ORIGINAL RESEARCH

DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF STATIC MAGNETS FOR THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE: RESULTS OF A PILOT STUDY

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Context • *Outpatient clinical studies of magnet therapy, a complementary therapy commonly used to treat osteoarthritis (OA), have been limited by the absence of a credible placebo control.*

Objective • *Our objective was to assess the feasibility and promise of studying static magnetic therapy for knee OA and determine the ability of a new placebo-magnet device to provide concealment of group assignment.*

Design • *Randomized, double-blind, placebo-controlled clinical trial.*

Setting • *Academic teaching hospital in Boston.*

Participants • *We enrolled 29 subjects with idiopathic or post-traumatic OA of the knee.*

Interventions • *Subjects received either high-strength magnetic (active) or placebo-magnetic (placebo) knee sleeve treatment for 4 hours in a monitored setting and self-treatment 6 hours daily for 6 weeks.*

Main Outcome Measures • *Primary outcomes were change in knee pain as measured by the WOMAC Osteoarthritis Index Pain Subscale at 6 weeks and extent of group concealment at study end.*

Results • *At 4 hours, VAS pain scores (±SE) on a 5-item scale (0-500, 500 worst) decreased 79±18 mm in the active group and 10±21 mm in the placebo group ($P<0.05$). There were no significant differences in any primary or secondary measure of efficacy between the treatment groups at 6 weeks. Despite widespread testing for magnetic properties, at study end, 69% of the active group and 77% of the placebo group ($P>0.2$) believed that they had been assigned to the active treatment group.*

Conclusion • *Despite our small sample size, magnets showed statistically significant efficacy compared to placebo after 4 hours under rigorously controlled conditions. The sustained efficacy of magnetic therapy for knee osteoarthritis could be assessed in an adequately powered trial utilizing an appropriate control such our new placebo-magnet device. (Altern Their Health Med. 2004;10(2):36-43.)*

Osteoarthritis (OA) is the most prevalent musculoskeletal disease, affecting 10% of Americans and 55% of those older than 70.[1] The morbidity and economic costs resulting from chronic pain and disability make this a major healthcare concern.[2] Use of magnetic therapy by those exploring alternative treatments for arthritis is increasingly popular. Unpublished data from a random national survey of complementary and alternative medicine use suggests that in 1997, 1.1 million Americans (0.6% of adults) had used magnetic therapy and spent an estimated 155 million dollars on supplies for this therapy in the last year, primarily for the treatment of musculoskeletal conditions.[3] Similarly, a recent survey of patients with rheumatologic conditions seen by rheumatologists reported that 29% had used magnets or copper bracelets, second only to chiropractic as the most commonly used complementary and alternative medicine (CAM) therapy in these patients.[4]

Although the surge in interest in magnetic therapy appears

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to have been fueled primarily by media attention[5-7] and mass marketing rather than by convincing data, there is scientific evidence that suggests static magnetic therapy can affect biological systems, thereby potentially affecting pain due to osteoarthritis. Our current understanding of physics and biology suggest that there are 4 *primary* mechanisms by which static magnetic fields could influence biological systems.[8,9] These primary mechanisms include; 1) altering radical dependent biochemical processes including the activity of certain enzymes through the radical pair mechanism; 2) altering the characteristics of lipid membranes; 3) exerting torque on small amounts of magnetite and iron contained in specific cells; and 4) exerting lateral force on charged particles in motion such as electrolytes in plasma. Of these, the enzyme mediated mechanism has the best experimental support at conventional magnetic fields strengths.[9-14] These primary mechanisms are theorized to influence important biologic processes in several ways. In-vitro experimental evidence suggests that static magnetic fields can do the following: decrease the firing rate of certain neurons, particularly c-type chronic pain neurons; change the rate of enzyme-mediated reactions which may play a role in inflammatory cascades and free radical generation; modulate intracellular signaling by affecting the functioning of calcium channels in cell membranes; and cause small changes in blood flow.[14-35] Further validation of these potential mechanisms of action may have relevance to therapeutics. If efficacy in osteoarthritis occurs via effect on intracellular signaling or effects on inflammatory cascades, than magnetic fields must penetrate deep into tissue spaces in order to be therapeutic. Conversely, if effects relate primarily to effects on sensory neurons, than magnetic fields may only need to need to have superficial penetration in order to have beneficial effects.

Clinical trials evaluating static magnetic therapy for OA of the knee have been limited but promising. Utilizing continuous monitoring to assure effective masking of treatment assignment, one double-blind placebo-controlled crossover trial of a static magnetic therapy lasting 24 hours evaluated 15 patients with OA of the knee. Although their overall results were not significant, their primary outcome of knee pain showed a trend toward improvement as early as one hour into treatment.[36] A more recent study enrolled 43 subjects with self-reported knee OA and randomized them to either static magnet therapy or placebo for 2 weeks of home treatment.[37] While the treatment group had statistically significant symptom decreases compared to placebo at study end, their placebo group reported only a 10-20% decrease in symptoms—a smaller decrease in pain symptoms than other placebo medical device interventions typically demonstrate.[38] The low placebo response rate, combined with the ease with which subjects could determine whether they had placebo through testing for magnetic properties at home, calls into question whether this was a placebo-controlled trial or simply a controlled trial.

Static magnetic therapy has been tested for other conditions including rheumatoid arthritis,[39] fibromyalgia,[40] low back pain,[36,41] post polio pain,[42] inflammatory knee arthritis,[43] plantar fascitis,[44] neck and shoulder pain,[45] and diabetic neuropathy[46,47] with mixed results. Overall, clinical studies of static magnetic therapy to date have been limited by the lack of a placebo treatment that can provide effective group concealment.

Electromagnetic therapy is closely related to static magnetic therapy and offers additional potential mechanisms of action for therapeutic effect, but is more expensive and significantly less available to consumers. Electromagnetic therapy for knee OA has been studied in 3 double-blind placebo controlled trials, which together evaluated 284 patients.[48-50] In these trials, which also employed short carefully monitored treatment periods to ensure effective masking, electromagnetic therapy showed statistically significant improvement compared to placebo as early as minutes after treatment with significant effects of treatment persisting for as long as one month.

Because magnets represent a popular, inexpensive, new therapy that holds promise for helping those with osteoarthritis, we studied static magnetic therapy to treat patients with OA of the knee. Our objective was to determine the feasibility and promise of studying magnetic therapy for the treatment of knee OA in a rigorously designed randomized controlled trial utilizing a newly designed placebo device.

METHODS AND MATERIALS

Participants

Twenty-nine subjects with idiopathic or post-traumatic knee osteoarthritis were recruited from the Beth Israel Deaconess Medical Center and surrounding Boston metropolitan community. The eligibility criteria for participation in the study were: 1) age 21 years or more; 2) pain in the affected knee for at least 3 months resulting in at least moderate pain (patient reported at least 3 on a scale from 0 to 10), modification of daily activities, or the need to take pain medications on at least 25 days of the month; 3) a willingness to refrain from usual analgesics for the study period; 4) American College of Rheumatology clinical criteria for idiopathic OA of the knee;[51] and 5) radiographic evidence of knee OA with minimum findings of joint space narrowing in conjunction with osteophytic lipping. All subjects received a standing anterior-posterior knee film graded by Kellegren-Lawrence criteria to allow comparisons of radiographic OA severity.[52] Exclusion criteria were, 1) history of surgery, injection, or trauma to the study knee within the last 2 months; 2) inability to perform a 50' walk test without use of an assistive device; 3) diagnosis indicating other pathology to explain knee pain such as sciatica, fibromyalgia, venous insufficiency, or an inflammatory arthropathy; 4) plan for surgeries and any other interventions for the knee within the 6 week study period; 5) pregnancy; and 6) presence of a pacemaker.

All subjects were recruited for participation via mail followed by telephone interviews. Eligible subjects were scheduled for a visit during which eligibility and interest were confirmed, consent was obtained, and the participant was fitted for a customized knee sleeve. The study procedures were approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations.

INTERVENTIONS

Two interventions were compared. Subjects in the treatment group received a high-strength magnetic knee sleeve while subjects in the placebo group received a placebo magnetic knee sleeve. Knee sleeves were made from a soft cotton/latex blend material, customized for the patient's knee size, and had either high-strength magnet or placebo-magnet inserts permanently sewn into two pockets in locations corresponding to the medial and lateral aspects of the knee. Knee sleeves and inserts were visually identical, with study investigators only able to differentiate between active and placebo via careful experimentation with metal instruments. A pictorial of the insert is shown in Figure 1, with details of construction provided in Appendix A.

DESIGNING A SUITABLE SHAM DEVICE

Our analysis of all widely available commercial products suggested that there was not currently a product on the market designed to maximize efficacy potential. Our findings on the quality of commercially available devices were generally consistent with the findings of Blechman and colleagues.[53] Moreover, no credible sham device could be identified to be used as a suitable control (placebo). Therefore, we undertook to design a magnetic treatment that would maximize any potential therapeutic benefits of magnetic treatment (maximum intensity, maximum gradient), and to design a credible sham device to mimic its appearance and qualities. The high-strength magnetic knee sleeve was designed to saturate the entire knee joint space with a magnetic field having both high intensity and high gradients, two factors most likely to be responsible for any treatment effect of static magnetic therapy. For this discussion, magnetic field intensity represents the absolute value of the magnetic field at a given point in space. Remembering that the magnetic field itself is static and by definition unchanging in nature, magnetic field gradient represents the change in measured intensity as the measurement instrument moves in space from point A to point B. The 'North' magnetic field of the high-strength magnets were chosen to face toward the knee joint to concur with common practice in the magnetic therapy community.[54] Measurement of the magnetic fields utilized in the study was conducted by JW in the Stanford University Department of Radiation Oncology using a FW-Bell Gaussmeter on two high-strength and two placebo-magnet inserts that were randomly selected. With the high-strength magnetic knee sleeve on, a large adult knee was exposed to magnetic field intensities ranging from approximately 40 to 850 Gauss (G) and magnetic gradients as high as 100G/mm. Saturation of the entire knee space with this high-intensity magnetic field represented far superior coverage compared to any commercially available product. In addition, our maximum gradients of 100 G/mm were on the order of in-vitro experimental gradients of 30 G/mm which resulted in maximum suppression of action potential firing and well above the minimum experimental gradient 'threshold' of 0.2 G/mm required to suppress action potential firing.[28] Figure 2 illustrates the magnetic field intensity on the inside of the active and placebo knee sleeves starting at the skin surface. For purposes of comparison, the earth's magnetic field ranges from 0.5-0.6 G,55 while a typical refrigerator magnet has a maximum field of 100 G.

The placebo knee sleeve was designed to provide a strong magnetic field on the surface facing away from the knee joint, thereby making it appear to offer magnetic therapy, but to impart no significant magnetic field to the knee joint. In arriving at this design, we reasoned this would increase the rigor of our concealment if subjects tried to 'investigate' on their own whether they had a real or decoy magnet. Our aim was to subject the knee of placebo subjects to magnetic field intensities no larger than earth strength of 0.5 G. This was accomplished by an innovative design utilizing a 'checkerboard' array of high-strength magnets (diagrammed in Figure 1 and described in Appendix A). With the placebo magnet knee sleeve on, the knee was exposed to a maximum magnetic field intensity of 0.65 G at the skin surface. However, knee tissue exposed to magnetic fields of this intensity were quite limited in scope: approximately 0.001% of the knee space from the surface of the skin inwards was exposed to fields greater than earth strength (0.5G) and 0.3% of the knee space was exposed to fields greater than earth strength (0.25G). Peak magnetic field gradient values were less than 0.2 G/mm.

Both the high-strength magnetic knee sleeve and the placebo magnet knee sleeve emitted comparable magnetic fields on their external surface upon testing with metal objects. For example, 1.9 pounds of force were required to detach both the high-strength magnet sleeve and the placebo magnet knee sleeve away from a vertical refrigerator surface. As such, both devices passed the test of literally 'sticking' to the refrigerator door. Importantly, the placebo knee sleeve could not be comfortably worn inside out—therefore conversion of the placebo knee to an active knee sleeve could not occur.

Subjects were asked to refrain from their usual analgesic medications during the treatment period and the 3-7 day washout period, which preceded the treatment period. As an alternative, subjects were given acetaminophen 500-1,000 mg every 6 hours as needed for breakthrough pain, except for 48 hours before each visit when they were asked to refrain from using even the acetaminophen. Although subjects were not excluded if they were unable to refrain from their usual analgesic medications, they were strongly urged to use them only when absolutely necessary and if acetaminophen failed.

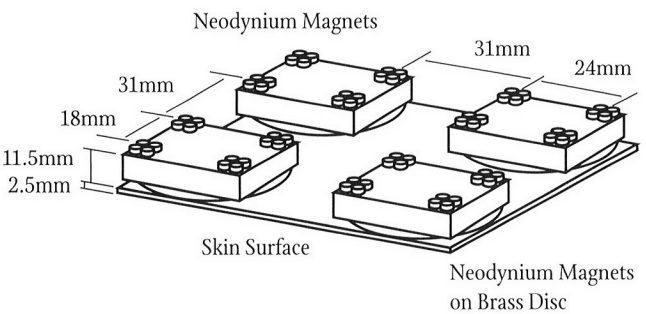


FIGURE 1 Study Insert[1]

[1]Active and placebo insert identical except for different metals as described in Appendix A.

Subjects started the treatment period during their second visit to the hospital, at which time the sleeve was slid onto the knee with the help of a research assistant, blinded to subjects random assignment. For the first 4 hours after the knee sleeve was placed around the knee, subjects were closely observed by a research assistant to assure that no patient testing of the knee sleeves occurred. This first 4 hour period was specifically designed to assure that subjects remained blind to their group assignment. Subjects requiring short breaks during the 4-hour monitoring period had their knee sleeves removed while out of the room and away from monitoring. In order to provide a spectrum of activities besides sitting and standing upon which to rate knee pain and discomfort while in the hospital, subjects walked approximately 200 feet and walked up and down one flight of stairs both before and after the 4-hour monitoring period in addition to their routine activities. Subjects wore the knee sleeves during all assessments (4-hour, 1 week, 6 weeks) and rarely took more than one 5-minute break during the 4-hour monitoring period. After the monitoring period, subjects returned home to their usual activities and were asked to wear the wrap at least 6 hours a day every day for the next 6 weeks, preferentially at times when their knee was bothering them. Subjects were asked not to seek out new therapies for pain or knee arthritis during the study period unless absolutely necessary, use the sleeve only on their designated study knee, and to refrain from 'testing' the magnetic properties of the knee sleeve. After conclusion of the study, all subjects received a knee sleeve that contained the high-strength magnetic treatment, regardless of their initial group assignment.

OBJECTIVES

Our objective was to determine the feasibility and promise of studying magnetic therapy for the treatment of knee OA in a rigorously designed randomized controlled trial. We hypothesized that magnetic therapy would show evidence of efficacy throughout the trial, with 6-week measurements showing greater effects than 4-hour measurement. However, since we planned a feasibility study, we did not expect sufficient power to show statistically significant differences between groups. A second objective was to determine whether our new placebo-magnet device would function as a credible sham in a clinical trial.

OUTCOMES

One knee was chosen for treatment in the study, with all measurements focused on that knee. Outcomes were measured at 4 hours, 1 week, and 6 weeks. The primary outcomes were change in the WOMAC Osteoarthritis Index (Version 3.1) pain subscale score at 6 weeks and change in pain measured on a visual analogue scale (VAS) at 4 hours. The WOMAC Osteoarthritis Index is a disease-specific health status measure for patients with OA of the hip or knee.[55] It contains 24 items in VAS format that probe patient-relevant symptoms in the areas of pain (5 items), stiffness (2 items), and physical function (17 items). Our 4-hour VAS pain items are identical to the Western Ontario MacMaster questionnaire (WOMAC) items except that they asked patients to reflect only on symptoms in the last 1 hour. On the WOMAC and our visual analogue scale (VAS) items, pain scores range from 0-500, stiffness scores range from 0-200, and physical function scores range from 0-1700, with higher scores representing worse symptoms.

Secondary outcome measures included physical function and stiffness subscales of the WOMAC; global assessment of change in knee OA status assessed on a 7 point scale (1 improved markedly; 7 worsened markedly); VAS assessment of the overall helpfulness of the treatment with higher scores representing greater perceived helpfulness, use of acetaminophen and other analgesics assessed by daily diaries and pill counts, 50' walk test time, presence of any adverse or unusual effects, and extent of compliance with knee wrap application over the trial period as assessed by recall questions and daily diary entries. Extent of group concealment was assessed by 2 standardized questions with high face validity and the strongest historical precedence.[57,58] Due to circadian variations in OA pain perceptions, data were collected on similar days of the week and similar times of the day to the greatest extent possible.[56]

RANDOMIZATION AND BLINDING:

The statistician generated the randomization sequence and placed the results into sequentially numbered envelopes. The randomization sequence was created using a permuted block sequence from a random number generator. A research assistant who had no other tasks or patient contact throughout the study conducted group assignment, placed the active or placebo inserts into the customized knee sleeve, and placed the device in a numbered and sealed box. Subjects were assigned to active or placebo treatment arms 4-6 days before their second visit to the hospital, when treatment was to be started. This delay was required so that the high-strength magnet or placebo-magnet inserts could be sewn permanently into the customized knee sleeve. A different research assistant blinded to overall study design assisted subjects in sliding the knee sleeve around their knee at the beginning of the treatment period. Initial placement was conducted carefully to avoid any chance of discovering true group assignment. The study coordinator conducted all other study procedures including enrollment and study visits. Procedures were designed so as to maximize blinding for all study subjects and study personnel. Actual extent of masking was assessed via questions for both subjects and study personnel probing issues related to probable group assignment.

STATISTICAL METHODS:

Continuous variables such as change scores in WOMAC subscales and ordinal variables such as global assessment of change scores were compared via a Wilcoxon rank sum test. Categorical variables were evaluated via Fisher's exact test.

RESULTS

Patients

A total of 29 subjects were enrolled between March and November 2001. Three subjects were fitted for a knee wrap and

randomized, but dropped out before the second visit when they were to begin treatment. Subjects dropping out before treatments began (2 active group, 1 placebo group) were not included in analyses. Of the 26 subjects who were randomly allocated and began treatments at the second visit, all completed the study protocol and were analyzed for the primary outcomes.

Thirteen subjects were randomized to receive high-strength active magnet (active) and 13 subjects were randomized to receive placebo magnet (placebo). As shown in Table 1, baseline characteristics in the two groups were similar with the exception of knee x-ray severity as graded by the Kellegren-Lawrence Criteria, which revealed greater severity in the active group ($P<0.05$).

TABLE 1 Baseline patient characteristics at start of treatment by group assignment

Characteristic[1]	Active Magnet (n=13)	Placebo Magnet (n=13)	*P*-value
Median age (range), y	62 (50-74)	63 (48-75)	> 0.2
Sex (% male)	31	31	> 0.2
Body mass index, median (range), kg/m^2	30.1 (25.6-41.0)	29.6 (21.1-38.7)	> 0.2
Disease duration, median (range), months	48 (12-300)	48 (6-240)	> 0.2
Pattern of knee pain symptoms (%)			> 0.2
Continuous	31	8	
Flares with symptom-free periods	31	61	
Flares with return to daily pain	38	31	
Hips or other knee affected by chronic pain (%)	69	77	> 0.2
Patient expectations (%)			
Expecting moderate improvement or better with treatment	69	46	> 0.2
Physical exam findings (%)			
Effusion	15	31	> 0.2
Tenderness	31	38	> 0.2
Warmth	-	-	
Kellegren/Lawrence xray grade (%)			0.03
I	-	23	
II	15	38	
III	77	31	
IV	8	8	

EXTENT OF GROUP CONCEALMENT:

On average, subjects wore their knee sleeves 10.5 hours/day in the active group and 7.6 hours/day in the placebo group ($P< 0.1$). At study end, 69% of the active and 77% of the placebo group guessed they 'Probably' or 'Certainly' had received the active treatment ($P> 0.2$) (Table 2). When those selecting that they had 'absolutely no idea' whether they received the active or placebo wrap in the first question were asked the second question which required forced guessing as to their treatment assignment, all in the active group (n=1) guessed they had the active wrap and all in the placebo group (n=3) guessed they all received the placebo wrap. Although subjects were specifically asked not to test their knee sleeve for magnetic properties during the trial, 69% of the active group and 46% of the placebo group admitted to purposefully or accidentally doing so during the trial. Sensing magnetic fields during testing of their wraps, subjects in both groups most often reported that the wrap had a magnetic field 'about as strong as a typical refrigerator magnet', as opposed to a minority who thought the magnetic field was either stronger or weaker than a typical refrigerator magnet. Of those in the active group who reported testing their wrap for magnetic properties, 77% guessed they had received the active wrap at study end, while in the placebo group 83% of those who tested the wrap guessed they had the active wrap at study end. When giving reasons for their guess of group assignment at study end, subjects reported that results of magnetic field testing and sense of improvement (or lack thereof) over the course of the trial both played prominent roles. At study end, the research coordinator guessed that 46% of the active group and 61% of the placebo group had been assigned to the active group, basing decisions primarily on extent of patient enthusiasm about their own clinical status.

EFFICACY

Outcomes after 4 hours of monitored treatment are shown in Table 3. Change in VAS pain on a 5-item instrument, one of our primary outcomes, as well as global assessment of change scores, overall helpfulness by VAS, and percent who would recommend to a friend were all significantly superior in the active group compared to the placebo group. Other outcomes at 4 hours demonstrated superior results in the active group, although differences were not significant.

Outcomes at 1 and 6 weeks for the WOMAC Osteoarthritis Index are shown in Table 4. No primary or secondary outcome demonstrated significant differences between the active and placebo groups at 1 or 6 weeks. Furthermore, while both active and placebo groups reported modest improvements by 6 weeks, our measures did not demonstrate any evidence of a trend toward benefit in the active group compared to the placebo group.

Adverse Effects

No subjects experienced any clinically important adverse effect as a result of participation in the trial. Three persons in the placebo group and 2 people in the active group reported mild discomfort while wearing the cotton/elastic knee sleeve. In all cases, the discomfort disappeared immediately upon removal of the knee sleeve. Two subjects (both in the placebo group) were bothered enough as to decrease their use of the wrap to an average of 3 hours/day. All other subjects in both groups were able to wear the wrap for at least 5 hours/day on average.

CONCLUSION

Our pilot double-blind, placebo-controlled study of static magnetic therapy for knee osteoarthritis demonstrated that magnetic therapy can be studied under true double blind conditions. Despite widespread testing for magnetic properties among study subjects, at study end, 69% of the active and 77% of the placebo

group guessed they 'Probably' or 'Certainly' had received the active treatment ($P > 0.2$). Our efficacy analysis demonstrated statistically significant changes in the active group compared to the placebo group at 4 hours but statistically significant benefits were not sustained in any primary or secondary measure of efficacy at 1 or 6 weeks.

Despite widespread acknowledgement of the potential for placebo effects to influence treatment outcomes, double-blind placebo-controlled trials have historically paid little attention to the ability of their 'placebo' controls to provide true group concealment. If subjects in the placebo arm of a research cohort believe they were assigned to the inactive placebo group, they may no longer be subject to placebo effects equal to the active treatment group. To the extent that this occurs preferentially to the placebo group, double-blind, placebo-controlled trials are more appropriately categorized as single-blinded, controlled trials—a much lower standard of evidence in the current scientific hierarchy. When investigators have evaluated how well their placebo controls actually concealed group assignment, they often find they utilized imperfect placebo controls. For instance, in a two-arm trial of propranolol vs. placebo for the prevention of post-myocardial infarction mortality with 3230 subjects, 64% of the active group and 41% of the placebo group guessed they had 'Probably' or 'Certainly' been prescribed propranolol.[57] Evaluation of a sham Transcutaneous Electrical Nerve Stimulation unit by an identical questioning process resulted in even larger discrepancies in extent of group concealment.[58]

A recently published meta-analysis, while shedding doubt on the magnitude of placebo effects for all conditions, reported that placebo effects are significant and strongest when pain is the outcome.[59] Furthermore, research has shown that placebo effects may be larger when the treatment involves a medical device.[38] Therefore, we felt that close attention to placebo treatment was particularly important in our clinical trial evaluating a medical device for the treatment of pain associated with arthritis.[60] Our finding that 69% of the active group and 46% of the placebo group admitted to testing their wrap for magnetic properties (despite being asked to refrain from doing so) confirmed that a believable magnetic placebo device was necessary. The success of our device in maintaining group concealment even among those testing it for magnetic properties (acknowledging the limitations related to our small sample size) suggests that it is an effective placebo and that it could be used with confidence in future placebo-controlled trials of magnetic therapy.

The efficacy results of static magnetic therapy were mixed in our pilot study. VAS pain by a 5-item instrument, one of our primary outcomes, was significantly improved in the active group compared to the placebo group after 4 hours of treatment in a closely monitored setting, despite our small sample. In addition, all other outcomes at 4 hours showed statistically significant or trends toward superior results in the active group compared to the placebo group. However, no outcome at 1 or 6 weeks showed significant differences between groups. These findings were contrary to our a-priori hypothesis that any significant benefit of magnetic therapy would increase rather than decrease over the course of the trial. One potential explanation for these findings would be if there were a 'toxic' dose of magnetic treatment above which pain and inflammation worsened. In this case, 4 hours of initial treatment might be optimal and show good results, but 15 or 20 hours a day for 6 weeks might be harmful. However, our stratified analysis suggested that the opposite was true: those reporting wearing the wrap more than the median time per day in both the active and placebo group had greater improvements in all WOMAC subscales at 6 weeks compared to those wearing less than the median time per day (results not shown). A more plausible explanation for no difference in efficacy at 6 weeks is that natural history, placebo effects, and regression to the mean over the course of the trial overwhelmed any differences between the groups in our small sample. We find the statistically significant results at 4 hours under rigorously controlled circumstances promising and believe they support further study of static magnet

TABLE 2 Perception of Treatment Group Assignment at 6 Weeks

	Actual Treatment Group Assignment	
Patient Guess (%)	**Active Magnet (n=13)**	**Placebo Magnet (n=13)**
	Guess of Group Assignment*	
Certainly Active	46 (6)	23 (3)
Probably Active	23 (3)	54 (7)
Absolutely no idea	8 (1)	23 (3)
Probably Placebo	15 (2)	-
Certainly Placebo	8 (1)	-
Total	100 (13)	100 (13)

* Text of question: "Before giving you the wrap we told you that you would be randomly assigned to receive either the 'active' treatment wrap or an inactive 'placebo' wrap. What treatment do you think you were given for this study?"

TABLE 3 Outcomes at 4 Hours

Outcome	Active Magnet (n=13)	Placebo Magnet (n=13)	*P*-value
Pain			
Baseline pain by 5-item VAS (mean ±SE), mm	223 ±31	217 ±43	
Change in pain	-79 ±18	-10 ±21	0.03
Physical Function			
Baseline physical function by 5-item VAS (mean ±SE), mm	209 ±31	211 ±40	
Change in physical function	-58 ±21	-8 ±20	0.16
Change in walk time (mean ±SE), sec	-0.6 ±0.4	0.6 ±0.6	> 0.2
Global assessment of change %, (n)			0.002
Improved markedly	8 (1)	-	
Improved moderately	23 (3)	-	
Improved slightly	62 (8)	33 (4)	
No change	8 (1)	59 (7)	
Worsened	-	8 (1)	
Overall helpfulness (mean ±SE), mm	51 ±7	25 ±6	0.03
Would recommend to friend (% yes)	54	-	0.005

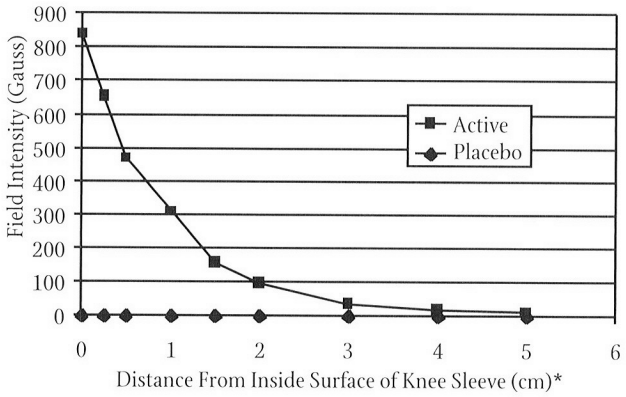
therapy. Future studies could confirm our short-term findings and be powered to more definitively test for sustained effects.

Our clinical trial has several weaknesses. First, this was a pilot trial that had low statistical power to determine efficacy of magnetic therapy. Similarly, promising results regarding the ability of our placebo device to provide group concealment were limited by a small sample size. Second, analysis of treatment group differences revealed that the active group had statistically more severe knee radiographic findings at baseline compared to the placebo group. However, others have found that radiographic severity has only a weak correlation with degree of symptomatology among those with OA.[59] In support of this, our treatment groups had similar baseline scores on WOMAC pain, stiffness, and physical function subscales. Therefore, while group differences in radiographic severity had the potential to bias efficacy results, we feel they were unlikely to have had a marked effect. Third, our placebo magnet was designed to test a specific theory of magnetic field effects. Although subjects in the placebo group experienced no significant magnetic field within the knee joint, they did encounter a strong magnetic field approximately 1 cm outside the knee joint. Therefore, our placebo was specifically designed to investigate whether magnetic fields that penetrate the body are able to influence the symptoms of OA. This design was supported by previously discussed mechanisms whereby magnetic fields penetrating cells could influence biological processes and a lack of plausible mechanisms supporting the notion that magnetic fields not penetrating the body can influence biological processes. However, some traditions of energy healing are intended to affect energy fields that are purported to surround and penetrate the human body.[62] Addressing concerns of those who believe in the existence of energy fields is difficult because of the heterogeneity of beliefs within the field and because despite many claims, any credible evidence for the existence of such fields continues to be lacking. Nonetheless, we believe that most proponents of energy healing will generally accept our methodology because, unlike oscillating magnetic fields, static magnetic fields do not have the ability to transfer energy through resonance mechanisms.[8]

TABLE 4 Outcomes at 1 and 6 Weeks

Outcome	Active Magnet (n=13)	Placebo Magnet (n=13)	*P*-value
WOMAC Scores			
Pain			
Baseline (mean ±SE), mm	251 ±28	252 ±36	
Change at 1 week*	-95 ±32	-68 ±24	> 0.2
Change at 6 weeks*	-133 ±32	-125 ±28	> 0.2
Stiffness			
Baseline (mean ±SE), mm	96 ±11	112 ±17	
Change at 1 week *	-43 ±10	-20 ±14	0.14
Change at 6 weeks *	-47 ±9	-35 ±13	> 0.2
Physical Function			
Baseline (mean ±SE), mm	820 ±117	896	
Change at 1 week *	-288 ±88	-220 ±78	> 0.2
Change at 6 weeks*	-359 ±99	-353 ±80	> 0.2
Other Outcomes a 6 weeks			
Global assessment of change %, (n)			> 0.2
Improved markedly	31 (4)	23 (3)	
Improved moderately	15 (2)	31 (4)	
Improved slightly	15 (2)	15 (2)	
No change	8 (1)	31 (4)	
Worsened	31 (4)	-	
Change in 50' walk time (sec)	-2.3 ±0.7	-0.9 ±0.6	0.18
Overall helpfulness (mm)	57 ±9	58 ±9	> 0.2
Would recommend to friend (% yes)	53	46	> 0.2
Acetaminophen 500mg tablets used (tablets/day)	1.1 ±0.4	1.0 ±0.3	> 0.2
Analgesics besides acetaminophen required (% using during 6-week treatment period)	46	15	0.2

* Change from baseline score



*0.0 cm corresponds to skin surface

FIGURE 2 Knee Sleeve Peak Magnetic Field

In summary, our pilot study demonstrated that a randomized, double-blind, placebo-controlled trial of static magnetic therapy can be conducted but requires special considerations such as the use of a carefully designed placebo device. Our efficacy analysis demonstrated small but statistically significant effects that were not sustained at 1 or 6 weeks. Future trials with adequate statistical power could determine whether there are small to moderate sized effects of this commonly used complementary medicine treatment.

Acknowledgments

Dr Wolsko was supported by an Institutional National Research Service Award for Training in Alternative Medicine Research (T32 AT00051), National Institutes of Health, Bethesda, MD. Dr Phillips is supported by a Mid-Career Investigator Award (K24 AT00589) from the National Center for Complementary and Alternative Medicine, National Institutes of Health, Bethesda, MD; and unrestricted educational grants from the John E. Fetzer Institute and American Specialty Health Plans.

APPENDIX A:

The customized knee sleeves were made from a commercially available light-weight cotton/latex blend knee sleeve as the starting material. Each knee sleeve received two identical inserts. Each high-strength magnet insert incorporated four 1"x 0.1"

nickel-plated Neodynium disc magnets and 64 partially demagnetized 0.12"x 0.06" nickel-plated Neodynium disc magnets. Each placebo magnet insert incorporated four 1"x 0.1" brass discs and sixty four 0.12"x 0.06" nickel-plated Neodynium disc magnets. All active and placebo inserts were constructed at our center in a standardized fashion using the appropriate metals, light-weight wood, cheesecloth, superglue, and a latex encasement. An independent professional seamstress performed permanent placement of the inserts into stretch lycra pockets located on the medial and lateral aspects of the knee sleeves.

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