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Effects of PEMF on Patients With Osteoarthritis: Results of a Prospective, Placebo-Controlled, Double-Blind Study

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This study aimed to evaluate effects of pulsed electromagnetic fields (PEMF) in a double blind study on patients with knee joint osteoarthritis. The MAGCELL ARTHRO electrode-less therapy delivered a sinusoidal magnetic field, varying in frequency between 4 and 12 Hz. In 1 cm tissue depth, magnetic flux density was 105 mT. A total of $n = 57$ patients were randomly assigned to the verum, PEMF or placebo group (placebo device). Their average age was 61.6 ± 12.0 years. According to American College of Rheumatology criteria the osteoarthritis level was 2.8 ± 0.8. Treatment was performed twice a day for 5 min over a period of 18 days. Treatment with the MAGCELL device versus control (sham exposed) showed a highly significant reduction in pain ($P < 0.001$), a significant reduction in stiffness ($P = 0.032$) and a significant reduction in disability in daily activities ($P = 0.005$) according to the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scales—with a good overall treatment tolerance. In the placebo group there was no evidence of a significant change between the initial and final examination in any of the three above-mentioned WOMAC scales. Results of this partly randomized placebo-controlled double-blind study show clinically at any rate, that use of PEMF lead to highly significant better results in the treatment group compared to the placebo group with regard to the total WOMAC global score and especially for visual analogue scale. Patient assessment of the "effectiveness" was rated in 29.5% as very good and good in 27.3% compared to 0.0% and 15.4% in controls. This therapy is thus a useful complementary treatment option with no side effects. Bioelectromagnetics. 36:576–585, 2015. © 2015 Wiley Periodicals, Inc.

Key words: MAGCELL; osteoarthritis; magnetic field therapy; electrotherapy; inflammation

INTRODUCTION

Osteoarthritis is a dynamic but gradual, non-inflammatory, degenerative disease of cartilage and other joint tissue, particularly in the aged, interspersed with inflammatory phases. Cartilage degeneration through complete disintegration may be triggered by unknown causes ("primary or idiopathic osteoarthritis"; approximately 80% of all cases) and known causes ("secondary osteoarthritis"; approximately 20% of all cases) [Ferraz et al., 1990]. The disease finally results in loss of joint function. Generally the joint is braced or, insofar as it is possible, replaced. Osteoarthritis is the most common pathological finding related to the musculoskeletal system, and its incidence is growing steadily [Engelhardt, 2003]. A distinction is made between clinically silent (=asymptomatic) and activated (=inflamed) and clinically manifest osteoarthritis accompanied by constant pain. Every stage calls for a separate individual therapy. Fast pain alleviation in symptomatic phases is of decisive importance from the patient's point of view.

Until now, primary conservative therapy has focused on pain reduction with a little impact on causal therapy concepts. Moreover, medicamentous therapy often entails serious side effects. Effectiveness of pulsed electromagnetic fields (PEMF) is a controversial subject of discussion, which tends to be viewed critically in scientific circles. A look at the literature [Quittan et al., 2000; Hulme et al., 2002;

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McCarthy et al., 2006] reveals major differences with regard to field strengths, frequencies, application areas, extent, duration, therapy frequency, outcome variables, and their assessment, and in methodological quality. Results regarding effectiveness differ according to the inclusion criteria underpinning studies. However, recent studies further corroborate a positive outcome of PEMF therapy in osteoarthritis—although using different frequencies and devices [Nelson et al., 2013].

Different interpretations of how PEMF acts are available: In the case of cultured tendon fibroblasts, following PEMF exposition de Girolamo et al. [2013], among others, established increased collagen I expression and increase of anti-inflammatory prostaglandins, and a huge rise in the Vascular Endothelial Growth Factor (VEGF)—A-mRNA transcription. These findings also indicate a tendency towards proliferation and increase in vascular density. Positive PEMF influence is also reported on anabolic activity of chondrocytes, a chondroprotective effect on joint cartilage and on spontaneous osteoarthritis in animal models [De Mattei et al., 2001, 2003, 2007; Ciombor et al., 2003; Fini et al., 2005, 2008; Nicolin et al., 2007; Benazzo et al., 2008; Ongaro et al., 2011]. At the same time, the catabolic effect of IL-1b is reduced [Boopalan et al., 2011; Ongaro et al., 2011]. Furthermore an increased gene expression in members of the Transforming Growth Factor (TGF-ß) family is affected [Aaron and Ciombor, 2004]. Local expression of TGF-ß hereby also results in improved bone fracture healing [Boopalan et al., 2009], whereby the proliferation, differentiation and synthesis of cartilage matrix proteins [De Mattei et al., 2001; Ciombor et al., 2002] are improved.

Aforementioned impact mechanisms combined with increased blood circulation (see pilot studies referred to below) and the signal cascade of nitrogen oxide (NO) might be an important strand of the PEMF effect. With regard to the release of NO in pilot studies of PEMF therapy tested here [Graubner et al., 2007; Funk et al., 2014] a strong boost in blood circulation was evidenced, which can be attributed to an improvement in haemodynamics and rheology. In this context an activation of the vasodilatative NO may be of significance [Grohmann et al., 2000]. Indeed, our group also showed a direct increase in NOs produced by endothelial cells in an in vitro study [Funk et al., 2014]. To be considered are also cell-stimulatory effects caused by weak electrical signals that may influence cellular processes over second messenger-transported cell differentiation and immunomodulation (see above) [Weintraub and Cole, 2008; Graak et al., 2009].

The therapy device used in this study generates a time-varying magnetic field with a flux density of 105 mT at the therapeutically relevant depth of 1 cm. Electrical current densities induced thereby are considerably higher than 10 mA/m^2, classing them within the effective range [Lakes and Saha, 1978; Bassen et al., 1992; Schimmelpfeng and Dertinger, 1997; Ohgaki and Kleihues, 2005]. The different therapy concept and positive results of an un-controlled pilot study [Hitrov and Portnov, 2008] (parameter of pain, on a visual analogue scale, VAS, from 7,1 at baseline to 2,6 after 10 days and significant reduction of WOMAC score from 715,6 at baseline to 131,5 after 10 days) gave rise to the idea of examining the effects of the therapy device on patients with osteoarthritis of the knee joint in a study of an appropriate methodical standard. We raised the question if there is really a significant improvement in WOMAC score after treatment with the MAGCELL ARTHRO therapy device.

METHODS

Overall Description

Patients with osteoarthritis in their knee joint were recruited (no payment was given to the study participants) and divided randomly into two groups. Then they received therapy with the MAGCELL device (verum group) or with a similar device—identical exterior—except magnetic segments in the rotating magnet (verum group—see below) were replaced by non-magnetic metal segments (placebo group).

Therapy Procedure

The MAGCELL device uses time-varying magnetic fields of 105 mT flux density in 1 cm tissue depth to induce biologically effective electric current densities (for examples of computation see Bassen et al. [1992] or Schimmelpfeng and Dertinger [1997]) (Fig. 1). Current densities provided by the MAGCELL device are well above the level of 10 mA/cm^2. Thus responses are ensured that are internationally qualified as biologically efficient. In blood and body fluids, induced current density are many times higher even [Lakes and Saha, 1978; Ohgaki and Kleihues, 2005]. Since the synovial fluid is considered the therapeutic target in this study, specific electric conductivity of body fluids (1.5 S/m) can be used for calculations of the current density. Using, in addition, typical MAGCELL features, namely 105 mT magnetic flux density, 8 Hz average frequency and 6 cm diameter of

Fig. 1. MAGCELL ARTHRO therapy device.

the magnetically active area, then the therapeutically relevant current density can be estimated to be 120 mA/m^2. This is more than one order of magnitude higher than "threshold" of 10 mA/m^2.

Solely on account of its effective strength, which is four to several hundred times that of standard commercially available equipment like magnetic field mats and coils, the therapy device is more powerful than the latter. As a general reference: magnetic field mats generally feature output effective strengths in the micro-tesla range (μT). Most coil devices for home use few millitesla to up to approximately 40 mT. On account of the effective strength generated and different therapy concept we opt for the term "electrode less electrotherapy."

The therapy process used bears no resemblance to Magnetic field Resonance Tomography, Pulsating Signal Therapy, MultiBioSignal Therapy, or similar methods.

Treatment

Verum group patients received treatment with the genuine MAGCELL ARTHRO (PHYSIOMED, Schnaittach, Germany). In this hand-held and battery-driven device no coils are used for field generation. Instead, four 45° segments of a special magnetic material are mounted symmetrically on a pivoting disc (6 cm in diameter) supported on bearings In the MAGCELL device, the disc area of 28 cm^2 (diameter ca. 6 cm) is magnetically active and fully available for treatment. Disc rotation is varied in 2 Hz steps to produce frequencies between 4 and 12 Hz.

By rotating the disc via a direct current motor controlled by a microcontroller, a nearly sinusoidal magnetic field is generated with a magnetic flux density of 420 mT (peak-to-peak) on the device surface. At 1 cm distance (the therapeutically recommended tissue depth), still 105 mT flux density prevails. At 2 cm distance (depth in tissue), the flux density is 40 mT, with a corresponding current density of roughly 43 mA/m^2. At depths beyond 2.5 cm, current density falls below 10 mA/m^2. This information stems from measurements of the flux density at various distances from the surface in synovia and joint tissue-like material and representing values within tissue during the typical cycle of the MAGCELL device.

Magnetic flux density was measured with a magnetometer (MP—U, List-Magnetik, Leinfelden, Germany). Current density was calculated by the law of induction.

In the placebo group, the study participants only received a sham therapy with a placebo device. Devices were absolutely identical other than the sham device featured a non-magnetic material instead of the four 45° segments in a magnetic material. So no difference was noticeable, neither visually, nor with regard to weight, operating noise etc. In addition, the patients could not perceive the PEMF created by MAGCELL in either groups.

For all (verum- and placebo treated) participants, therapy lasted for a period of 18 days. Treatment took place twice daily for 5 min for all. Upon pressing the start button the device ran and stopped automatically after 2.5 min (application 2 times consecutively). After the first treatment, the area was changed and device started for a second time. Treatment areas included anterior surface of the joint (cartilage at the top of the lateral femur (Epicondylus lateralis femoris)) and the interior surface of the joint (directly below the femur cartilage (Epicondylus medialis femoris)).

Setting and Measuring Times

Main examinations (initial examination = IE, final examination = FE) and treatment were performed in the Tagesklinik Esplanade, Berlin-Pankow (Germany). Recruitment took place from October 2008 to the end of February 2009. The treatment was conducted over a period of 18 days and consisted of 2 sessions daily of 2×2.5 min. Data were recorded before beginning of the study (initial test) and after 18 days (final test). The experience from our previous pilot study suggested the period of 18 days.

Patient Recruitment

All study participants were long-standing patients treated at the investigating clinic. Contact was established during these patients' quarterly consultation with their doctors, or when patients came due to acute worsening of the complaint. During consultation the study was explained and written information given to the patient (patient education). Patients could arrange a new appointment indicating their willingness to take part in the study. At this appointment, patient consent form and data privacy declaration were signed, in part randomization and initial examination conducted.

Randomization and Blinding

Treatment was assigned by a draw. Study participants were asked to pick an envelope out of an appropriate container. Envelopes were drawn and kept. The envelopes were identical and could not be told apart. Lots contained software-generated random codes. According to the random code the study participant received a "package" with the same code. This contained all relevant documentation literature and the corresponding therapy device (verum or placebo). After running first groups in verum and placebo with $n = 13$ in each group for 9 days a first unblinding evaluation showed significant improvement in most parameters and by ethical reasons, an additional 31 people were assigned to the verum group which run overlapping the rest of the 18 days of the first groups and 9 days further to complete identical treatment time of 18 days.

All participants were attended by two, trained doctor's assistants (drawing lots, coordination and collecting examination documents, device dispensing and collection). Neither the doctor's assistants, doctor in charge, nor patients knew to which group the latter belonged. Exterior of the device (in verum or placebo machines) was absolutely equal, so the study was effectively a double-blind one.

Inclusion and Exclusion Criteria

Included were patients with osteoarthritis in their knee joint, severity level (till score 5–arthritis of several joints) according to American College of Rheumatology (ACR) criteria [Neogi et al., 2010] and willingness to take part in study. Patients were excluded in case of pregnancy or possibility thereof, infection in the area treated, presence of general inflammatory processes in area to be treated, not considered to be due to an inflammatory phase of osteoarthritis, and patients susceptible to thrombosis or spasms.

Variables

Primary outcome criterion of the study was a reduction of osteoarthritis-associated pain—recorded by the "pain" domain in the WOMAC index [Stucki et al., 1996]—i.e., difference between basic value (initial test) and value after 18 days of treatment (final test). The WOMAC index is a fully standardized international disease-specific self-assessment tool for recording symptoms and functional disability for knee and hip osteoarthritis [Stucki et al., 1996; Bellamy, 2005]. A German version with a 100 mm VAS was used. The WOMAC questionnaire comprises 24 questions based on three scales. Aside from a global score, scores can also be calculated for the categories of pain, stiffness, and function. High values indicate poor function or severe pain symptoms. Secondary outcomes were defined as followed: effectiveness and tolerance parameters were recorded by posing questions of "What was the overall impression and tolerance of the therapy in the patient's view?" and "How was the therapy tolerated overall?"

Statistics

Individual scales in the WOMAC questionnaire and differences recorded between the two examinations were represented as illustrative quantitative variables on the basis of a mean value and standard deviation, minimum and maximum, quartiles including median, and checked for normal distribution via the Shapiro Wilk test. On account of significant deviations from a normal distribution, subsequent statistical analysis was performed on the basis of non-parametric methods. With regard to WOMAC scale values and differences recorded in the examinations, the two groups were compared to the Mann and Whitney test, while Wilcoxon test for pair differences was used for comparison of scale values for initial examination with those of the final examination within the groups. Due to the low expected frequencies, comparison of both treatment groups in terms of effectiveness and tolerance was performed according

to exact test after Fischer, while Likert scales were used to illustrate absolute and percent frequencies for the characteristics. Likert scale is the sum of response fields in a subjective rating scale (in our case from very good, to "good" to "moderate," "fairly poor," and "very poor"). Bilateral testing was always employed, with a significance level of 5% as basis. Alpha adjustment for multiple testing in respect of the primary end points (WOMAC scales) was performed according to Bonferroni and Holm method. IBM SPSS Statistics 21 (SPSS, IBM, Chicago, IL) was used to perform the statistical calculations.

Normal distribution with the same standard deviation was assumed for both groups in size calculation. Various works were taken into account in respect of the improvement potential for outcome variables [Bellamy and Buchanan, 1988; Ferraz et al., 1990; Angst et al., 2002; Altman et al., 2004; Bellamy, 2005]. Variables for indicating pain were: during walking, using stairs, in bed, sitting or lying, and standing. Sample size planning was based on the assumption that bilateral 2-SampTTest was to be used for assessment. Significance level was fixed at $\alpha = 5\%$, power (1-β) to 80%. For this study, at least 28 assessable patients per group were taken as the optimum random sample size for the primary outcome. Drop-out rate in this intervention (5% = 1.25 participants) and time period was based on the pilot study and general experience of such short intervention periods. Targeted total random sample size was thus $n = 60$ people ($n = 30$ per group). The G*Power 3.0.8. program from the Heinrich Heine University Düsseldorf (Düsseldorf, Germany) was used to calculate the optimum random sample size.

Statistical analysis was conducted according to the "Intention-to-Treat" principle whereby missing values were not substituted.

Clinical study protocol was approved by the Ethics Committee of the official Berlin Medical Association (Ärztekammer Berlin, Number: Eth-016/08).

RESULTS

A total of 73 patients were asked if they were willing to take part in the study. Of those, 16 people declined. A total of 44 people drew a verum treatment, although the calculated random sample size was already exceeded, so 13 patients were available for analysis in the placebo group.

Patient Characteristics at the Beginning of the Study

Table 1 illustrates main patient characteristics at beginning of study.

Primary outcome criterion in this study derived from the WOMAC score. Table 2 shows distribution of WOMAC scales of pain, stiffness, daily activities and total score for both study groups at times T0 and T1. The higher the score values, the greater the patients' physical disability.

In the verum group, a significant *reduction* was observed in all WOMAC scores ($P < 0.001$ for pain, stiffness, daily activities, and total score). Distribution of WOMAC score differences recorded in two treatment groups is shown in Table 3. In WOMAC total score, patients in verum group achieved a median improvement of 21.8 points.

On the other hand, in the placebo group a median increase in WOMAC pain score of 0.9 points was recorded. During treatment "pain" in this group therefore increased. In respect to stiffness and daily activities, a reduction of score was observed, the median lying between 0.2 and 1.1 points. By contrast, total score revealed deterioration in the placebo group, median value being 0.7 points. None of these changes proved significant in this group (Wilcoxon test for pair differences, $P > 0.05$).

Comparison of verum versus placebo group reveals significant differences in all WOMAC scales and shows highly significant pain reduction even after adjustment for multiple testing. Table 4 provides an overview of statistical comparisons; tests and *P*-values are specified.

Subjective Rating by Patients (Likert Scale)

Possible answers were recorded on the basis of a 5-stage Likert scale. Results of patients' self-assessment of the final examination are illustrated in Table 5. With regard to effectiveness of the treatment, there was a highly significant difference between verum

TABLE 1. Distribution of Age, Gender, and ACR Severity Level of Partly Randomized Patients at Beginning of Study

Parameter	Index	Verum group	Placebo group	Total
Age (years)	MV ± SD	63.4 ± 12.1	55.5 ± 10.8	61.1 ± 12.0
Gender	w N (%)	15 (34.1%)	5 (38.5%)	20 (35.1%)
	m	29 (65.9%)	8 (61.5%)	37 (64.9%)
ACR severity level	MV ± SD	3.0 ± 0.8	2.3 ± 0.6	2.8 ± 0.8

MV, mean value; SD, standard deviation.

TABLE 2. Distribution of WOMAC Scores for T0 and T1 for Both Patient Groups

Group	WOMAC		N	Mean value	Standard deviation	Min	Max	Percentile 25.	Percentile 50. (Median)	Percentile 75.
Placebo	Pain	T0	13	9.8	8.2	2.1	27.8	5.2	6.4	11.9
		T1	13	11.1	10.3	1.8	36.2	4.3	7.6	13.7
	Stiffness	T0	13	3.6	3.1	0.4	10.9	1.4	2.6	5.8
		T1	13	3.4	2.8	0.5	8.5	1.8	2.3	5.5
	Daily activities	T0	13	43.5	26.8	13.8	93.7	18.5	30.9	63.6
		T1	13	41.8	28.6	9.1	106.1	21.0	30.5	57.5
	Total score	T0	13	56.9	36.7	19.4	132.4	26.0	38.8	79.0
		T1	13	56.2	40.4	15.7	150.4	28.0	41.8	73.1
Verum	Pain	T0	44	14.5	8.6	0.8	37.3	7.0	15.0	18.9
		T1	44	8.8	7.7	0.1	32.2	2.8	6.2	14.3
	Stiffness	T0	44	3.8	2.5	0.0	11.1	1.7	3.5	5.5
		T1	44	2.5	3.0	0.0	11.7	0.6	1.3	3.8
	Daily activities	T0	44	47.1	21.6	8.8	94.7	32.0	47.7	57.5
		T1	42	31.4	25.6	5.2	96.4	13.2	21.4	43.3
	Total score	T0	44	65.4	30.8	11.0	133.1	42.6	67.2	84.1
		T1	42	42.9	35.5	6.8	135.5	16.2	28.7	62.6

versus placebo group (exact Fisher test, $P = 0.040$), while the difference observed for tolerance between these two groups proved not to be significant ($P = 0.316$). Box plots of Figure 2 reveal obvious improvements in the verum group in comparison to placebo group. Even over three-quarters of patients scored a success in WOMAC pain and daily activities scales, represented by the third quartile under the zero line. On the other hand, the median difference close to the zero line in the placebo group indicates that half of the patients experienced no change at all or even a deterioration in WOMAC values.

Undesirable Side Effects

This study revealed no undesirable occurrences or side effects in connection with therapy.

DISCUSSION

Application of our electrode-less PEMF therapy (verum group) in the present study showed a significant and relevant improvement in pain category of the WOMAC questionnaire, and significant improvements in mobility, daily activities categories and global score. No notable changes could be recorded in any of the WOMAC scales in the placebo group.

In the verum group 56.8% of patients assessed effectiveness to be at least "good," whereas only 15.4% did so in the placebo group; 54.6% of the verum group patients rated tolerance to be at least "good," in comparison to 38.5% in the placebo group.

In the verum group the therapy led to an improvement in symptoms and functional condition. No side effects were observed. Slight improvements in values of the treatment group in WOMAC global score parameters in comparison to those in the pilot study [Hitrov and Portnov, 2008] are accounted for by lower initial values, and thus for less pronounced symptoms of the patient group at the baseline. Improvement rate in the verum group can be regarded as relevant in comparison to other treatment regimens with significant improvement described in literature

TABLE 3. Distribution of WOMAC Scale Differences Recorded in the Placebo and Verum Groups

Group	Diff. WOMAC AU-EU	N	Mean value	Standard deviation	Min	Max	Percentile 25.	Percentile 50. (Median)	Percentile 75.
Placebo	Pain	13	1.3	3.1	−3.3	8.4	−0.8	0.9	3.5
	Stiffness	13	−0.2	1.1	−2.8	1.4	−0.8	−0.2	0.6
	Daily activities	13	−1.8	7.8	−20.0	12.4	−4.7	−1.1	2.6
	Total score	13	−0.7	8.8	−20.1	18.0	−5.5	0.7	3.7
Verum	Pain	44	−5.7	5.9	−22.7	2.5	−10.0	−3.3	−1.2
	Stiffness	44	−1.3	1.9	−4.9	3.5	−2.6	−1.1	0.1
	Daily activities	42	−16.4	16.1	−50.1	8.3	−30.0	−16.7	−2.0
	Total score	42	−23.5	22.6	−69.2	7.9	−43.1	−21.8	−3.1

TABLE 4. Overview of Statistical Comparisons Performed (*P* values)

Comparison	Test	WOMAC pain	WOMAC stiffness	WOMAC daily activities	WOMAC total score
Placebo T0 vs. T1	Wilcoxon test for pair diff.	$P = 0.147$	$P = 0.779$	$P = 0.507$	$P = 0.834$
Verum T0 vs. T1		$P < 0.001$ /$p_{adj} < 0.001$	$P < 0.001$ /$p_{adj} < 0.001$	$P < 0.001$ /$p_{adj} < 0.001$	$P < 0.001$ /$p_{adj} < 0.001$
Diff. T0-T1 placebo vs. verum	U-Test	$P < 0.001$ /$p_{adj} < 0.001$	$P = 0.032$ /$p_{adj} = 0.032$	$P = 0.005$ /$p_{adj} = 0.010$	$P = 0.001$ /$p_{adj} = 0.003$

[Ehrich et al., 2000; Angst et al., 2002; Altman et al., 2004; Tubach et al., 2005].

Our results reveal a benefit in the use of PEMF as a complementary therapy in treatment of acute osteoarthritis of knee joint, severity level 2–4 according to ACR criteria [Bellamy and Buchanan, 1988] in the relapse stage. However, a sufficient average flux density (± 105 mT), as provided by the MAGCELL ARTHRO device used in the study, must be ensured. The therapy option is of particular relevance due to its effect on patient's pain, who particularly when exposed to chronic, high doses, suffer from intolerance or the side effects of painkillers (e.g., non-steriodal anti-rheumatic drugs). Improvements in mobility and ability to perform daily activities, as well as pain alleviation, benefit both mechanical forms of therapy like passive physical movement and physical training performed by the patient [Rohde, 2003]. However, in a Cochrane study, Rutjes et al. [2009] showed that treatment with transcutaneous electrostimulation for osteoarthritis of the knee was not effective for pain relief.

On the other hand, several recent studies showed the effectiveness of the PEMF treatment in clinical assessment of arthritis, osteoarthritis or sciatica, or neuropathy [Weintraub and Cole, 2008; Graak et al., 2009; Ozguclu et al., 2010; Omar et al., 2012]. Despite evidence of clinical effectiveness, the exact physiological impact of PEMF in a sufficient strength (of the electromagnetic field) in the case of osteoarthritis has still not been fully explored and requires further examination—this is true especially for applied frequencies, flux densities, and therapy periods. However, recent publications showed an increasing amount of data, which favour PEMF therapy. In fact, Veronesi et al. [2014] showed in guinea pigs that PEMF (75 Hz) ameliorated all symptoms of knee osteoarthritis. In clinical studies, Iannitti et al. [2013] applied PEMF at varying carrier (high) and modulation (low) EMF frequencies. The treated knee of the osteoarthritis patients had less pain, less stiffness, and an increased physical function. Two meta analyses by Negm et al. [2013] (7 studies analyzed) and Ryang We et al. [2013] (14 studies analyzed) support efficacy of PEMF in management of knee osteoarthritis. The only point to mention was that in the Negm study, the parameter pain was only slightly ameliorated.

In respect of the PEMF treatment period, the latest works refer to the superiority of very short (3 min, twice daily), very intensive (up to 1 T) applications. PEMF stimulation, on the other hand, exerts field exposure of a longer duration. This is also alleged to lead to stem cell induction (mesenchymal stem cells), whereby improved proliferation pertaining to the cartilage in comparison to the induction of bone formation (in the case of long-term field exposure) could be established [Chen et al., 2013].

Results of this partly randomized placebo-controlled double-blind study show clinically at any rate, that use of PEMF of sufficient strength (105 mT) leads to highly significant better results in

TABLE 5. Patient Assessment of the "Effectiveness" and "Tolerance" Parameters

	Effectiveness		Tolerance	
Rating	Verum group; N (%)	Placebo group; N (%)	Verum group; N (%)	Placebo group; N (%)
Very good (1)	13 (29.5)	0 (0.0)	5 (11.4)	2 (15.4)
Good (2)	12 (27.3)	2 (15.4)	19 (43.2)	3 (23.1)
Moderate (3)	6 (13.6)	7 (53.8)	10 (22.7)	4 (30.8)
Fairly poor (4)	12 (27.3)	4 (30.8)	10 (22.7)	4 (30.8)
Very poor (5)	1 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)

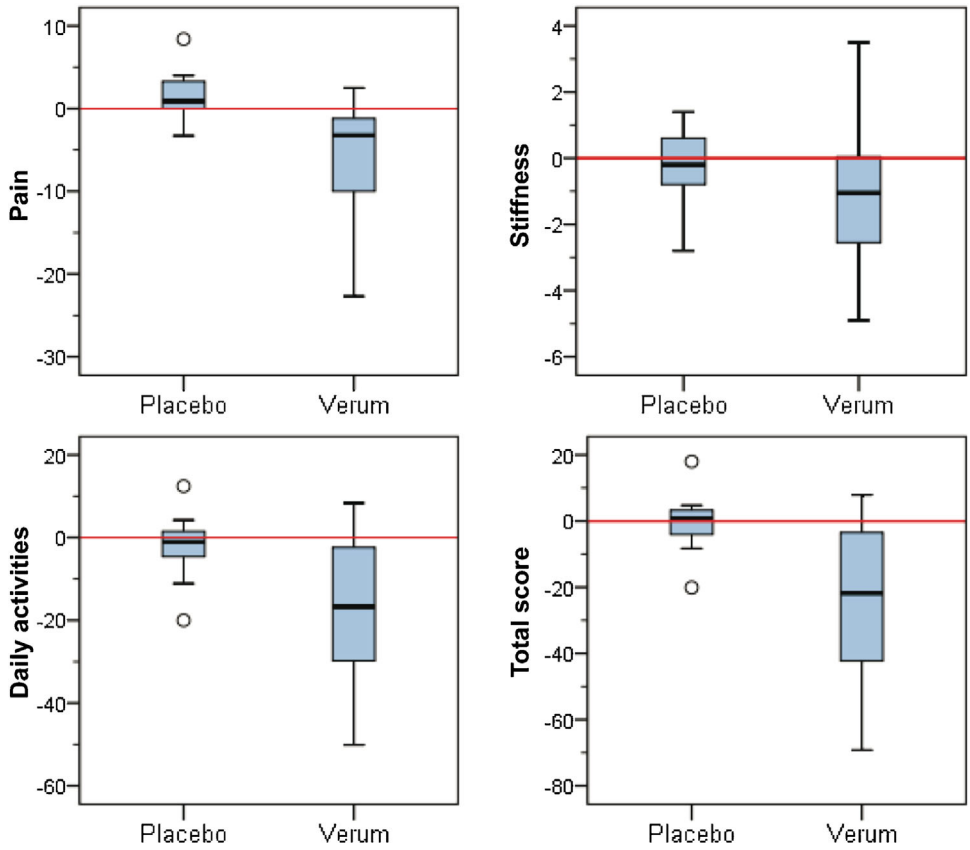

Fig. 2. Comparison of differences recorded in WOMAC scales between initial and final examinations for two groups treated. Zero line indicates initial score. Whisker box plot shows at top of the box the 1. quartile, at the bottom the 3. quartile. Thick line in middle depicts median. Length of whisker indicates maximum (**top**) or minimum (**bottom**) values. Small circles are individual outliers.

the treatment group compared to the placebo group with regard to the total WOMAC global score and especially for VAS. The therapy can thus constitute a useful complementary treatment option with no side effects in treatment of acute osteoarthritis in the knee joint. Devices used in the study may be used for personal therapy without any risk. A further strength of our therapy method is the light, hand-held, and electrode-less device itself, which can be used in any daily situation and even through clothes. On the other hand, this device has a limited range of frequencies—especially to higher levels—compared to coil and electrode systems like those used in the study of Iannitti et al. [2013].

Regarding cell and molecular biological implications (see above)—and regarding inflammation—it is difficult to generalize these results for other arthritic conditions. Further studies to follow up the present results are planned and will start soon. Also further studies are planned to test the MAGCELL in other arthritic conditions.

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