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MAGNETIC THERAPY FOR EDEMA IN INFLAMMATION:
A PHYSIOLOGICAL ASSESSMENT

Rolando E. Rumbaut^{1,2} and Dragan Mirkovic³

¹Medical Care Line, Michael E. DeBakey VA Medical Center, Houston, TX 77030;

²Departments of Medicine and Pediatrics, Baylor College of Medicine, Houston, TX 77030;

³Department of Radiation Physics, The University of Texas M.D. Anderson Cancer Center,
Houston, TX 77030.

Corresponding author:

Rolando E. Rumbaut, M.D., Ph.D.

Baylor College of Medicine

Children's Nutrition Research Center

1100 Bates Ave., Room 6014

Houston, TX 77030

Phone: (713) 798-0316

Fax: (713) 798-0337

email: rrumbaut@bcm.tmc.edu

Edema (tumor) is one of the four cardinal components of inflammation described by Celsus (~25 BC-50 AD) (4). Conventional management of edema in inflammation usually includes treating the underlying condition and use of anti-inflammatory agents. In addition, many patients use complementary and alternative medicine approaches, including magnetic therapy, for inflammatory disorders (12, 17). Magnetic healing appears to date to ancient Greece (12), and a mechanistic effect on resolution of edema in inflammation was described by William Gilbert in 1600, who proposed that the loadstone (magnetite, a naturally occurring magnetic mineral) served to “heal the ruptured tissues by exsiccation, so causing the wound to close and dry up” (6). Presently, magnetic therapy is a popular healing technique, estimated to result in \$300 million in annual sales in the United States, and \$5 billion worldwide (1, 19).

In general, magnets can be divided into electromagnets, permanent, and temporary magnets; in each case the magnetic field is a consequence of moving electric charges (3). In electromagnets, the magnetic field is produced by an electric current moving through a wire and in permanent and temporary magnets it is generated by a subatomic, quantum mechanical motion of electrons. The magnetic field created by an electromagnet can be manipulated by changing the electric current. Most applications in science and engineering use this kind of magnet; the time-varying electromagnetic fields can be pulsed, gradient, alternating, and rotating. Published clinical data support the use of pulsed electromagnetic field therapy for selected patients with certain orthopedic conditions (8, 10). In contrast, the most common type of magnetic therapy used for healing involves permanent magnets generating static magnetic fields (SMF), in which magnetic fields do not vary with time. A broad variety of devices for SMF therapy are available, including bracelets, straps (wrist, knee, elbow, back, etc.), insoles, pillows and mattresses. Use of this therapy is prevalent; one study reported that 18% of outpatients in rheumatology clinics

used magnets or copper bracelets (17), and another found that 30% of patients with peripheral neuropathy used magnet therapy (2). The popularity of SMF therapy is appreciated by searching the Internet with the terms “magnetic therapy inflammation”, which yields a plethora of dramatic claims and testimonials of their efficacy (5). However, these claims are not supported firmly by clinical research; conflicting results are illustrated by a recent systematic review of randomized controlled trials, which failed to demonstrate efficacy of SMF over control groups (16). Limitations of many clinical studies include subjective end-points, subject awareness of the “blinded” treatment group (e.g., sham magnets do not attract keys or paper clips), low patient numbers, and inconsistent characterization of magnetic field strength (5, 7).

Static magnetic fields may interact with a variety of potential targets in living tissues (18), and may induce physiological effects on many biological systems, including the microcirculation (13). As in the clinical trials, the magnetic field strength used in these reports varies widely. Magnetic field strength, or magnetic flux density, can be conceptualized as the number of magnetic lines of force per unit area. The SI unit, tesla (T), predominates in science and engineering, though the gauss (G) still appears frequently in the literature, in particular when describing weak magnetic fields ($1\text{T} = 10,000\text{ G}$). The strength of magnetic fields in nature varies over many orders of magnitude. The strength of the earth’s magnetic field is $\sim 50\ \mu\text{T}$; ferrite or ceramic magnets typically exhibit field strengths of 50 to 100 mT, and permanent magnets made from alloys of rare earth elements can range from 0.2 to 1.2 T. Electromagnets used in magnetic resonance imaging (MRI) usually range between 0.5 and 2 T (3); current guidelines from the U.S. Food and Drug Administration consider MRI device operation below 8T as non-significant risk (20). It is worth noting that magnetic field strength decreases significantly at a distance to the magnet; field strength is proportional to the inverse square or

third power of the distance, dependent on the proximity of the magnet, its orientation and geometry. Hence, the strength of the magnetic field applied to tissues of interest may vary considerably with the geometry of the experimental setup, and be markedly less than the reported field strength of the magnet. The magnetic field strength reported in most clinical and experimental studies of SMF range from 1 to 400 mT (13, 16). Several reports describe effects of SMF on vascular tone, though both vasodilatation and vasoconstriction have been reported (13). This apparent discrepancy may be explained by data reported by several groups (reviewed in (13)) that SMF had a biphasic effect on vascular tone as a function of resting tone. In an earlier study, Morris and Skalak (14) showed that SMF increased tone in vessels that were initially vasodilated, and thus suggested a potential effect in resolution of inflammatory edema.

In the current issue of *The American Journal of Physiology: Heart and Circulatory Physiology* (15), Morris and Skalak expand greatly their prior observations. They provide an elegant, carefully controlled evaluation of the physiologic effects of well-defined static magnetic fields (see Figure 1) on inflammatory agonist-induced edema in a rat hindpaw model. SMF therapy (10-70 mT) reduced histamine-induced edema by 20-50%, and carrageenan-induced edema by 33-37%. The duration of field therapy required for maximal attenuation of edema corresponded to 50% of the time to peak edema: 15 minutes was most effective for histamine (which induced peak edema at 30 minutes), while 2 hours were required for carrageenan (peak edema at 4 hours). Further, effective reduction of edema required SMF application immediately following induction of inflammation; SMF applied prior to injection or at the time of maximal edema had no effect on the responses. If the temporal profile of efficacy is confirmed in other models, this may limit the applicability of SMF therapy for inflammatory edema to conditions in which treatment may be administered immediately following the onset of inflammation. Of

interest, one small clinical trial with positive outcome had such a design; SMF therapy (15-40 mT) or sham magnets were initiated in the immediate postoperative period in patients undergoing suction lipectomy (11); significant improvement in edema was noted in patients randomized to SMF. These interesting findings remain to be substantiated. In addition to the temporal efficacy profiles, Morris and Skalak evaluated dose-dependent effects of SMF on edema. A magnetic field strength of 70 mT attenuated edema to a greater degree than 10 mT, but the highest magnetic field strength (400mT) failed to have an effect. Further, data from their pharmacological experiments (Figure 5) suggest a role for L-type calcium channels, though not nitric oxide, as mediators of the effects of SMF on edema. These initial mechanistic studies may provide the basis for subsequent experiments aimed at defining additional cellular mechanisms (and the cell types involved) in the physiological effects of SMF on the microcirculation. Based on their prior study and those by others, the authors emphasized changes in vascular tone as a potential explanation for the physiological effects of magnets on edema. However, as acknowledged in the manuscript, it remains to be determined whether SMF therapy influences microvascular permeability, which is enhanced typically by inflammatory agonists such as those used in the present study (9). Attenuation of hyperpermeability is a plausible alternative explanation for the physiologic effects of SMF therapy on edema reported in this study.

In summary, the manuscript by Morris and Skalak (15) provides a rigorous scientific evaluation of the physiologic effects of SMF therapy on edema in inflammation, with novel observations of temporal and dose-dependent efficacy profiles as well as insight into potential mechanisms involved. Their work may provide the basis for future experimental and clinical investigations of static magnetic field therapy, a complementary and alternative medicine approach of great popularity despite current lack of firm clinical data to support its efficacy.

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