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Evaluation of the effectiveness of three-dimensional pulsating electromagnetic fields of the MultiBioSignal Therapy (MBST) in respect to the regeneration of cartilage structures

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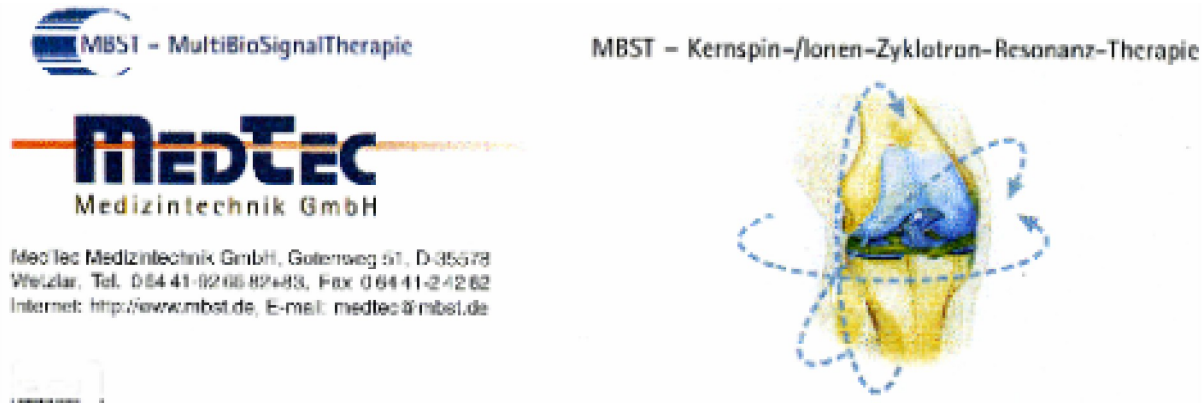

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Gonarthosis – PEMF Treatment – MBS Therapy – MBST - CT –Chondrogenesis

Abstract

Although pulsating electromagnetic fields (PEMF) have been used for quite some time in the therapy of bone fractures, there has not yet been any scientific study in respect to the applicability to cartilage structures in vivo in human beings. Therefore, in this study, 14 female patients suffering from a gonarthrosis ((Wirth stages II and III) were submitted to a PEMF treatment in nine consecutive treatment sessions. The treatment was carried out using the appliance MBST 1-CELLREMAKE, produced by MedTec Medizintechnik GmbH. The effectiveness of this intervention was evaluated using the procedure published by ECKSTEIN et al. (1998). The ECKSTEIN procedure allows for a three-dimensional reconstruction and thus a quantification of the cartilage structure over time, using data compiled with the nuclear resonance tomograph. The data here presented clearly indicates that distinct positive adaptations of the cartilage structures in respect to thickness, volume, and area occurred. These positive results are credited to the usage of the complex PEMF technology in the therapy procedure. It is assumed that this mechanism originates from the activation of intact or partly functional cartilage tissue cells as well as from an augmentation of the collagen synthesis. It must, however be noted, that it is evident that a special characteristic of the PEMF technology is required to initiate the adaptations as described.

1. Introduction

For more than twenty years, pulsating electromagnetic fields (PEMF) have been used, especially in the therapy of fractures. Their usage is based on the principle of electromagnetic stimulation with the intention of obtaining cell proliferation, calcification and the development of matrixes. This has been described in various studies (Basset & Becker, 1962; Krempen & Silver, 1981; Sharrad et al, 1981; Pollack, 1984). The signals thus stimulate a biological reaction, which can vary, and which is dependent on frequency, amplitude, field strength and the cell structure that is to be treated.

More recently, singular studies that deal with the influence of PEMF on other structures, and especially on cartilage, have been published, for example by SAKAI et al (1991). Hitherto, however, it was hardly possible to demonstrate quantitative changes of the cartilage outside the laboratory experiment. The majority of the results of these studies referred to subjective, semi-objective or symptomatic parameters, allowing merely indirect conclusions in respect to the regeneration of damaged cartilage structures. Therefore, in the present study, and for the first time on humans in vivo, MR-Technology will be used to demonstrate and evaluate precisely the influence of the therapy on arthrotic joint structures, using a special form of PEMF, referred to as MultiBioSignalTherapy.

2. Materials and Methods

The study was carried out on 14 female patients with a clinically confirmed record of gonarthrosis (Wirth stages II and III). The mean age of the patients was 54.4 years. All patients reported discomfort in the knee joint for more than 10 years and demonstrated a multitude of typical secondary symptoms such as pain, mobility reduction, and others. The rejection criteria for this study were: pregnancy, presence of any electronic implant, presence of metal in the area of treatment, and heart disorder. The therapy, using complex PEMF on the basis of ion-cyclotron frequency and nuclear resonance frequency was carried out using

a MultiBioSignal Therapy appliance from the company MedTec Medizintechnik GmbH, Germany type designation: Appliance MBST 1-CELLREMAKE.
The therapy consisted of nine (9) treatments sessions of one (1) hour each. They were carried out on consecutive days with a break at the week-end. For the treatment, the knee joint was rested in a specially designed treatment coil which was controlled by a control unit. Through the control unit, the treatment coil received the commands to generate the complex therapy fields that are typical for the MBS therapy. The control unit did also guarantee a predefined standard of therapy.

The MBS therapy is based on the use of static and highly complex, varying magnetic fields. It acts directly upon the living organism and biological structures. In order to make a treatment appliance available that transports ions and especially protons that have a directed impact on the mobility of the ions in any given body area of a humans or animals, the emitting energy of the special air coil is selected at such a high level as to ascertain that the energy induced in the electrolyte liquid augments the thermal energy, without, however allowing the thermal energy level to go beyond the limit values of a so-called cell specific amplitude window.

Immediately before the first treatment session and 10 weeks after the last therapy unit, the cartilage changes of the patients were examined by means of nuclear resonance tomography. In this procedure, the data regarding the characteristics of the cartilage structures was recorded in the way published in the studies of ECKSTEIN et al (1998) and LÖSCH et al (1997).

Nuclear resonance tomography was carried out using a 1.2T total body magnet whereby the following sequence data were applied: Flash 3 with frequency selective fat suppression, TR 45 m^3, TE 11 ms, Flip angle 30º. The acquisition time was 16 min (sagittal) at an in-plane resolution of 0.31 mm x 0.31 mm. The thickness of the layer was 3 mm (FOV = 16 cm, Matrix = 512 pixel).

With the help of this data recording method, three-dimensional reconstruction of the cartilage areas was achieved. On this basis, the volume of the cartilage as well as its thickness were determined, whereby the thickness was calculated using a 3D algorithm (see LÖSCH et al, 1997).

The statistical evaluation was carried out with a T-Test for dependent random samples, using SPSS.

3. Results

The results of the nuclear resonance tomography as given below are presented according to the areal structures. As stated above, the examination was made before and after the therapy of the patients.

Patella:
The mean thickness of the cartilage structure was 1.93 mm before the treatment and 2.24 mm after the therapeutic intervention with the help of PEMF. The changes are considered to be highly significant (see Table 1).
The change of the maximum (4.14 mm to 4.52 mm) and minimum (0.02 mm to 0.11 mm) thickness was comparably significant whereby here also, growth could be statistically proven ($p<0.05$).

Patella	Before Therapy	After Therapy	p-Value
mean thickness (mm) **x** **s**	 1.93 0,37	 2.24 0.39	<0.001
maximum thickness (mm) **x** **s**	4.14 0.81	4.52 0.88	<0.05
minimum thickness (mm) **x** **s**	0.02 0.08	0.11 0.16	<0.05
volume (mm^3) interpolated **x** **s**	 2109.28 660.75	 2459.48 655.60	<0.001
area (mm^2) Cartilage-Bone boundary **x** **s**	 912.67 170.34	 942.45 179.73	n. s.

Table 1. Mean values and standard deviations for the cartilage parameters at the patella - Comparison of the measurements made before and after the therapy. (N=14).

The volume, the computation of which was completed with yet another interpolation because of the higher measurement accuracy, also showed a significant change in value after the treatment as compared to the pre-treatment measurements. The volume increased from 2109.2 mm^3 to 2459.4 mm^3. The area surface of the cartilage at the patella was also greater after than before the treatment, the statistical proof however, could not be obtained ($p>0.05$).

Tibia med.	Before Therapy	After Therapy	p-Value
mean thickness (mm) **x** **s**	 1.25 0.30	 1.37 0.26	<0.05
maximum thickness (mm) **x** **s**	2.42 0.60	2.63 0.43	<0.05
minimum thickness (mm) **x** **s**	0.29 0.08	0.31 0.00	n. s.
volume (mm^3) interpolated **x** **s**	 1343.36 446.61	 1511.67 342.49	<0.05
area (mm^2) Cartilage-Bone boundary **x** **s**	 930.03 255.85	 906.54 105.55	n. s.

Table 3. Mean values and standard deviations for the cartilage parameters of the medial tibia joint surface – Comparison of the measurements made before and after the therapy. (N=14).

Tibia lat.	Before Therapy	After Therapy	p-Value
mean thickness (mm) **x** **s**	 1.64 0.49	 1.67 0.35	<0.01
maximum thickness (mm) **x** **s**	 3.30 0.98	 3.38 0.73	<0.01
minimum thickness (mm) **x** **s**	 0.31 0.00	 0.31 0.00	<0.01
volume (mm^3) interpolated **x** **s**	 1706.83 630.84	 1739.23 453.24	<0.05
area (mm^2) Cartilage-Bone boundary **x** **s**	 896.69 232.44	 897.29 165.35	n. s.

Table 2. Mean values and standard deviations for the cartilage parameters of the lateral tibia joint surface – Comparison of the measurements made before and after the therapy. (N=14).

Tibia:

The results obtained for the lateral and medial cartilage structures of the tibia (see tables 2 and 3) show developments that were like those obtained with the patella. Laterally, the tibia shows a mean cartilage thickness of 1.64 mm respectively 1.25 mm. After the treatment with PEMF the corresponding values were 1.67 mm respectively 1.37 mm. These values were statistically confirmed. These modifications also become apparent when considering the results for the maximum and minimum thickness and volume of the cartilage.

Femur	Before Therapy	After Therapy	p-Value
mean thickness (mm) **x** **s**	 1.62 0.25	 1.54 0.21	n. s.
maximum thickness (mm) **x** **s**	 3.61 0.38	 3.50 0.58	n. s.
minimum thickness (mm) **x** **s**	 0.27 0.11	 0.22 0.15	n. s.
volume (mm^3) interpolated **x** **s**	 9214.30 1862.46	 8349.79 1555.34	n. s.
area (mm^2) Cartilage-Bone boundary **x** **s**	–	–	–

Table 4. Mean values and standard deviations for the cartilage parameters of the femur – Comparison of the measurements made before and after the therapy. (N=14).

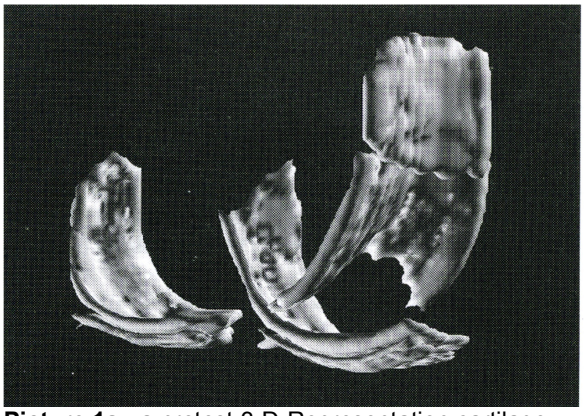
In this respect, the enormous augmentation (1343.3 mm^3 to 1511.6 mm^3) of the cartilage volume at the medial part of the tibia becomes apparent. This is a growth of 13%. Adaptation of the cartilage structure at the tibia could also be recognised, but a statistical confirmation, in this respect, could not be obtained ($p>0.05$).

Femur:
The results obtained in respect to the femur did not allow for any statistical confirmation (see table 4). This was, at least partially, caused by problems arising from the measurement technology, problems that cannot be discussed here.

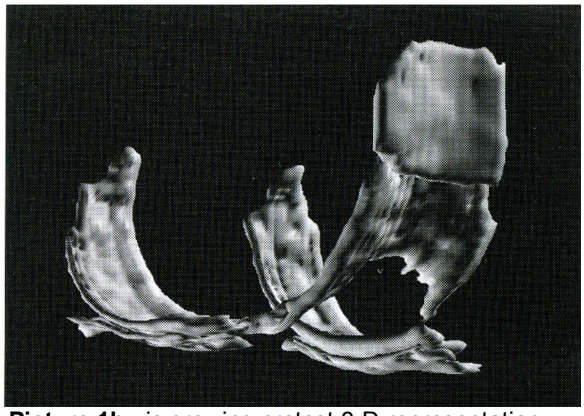
4. Discussion

The results clearly show that there is distinct growth in respect to the cartilage structures after the treatment with three-dimensional PEMF using the therapy equipment as indicated in Materials and Methods above. Such growth has hitherto not been described for humans in vivo. The reasons for this are also to be found in the fact that with the methods that were hitherto available, an acceptable quantification of cartilage structures could hardly be obtained. Since this problem has become an object of intensified scientific concern, it is now possible, with the help of nuclear resonance tomography, to close this gap forever. Especially the possibility to freely choose the layers as well as the relative low thickness of these layers, allow for augmented safety in respect to the accuracy of the results. The studies of TRÄGER et al (1995) and ECKSTEIN et al (1998) showed that the evaluation of joint cartilage as well as cartilage defects can be carried out with great accuracy. This method allows for the first time to differentiate the joint liquid from the joint cartilage by means of a distinct difference in signal. In that way, the joint liquid enhances the contrast and therefore allows a better evaluation and quantification of the cartilage structures. Especially ECKSTEIN et al (1998) obtained a highly reliable quantification of the cartilage volume and the cartilage thickness with the method that has been used in this study. The direct consequence is, that the method used in this study is to be regarded as an adequate technique for the quantification of cartilage, and furthermore allows for the determination of change and adaptation in respect to the tissue under examination. It is to be noted, however, that some difficulties were encountered in this study in respect to the quantification of the characterisation of the cartilage of the femur. These difficulties can also be deduced from the corresponding results. In respect to the highly reliable measurement parameters "cartilage thickness" and "cartilage volume" in connection with the patella and both tibia plateaux we obtained clear-cut results that also survived statistical scrutiny. This was only partly so in respect to measurements of the area. This, however, does also go conform with the results presented by ECKSTEIN at al (1998) and LÖSCH et al (1997) who, especially in respect to structures with more important curvatures, report technical problems by the measurements in relation to a three-dimensional quantification.
There have been some studies regarding the positive influence of PEMF on the treatment of cartilage defects (TROCK et al, 1993; SAKAI et al, 1991; RIZKALLA et al, 1991; and others). The results obtained were quantified in various ways in the studies referred to. In the present study, the results obtained in a treatment with complex PEMF on humans in vivo are quantified for the first time. The patients of the MBST study showed more or less distinct cartilage defects. All values measured before and after the treatment were below the values obtained from measurements of a healthy knee. ATHESIAN et al (1991) determined a mean thickness of the cartilage at the patella of 3.33 mm, at the lateral tibia plateau of 3.51 mm and at the medial tibia plateau of 2.42 mm.
The patients belonging to the test group of this study had values that were distinctly lower than the values presented by ATHESIAN et al (1991). The values obtained by those authors in respect to the other parameters that can be used for comparison, also show that the patients of our test group show considerable cartilage defects. It does, however, become clear, that after the therapeutic intervention, these values are closer to the normal reference values, and it is therefore evident, that the MBS therapy has induced positive adaptations.

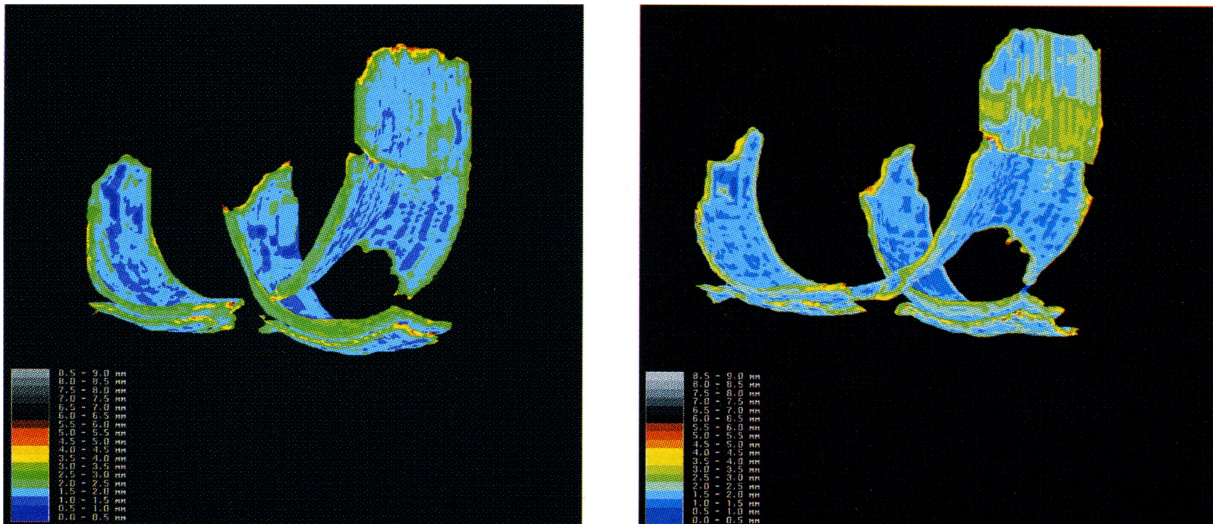
PEMF procedures have been part of successful fracture treatment for years. The fundamental principle in this respect is the recognition of the piezoelectric mechanism of the bone structures. The crystalline structures react to mechanic stress by generating electric activity (NAGAI & OTA, 1994). As stress causes electric activity, it is assumed that stress dependent morphological adaptations are equally generated by the stimulation originated by the electromagnetic fields in the method applied in this study (AARON et al, 1993). It is clear that the electric characteristics of cartilage structure are somewhat more complex than those encountered with bone structures. Nevertheless, one can also use those fundamental phenomena when dealing with cartilage. The organising matrix of the cartilage tissue consists of conglomerates of muco-polysaccharides and hyaluronic acid that are of importance for this mechanism. Mechanical stress caused by structures or molecules results in the immediate generation of electric activity (ROTHSCHILD, 1996). Tension differences within the collagen structures of the cartilage tissue also cause electric reactions. Accordingly, especially alternating electrical signals, caused by mechanical stress, cause the transport of electrical molecules in and out of the cartilage structures, and accordingly, they have a positive influence onto the metabolism. Electrical energy, brought in from the outside, causes, as in the case of bone, adaptations in the cartilage. In these adaptations the collagen structures in the cartilage tissue align according to the energy lines of the magnetic/electric field (LIU et al, 1996). Additionally, the metabolism is stimulated, causing a positive stimulation of the nutritional balance and an inhibition of the degeneration of cell structures. According to ROTHSCHILD (1996), the use of PEMF causes an augmentation of DNA synthesis in the cartilage of up to 20 % and an augmentation of collagen production of up to 300 %.



Picture 1a : a pretest 3-D-Representation cartilage cartilage structures



Picture 1b : is growing pretest 3-D-representation cartilage structures



Picture 1c : representation of the cartilage thickness before (left) and growing dark

Especially the latter phenomenon is (in accordance with the studies of LIU et al, 1966) responsible for the fact that within the scope of our study, there are such positive, quantifiable influences on the degenerated cartilage structures of the patients.

The adaptations of the cartilage structure could mainly be seen in the marginal regions, although corresponding adaptations to the stimulus could also be recorded from other areas.

The illustrations 1a through 1c show the three-dimensional pictures of the cartilage areas of a patient before and after the therapy. These results show that the treatment caused regeneration, respectively growth of the cartilage or cartilage-like structures, and that these adaptations were, at least in part, quite massive.
In the case of this 57 year old female patient a strong case of gonarthrosis with grade III chondropathy of the inner and outer slide bearing as well as a synovitis caused by irritation were diagnosed in the right. After the treatment, the illustrations show distinct regenerative processes of the cartilage structures. These results of these adaptations are furthermore conform with the subjective information from the patient.

It seems, however, that complex PEMF also activates all cartilage cells as has already be shown in animals (LIPIELLO et al, 1990). Furthermore, it seems that complex PEMF also has a positive influence on the regeneration of cartilage cells that have already been damaged. By using PEMF, LIPIELLO et al (1990) could demonstrate the production of Muco-polysaccharides that, otherwise can only be observed in juvenile cell structures. With the help of PEMF, true chondrogenesis can be proven. In this process, mesenchymatic cells are stimulated to chondrocytes in defective marginal areas, something that was suspected by ROTHSCHILD (1996). Hereby, however, one can also demonstrate qualitative differences in respect to the effectiveness of the electromagnetic fields. Only certain fields lead to the desired mechanisms.

The MBST Therapy appliances were characterised by the following components. The basis is a highly complex treatment apparatus with a specially designed air coil for the generation of a field with a static and a three-dimensional alternating field component using cyclotron resonance and nuclear spin resonance at the site of the tissue that is to be treated. This alternating field has a pre-defined cell biorhythm frequency. This is mainly chromatic, and amplitude modulated with a single modulation frequency in the area if ion-cyclotron- and nuclear spin frequency. Part of the functional mechanism serves the simultaneous augmentation of the internal energy of the cells within the area of treatment of the intracorpural electrolyte liquid and the augmentation of the energy of a predefined group of ions in order to enhance the transport of these ions at the cell membrane. The main idea behind this method is the transfer of as much energy as possible to the cells while maintaining the lowest possible field strength. It may, therefore, be concluded, that the PEMF-method (MBST) as used by us, is capable of inducing positive changes in the cartilage structures in respect to just about all parameters (cartilage thickness, cartilage volume, cartilage area.). These positive effect probably result 1) from the activation of intact cartilage cells or cartilage cells that are still capable of division, and 2) from an enhanced synthesis of collagen.

The results presented in this study show that the MultiBioSignal Therapy (complex PEMF method) can be used for the treatment of degenerated joint structures, whereby, however, the quantity and quality of the highly complex electromagnetic field must be considered to be of special concern (VALBERG, 1966). It is possible that the cartilage regeneration process is not even terminated at the end of the 10 weeks duration of this study. This question requires further examination. Furthermore, it seems that the method, consisting of a three-dimensional delineation of the cartilage characteristics and the subsequent quantification based on that three-dimensional delineation is very much suited to be used as a further diagnostic tool and is equally suited as a method to proof the effectiveness of therapeutic

interventions. The hitherto generally accepted statement "cartilage cannot regenerate" needs to be reconsidered in view of these new methods. It cannot be excluded that such reconsideration will lead to a different interpretation of the problem within the near future

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