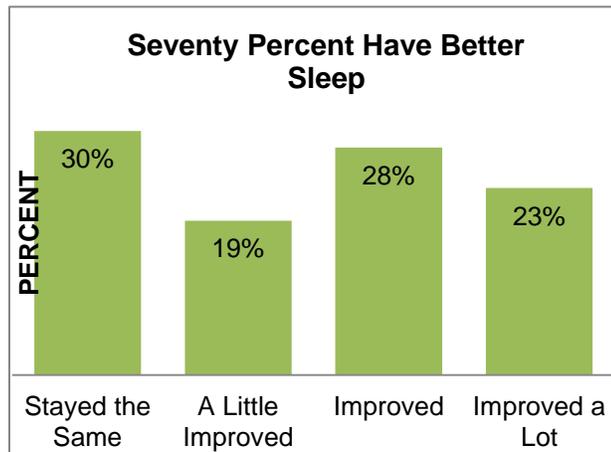
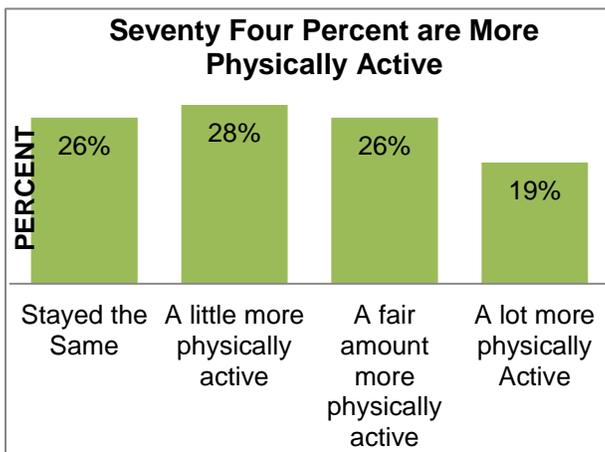
## One-Year Pain Management Assessment

The following shows exceptional pain relief and customer satisfaction.



After one-year, 73 users of the 86 respondents, eighty-five percent (85%) have reported purchasing 198 devices, or an average of 2.7 each. 85% of the 71% equates to approximately 54% (85% of the 71%, less 10% additional loss) of the 7-day trial device users becoming long-term users purchasing 2.7 devices per year.

Number	Responses	Total
1	20	20
2	19	38
3or 4	20	70
5 plus	14	70
	Total	<u>198</u>



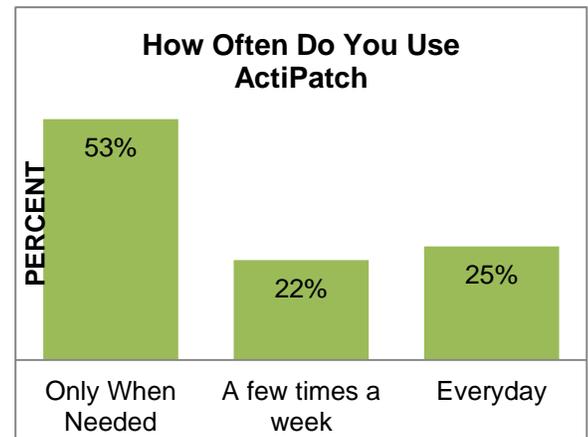
## Conclusion

These surveys show excellent *durability* of ActiPatch® Therapy without the loss of efficacy seen with NSAIDs, opioids, and other analgesic drugs. The majority of chronic pain sufferer experience:

- a clinically meaningful decrease in pain;
- a substantial improvement in the quality of life; and,
- a reduction in reliance on OTC and prescription medications, including opioids.

Taking these findings together, it can be concluded that ActiPatch® is an effective pain therapy for a variety of chronic musculoskeletal pain conditions.

The durable clinical benefit and QOL improvement translates into strong consumer acceptance and use over the long term.



## Menstrual Pain

- About half of menstruating women experience period pain (dysmenorrhoea)
- **61%** of these treat
- **12-14%** have severe menstrual pain
- **12%** incapacitated by pain for up to 3 days
- **64%** the pain is moderate to severe
- 47% school performance reduced
- 44% social performance reduced
- 37% report absenteeism
- Painful menstruation is the leading cause of lost time from school and work among women of childbearing age
- High dissatisfaction with current therapies demonstrates that current treatments are not very effective- there is a clear unmet medical need
- OTC menstrual pain market much larger than specific menstrual pain product market as many women take standard OTC analgesics

Menstrual pain market is *not* restricted to only those who are dissatisfied with current pain treatments *and* willing to try new/alternative treatments.

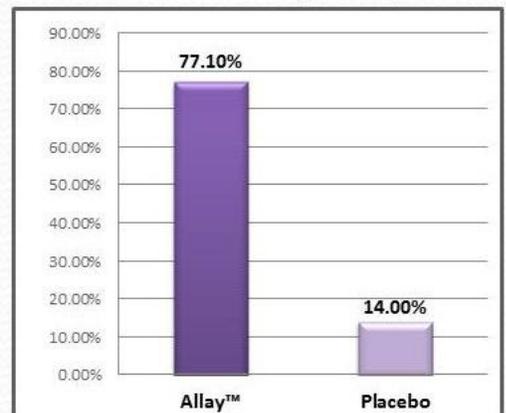
The market includes:

- Women taking drugs who are dissatisfied
- Women not willing or unable to take drugs
- Women who would, given the opportunity of a non-drug effective solution, switch from drugs and patches to Allay
- Women have to go onto the oral contraceptive pill when conventional analgesics fail, there are many women who would prefer not to be on the OCP

Additional considerations:

- Allay is low cost and cheaper than most OTC analgesics and very much cheaper than heat pads
- Allay is much easier to use than heat pads that need to be replaced every 8 hours and are uncomfortable in the summer
- Mothers do not want to medicate their daughters and Allay will be quickly recommended by word of mouth and through a schools program
- Allay will be picked up by all the major women's magazines and media sources
- Allay has an on/off switch so one device can last for 6-8 menstrual cycles
- Allay is a high-end, disruptive, innovative technology that works and should not be thought of or positioned as an *alternative* therapy

**Over 77% of women using Allay Menstrual Pain Therapy reported complete elimination or reduction in their menstrual pain symptoms (study size N=71)**



\*Multicenter, double blind, randomized and placebo controlled trial. Conducted by Dr Barry Epley and Dr Sheena Kong.

# Pulsed Radiofrequency Electromagnetic Field Therapy for Menstrual Pain, a Double Blind, Randomized and Placebo Controlled Study

Principle Investigators: Dr. Barry Eppley, Dr Sheena Kong (unpublished)

## Background

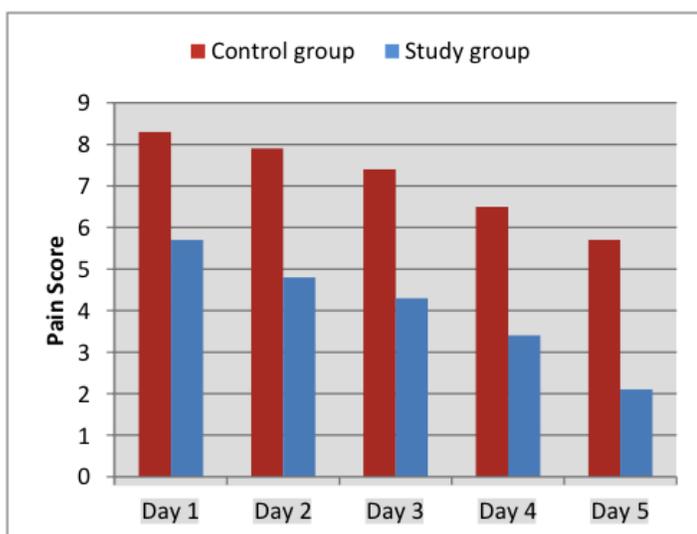
Primary Dysmenorrhoea, commonly referred to as menstrual cramping, is a medical condition characterized by pain from contractions in the lower abdomen occurring at the onset of menstruation in the absence of an identifiable pelvic disease. Sharp pains in the lower abdomen begin at the start of menstruation and may continue for up to 5 days. The pain can range from mild to severe and can interfere with many normal activities. While the majority of women who have menstrual periods experience some discomfort, an estimated 10% or more are temporarily disabled by the high level of pain they experience. A miniaturized, lightweight and battery pulsed shortwave radiofrequency electromagnetic field (PEMF) device – Allay has been developed as a wearable pain therapy. The device operates at the 27.12MHz radio frequency, 1000Hz pulse rate with a pulse width of 100µseconds. The electromagnetic field is delivered by a 12 cm loop wire antenna.

## Methods

A total of ninety-one (91) women were enrolled with moderately to severe dysmenorrhea. Subjects self-reported perceived levels of pain for each day of their menstrual cycle prior to participation in the clinical trial were collected. Subjects were then randomly assigned a number coded PEMF device, either active or placebo. The energy from the functioning device can't be felt by the recipient so subjects were unable to determine device allocation through use. The patients ranged in age from 18-34 years, with an average age of 26.2. Forty-eight (48) patients were assigned active devices while the remaining forty-three (43) received placebo devices. Subjects were asked to wear the PEMF device over the lower abdomen, from the onset of their symptoms, for 24 hrs per day for 5 days, and record their daily VAS pain scores on an 11 point scale (0 -10 scale). Subjects were not restricted in use of pain medications.

## Results

On average, pain was decreased significantly on a daily basis, with the study group reporting a 31% decrease in pain compared to the placebo group on day 1, 39% day 2, 42% day 3, 48% day 4 and 63% day 5. Average VAS scores for the 5 days of the study were, day 1 control v study group 8.3 v 5.7, day 2: 7.9 v 4.8, day 3: 7.4 v 4.3, day 4: 6.5 v 3.4 and day 5 5.7 v 2.1. The result indicate that over time 5 days the percentage of decrease in pain increases, suggesting that there is a strong correlation between duration of use of the PEMF device and amount of pain reduction. Overall 77% study group subjects reported a decrease in pain compared to 14% in the control group. No significant adverse events were reported.



**Figure 1.**

The mean pain level in the study group was significantly lower than on each day compared to the control group using the placebo device. Overall over the 5 days of the study period those in the study group experienced 43% less pain than those in the control group.

**Conclusion**

The clinical study demonstrated that the PEMF menstrual pain therapy is an effective and safe non-drug method for use in the treatment of primary dysmenorrhea. The results suggest that PEMF in this form can be used as a drug-free treatment method for women suffering from moderate dysmenorrhea. In more severe cases of dysmenorrhea, it can be a possible adjuvant treatment allowing for a reduction in the amount of oral pain medications used.

## Heel Pain

The device can be incorporated into the design of shoe insoles to treat foot pain and wounds:

- Plantar Fasciitis (product at market)
- Heel pain (product at market)
- Painful Diabetic Neuropathy (pipeline)
- Early Stage Diabetic Foot Ulcers (pipeline)
- Ulcer Prophylaxis in Diabetic Peripheral Polyneuropathy (pipeline)

Diabetic products of such global importance they could potentially receive reimbursement providing access to the healthcare market and premium pricing worldwide

- Plantar Fasciitis and Heel Pain
- **11-15%** of all foot symptoms requiring professional care
- **10%** of the general population
- Bilaterally in a third of cases
- Peak incidence occurs in women aged 40-60 years
- Affects women twice as much as men
- **7%** of population over age 65 report heel pain
- **10%** runner related injuries
- Diabetic related disease
- Diabetes prevalence: 8.5% of the population
- 20% increase in prevalence by 2030
- Peripheral neuropathy affects 10-50% of Diabetics (25%)
- 33% of patients with peripheral neuropathy get painful diabetic neuropathy
- 25% lifetime incidence foot ulcer, 2% annual incidence, chronic condition

