

Static Magnetic Fields for the Treatment of Pain

Michael McLean, M.D., Ph.D.,¹ Stefan Engström, Ph.D.,
and Robert Holcomb, M.D., Ph.D.

*Department of Neurology, Vanderbilt University Medical Center,
Nashville, Tennessee 37212*

Received May 11, 2001; accepted with publication May 14, 2001

Unlabeled/investigational or unapproved use of products will be presented in this article.

Therapeutic magnets constructed with permanent magnets that generate static magnetic fields have gained popularity in recent years. Federal authorities in the United States do not currently regulate sales. The marketed devices are not FDA approved. Nonetheless, there is a body of published data that supports potential therapeutic utility of static magnetic field-generating devices. This body of knowledge is critically reviewed here. Characterization of effective field metrics and mechanisms of interaction with biological substrates are incomplete. The design of magnetic placebos for masking in long-duration studies is essential. Current evidence suggests that there is merit in continuing to develop and test therapeutic magnetic devices. © 2001 Academic Press

Key Words: therapeutic magnets; magnetotherapy; pain management; Magna Bloc; Nikken; Bioflex; low back pain; magnetic placebos; medication-resistant neuropathic pain.

Application of static magnetic field-generating devices to the skin over painful areas of the body with tape or elastic wraps has become a popular method for the treatment of day-to-day pains. Many types of magnetic devices are available on the shelves of pharmacies, groceries, and department stores. Worldwide sales have been reported to exceed \$5 billion (1). Nonetheless, the fundamental basis for therapeutic use of magnetic fields has not been established to the extent necessary for acceptance by the conventional medical community. Also, though such devices appear to have no significant risk and their sale is not regulated at the present time, no static magnetic field-generating device has been approved by the FDA for marketing to treat a specific medical condition.

A number of criteria, including the following, must be met to achieve acceptability among medical prac-

tioners and regulatory agencies: (a) The magnetic field produced by each device must be characterized and its depth of penetration into tissue determined. (b) Biological effects of magnetic fields to be used in clinical trials must be demonstrated in relevant animal and cell models. (c) Effects of specific magnetic field-generating devices must be demonstrated in human subjects in pilot studies so that larger controlled studies can be designed to test positive findings. This same principle drives development of pharmaceuticals. For example, an antiepileptic drug is shown to have efficacy in animal models and in limited phase II testing (equivalent to pilot studies, including dose-ranging) before pivotal placebo-controlled trials are undertaken in phase III. (d) Large controlled studies must demonstrate superiority to placebos and, preferably, also other magnetic devices. To examine the current status of magnetotherapy for pain, we summarize our own efforts that have used these criteria and review recently published results of controlled trials. All of the devices described here are commercially available, and the research reviewed here was supported by private funds.

We have examined effects of a static magnetic field with marked spatial variation produced by a square array of four cylindrical permanent magnets (NdFeB) of alternating polarity (Magna Bloc; Figs. 1A, 1B).

Robert R. Holcomb is the inventor of the Magna Bloc. He is a major shareholder, and Michael J. McLean is a minor shareholder, in companies involved in commercialization of the device. This participation could result in monetary gain for them personally.

¹To whom correspondence should be addressed at Department of Neurology, Vanderbilt University Medical Center, 2100 Pierce Avenue, 351 MCS, Nashville, TN 37212. Fax: (615) 936-0223. E-mail: michael.mclean@mcm.vanderbilt.com.



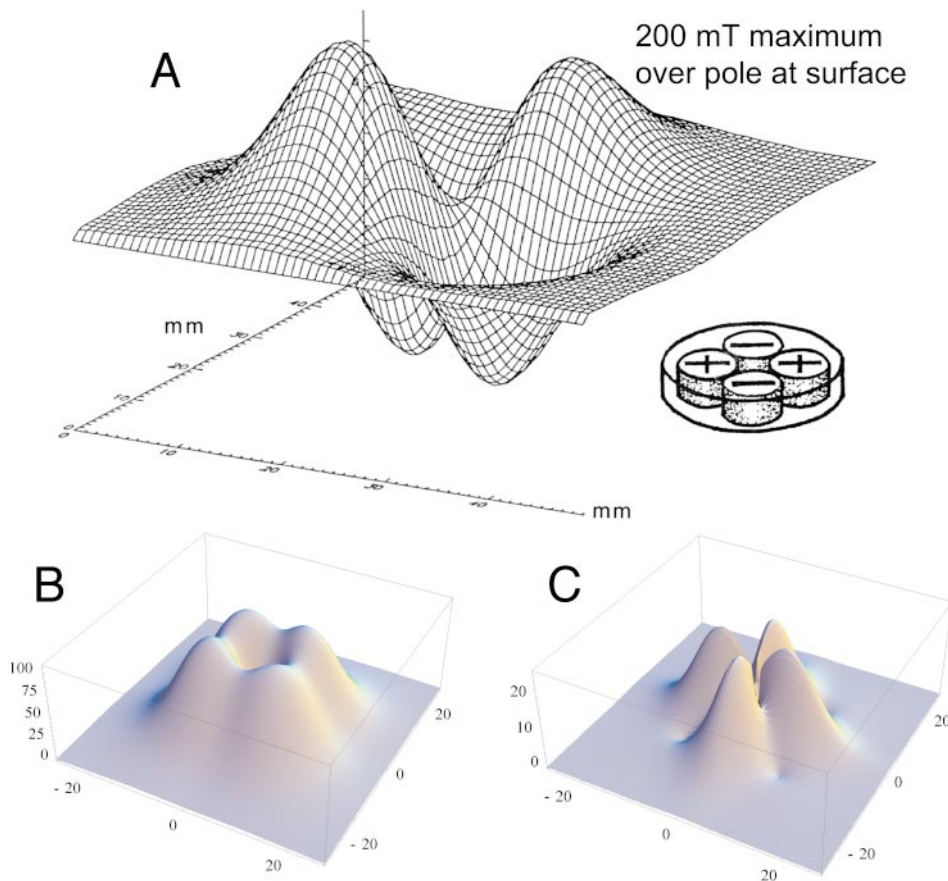


FIG. 1. (A) Field map produced by canning with a gaussmeter oriented in z plane shows the contour of the field measured 3 mm above the surface of the alternating quadrupolar array depicted in the cartoon. Scan courtesy of Dr. John Wikswo. (B) Calculated total fields showing field magnitude. This three-dimensional plot is important in showing the strong field between the poles (note slight decline in the saddle between two poles) and the steep decline of the field strength from the pole to the center. (C) Calculated regions in which gradient components of the field (dB/dx) are perpendicular to the field strength (B). Abscissa units: mm throughout; ordinate units: mT in (A) and (B), T/m in (C).

Positioning cultured neurons above the device along a perpendicular line drawn from the middle of the interpole line to the center (maximally effective region, MER) resulted in significant effects on the neurons. Lesser effects have been obtained by positioning the cells near the center or over the poles. Gradients (dB/dx , change of field strength with distance) in the magnetic field are important in determining biological efficacy (2). Modeling has shown that the MER coincided with regions in which the gradient (dB/dx) is predominantly perpendicular to the local field vector (Fig. 1C).

Placing cultured neurons at effective distances over the MER resulted in reversible, time-dependent blockade of electrically stimulated action potentials of cultured mouse dorsal root ganglion cells without altering resting membrane potential (3, 4) (Fig. 2A). Re-

sponses of neurons to the pain-producing substance capsaicin also were blocked reversibly over the MER (5) (Fig. 2B). Calcium-calmodulin-mediated myosin phosphorylation is enhanced by placing the reaction chamber over the MER (Engström *et al.*, submitted). Positioning of cultured neurons over the MER also protected against kainate-induced swelling and cell death (6). This neuroprotective effect may result from interaction of the magnetic field with multiple steps in a pathway leading to generation of inositol triphosphate and the release of intracellular calcium (6). These different lines of evidence suggest that the MER has unique properties that enhance or diminish biological activities. Other regions of the field had less or no effect on these different preparations (Fig. 2).

The mechanism(s) of interaction of the field with cell components is not known. Time dependence sug-

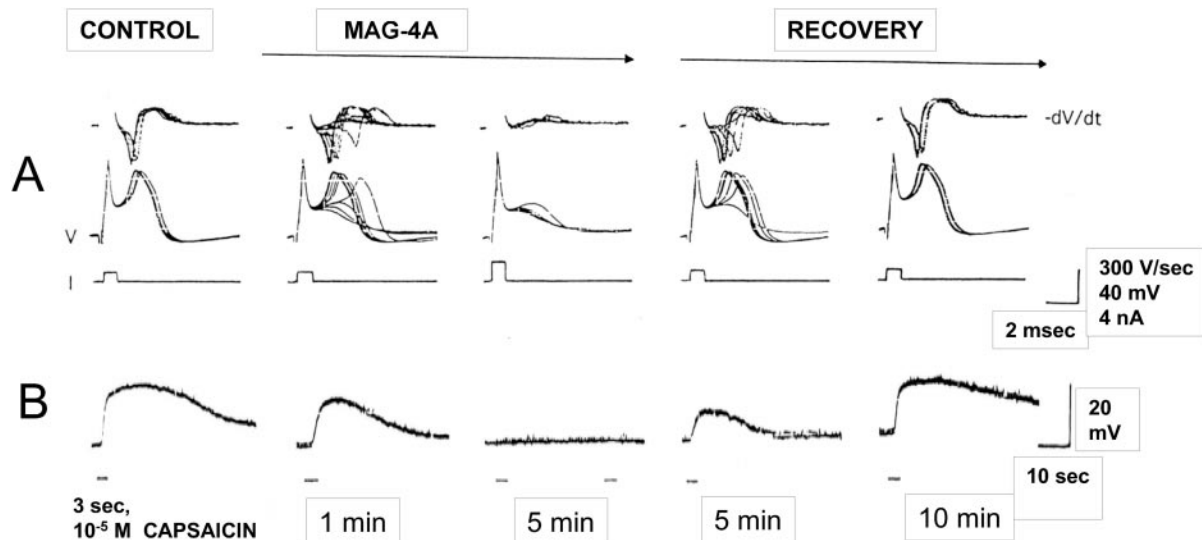


FIG. 2. Effects of exposure to the MER of field produced by the alternating quadrupolar array with the neuron 5 mm above the surface of the array. (A) Reversible blockade of electrically stimulated action potential (AP) firing by adult mouse dorsal root ganglion neurons in monolayer dissociated cell culture. Each panel shows multiple superimposed traces to assess fluctuations in latency. After control recordings (leftmost panel), the array was positioned beneath the neuron under study (Magnet Array, center panels). After 1 minute of exposure to the magnetic field, AP latency fluctuated and maximal rate of rise declined; some stimuli failed to elicit AP. After 5 minutes, 10 consecutive stimuli failed to elicit AP, despite doubling of stimulus intensity that was otherwise constant throughout. Recovery of AP occurred with abbreviation of latency and increasing rate of rise by 5 minutes and recovery to control status by 10 minutes. Top: dV/dt , maximal downward deflection = maximal rate of rise (indirect measure of inward sodium current generating AP upstroke). Middle: intracellularly recorded transmembrane voltage. Bottom: intracellularly applied depolarizing current pulses. Calibrations to right. (B) Responses of another neuron to 10^{-5} M capsaicin (calcium-dependent) applied intermittently by pressure ejection for 3 seconds (bars beneath traces). After control responses were obtained (leftmost panel), magnetic field exposure over the MER resulted in time-dependent reduction (second panel) and block (third panel). Partial recovery occurred 5 minutes (fourth panel) after and full recovery by 10 minutes after removal of the magnetic array. Calibrations shown at right. Times at bottom apply to respective columns of panels in rows (A) and (B).

gests slow changes in conformation of ion channels or enzymes, e.g., resulting in phosphorylation/dephosphorylation of sodium channels. A different static magnetic field (123 mT), with no detectable gradient, decreased activation of calcium channels of cloned pituitary cells (7) and reduced acetylcholine release at a neuromuscular junction in a calcium-dependent manner (8). In summary, these findings suggest a plausible mechanism or mechanisms by which magnetic fields change conformation of transmembrane and soluble proteins to produce significant biological effects. Also, modeling and multifactorial analysis of the field produced by the alternating quadrupolar array also suggest a possible metric by which the interaction with biological substrates occurs.

In a double-blind, placebo-controlled, randomized crossover pilot study of 54 patients with mechanical low back and knee pain, reduction of pain during treatment with devices consisting of the alternating quadrupolar array (referring to the poles facing the skin; Magna Bloc) was superior to that during treat-

ment with nonmagnetic placebos ($P < 0.03$) (9). A thick foam pad covered the devices to maintain masking. The study entailed two 24-hour periods of observation, 1 week apart. The order of treatments was randomized. Knee pain responded better than back pain. No significant adverse events occurred.

A larger study involved patients with mechanical low back pain only (10). The study design was similar to the pilot study. In the per protocol analysis, treatment with the Magna Bloc devices produced significantly greater pain relief than placebo by three instruments of measure: (a) at 3 hours by the visual analog scale (11, 12); (b) at 3 and 24 hours by the verbal response scale ($P = 0.02$ for both times) (13); and (c) by reduction of average pain over 24 hours based on self-reported patient diaries ($P < 0.01$). The internal consistency of the findings suggests that extended wearing of devices incorporating the alternating quadrupolar array may reduce chronic mechanical low back pain of moderate intensity. Characteristics of these two studies are listed in Table 1. Larger patient

TABLE 1
Controlled Studies of Efficacy of Static Magnetic Field-Producing Devices in the Treatment of Diverse Pains

	Type of pain	Study design	Number of subjects	Magnetic device ^a	Placebo device	Duration of masked period	Security of masking	Instrument(s) of measure	Outcome	Adverse events
Holcomb et al., 1991 (9)	Mechanical low back and knee PILOT STUDY	R, DM, PBO, XO	54 (41, low back; 13 with OA of the knee)	Magna Bloc, 7 devices over low back, 4 over knee	Nonmagnetic devices	Two 24-h periods, 1 week apart, continuous wearing	Intact per physician and patient "Intactness of Blind" forms	VAS (10-cm line)	Magnetic devices superior to PBO (P < 0.03)	Discomfort due to pad designed to protect blind
Valbona et al., 1997 (16)	Trigger point pain, postpolio syndrome PILOT STUDY	R, M, PBO, PG	50	Bioflex, discs and pads of 2 different strengths = 4 devices	Nonmagnetic discs and pads	45 min, continuous wearing	Assumed to be intact, patients under observation in waiting room	McGill Pain Questionnaire	Magnetic devices superior to PBO (P < 0.0001)	Not reported
Borsa and Liggett, 1998 (15)	Exercise-induced biceps pain and microinjury	R, SB, PBO, PG	45	Nikken, 5 cm × 8 cm × 3 mm pad	Nonmagnetic pads	72 h postexercise, continuous wearing	Not reported	VAS (10-cm line), range of motion, arm girth, force production	No significant differences reported	Not reported
Weintraub, 1999 (1)	Painful diabetic and nondiabetic neuropathy, burning and numbness/tingling assessed, both feet treated	R, XO with PBO (1 month on each foot), then 2 months with 2 active devices	10 diabetics, 9 other	Nikken Magstep insoles	Nonmagnetic insole	Masking and patient instructions not reported; 4-month study period, continuous wearing	Dubious with nonmagnetic PBO	Nonvalidated 5-point pain intensity scale (0 = none, 4 = worst)	No change during PBO treatments; significance reported vs nondiabetics (P < 0.02)	Devices intolerable due to pain (N = 2); withdrawals due to surgery for persistent infection (N = 2)
Collacott et al., 2000 (14)	Chronic low back, multiple pathologies PILOT STUDY	R, DM, PBO, XO	20	Nikken back pad (trapezoid, 19 × 11.5 × 14 cm, 2 mm thick)	Nonmagnetic pads	Two 1-week periods, 1 week apart; devices on 6 h/day 3 days/week	Not reported; dubious with nonmagnetic PBO	VAS, McGill Pain Questionnaire, range of motion testing	No significant differences reported	None
Holcomb et al., 2001 (9)	Mechanical low back pain	R, DM, PBO, XO	77 per protocol	Magna Bloc, 7 devices over low back in standard pattern	Nonmagnetic devices	Two 24-h periods, one week apart, continuous wearing	Intact per physician and patient "Intactness of Blind" forms	VAS (10-cm line); Verbal Response Scale, patient diaries (self-reported)	Magnetic devices superior to PBO at 3 h by VAS (P < 0.05), at 3 and 24 h by VRS (P < 0.02), P = 0.01 by diary	Discomfort due to pad designed to protect blind (N = 4)

^a R = randomized; DM = double-masked; SM = single-masked; PBO = placebo or placebo-controlled; XO = crossover; PG = parallel group.

populations are needed to minimize the impact of variability of pain, and longer studies are needed to assess duration of pain relief.

We contrast these findings with results of a pilot study of a different magnetic device (Nikken) for the treatment of chronic low back pain (14) (see Table 1). This study involved 20 individuals with low back pain associated with a variety of pathologies. Field strength was roughly 30 mT at the device surface, but there was no further characterization of the field or its depth of penetration and no reference to basic studies. Demagnetized devices served as placebos. This was a double-blind, placebo-controlled, crossover study in which subjects wore one device 6 hours per day on Monday, Wednesday, and Friday of one week and then the other device in similar fashion, with a 1-week washout period between the two treatments. There was no statistical difference between pain intensities reported by the visual analog scale during the two treatments. The rationale for treatment with the devices every other day is not clear, and this is the only study reviewed here in which wearing of the magnetic device was intermittent. The authors state that one possible reason for failure to see a difference in the treatments might be the limited penetrability of the magnetic field. If the field did not envelop the pain-generating structures, this pilot study would not constitute a test of efficacy of the magnetic field. Without characterization of the field produced by these devices, and given the heterogenous study population, the chance of a significant outcome from this study design was no better than chance.

Magnetic insoles (Nikken Magsteps) were employed to test efficacy against medication-resistant neuropathic pain in 10 patients with diabetes and 9 patients with other neuropathic disorders (1) (Table 1). In the first month, patients were randomized to treatment of one foot with a magnetic insole and the other with a nonmagnetic placebo insole. In the second month, the treatment devices were switched. In the final 2 months, both feet were treated with magnetic insoles. Patients were instructed to rate their pain twice daily using a 5-point scale. Pre- and posttreatment composite scores (30-day mean pain scores) were compared. Burning was assessed separately from numbness and tingling. Four individuals in the diabetic cohort withdrew: two because of surgery for residual foot infections, one because of inability to tolerate the insoles on painful feet, and one because of administrative issues. During the first 2 treatment months in which one foot or the other was treated with a placebo, there was no significant reduction of

the mean composite pain scores. Between the second and third months, pain scores of the diabetic group declined about 80%. Numbness and tingling also declined between months 2 and 3 in the diabetic group but not in the nondiabetic group. Nine of ten diabetics were said to have benefited (not defined) compared with three of nine among the nondiabetic neuropathic group. Pain returned after removal of the devices. Carryover effects could not be eliminated because there was no washout period between treatments. Use of placebos in only the first half of the study makes the analysis questionable. The fields and biological effectiveness of the active devices were not characterized in any detail. Pain intensities were mild (<1 on a scale of 0 to 5) and improvement could be difficult to discriminate in this range. In a long study such as this, it is doubtful that masking could be protected for 4 months with nonmagnetic placebos. The study was designed to evaluate the placebo, but patients could not distinguish between placebo and active treatment during the first 2 months. For these reasons, the report of a positive outcome is difficult to interpret. A larger study is in progress.

Magnetic devices of a different size (5×8 -cm Nikken pads), but presumably the same magnetic field characteristics as the two devices described above, were also used to determine effectiveness in decreasing postexercise pain (15). A single-blind placebo-controlled design was used. A protocol of concentric-eccentric exercise of the biceps brachiae was used to induce muscle soreness and microinjury. After completion of the exercise, patients were treated with either placebo or active magnetic device for 72 hours with assessments of pain, upper arm girth, range of motion, and static force production at 24-hour intervals. The 5×8 -cm device covered only the midbody of the biceps. No rationale is given for this procedure, and there is no indication that pilot studies involving different arrangements or the use of multiple magnetic pads were tried. The visual analog scale was used to assess pain. There was no statistically significant difference between treatments for any of the parameters measured. Without characterization of the magnetic field produced by the device, the depth of penetration could not be assessed. In the absence of laboratory studies, there are no parameters for thresholds of field strength or field gradient that could be anticipated to bring about a therapeutically beneficial result. No mention was made about intactness of the masking. Partial coverage of the biceps by the magnetic device could be insufficient to produce detectable therapeutic benefit. Under the conditions of the

experiment, no significant benefit was achieved. This does not prove that magnetic fields of similar or different design are without potential for treating musculoskeletal injuries and pain under optimal study conditions.

Lastly, magnets of a different design (Bioflex 30 or 50 mT at the surface of the devices) were tested for efficacy against trigger point pain in 55 patients with postpolio syndrome (16). The study was double-blind, randomized, placebo-controlled, and involved parallel groups. The primary instrument of measure was the McGill pain questionnaire. After baseline measures, patients were randomized to treatment with either active or nonmagnetic placebo devices. The devices were placed over trigger points. After 45 minutes of treatment, the devices were removed, and trigger points were again palpated to assess pain. Pain improved in 22 of 29 subjects treated with active devices and in 4 of 21 treated with the nonmagnetic placebos. Reduction of mean pain intensity during treatment with the active magnetic devices was statistically greater than that during treatment with the nonmagnetic placebos ($P < 0.0001$). The duration of pain relief after treatment of the active devices was not assessed. The authors concluded that magnetic fields of 30 to 50 mT applied over painful trigger points resulted in significant and prompt relief of pain in patients with postpolio syndrome. This study uses standardized assessment tools in a well-controlled environment in which masking appears to have been protected. The pressure applied to trigger points to elicit pain was not quantified or controlled, although investigators tried to be consistent. The brief period of treatment limits conclusions to the rate of onset of benefit and is not sufficient to guarantee protracted benefit. No adverse events were encountered. This statistically significant result in a pilot study encourages further investigation with skin-applied static magnetic field-generating devices.

CONCLUSIONS

Despite problems of study design that limit interpretability of the studies described above, this critique suggests that there is a growing body of data from the laboratory and from controlled trials that, even if rudimentary, justifies further research with therapeutic static magnetic field-generating devices. As indicated above, both efficacy and inefficacy of poorly characterized devices are uninformative. Better characterization of devices and the development of appropriate

magnetic placebos are required for future studies. Some studies lack the precedent of reducing pain in pilot studies. This means, in effect, that the investigators cannot know whether they are testing a demonstrable effect. We suggest that the plan of investigation outlined at the beginning of this discussion be followed in an effort to adduce compelling mechanistic and clinical trial data. This is necessary to compete for public/federal funding and to achieve federal regulatory approval.

At the heart of understanding apparent discrepancies lies the problem of learning how to study these devices. Therapeutic magnets are applied locally. They have the advantage of being free of adverse effects of systemically administered analgesic medications, such as gastritis. But the devices must be positioned critically to have any chance of providing benefit. As a result of distribution throughout the body, pharmaceuticals may affect more than one target along the pain-processing pathway. To do so with magnetic devices requires positioning multiple devices over different points along the processing pathway. The magnetic fields may only be effective in the limited tissue volumes they envelop, a feature that should minimize adverse events. Every aspect of study design must be optimized for the specific device being tested. Finding appropriate conditions to test specific fields is the first step toward the design of informative studies.

REFERENCES

1. Weintraub M. Magnetic biostimulation in painful diabetic peripheral neuropathy: a novel intervention—a randomized, double-placebo crossover study. *Am J Pain Manage* 1999;9:8–17.
2. Cavopol AV, Wamil AW, Holcomb RR, McLean MJ. Measurement and analysis of static magnetic fields that block action potentials in cultured neurons. *Bioelectromagnetics* 1995;16:197–206.
3. McLean MJ, Holcomb RR, Wamil AW, Pickett JD. Effects of steady magnetic fields on action potentials of sensory neurons in vitro. *Environ Med* 1991;8:36–44.
4. McLean MJ, Holcomb RR, Wamil AW, Pickett JD, Cavopol AV. Blockade of sensory neuron action potentials by a static magnetic field in the 10 mT range. *Bioelectromagnetics* 1995;16:20–32.
5. Wamil A, McLean M, Holcomb R. Blockade of capsaicin responses of cultured sensory neurons by a static magnetic field. Submitted for publication.
6. McLean MJ, Holcomb RR, Engström S, Sanderson L, McDonald PW, Thomas RM. A static magnetic field reduces neuronal swelling and death produced by kainic acid. Paper presented at the Proceedings of the Millennium International Workshop on Biological Effects of Electromagnetic Fields; 2000 Oct 17–20, Heraklion, Crete, Greece, pp 502–8.

7. Rosen AD. Inhibition of calcium channel activation in GH3 cells by static magnetic fields. *Biochim Biophys Acta* 1996;1282:149–55.
8. Rosen AD. A proposed mechanism for the action of strong static magnetic fields on biomembranes. *Int J Neurosci* 1993;73:115–19.
9. Holcomb RR, Parker RA, Harrison MS. Biomagnetics in the treatment of human pain—past, present, future. *Environ Med* 1991;8:24–30.
10. Holcomb RR, McLean MJ, Engström S, Morey J, Williams D, McCullough B. Treatment of mechanical low back pain with a static magnetic field. *Arch Phys Med Rehab* 2001.
11. Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. *Pain* 1983;16:87–101.
12. Chapman CR, Casey KL, Dubner R, Foley KM, Gracely RH, Reading AE. Pain measurement: an overview. *Pain* 1985;22:1–31.
13. Ohnhaus EE, Adler R. Methodological problems in the measurement of pain: a comparison between the verbal rating scale and the visual analogue scale. *Pain* 1975;1:379–84.
14. Collacott EA, Zimmerman JT, White DW, Rindone JP. Bipolar permanent magnets for the treatment of chronic low back pain: a pilot study. *JAMA* 2000;283:1322–5.
15. Borsa PA, Liggett CL. Flexible magnets are not effective in decreasing pain perception and recovery time after muscle microinjury. *J Athletic Training* 1998;33:150–5.
16. Vallbona C, Hazlewood CF, Jurida G. Response of pain to static magnetic fields in postpolio patients: a double-blind pilot study. *Arch Phys Med Rehabil* 1997;78:1200–3.



For more information visit
www.neuromagnetics.com