

Clinical evaluation of a noninvasive technology for the treatment of chronic joint symptoms

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Abstract: A device that emits thermal kinetic energy and photonic energy has been developed for the treatment of chronic knee pain. We conducted a clinical trial pilot study in which 69 patients with chronic knee pain were randomly allocated to one of four treatment groups with approximately 17 patients per group. One group was treated with the operational device; a second group was treated with the device emitting only thermal kinetic energy; a third group was treated with the device configured to emit only photonic energy; and the fourth group was treated with a complete sham device. Several parameters, eg, number of steps climbed, knee circumferences, pain rank during flexion, and flexion angle achieved prior to pain perception, were assessed immediately prior to treatment and immediately after the application of a 25-minute treatment under fully blinded conditions. Analysis of variance with the Tukey multiple comparisons procedure was used for comparing treatment results. The fully or partially activated device was superior to the sham device in patients with chronic knee pain. The results suggest that this device may have benefit for patients with chronic knee pain, and that larger, more robust studies of the device are warranted.

Keywords: joint pain, knee pain, noninvasive joint pain therapy, osteoarthritis, digital medicine therapy

Introduction

Almost one in three adult Americans suffer from joint-related problems associated with a wide array of signs and symptoms arising from injury and/or disease. These are referred to as arthritis/chronic joint symptoms.¹ Signs and symptoms of varying intensities can afflict one or several joints, and include pain, swelling, redness, restricted movement, clicking or crunching, a catching sensation, reduced capacity for repetitive or enduring action(s), limitation of activities, failure of the joint to perform, radiographic changes, magnetic resonance imaging abnormalities, and abnormal arthroscopic findings. These problems may be engendered because of work, activities of daily living, or recreational activities.

Currently, the cost of treating chronic painful conditions in the US is \$635 billion a year.² Joint pain accounts for a significant portion of the cost and 42% of the incidence.³ The knee joint is the most predominant joint affected with osteoarthritis, accounting for 25% of patients reporting a persistent disabling episode per year.^{4,5}

Current therapeutic modalities for managing joint pain include physical therapy, intra-articular injections, surgery, and medications, including over-the counter (OTC) medications, nutraceuticals, nonsteroidal anti-inflammatory drugs, prescription medications, and opioid analgesics. Although some may be inexpensive and perceived to be

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innocuous, others may be costly, partially effective, interact with other medications, elicit serious adverse effects on multiple organs,⁶⁻⁸ and responsible for a significant amount of morbidity and mortality.⁹⁻¹¹ Opioid analgesics do not promote healing and are associated with unacceptable morbidity and mortality.¹²⁻¹⁵ The Centers for Disease Control and Prevention now reports that more Americans die from painkiller overdose than from heroin and cocaine combined.¹³ Intra-articular injections and surgery are beset by problems of cost, efficacy, and safety.¹⁶⁻²⁰

In view of current joint pain therapeutic dilemmas, Physicians' Technology Inc (Monroe, MI) focused on developing technology for joint pain.²¹ An earlier third-generation device (MedLite[®]) received Food and Drug Administration clearance, and was tested in a small, complete, three-way, crossover study against placebo and OTC-strength ibuprofen. The study demonstrated statistically significant device superiority to placebo and ibuprofen for knee pain.²² More recently, a more robust fifth generation of the device was developed, which employs sensing technology and a biomedical computer that drives noninvasive neurovascular stimulation grounded in multiple dynamic energies. The fifth-generation device (the WilloMD[™]) delivers dynamic photonic energy and dynamic thermal kinetic energy, based on a proprietary algorithm, in concert with energy and sensory input data. Dynamic photonic energy comprises the transmission of particles of light (photons) in packets. These packets consist of particles in a spectrum of wavelengths ranging from the visible to the invisible spectrum. The particles are employed using a plurality of parameters, including magnitude (joules), patterns, sweeps, cascades, duty cycles, frequencies, alternations, and time. The energy transmission changes thousands of times per second. Dynamic thermal kinetic energy comprises joules of heat generated from multiple sources: resistance heat, ambient heat, and thermal mass heat. Thermal properties are manipulated through multiple cycles, deployed in changing joule packets, and delivered in concert with the photonic components.

We herein describe the design, execution, and results of a pilot clinical trial to test the effectiveness of the device in the treatment of chronic knee symptoms. The study was designed to evaluate the hypothesis that this noninvasive treatment approach for knee pain significantly reduces knee pain (standing or flexion), improves mobility (knee flexion), and enhances performance (stair climbing).

Methods

The Investigational Review Board of Mercy Health Partners (Toledo, OH) approved this study, and all participating

subjects gave informed consent. The study was conducted within the emergency department facilities of Mercy St Anne Hospital, Toledo, OH.

Patients

Sixty-nine patients were involved in the study, based on a power analysis, with a power of 0.8 and the probability of a type I error (α) set at 0.05.

Potential study candidates were evaluated by standard medical techniques and protocols, and the pool of patients was drawn from referrals made by Mercy St Anne Emergency Department physicians or recruitment from the general population.

A total of 69 (50 female and 19 male) patients completed the protocol. Inclusion and exclusion criteria are listed in Tables 1 and 2.

Patients were randomized into four groups following evaluation and standard treatment of trauma and disease of the knee as follows:

1. Group B received treatment with the experimental device that was configured to provide both forms of energy (dynamic photonic energy and dynamic thermal kinetic energy).
2. Group C received treatment with the experimental device that was configured to deliver only dynamic thermal kinetic energy.
3. Group D received treatment with the experimental device configured to deliver only dynamic photonic energy.
4. Group A received treatment with a complete sham device, delivering neither dynamic thermal kinetic nor dynamic photonic energy; however, the information liquid crystal display (LCD) screen was programmed to remain active in the same manner as the active and partially active devices.

All study group personnel and study patients were blinded regarding the active, partially active, or inactive status of each

Table 1 Patient inclusion criteria

Item	Inclusion criteria
Age	15–85 years old
Ethnicity	Any
Healthy	No serious medical condition apart from <ul style="list-style-type: none"> • Arthritis • Fractures around the knee • Gout and pseudogout of the knee • Ligament strains and muscle sprains of the knee • Osgood-Schlatter disorder • Osteoarthritis of the knee • Overweight and obesity • Patella-femoral syndrome

Table 2 Patient exclusion criteria

Item	Details
Consent	Unable to give informed consent
Age	<15 or >85 years old
Medication	<ul style="list-style-type: none"> • Use (prescription, OTC, or nutraceutical) within 24 hr prior to active study that could alter pain perception • If they had used illicit or recreational drugs within two weeks prior to study enrollment • If they had a history of chronic alcohol use (defined as greater than the equivalent of three cans of beer per day)
Knee pain was associated with	<ul style="list-style-type: none"> • Septic knee joint • Infection about the knee • Frozen knee joint
Other	Patients had any other condition or situation that investigators viewed as a confounding factor or as a risk to the subject
Pregnancy	<ul style="list-style-type: none"> • Confirmed pregnant • Lactating • Unable to exclude pregnancy

study device. The LCD screen on all devices remained illuminated after the attachment of the device to each patient's knee. However, at the initiation of treatment, the LCD screens were covered with opaque tape until the devices cycled off, to further prevent patients from drawing inferences about the activity of the device. Thereby, the LCD component of the device was effectively masked to both the study participants and the study personnel during the treatment.

The thermal energy component was active in Groups B and C. Even though the temperature display on the LCD was masked, it is possible that subjects in these groups may have detected warmth. However, because there was no cross-communication between or within the groups, nor was there any discussion by the study personnel regarding any subjective observations during the treatments, we do not feel there was significant impact on the results.

Patients in each group were maintained on their standard medical care except that they were instructed to withhold analgesics and narcotics for 24 hours prior to their use of the study device.

Devices were applied to the knee for 25 minutes. This pilot study was designed to compare only a single 25-minute treatment between the four different iterations of the device (a fully active device, a placebo device with no energies active, a device with only dynamic thermal kinetic energy active, and a device with only dynamic phonetic energy active). For convenience we elected to use the device's 25-minute treatment default setting. Observations were made prior to treatment and immediately thereafter.

Parameters assessed

Any staff member assessing a given parameter assessed that same parameter in all study patients. Parameters that were assessed are listed in Table 3.

Data were recorded from one summary sheet and 69 case report forms into Excel® (Microsoft Corporation, Redmond, WA). Variables included were demographic data, all pre- and post-treatment data, and results of an exit survey (questionnaire). Data were then transferred to Minitab® (Minitab Inc, State College, PA) and examined for consistency and errors. Corrections were made in Minitab. Variables that were constant or nearly constant were eliminated from analysis. These were: (1) crepitus (only three non-zero observations), (2) erythema (no nonzero observations), and (3) question No 4 from the exit survey (for which there were only five "yes" responses). Age was computed from birth dates and exam dates.

One outlier datum was removed for the analysis of the degree (angle of flexion) at which pain develops (Figure 3). For patient No 51 the angle was recorded as changing from 160° to 50°. Even if correct, the extreme nature of this outlier caused severe difficulties with the standard data analysis.

Demographic data were compiled. Pre-/post-data were analyzed for any differences between treatment groups. Survey data were analyzed for differences between treatment groups.

Minitab was used for all displays and analyses. Analysis of variance with the Tukey multiple comparisons procedure was used for comparing the four treatments. To determine whether there was a way to include the extreme outlier data (mentioned previously) for the parameter change in degree at which pain develops, a nonparametric Kruskal–Wallis

Table 3 Parameters assessed

Item	Detail
Number of steps climbed	
Knee circumferences	<ul style="list-style-type: none"> • Mid knee • Inferior knee • Superior knee
Erythema	
Edema	
Crepitus	
Pain while standing	
Flexion angle before pain perception	
Pain rank during flexion	
Self-assessed pain by quadrant	<ul style="list-style-type: none"> • Upper Lateral (UL) • Lower Lateral (LL) • Center • Upper Medial (UM) • Lower Medial (LM)

test was performed with the extreme outlier data included in the data set.

Results

Patients

Sixty-nine patients were observed on five dates occurring between September 10, 2010 and October 12, 2010. Of the 69 patients completing the trial, 50 patients were female. Ethnicities were as follows: Caucasian, 54; African American, seven; and Hispanic, four. Four patients did not list an ethnicity.

Sixty patients indicated that they had osteoarthritis, and for 52 patients this was listed as their only knee-related problem. Four patients indicated that they had only ligament strains (stretching or tearing of a musculo-tendinous structure) or sprains (stretching or tearing of a ligament). The remaining patients listed more than one knee-related problem. Unilateral right knee pain was reported in 36 of 69 (52%) patients, with the remainder reporting bilateral knee pain. Performance measurements were conducted in a uniform fashion in all patients. Protocols were in place that addressed symptoms laterality.

Allocations of patients into each of the four treatment groups were relatively uniform, with 17 patients receiving sham treatment (A) (only the LCD screen was operant); 19 patients each receiving full active treatment (B) or thermal kinetic energy only treatment (C); and 14 patients receiving dynamic photonic treatment (D) only.

Ages ranged from 16.4 years to 84.2 years with a mean and standard deviation of 56.8 years and 12.6 years, respectively. No age, gender, or ethnicity-related differences in responses were found.

Patient responses to an exit survey (questionnaire) revealed great satisfaction with the effectiveness of the device and its ease of use (see Table 4).

Numerical measurements

Key analysis of variance findings for the following measurements are exhibited in Figures 3–6. Although response variability for each group size of ~17 patients may have precluded establishing statistically significant differences among treatments for all parameters measured, it is clear that the fully active or partially active device yielded outcomes that consistently trended better than the sham device. Specifically, the angle of flexion at which pain occurred was least (smallest) for the sham device compared with the active or partially active devices, though this difference did not attain statistical significance ($P = 0.18$; $P = 0.13$ for inclusion of the extreme outlier using the Kruskal–Wallis test).



Figure 1 The WillomD.

The change in the number of steps that could be negotiated was statistically greater for patients treated with partially or fully activated devices versus sham devices ($P = 0.019$), with the dynamic thermal kinetic only device performing statistically better than the sham device, and the fully active device performing borderline better than the sham device.

Pain on standing was most tolerable for patients treated with the fully active and dynamic thermal kinetic only devices compared with the sham device, and these differences approached statistical significance ($P = 0.057$).

Finally, self-assessed pain on flexion was greatest for patients treated with the sham device ($P = 0.04$) compared with the fully or partially active devices.

There were no statistically different findings or obvious trends for any of the other parameters measured.



Figure 2 Illustrating application of the WillomD to the knee.

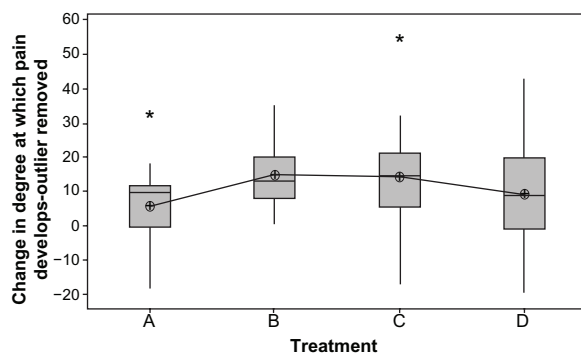


Figure 3 Box and whisker plot of the change (post treatment compared to pretreatment) in the self-assessment of pain on standing. Upper and lower limits of boxes denote first and third quartiles or 25th and 75th percentiles, respectively. Upper and lower limits of whiskers denote 1.5× the interquartile range. Horizontal lines within boxes denote median values. Plotting symbols within boxes denote mean values. Asterisks denote individual outliers. Treatments were as follows: (A) sham; (B) fully active device; (C) thermal energy (heat) only; and (D) photonic energy (light) only.

Notes: $P = 0.18$ by ANOVA with less pain on standing perceived among the patients treated with the fully active device (B) and the thermal energy (heat) only device (C) relative to the sham device (A). This outcome bordered on statistical significance. Change in degree to which pain develops (outlier removed).

Key subjective results from the exit surveys (questionnaires) are given in Table 4. A χ^2 test of homogeneity between the four treatment groups demonstrated satisfactory homogeneity regarding the questions exhibited in Table 4.

Discussion

This small Phase I trial was undertaken to evaluate the effectiveness of a device (WilloMD™) that delivers algorithmically computed dynamic photonic energy and dynamic thermal kinetic energy that is customized, via sensor-driven feedback

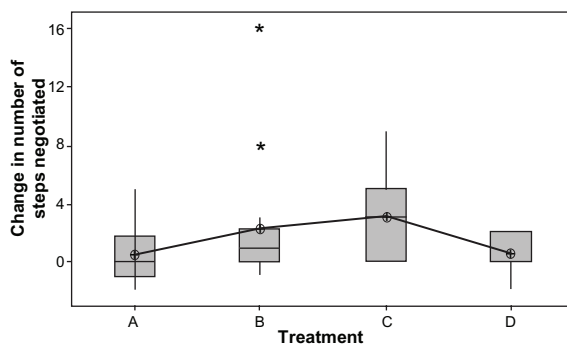


Figure 4 Box and whisker plot of the change (post treatment compared to pretreatment) in the number of steps that could be tolerated (negotiated). Upper and lower limits of boxes denote first and third quartiles or 25th and 75th percentiles, respectively. Upper and lower limits of whiskers denote 1.5× the interquartile range. Horizontal lines within boxes denote median values. Plotting symbols within boxes denote mean values. Asterisks denote individual outliers. Treatments were as follows: (A) sham; (B) fully active device; (C) thermal energy (heat) only; and (D) photonic energy (light) only.

Notes: Statistically significant differences were detected ($P = 0.019$) by ANOVA with the number of steps tolerated greater for treatment (C) than (A), and borderline greater for treatment (B) compared to treatment (A). Change in number of steps negotiated.

Table 4 Tabulation of patient exit survey (questionnaire) responses

Item	Responses			
Device effect on knee pain relative to pills	Better	Equal	Not as good	No answer
Degree of improvement in mobility	Great	Little	None	No answer
Ease of use	Easy	Somewhat difficult	Difficult	
Would use device in future	Yes	No		No answer
	61	7		1

technology, to treat pain/discomfort of knees stemming from osteoarthritis and other conditions. Chronic pain is reported by nearly one-quarter of the population, and is growing to near epidemic proportions.⁴ Moreover, over 42% of all such pain is, in fact, joint pain.⁴ The current therapeutic modalities for joint pain fundamentally invoke either physical therapy, medications, or surgery. Each modality carries its own risks and other inherent problems such as high costs and morbidity. Medications used can include anything from nutraceuticals to OTC analgesics and/or nonsteroidal anti-inflammatory drugs to opioid analgesics. It is becoming increasingly acknowledged that opioid use is now beset with the twin problems of dependence and accidental overdoses.

The device used in this trial is the fifth and most robust iteration of a noninvasive, easy to apply treatment that was developed by Physicians' Technology Inc, to help manage joint pain. An earlier version of the device (MedLite™) had been

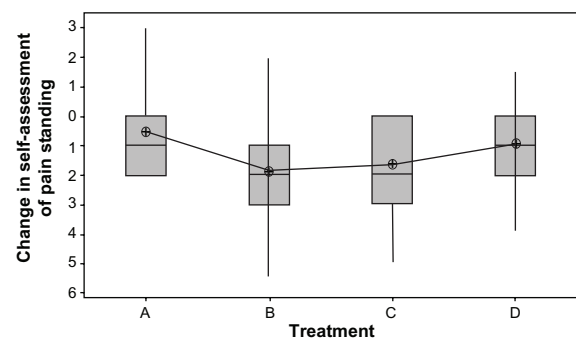


Figure 5 Box and whisker plot of the change (post treatment compared to pretreatment) in the self-assessment of pain on standing. Upper and lower limits of boxes denote first and third quartiles or 25th and 75th percentiles, respectively. Upper and lower limits of whiskers denote 1.5× the interquartile range. Horizontal lines within boxes denote median values. Plotting symbols within boxes denote mean values. Asterisks denote individual outliers. Treatments were as follows: (A) sham; (B) fully active device; (C) thermal energy (heat) only; and (D) photonic energy (light) only.

Notes: $P = 0.057$ by ANOVA with less pain on standing perceived among the patients treated with the fully active device (B) and the thermal energy (heat) only device (C) relative to the sham device (A). This outcome bordered on statistical significance. Change in self-assessment of pain standing.

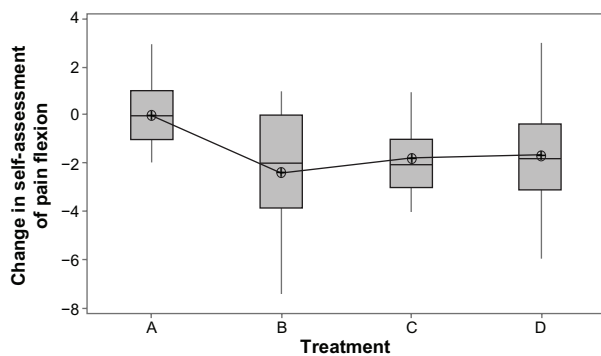


Figure 6 Box and whisker plot of the change (post treatment compared to pretreatment) pain perceived during joint flexion. Upper and lower limits of boxes denote first and third quartiles or 25th and 75th percentiles, respectively. Upper and lower limits of whiskers denote 1.5 \times the interquartile range. Horizontal lines within boxes denote median values. Plotting symbols within boxes denote mean values. Asterisks denote individual outliers. Treatments were as follows: (A) sham; (B) fully active device; (C) thermal energy (heat) only; and (D) photonic energy (light) only.

Notes: $P = 0.04$ by ANOVA with borderline less pain perceived for both treatments (B) and (C) compared to treatment (A). Change in self-assessment of pain flexion.

tested in a small number of patients with knee pain. It was found in a complete three-way crossover trial to yield significantly better results for pain and range of motion when compared with either an OTC-strength capsule of ibuprofen or a placebo of the ibuprofen capsule.²¹ The current study was initially powered to be able to distinguish significant treatment differences among each of four different groups of homogeneous but randomly allocated patients. Initial estimates of response variability (self-estimates of pain and movement) may have been too small, leaving the study, in effect, slightly underpowered. The overall ad hoc effect coefficient of variation had been estimated at 35%, whereas post hoc it was closer to 50%.

However, the median values were improved for the fully activated device relative to sham for every parameter. In addition, the medians for partially active devices were also in the direction of improvement compared with sham. Therefore, there is consistency to the direction of the changes. We feel comfortable that this indicates a trend.

Nevertheless, some significant comparative treatment effects were revealed, and in cases where statistical significance could not be demonstrated, relatively consistent treatment trends could, nevertheless, be seen. Unequivocal beneficial treatment effects were observed for the partially activated (thermal kinetic only) or fully activated device relative to the sham device regarding the number of steps tolerated ($P = 0.019$) (Figure 4). Results very closely approached statistical significance for pain on standing with both the fully active device and thermal kinetic only device performing better than the sham device ($P = 0.057$) (Figure 5).

The median values for the fully active device (treatment B) trended better than for the photonic active only (treatment D) and the thermal kinetic active only (treatment C) only devices. The inference we draw from this is that results tend to be better when both energies are used for all parameters measured except the number of steps negotiated.

Overall, the device statistically outperformed the sham form ($P = 0.04$) with regard to the degree of angle flexion tolerated before pain perception, with the fully active device and the partially active device (thermal kinetic only) borderline outperforming the sham device (Figure 6). The most consistently improved outcomes occurred with the use of the fully activated device compared with the partially activated devices, suggesting that there may be some synergistic benefit arising from the combined modalities (ie, thermal kinetic plus photonic energies).

Two Phase I trials of devices that provide noninvasive neurovascular stimulation have now both demonstrated device effectiveness for knee pain and knee mobility, even when applied for relatively short periods of time: 25 minutes in the current study.

The results of this pilot study, though positive, suggest that more robust studies to further validate the effectiveness of the technology are warranted.

In clinical use, patients have exercised the option of undergoing multiple back to back treatments and selecting their own desired treatment schedule. More robust and cumulative favorable outcomes have been clinically observed prior to and subsequent to this pilot study. We expect that the result of this pilot study would have been more robust if clinical testing had included varying treatment times of application. In view of this and the pilot study results, future Phase II and Phase III studies with larger cohorts are planned.

Clearly, a new noninvasive, nonsystemic, and affordable modality for pain management that will be unencumbered by the sometimes life-threatening risks and high costs of other modalities of pain management would be a welcome addition to the treatment armamentarium for joint pain.

Disclosure

This study was funded by Physician's Technology Inc, Dr Kenneth Chelucci was the principal investigator. Dr Kenneth Bachmann assisted with the study design. Dr Donald White assisted with study design and provided the statistical analysis. Dr Ronald Shapiro is a co-founder of Physician's Technology Inc.

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