

**Preliminary Results for the Reduction of Phantom Limb Pain  
by Electromagnetic-Own-Signal-Treatment Under Clinical  
Circumstances**

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7 **Preliminary Results for the Reduction of Phantom Limb Pain by**  
8 **Electromagnetic-Own-Signal-Treatment Under Clinical Circumstances**  
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## Abstract

When amputees sense an intense pain in their missing body part, this phenomenon is called phantom pain. Despite the numerous treatments for the reduction or elimination of phantom pain, there is little clinical proof supporting the effectiveness of these treatments. Based on our years of experience testing a technique called Electromagnetic-Own-Signal-Treatment (EMOST), our preliminary results showed a reduction in phantom pain using the EMOST method under clinical circumstances. The EMOST method is based on the collection of non-linear, electromagnetic cellular signals from the patients, which are then processed by device and returned to patients without any substantial changes. These collected, processed and returned non-linear electromagnetic signals might be more effective in potential therapeutic applications than in diverse, artificial low-frequency and low-intensity electromagnetic fields.

**Keywords** Phantom pain, Electromagnetic-Own-Signal-Treatment (EMOST), low-frequency and low-intensity electromagnetic fields (LFI-EMFs), redox-related neural plasticity

## Introduction

The amputation of a limb is generally followed by a sensation that the deafferented body part is still present. Phantom limbs are perceived by up to 98% of amputees following amputation (Ramachandran and Hirstein, 1998). However, phantom limb sensations can also occur following spinal cord injury, nerve avulsion and in children with congenital limb aplasia (Moore et al., 2000; Melzack, 1992; Melzack et al., 1997). The phantom sensations usually resolve without treatment, except in cases in which phantom pain develops.

When amputees sense an intense pain in their missing body part, the phenomenon is known as phantom pain. Phantom pain is more frequent in patients with preamputation pain and is less likely in cases in which the amputation was performed when the patient was very young. While phantom pain is most common after the amputation of a leg or an arm, it can also occur after the surgical removal of a breast, rectum, testicle, penis, or eye, among others (Edward, 1997). The phantom pain aftereffect occurs in 50-80% of the patients who have undergone this type of surgery, and the most frequently reported types of pain include burning, tingling, and cramping (Sherman, 1994). Various other pains and types of sensation such as shocking, itching, shooting, squeezing, and throbbing, among others, can also occur. Although a high percentage of amputees experience phantom pain, every patient has a unique description concerning his/her particular sensations and the pain experienced, as well as the intensity and frequency of the sensations. Phantom pain generally resolves without treatment, except in cases in which chronic phantom pain develops.

There is increasing evidence that both peripheral and central neural mechanisms are involved in phantom pain, but the pathophysiological mechanisms of phantom pain remain unknown (Devor and Seltzer, 1999; Dhillon et al. 2005; Davis et al., 1991; Mackert et al.,

2003; Mercier et al., 2006; Karl et al., 2001). One possible peripheral mechanism is that neuromas (*a growth of the nerve tissue*) form from injured nerve endings at the stump site after the amputation of a limb and fire abnormal action potentials. In addition to peripheral processes, spinal mechanisms have also been considered to influence phantom pain (Bittar et al., 2005). Phantom limb pain is also strongly correlated with changes in the representational plasticity (*cortical reorganization*) in the somatosensory and motor cortices (Karl et al., 2001). According to the neuromatrix theory, there is an extensive, genetically predetermined, network that interconnects the thalamus-cortex-limbic system, and phantom pain could arise from an atypical reorganization of this neuromatrix (Melzack, 1992; Bittar et al., 2005). Psychological factors have also been investigated. Whereas psychological factors do not appear to cause the phantom pain, these factors might affect the severity and the progression of the pain (Sherman et al., 1987).

Although diverse treatments have been presented, there is little clinical proof supporting the benefits of pharmacological treatments, surgery or interventional techniques, electroconvulsive therapy, electrical nerve stimulation, far infrared ray therapy, pulsed radiofrequency ablation, or psychological therapies (*for instance, mirror box therapy*), among other treatments (Gnezdilov et al., 1995; Rasmussen and Rumman, 2000; Wiech et al., 2004; Irlbacher et al., 2006; Wilkes et al., 2008; Huang et al., 2009; Seidel et al., 2009; de Roos et al., 2010).

However, there is currently a gap between practice and research in the area of phantom limb pain. Here, we report the preliminary results for phantom pain reduction by Electromagnetic-Own-Signal-Treatment (EMOST) under clinical circumstances.

## Materials and Methods

### *Patients*

Limb amputees (with vascular and arterial disease, diabetes and accidents) were recruited at the National Institute for Medical Rehabilitation in Budapest, Hungary. The limb amputees (experimental amputees (n=10) and control amputees (n=3)) were randomized to receive either an active EMOST treatment or a sham treatment. The experimental amputee group included 10 out-patients, 5 males and 5 females, with an age range from 47 to 69 years (mean  $\pm$  SD:  $58.4 \pm 6.91$  years). The control amputee group included 3 out-patients, 2 males and 1 female, with an age range from 47 to 73 years (mean  $\pm$  SD:  $63.3 \pm 1.22$  years).

### ***Apparatus***

The EMOST device (BioLabor-MCC HI 2.5.2) was used in the experiments. It contains three basic elements: (1) an input electrode, (2) signal-processing circuits and (3) an output electrode. The input signals (*described as endogenous*) are thought to originate from patients who are placed in direct contact with the specially designed flat electrodes. The EMOST device (*which is controlled by a personal computer*) operates with the non-linear, electromagnetic signals of the patient within a defined frequency range, i.e., from 1 Hz to 1 MHz. The parameters and exposure times can be pre-programmed. The collected input signals of patients, can be filtered using pre-programmed, low-frequency ranges by device circuits. Output signals are emitted by an identical flat electrode. The electromagnetic intensity range of the device is 0.1-10 microteslas. A photograph of the EMOST apparatus is shown Figure 1.

### ***Treatments***

The present research conformed to the Helsinki Declaration outlining the principles for medical research involving human subjects. All of the subjects completed an informed consent form prior to participation in the study. The patients were treated using a pre-programmed, noninvasive EMOST method (Fig. 2) for six sessions. Each session was approximately 45 min, between all treatments with a one-day pause. Pain intensity was quantified upon admission using a 0-10 verbal numerical rating scale (Fig. 3). The patients were asked to rate their pain on the verbal NRS prior to the therapy and after they had completed the six treatments. During and after the patients had completed the six treatments, they did not receive any additional treatments related to the reduction or elimination of phantom limb pain.

### **Results**

The Student's t-test (Microsoft Excel) was used to analyze the data. The reduction of phantom limb pain by EMOST was statistically significant (\* $P < 0.05$ ) as compared to the controls. The frequency of phantom limb pain was reduced in three patients after treatment with EMOST. Although our primary goal was to reduce phantom limb pain via EMOST treatments, most of the patients also reported a marked improvement in their sleep and mood quality, or a reduction in the frequency of phantom pain (PP↓) after the treatments. No significant improvements in the reduction of phantom limb pain or sleep and mood improvement were reported in the control group. The results obtained after six EMOST treatments are summarized in Table 1.

## Discussion

### *Extremely low-frequency electromagnetic fields*

Electromagnetic fields can be generated by various mechanisms in living cells. According to the laws of physics, when charged particles (*ions, dipole or multipole molecules*) move at a nonlinear speed, they generate electromagnetic fields. However, most biomolecules are charged, or have dipoles or multipoles, and they move and vibrate in nonlinear manners. However, nonlinear nanomechanical motions and vibrations of electrically polar or charged cellular structures (*for instance, cell membrane vibrations*) and oscillating biochemical reactions and excited molecules are very important sources for a wide range of electromagnetic frequencies, from Hz to THz, in cells (Fraser and Frey, 1968; Levin and Korenstein, 1991; Albrecht-Buehler, 1992; Isojima et al., 1995; Cohen and Popp, 1997; Kobayashi et al., 1999; Belousov et al., 2000; Pokorný et al., 2001; Lipkova and Cechak, 2005; Pelling et al., 2005). Thus, living cells display a particularly weak non-linear electromagnetic activity in a wide spectrum of frequencies that can be generated by diverse cellular mechanisms that are associated with biochemical processes.

Although the health effects of low-frequency and intensity electromagnetic fields (LFI-EMFs) are controversial, increasing evidence suggests that non-ionizing LFI-EMFs can influence numerous cell functions and are capable of initiating various healing processes, such as the delay of fractures, induction of analgesia, acceleration of wound re-epithelialization, inhibition of inflammatory processes, reduction of fatigue, improvement of multiple sclerosis and chronic pulmonary disease, among others (1984; Selvam et al., Reiter, 1993; Satter Syed et al., 1999; Lappin et al., 2003; Kumar et al., 2005; Alfieri et al., 2006; Zhang et al., 2007; Markov, 2007a; Orgel et al., 2007; Tsang et al., 2009; Huo et al., 2009; Sutbeyaz et al., 2009; Jing et al., Mach and Persinger, 2009; Mancuso et al., 2009; 2010; Patruno et al., 2010).

Many potential causes have been suggested to explain the influence of LFI-EMFs in living systems, for example, Eddy electric currents, classical and quantum oscillator models, by the help of biomagnetites, cyclotron resonance, the interference of quantum states of bound ions and electrons, coherent quantum excitations, stochastic resonance, parametric resonance, bifurcation, and magnetosensitive free-radical and redox processes, among others (Binhi, 1999; Bókkon and Salari, 2010). Despite these explanations, the primary effect of LFI-EMFs on cell functions remains unclear. However, several effects of extremely low-frequency electromagnetic therapies may be explained (*or connected*) by redox regulation and

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2  
3 membrane processes (2006; Patruno et al., 2009; De Nicola et al., 2010; Di Loreto et al.,  
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5 Morabito et al., 2010).

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7 Numerous experiments have provided evidence that reactive oxygen species (ROS)  
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9 and reactive nitrogen species (RNS) and their derivatives act as fundamental signals  
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11 (*secondary messengers*) during physiological (*and pathophysiological*) processes in  
12  
13 intracellular signaling and intercellular communication processes (Hidalgo et al., 2000;  
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15 Hancock et al., 2001; Dröge, 2002; Kamsler and Segal, 2007; Valko et al., 2007; Kishida and  
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17 Klann, 2007; Forman et al., 2008; Bókkon and Antal, 2010). Because the primary effect of  
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19 LFI-EMFs can be explained by redox regulation and membrane processes, LFI-EMFs may  
20  
21 have an important effect on redox mechanisms.

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23 A growing body of evidence indicates that cell membranes play a key role in the  
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25 transduction and amplification of LFI-EMF field signals (Bauréus Koch et al., 2003; Foster,  
26  
27 2003; Mathie et al., 2003). Specifically, LFI-EMFs can affect the length of cell membranes  
28  
29 and the number and variety of membrane-bound receptors. However, the activation of many  
30  
31 cell surface receptors (for *instance, G protein-coupled receptors and receptor tyrosine*  
32  
33 *kinases, among others*) induces an influx of  $\text{Ca}^{2+}$  into the cells and the release of  $\text{Ca}^{2+}$  from  
34  
35 the endoplasmic reticulum. Because ROS and calcium signals are intimately interconnected  
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37 and calcium and ROS constitute the most significant intracellular signaling molecules in the  
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39 regulation of various cellular functions (Gordeeva et al., 2003; Michael et al., 2003; Yan et  
40  
41 al., 2006; Feissner et al., 2009), the effect of LFI-EMFs on cell membranes and membrane-  
42  
43 bound receptors may cause these radiations to stimulate  $\text{Ca}^{2+}$ -related pathways and free  
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45 radical and redox-regulated processes. Several cell surface receptors are regulated by redox  
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47 processes (Choi and Lipton, 2000; Dröge, 2002; Nakashima et al., 2002; Kishida et al., 2005;  
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49 Yang, et al., 2006; Cecilia et al., 2008; Monteiro et al., 2008; Bókkon and Antal, 2010; Shi et  
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51 al., 2010).

52  
53 In addition, ELFI-EMF can have effects on the molecular transition states and can  
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55 affect the kinetic processes of enzymes without thermodynamic kT energy. Importantly,  
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57 magnetic fields are more effective when the tissue is out of equilibrium (Markov, 2007b).  
58  
59 Consequently, LFI-EMFs experiments in healthy individuals do not reflect the potential  
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response of patients who have endured an injury or disease. Because the cell type-specific  
redox status is responsible for the effects of diverse electromagnetic expositions (Simkó,  
2007), it is possible that the effects of diverse electromagnetic fields are dependent on the cell  
type and the temporary spatiotemporal redox (*and free radicals*) patterns of cells.

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3 It is important to note the role of exposure time during LFI-EMF therapies is very  
4 critical. Radiations with a short-term exposure (*according to our experience, less than 45 min*)  
5 can facilitate (*for instance, through redox activation processes*) the immune system and  
6 cellular processes, but a long-term or continuous exposure to LFI-EMFs results in a decline in  
7 cytoprotection (Regoli et al., 2005; Di Carlo et al., 2008). Long-term electromagnetic  
8 radiations may shift the redox and calcium balance, which could cause additional cellular  
9 malfunctions.  
10

11  
12 In most ELFI-EMF experiments or treatments, various devices employ diverse  
13 artificial frequencies, which are waveforms that are modulated with respect to the frequency  
14 or the amplitude. LFI-EMFs with different characteristics, including different waveforms,  
15 frequencies and modulations, can have diverse (*or even opposing*) effects on biochemical  
16 signal processes during experiments. In other words, the effects of electromagnetic fields are  
17 associated with the type of electromagnetic field that is applied (Walther et al., 2007).  
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19  
20 However, it is impossible to investigate the whole range of artificial LFI-EMFs for  
21 potential therapeutic applications. It seems reasonable to use non-linear electromagnetic  
22 signals from cells of the body for potential therapeutic applications that may be more effective  
23 than the diverse, artificial types of LFI-EMFs signals. However, the EMOST method is based  
24 on the utilization of the non-linear, electromagnetic signals of the patients.  
25

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27 During various diseases, cells not only demonstrate altered biochemical processes but  
28 also produce altered non-linear electromagnetic complex patterns. Thus, the EMOST method  
29 can strengthen the electromagnetic communication in impaired cells with altered  
30 electromagnetic signals and can restore normal communication with surrounding cells.  
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33 Because each patient with phantom pain has a unique description concerning his/her  
34 particular sensations and the pain experienced, and because the effects of electromagnetic  
35 fields are related to the type of electromagnetic field applied, it is possible that the treatment  
36 of particular phantom pain sensations will require specific methods. However, our EMOST  
37 device may guarantee specific methods, because it is based on the non-linear,  
38 bioelectromagnetic fields of the patients' own living systems.  
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3 ***Phantom pain, neuromatrix theory, representation of body image, visual dreams, redox***  
4 ***processes, EMOST***  
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7 The precise cause of phantom pain is incompletely understood, but most researchers agree  
8 that phantom pain and phantom sensations could originate from the central nervous system.  
9 LFI-EMFs can affect the length of cell membranes and various membrane-bound receptors as  
10 well as free radical and redox processes. During several years of EMOST application, we  
11 have found that our method generally affects the quality of sleep and mood in test subjects. It  
12 is remarkable that EMOST treatments not only significantly reduced phantom pain, but that  
13 most of the patients also reported these additional benefits (mainly about improvement of  
14 their sleep and mood quality) after six treatments (Table 1).  
15

16  
17 Recently, Ikeda et al. (2005) suggested that brain oxidation could be an initial process  
18 in sleep induction. They proposed that a mild enhancement of reactive species during  
19 wakefulness in the neuronal network that regulates sleep might trigger sleep induction. In  
20 other words, reactive species-related redox homeostasis plays an essential role in sleep/wake  
21 regulation.  
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24 Phantom limb pain can also occur in individuals who are born without limbs.  
25 Neurologists have hypothesized that the perception of our limbs can be hard-wired into our  
26 brain. According to the neuromatrix theory (Melzack, 1990), the representation of body image  
27 is genetically determined and can be modified by sensory input to generate a neurosignature.  
28 The regular neurosignature may be responsible for painless phantom limb sensations, whereas  
29 phantom pain could be due to an anomalous reorganization of the neuromatrix.  
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32 Michael Jouvet (1998) suggested that during sleep, an iteration process occurs at the  
33 DNA level that maintains and programs hereditary behavior. His notion may be related to the  
34 neuromatrix theory. Namely, during sleep, a neurocomputational process can maintain and  
35 reinforce the neurosignature and complex neuro-DNA patterns.  
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38 Mulder et al. (2008) reported that a large number of amputees continue to experience a  
39 body with all of the limbs intact during in their dreams. The visual perception from the eyes  
40 or the imagination generated internally employs the same (or a very similar) neural substrate  
41 in the visual cortex (Ganis et al., 2004; Slotnick, et al., 2005; Borst and Kosslyn, 2008). In  
42 addition, in dream images, deficits occur that correlate with the damaged visual areas of the  
43 cortical brain. These phenomena indicate that the same (*or a very similar*) neural substrate of  
44 the visual cortex is used for the visual content of the dream image (Llinas and Pare, 1991).  
45 Such findings suggest that during sleep, visual dreams continue and/or reinforce the  
46 representation of a missing limb. After a limb has been amputated, the visual system from the  
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3 eyes recognizes the lack of the limb, but the subconscious proprioceptive system and visual  
4 dreams (*which are also produced by the subconscious*) do not, because the subconscious brain  
5 mechanisms (proprioceptive system, neurosignature) have not yet changed.  
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8  
9 It is possible that one of the major effects of the EMOST method (*which is based on*  
10 *the non-linear, bioelectromagnetic fields of the subject*) is to influence redox processes in  
11 cells and tissues. However, reactive species and their derivatives act as fundamental signals  
12 (*secondary messengers*) in physiological (*and pathophysiological*) processes and are  
13 particularly important in redox signal systems. During EMOST treatments, the feedback of  
14 non-linear, extra weak electromagnetic fields of cells and tissues can strengthen the cellular  
15 bioelectromagnetic and redox communication between cells and can influence the redox  
16 balance of the entire body via the circulating blood. One outcome of these processes is that  
17 EMOST affects sleep and mood processes.  
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25 There are converging lines of evidence to support the hypothesis that sleep promotes  
26 brain plasticity. Glutamate is one of the main excitatory neurotransmitters in the visual cortex  
27 (Baughman and Gilbert, 1980), and the NMDA glutamate receptor is the most important  
28 molecular structure in controlling synaptic plasticity and memory functions. However, redox  
29 modulation has been recognized as a fundamental system in the regulation of the NMDA  
30 receptor (Choi and Lipton, 2000; Bókkon and Antal, 2010). In addition, glutamate receptors  
31 are reactivated during sleep-associated consolidation processes (Gais et al., 2008). It is  
32 possible that some of the important effects of the EMOST method are achieved via the redox  
33 balance of the body and redox-related plasticity during sleep.  
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41 In addition, weak magnetic fields with an optimal frequency and intensity have  
42 ameliorating effects on melatonin-related diseases (Persinger, 2006). However, melatonin is  
43 involved in the regulation of sleep, and can modulate hippocampus NMDA receptors, as well  
44 as brain and blood oxidative stress levels in ovariectomized rats. Furthermore, melatonin  
45 improves the antioxidant status (*balance of the oxidant-antioxidant status*) in the brain and  
46 liver (Subramanian et al., 2007; Dilek et al., 2010). According to Huse et al. (2001), opioids  
47 are effective in the treatment of phantom limb pain and may influence the cortical  
48 reorganization. However, various EMFs can affect the nociceptive sensitivity and analgesia  
49 via opioid-mediated responses (Del Seppia et al., 2007). However, what the brain could need  
50 a change in neurosignature following amputation.  
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## Summary

As a result of the described study, we present our preliminary results regarding the effectiveness of the EMOST method (*which utilizes the non-linear, electromagnetic fields of the subjects*) for the reduction of phantom limb pain under clinical circumstances. Although many additional experiments are needed, the results presented herein suggest that EMOST treatment can be effective not only for the reduction of phantom limb pain but also for the improvement of sleep and mood quality in test subjects. Because LFI-EMFs affect cell membranes, membrane-bound receptors and free radical and redox processes, the cell type-specific redox status is likely responsible for the effects of various electromagnetic fields. Therefore, the EMOST method potentially affects redox processes. Because redox homeostasis plays a fundamental role in physiological (*pathophysiological*) processes and sleep/wake regulation, brain oxidation can be an initial process in sleep induction, and sleep promotes brain plasticity, these results suggest that some important effects of EMOST are to improve redox and redox-related plasticity (*reorganization*) during sleep.

However, nonlinear electromagnetic methods may potentially provide a new method for the treatment of various problematic disorders and may integrate complementary and classic methods.

## Conflict of interest

None of the authors had any personal or financial conflicts of interest. The authors alone are responsible for the content.

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## References

- Albrecht-Buehler, G. (1992). Rudimentary Form of Cellular 'Vision'. *Proc. Natl. Acad. Sci. USA* 89:8288–8293.
- Alfieri, R. R., Bonelli, M. A., Pedrazzi, G. et al. (2006). Increased levels of inducible HSP70 in cells exposed to electromagnetic fields. *Radiat. Res.* 165:95–104.
- Baughman, R. W., Gilbert, C. D. (1980). Aspartate and glutamate as possible neurotransmitters of cells in layer 6 of the visual cortex. *Nature* 287:848–850.
- Bauréus, K. C. L., Sommarin, M., Persson, B. R. et al. (2003). Interaction between weak low frequency magnetic fields and cell membranes. *Bioelectromagnetics* 24:395–402.
- Belousov, L., Popp, F., Voiekov, V., Wijk, R. V. (2000). *Biophotonics and Coherent Systems*. Moscow University Press.
- Binhi, V. N. (1999). An analytical survey of theoretical studies in the area of magnetoreception. In: *Electromagnetic Fields: Biological Effects and Hygienic*

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2  
3       *Standardization*. Repacholi, M.H, Rubtsova, N.B., Muc, A.M. eds. (pp:155–170)  
4       Switzerland, Geneva: World Health Organization.  
5  
6       Bittar, R. G., Otero, S., Carter, H. et al.(2005). Deep brain stimulation for phantom limb pain.  
7       *J. Clin. Neurosci.* 12:399–404.  
8       Bókkon, I., Salari, V. (2010). Information storing by biomagnetites. *J. Biol. Phys.* 36:109–  
9       120.  
10       Bókkon, I., Antal, I. (2010). Schizophrenia: redox regulation and volume transmission. *Curr.*  
11       *Neuropharmacol.* In press.  
12       Borst, G., Kosslyn, S.M. (2008). Visual mental imagery and visual perception: structural  
13       equivalence revealed by scanning processes. *Mem. Cognit.* 36:849–862.  
14       Calero, C. L., Calvo, D. J. (2008). Redox modulation of homomeric  $\rho 1$  GABAC receptors. *J.*  
15       *Neurochem.* 105:2367 – 2374.  
16       Choi, Y. B. (2000). Lipton, S.A. Redox modulation of the NMDA receptor. *Cell. Mol. Life*  
17       *Sci.* 57:1535–1541.  
18       Cohen, S., Popp, F. A. (1997). Biophoton emission of the human body. *J. Photochem.*  
19       *Photobiol. B.* 40:187–189.  
20       Davis, K. D., Kiss, Z. H., Luo, L. (1998). Phantom sensations generated by thalamic  
21       microstimulation. *Nature* 391:385–387.  
22       De Nicola, M., Cordisco, S., Cerella, C. et al. (2006). Magnetic fields protect from apoptosis  
23       via redox alteration. *Ann. N. Y. Acad. Sci.* 1090:59–68.  
24       de Roos, C., Veenstra, A. C., de Jongh, A. et al. (2010). Treatment of chronic phantom limb  
25       pain using a trauma-focused psychological approach. *Pain Res. Manag.* 15:65–71.  
26       Del Seppia, C., Ghione, S., Luschi, P. et al. (2007). Pain perception and electromagnetic  
27       fields. *Neurosci. Biobehav. Rev.* 31:619–642.  
28       Devor, M., Seltzer, Z. (1999). Pathophysiology of damaged nerves in relation to chronic pain.  
29       In: Wall, P.D., Melzack, R. eds. *Textbook of pain* (pp. 129–164). Edinburgh: Churchill  
30       Livingstone.  
31       Dhillon, G. S., Kruger, T. B., Sandhu, J. S. et al. (2005). Effects of short-term training on  
32       sensory and motor function in severed nerves of long-term human amputees. *J.*  
33       *Neurophysiol.* 93:2625–2633.  
34       Di Carlo, A., White, N., Guo, F. et al. (2002). Chronic electromagnetic field exposure  
35       decreases HSP70 levels and lowers cytoprotection. *J. Cell. Biochem.* 84:447–454.  
36       Di Loreto, S., Falone, S., Caracciolo, V. et al. (2009). Fifty hertz extremely low-frequency  
37       magnetic field exposure elicits redox and trophic response in rat-cortical neurons. *J. Cell.*  
38       *Physiol.* 219:334–343.  
39       Dilek, M., Naziroğlu, M., Baha Oral, H. et al. (2010). Melatonin modulates hippocampus  
40       NMDA receptors, blood and brain oxidative stress levels in ovariectomized rats. *J.*  
41       *Membr. Biol.* 233:135–142.  
42       Dröge, W. (2002). Free Radicals in the Physiological Control of Cell Function. *Physiol. Rev.*  
43       82:47–95.  
44       Lee, E. M. (1997). Pathogenesis and mechanisms of phantom pain. *Curr. Pain Headache Rep.*  
45       1:310–319.  
46       Feissner, R. F., Skalska, J., Gaum, W. E. et al. (2009). Crosstalk signaling between  
47       mitochondrial  $Ca^{2+}$  and ROS. *Front. Biosci.* 14:1197–218.  
48       Forman, H. J., Fukuto, J. M., Miller, T. et al. (2008). The chemistry of cell signaling by  
49       reactive oxygen and nitrogen species and 4-hydroxynonenal. *Arch. Biochem. Biophys.*  
50       477:183–195.  
51       Foster, K. R. (2003). Mechanisms of interaction of extremely low frequency electric fields  
52       and biological systems. *Radiat Prot Dosimetry.* 106:301–310.  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 Fraser, A., Frey, A. H. (1968). Electromagnetic emission at micron wavelengths from active  
4 nerves. *Biophys J.* 8:731–734.
- 5 Gais, S., Rasch, B., Wagner, U. et al. (2008). Visual-procedural memory consolidation during  
6 sleep blocked by glutamatergic receptor antagonists. *J. Neurosci.* 28:5513–5518.
- 7 Ganis, G., Thompson, W. L., Kosslyn, S. M. (2004). Brain areas underlying visual mental  
8 imagery and visual perception: an fMRI study. *Brain Res. Cogn. Brain Res.* 20:226–241.
- 9 Gnezdilov, A. V., Syrovegin, A. V., Plaksin, S. E. et al. (1995). Evaluation of the  
10 effectiveness of transcutaneous electroneuroanalgesia in phantom pain syndrome.  
11 *Anesteziol. Reanimatol.* 2:97–102.
- 12 Gordeeva, A. V., Zvyagilskaya, R. A., Labas, Y. A. (2003). Cross-talk between reactive  
13 oxygen species and calcium in living cells. *Biochemistry (Mosc).* 68:1077–1080.
- 14 Hancock, J.T., Desikan, R., Neill, S. J. (2001). Role of reactive oxygen species in cell  
15 signalling pathways. *Biochem. Soc. Trans.* 29:345–350.
- 16 Hidalgo, C., Carrasco, M. A., Muñoz, P. et al. (2000). A role for reactive oxygen/nitrogen  
17 species and iron on neuronal synaptic plasticity. *Antioxid. Redox Signal.* 9:245–255.
- 18 Huang, C. Y., Yang, R. S., Kuo, T. S. et al. (2009). Phantom limb pain treated by far infrared  
19 ray. *Conf. Proc. IEEE Eng. Med. Biol. Soc. 2009* 1589–1591.
- 20 Huo, R., Ma, Q., Wu, J. J. et al. (2009). Noninvasive Electromagnetic Fields on Keratinocyte  
21 Growth and Migration. *J. Surg. Res.* Mar 21. [Epub ahead of print]
- 22 Huse, E., Larbig, W., Flor, H. et al. (2001). The effect of opioids on phantom limb pain and  
23 cortical reorganization. *Pain* 90:47–55.
- 24 Ikeda, M., Ikeda-Sagara, M., Okada, T. et al. (2005). Brain oxidation is an initial process in  
25 sleep induction. *Neuroscience* 130:1029–1040.
- 26 Irlbacher, K., Kuhnert, J., Röricht, S. et al. (2006). Central and peripheral deafferent pain:  
27 therapy with repetitive transcranial magnetic stimulation. *Nervenarzt* 77:1196, 1198–  
28 1203.
- 29 Isojima, Y., Isoshima, T., Nagai, K. et al. (1995). Ultraweak biochemiluminescence detected  
30 from rat hippocampal slices. *NeuroReport* 6:658–660.
- 31 Jing, D., Shen, G., Huang, J. et al. (2010). Circadian rhythm affects the preventive role of  
32 pulsed electromagnetic fields on ovariectomy-induced osteoporosis in rats. *Bone* 46:487–  
33 495.
- 34 Jouvet, M. (1998). Paradoxical sleep as a programming system. *J. Sleep Research* 7:1-5.
- 35 KamslerA., M. (2007). Segal, Control of neuronal plasticity by reactive oxygen species.  
36 *Antioxid. Redox Signal.* 9:165–167.
- 37 Karl, A., Birbaumer, N., Lutzenberger, W. et al. (2001). Reorganization of motor and  
38 somatosensory cortex in upper extremity amputees with phantom limb pain. *J. Neurosci.*  
39 21:3609–3618.
- 40 Kishida, K. T., Klann, E. (2007). Sources and targets of reactive oxygen species in synaptic  
41 plasticity and memory. *Antioxid. Redox Signal.* 9:233–244.
- 42 Kishida, K. T., Pao, M., Holland, S. M. et al. (2005). NADPH oxidase is required for NMDA  
43 receptor-dependent activation of ERK in hippocampal area CA1. *J. Neurochem.* 94:299–  
44 306.
- 45 Kobayashi, M., Takeda, M., Sato, T. et al. (1999). In vivo imaging of spontaneous ultraweak  
46 photon emission from a rat's brain correlated with cerebral energy metabolism and  
47 oxidative stress. *Neurosci. Res.* 34:103–113.
- 48 Kumar, V. S., Kumar, D. A., Kalaivani, K. et al. (2005). Optimization of pulsed  
49 electromagnetic field therapy for management of arthritis in rats. *Bioelectromagnetics*  
50 26:431–439.
- 51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 Lappin, M. S., Lawrie, F. W., Richards, T. L. et al. (2003). Effects of a pulsed  
4 electromagnetic therapy on multiple sclerosis fatigue and quality of life: a double-blind,  
5 placebo controlled trial. *Altern. Ther. Health Med.* 9:38–48.
- 6  
7 Levin, A., Korenstein, R. (1991). Membrane fluctuations in erythrocytes are linked to  
8 MgATP-dependent dynamic assembly of the membrane skeleton. *Biophys. J.* 60:733–737.
- 9  
10 Lipkova, J., Cechak, J. (2005). Existence of Electromagnetic Radiation in Humans in. ELF  
11 Band. *Progress In Electromagnetics Research Symposium.* 1:227–230.
- 12  
13 Llinas, R. R., Pare, D. (1991). Of dreaming and wakefulness. *Neurosci.* 44:521–535.
- 14  
15 Mach, Q. H., Persinger, M. A. (2009). Behavioral changes with brief exposures to weak  
16 magnetic fields patterned to stimulate long-term potentiation. *Brain Res.* 1261:45–53.
- 17  
18 Mackert, B. M., Sappok, T., Grüsser, S. et al. (2003). The eloquence of silent cortex: analysis  
19 of afferent input to deafferented cortex in arm amputees. *Neuroreport* 14:409–412.
- 20  
21 Mancuso, M., Ghezzi, V., Di Fede, G. (2007). Utilization of extremely low frequency (ELF)  
22 magnetic fields in chronic disease; five years experience: three case reports. *Electromagn.*  
23 *Biol. Med.* 26:311–313.
- 24  
25 Markov, M. S. (2007a). Expanding use of pulsed electromagnetic field therapies.  
26 *Electromagn. Biol. Med.* 26:257–274.
- 27  
28 Markov, M. S. (2007b) Pulsed electromagnetic field therapy history, state of the art and  
29 future. *Environmentalist* 27:465–475.
- 30  
31 Mathie, A., Kennard, L. E., Veale, E. L. (2003). Neuronal ion channels and their sensitivity to  
32 extremely low frequency weak electric field effects. *Radiat. Prot. Dosimetry.* 106:311–  
33 316.
- 34  
35 Melzack, R. (1990). Phantom limbs and the concept of a neuromatrix. *Trends Neurosci.* 13:  
36 88–92.
- 37  
38 Melzack, R. (1992). Phantom limbs. *Sci. Am.* 266:120–126.
- 39  
40 Melzack, R., Isreal, R., Lacroix, R. et al. (1997). Phantom limbs in people with congenital  
41 limb deficiency or amputation in early childhood. *Brain* 120:1603–1620.
- 42  
43 Mercier, C., Reilly, K. T., Vargas, C. D. et al. (2006). Mapping phantom movement  
44 representations in the motor cortex of amputees. *Brain* 129:2202–2210.
- 45  
46 Berridge, M. J., Bootman, M. D., Roderick, H. L. (2003). Calcium signalling: dynamics,  
47 homeostasis and remodelling. *Nat. Rev. Mol. Cell. Biol.* 4: 517–529.
- 48  
49 Monteiro, H. P., Arai, R. J., Travassos, L. R. (2008). Protein tyrosine phosphorylation and  
50 protein tyrosine nitration in redox signaling. *Antioxid. Redox Signal.* 10:843–889.
- 51  
52 Moore, C. I., Stern, C. E., Dunbar, C. et al. (2000). Referred phantom sensations and cortical  
53 reorganization after spinal injury in humans. *Proc. Natl. Acad. Sci. USA* 97:14703–14708.
- 54  
55 Morabito, C., Rovetta, F., Bizzarri, M. et al. (2010). Modulation of redox status and calcium  
56 handling by extremely low frequency electromagnetic fields in C2C12 muscle cells: A  
57 real-time, single-cell approach. *Free Radic. Biol. Med.* 48:579–589.
- 58  
59 Mulder, T., Jacqueline Hochstenbach, Pieter U. Dijkstra, Jan H.B. Geertzen. 2008 Born to  
60 adapt, but not in your dreams. *Consciousness Cognition* 17:1266–1271.
- Nakashima, I., Kato, M., Akhand, A. A. et al. (2002). Redox-linked signal transduction  
pathways for protein tyrosine kinase activation. *Antioxid. Redox Signal.* 4:517–531.
- Orgel, M. G., O'Brien, W. J., Murray, H. M. (1984). Pulsing electromagnetic field therapy in  
nerve regeneration: an experimental study in the cat. *Plast. Reconstr. Surg.* 73:173–183.
- Patruno, A., Amerio, P., Pesce, M. et al. (2010). Extremely low frequency electromagnetic  
fields modulate expression of inducible nitric oxide synthase, endothelial nitric oxide  
synthase and cyclooxygenase-2 in the human keratinocyte cell line HaCat: potential  
therapeutic effects in wound healing. *Br. J. Dermatol.* 162:258–266.
- Pelling, A. E., Sehati, S., Gralla, E. B. et al. (2005). Time dependence of the frequency and  
amplitude of the local nanomechanical motion of yeast. *Nanomedicine* 1:178–183.

- Persinger, M. A. (2006). A potential multiple resonance mechanism by which weak magnetic fields affect molecules and medical problems: the example of melatonin and experimental "multiple sclerosis". *Med Hypotheses*. 66:811–815.
- Pokorný, J. J., Hašek, F., Jelínek, J., et al. (2001). Electromagnetic activity of yeast cells in the M phase. *Electro- and Magnetobiology* 20:371–396
- Ramachandran, V. S., Hirstein, W. (1998). The perception of phantom limbs. The D. O. Hebb Lecture. *Brain* 121:1603–1630.
- Rasmussen, K. G., Rummans, T. A. (2000). Electroconvulsive therapy for phantom limb pain. *Pain* 85:297–299.
- Regoli, F., Gorbi, S., Machella, N. et al. (2005). Pro-oxidant effects of extremely low frequency electromagnetic fields in the land snail *Helix aspersa*. *Free Radic. Biol. Med.* 39:1620–1628.
- Reiter, R. J. (1993). Static and extremely low frequency electromagnetic field exposure: reported effects on the circadian production of melatonin. *J. Cell. Biochem.* 51:394–403.
- Satter Syed, A., Islam, M. S., Rabbani, K. S. et al. (1999). Pulsed electromagnetic fields for the treatment of bone fractures. *Bangladesh Med. Res. Counc. Bull.* 25:6–10.
- Seidel, S., Kasprian, G., Sycha, T. et al. (2009). Mirror therapy for phantom limb pain--a systematic review. *Wien. Klin. Wochenschr.* 121:440–444.
- Selvam, R., Ganesan, K., Narayana Raju, K. V. et al. (2007). Low frequency and low intensity pulsed electromagnetic field exerts its antiinflammatory effect through restoration of plasma membrane calcium ATPase activity. *Life Sci.* 80:2403–2410.
- Sherman, R. A., Sherman, C. J., Bruno, G. M. (1987). Psychological factors influencing chronic phantom limb pain: an analysis of the literature. *Pain* 28:285–295.
- Sherman, R.A. (1994). What do we really know about phantom limb pain? *Pain Rev.* 1:261–274.
- Shi, Y., Yu, J., Jia, Y. et al. (2010). Redox-regulated lipid membrane binding of the PICK1 PDZ domain. *Biochemistry* 49:4432–4439.
- Simkó, M. (2007). Cell type specific redox status is responsible for diverse electromagnetic field effects. *Curr. Med. Chem.* 14:1141–1152.
- Slotnick, S. D., Thompson, W. L., Kosslyn, S. M. (2005). Visual mental imagery induces retinotopically organized activation of early visual areas. *Cereb. Cortex* 15:1570–1583.
- Subramanian, P., Mirunalini, S., Pandi-Perumal, S. R. et al. (2007). Melatonin treatment improves the antioxidant status and decreases lipid content in brain and liver of rats. *Eur. J. Pharmacol.* 571:116–119.
- Sutbeyaz, S. T., Sezer, N., Koseoglu, F. et al. (2009). Low-frequency pulsed electromagnetic field therapy in fibromyalgia: a randomized, double-blind, sham-controlled clinical study. *Clin. J. Pain.* 25:722–728.
- Tsang, E. W., Koren, S. A., Persinger, M. A. (2009). Specific patterns of weak (1 microTesla) transcerebral complex magnetic fields differentially affect depression, fatigue, and confusion in normal volunteers. *Electromagn. Biol. Med.* 28:365–373.
- Valko, M. D., Leibfritz, J., Moncol, M. T. et al. (2007). Free radicals and antioxidants in normal physiological functions and human disease, *Int. J. Biochem. Cell. Biol.* 39:44–84.
- Walther, M., Mayer, F., Kafka, W. et al. (2007). Effects of weak, low-frequency pulsed electromagnetic fields (BEMER type) on gene expression of human mesenchymal stem cells and chondrocytes: an in vitro study. *Electromagn. Biol. Med.* 26:179–90.
- Wiech, K., Kiefer, R. T., Töpfner, S. et al. (2004). A placebo-controlled randomized crossover trial of the N-methyl-D-aspartic acid receptor antagonist, memantine, in patients with chronic phantom limb pain. *Anesth. Analg.* 98:408–413
- Wilkes, D., Ganceres, N., Solanki, D. et al. (2008). Pulsed radiofrequency treatment of lower extremity phantom limb pain. *Clin. J. Pain.* 24:736–739.

- 1  
2  
3 Yan, Y., Wei, C. L., Zhang, W. R. et al. (2006). Cross-talk between calcium and reactive  
4 oxygen species signaling. *Acta Pharmacol. Sin.* 27:821–826.  
5  
6 Yang, Z., Asico, L.D., Yu, P., et al. (2006) D5 dopamine receptor regulation of reactive  
7 oxygen species production, NADPH oxidase, and blood pressure. *Am. J. Physiol. Regul.*  
8 *Integr. Comp. Physiol.* 290:R96–R104.  
9  
10 Zhang, X., Zhang, J., Qu, X. et al. (2007). Effects of different extremely low-frequency  
11 electromagnetic fields on osteoblasts. *Electromagn. Biol. Med.* 26: 167–177.  
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### 15 **List of figure legends**

16  
17 **Figure 1.** The EMOST device (BioLabor-MCC HI 2.5.2) is controlled by a personal  
18 computer.  
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22 **Figure 2.** Photograph of an amputee undergoing an EMOST treatment.  
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27 **Figure 3.** Verbal numerical rating scale.  
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31 **Table 1.** This table summarizes the phantom pain intensity observed after completion of six  
32 EMOST treatments and additional improvements reported by the patients. The reduction of  
33 phantom limb pain by EMOST was statistically significant (\*P < 0.05) as compared to the  
34 controls.  
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Figure 1.



Figure 2. Input and output electrodes on the hands

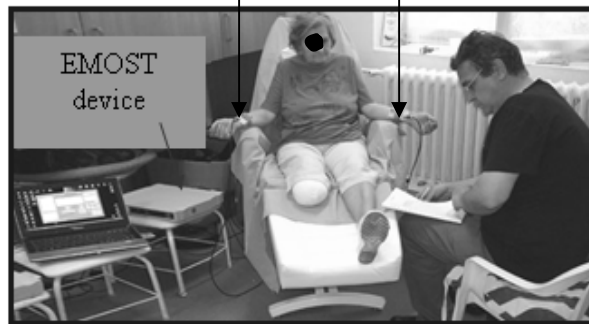


Figure 3.

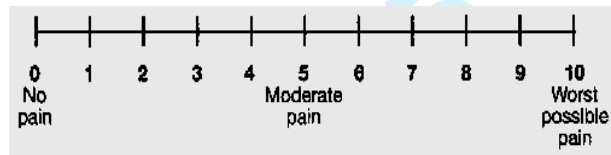


Table 1.

	Patients	Phantom pain intensity before the treatments	Phantom pain intensity after six completed EMOST treatments	Interval between the amputation date and the EMOST treatments	Additional improvements reported by patients after six EMOST treatments	Disease or Accident
<b>Patients with EMOST treatments</b>	I.	6	0	1 month	Sleep	Diabetes
	II.	7	3	1/2 year	Sleep	Arterial
	III.	8	4	2 years	Mood	Diabetes
	IV.	6	2	1 month	Sleep, Mood	Arterial
	V.	1	0	8 years	Sleep, Mood	Arterial
	VI.	3	2	1 month	Sleep, Mood PP frequency↓	Arterial
	VII.	7	2	1 month	Sleep, Mood	Diabetes
	VIII.	7	4	1 month	Mood	Accident
	IX.	7	0	3 years	Sleep PP frequency↓	Diabetes
	X.	7	6	5 years	Mood	Diabetes and arterial
		SD 5.9±2.18	SD 2.3±2.00			
<b>Patients without EMOST treatments (controls)</b>	CI.	4	3	2 months	————	Diabetes
	CII.	6	5	1/2 month	————	Arterial
	CIII.	3	3	1 month	————	Accident
		SD4.33±1.52	SD 3.66±1.15			