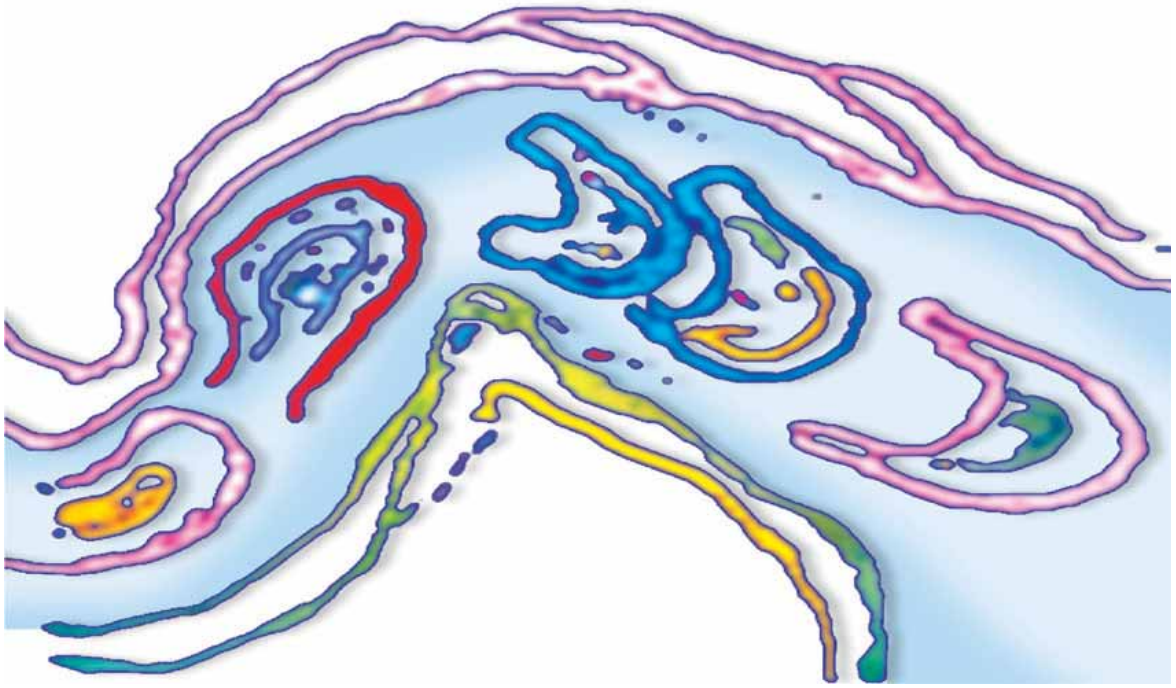
**Dr. med. R. Klopp**

# Complementary
# Physical Stimulation
## of constricted or disordered
# Microcirculation



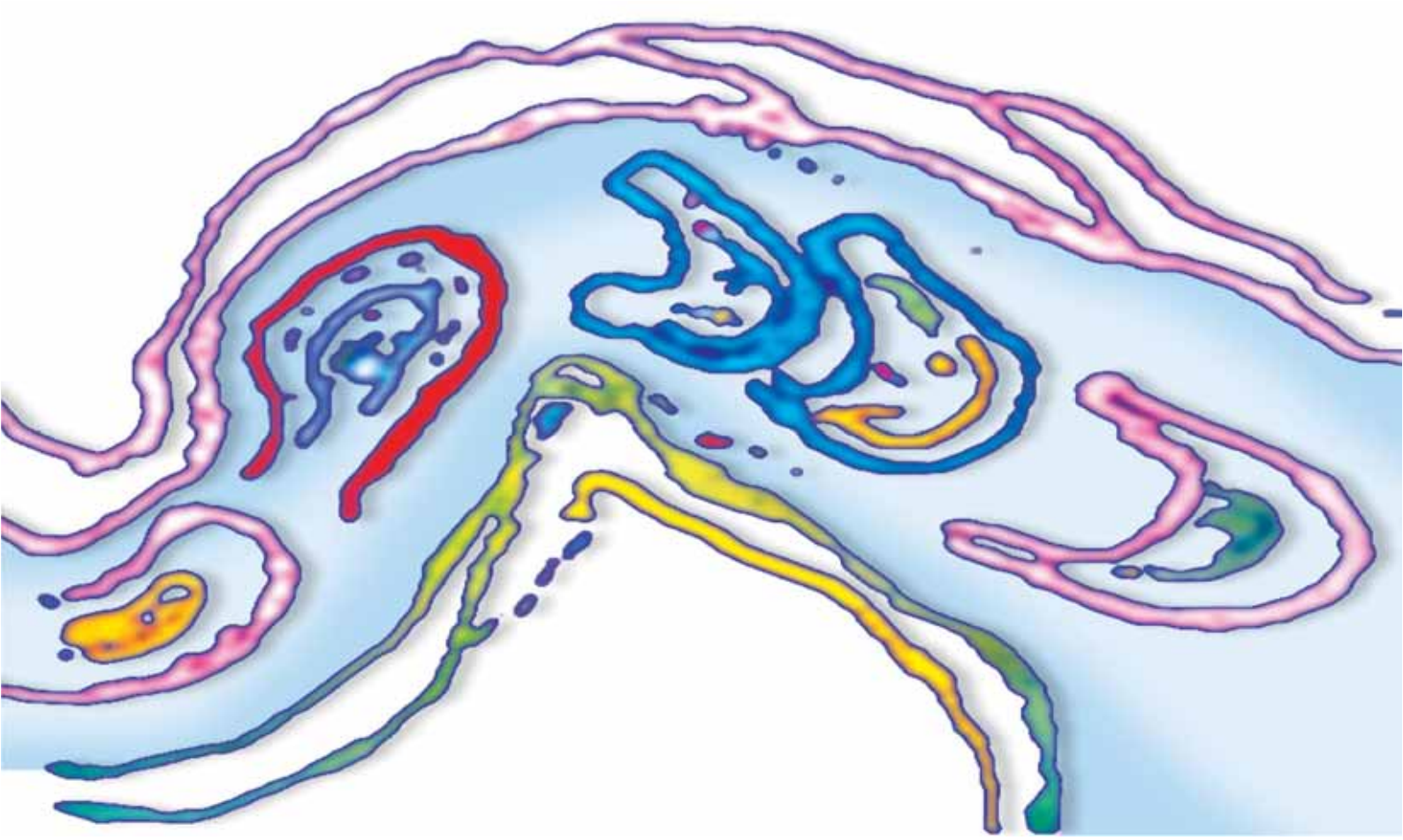
**Introduction to biomechanical, physiological and pathophysiological bases as well as selected treatment options**

**1st Edition excerpt from the german textbook "Microcirculation in the Focus of Research"**
**ISBN 978-3-033-014**

Dr. med. R. Klopp

# Microcirculation

## Research and Development of BEMER



Introduction to biomechanical, physiological and pathophysiological bases as well as selected treatment options

1st Edition excerpt from the german Mikrozirculation book - ISBN 978-3-033-01464-0

**Important note for the reader:**

The interpretation of scientific data and the therapy options mentioned in this book are the opinion of a researcher (the author is the director of the Institute for Microcirculation in Berlin, Germany). As is the case in other scientific disciplines, findings in medicine, especially in the area of microcirculation, are subject to change based on new research results and clinical experience. The author of this book took great care in reflecting the most current state of knowledge in his discussions of possible therapy options (medical indications, dosage, undesired effects).

Despite this, no guarantees can be provided. No liability of any kind will be accepted by the author, the publisher or its representatives for physical injury, damage to property or economic loss.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*This book is only an excerpt from the book "Mikrozirkulation - Im Fokus der Forschung" written by Dr. med. R. Klopp. This portion of the book focuses on the BEMER 3000 and its effects on microcirculation.*

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# Table of Contents

# Preface

"How should I know what I am thinking before I hear what I am saying." These were the words the scoffing HEINRICH VON KLEIST put into the mouth of his village judge in the "The Broken Jug".
The author of the aforementioned book has run across this kind of village judge more than once throughout his professional life. More recently, numerous "Adams" have surfaced, sharing their pseudo-scientific ideas of "magnetic field therapy", thereby discrediting scientifically based research in this area to a certain extent. This has become one of the reasons individuals from the field of academic medicine are skeptical toward or even reject new research results regarding therapy-relevant effects of pulsing electromagnetic fields. Scientific publications as well as popular science reports face the task of "separating the chaff from the wheat" and to clearly distinguish their object of research, their research methods as well as their measurement results and interpretation from the kind of pseudo-thesis that is hostile to science. This includes presenting scientifically based statements about several of the commercially available "magnetic field therapy devices," whose manufacturers make outrageous claims about alleged effects and effectiveness of their products. The author of this book sides with those who are committed to pure science.

The biggest enemy of science is…..well, not the simple-minded blithering idiot. He is only annoying. It is also not the opponent from a scientific standpoint, because he is only an ally in the quest for deeper insights. The biggest enemies of science are the semi-educated laymen. We know them all too well: they are experts on everything, want to be part of everything, know everyone and everything, have been everywhere and have seen everything….. Luckily, most of these individuals are lazy and therefore cause a limited amount of damage. They are merely a nuisance. If ignorance is paired with paranoid activity, however, the nuisance becomes a danger. In the interest of those who use therapy devices this danger must be eliminated.

The book at hand reflects a snapshot of the current state of research regarding "the influence of certain changing electromagnetic fields on microcirculation." The presented results and their interpretations are based on our own scientific testing over the past few years and further investigation is required. We are still

far from a self-contained theory about the effects of pulsing electromagnetic fields on microcirculation. Some gaps in our theory patterns will need to be bridged by hypotheses.

This field of study is “fluid” so that new developments are expected to come from continuing research.

The depiction of the current state of research is complicated and therefore cannot be made without reservations. This book will forgo superficial, entertaining, catchy and “glib” formulations in order to avoid misleading the reader about the inevitable difficulties of understanding foundations of scientific relationships and not yet fully resolved questions. Furthermore, the author would expressly like to point out that this book is not meant to encompass “everything” about the subject. Instead, some of the most essential aspects in the author’s opinion were selected, which are currently being examined in this subject area of science. Instead of presenting a string of lexical singularities, preference was given to the basic understanding of exemplary legitimate correlations and formulated hypothesis. The reader thus cannot be spared form being lectured about some scientific fundamentals.
Consequently, this book presents a type of outline of the current state of research. A more detailed presentation of the microcirculation and its therapeutic effects can be found in the author’s monograph “The Microcirculation” which will be published shortly.

Despite his 30 years as a researcher in the field of microcirculation, the author does not view himself as knowing everything, in other words, he is a scientist.
Aside from truthfulness, the most important criterion for a scientist is not what some would initially think – an out-of-touch subject focus coupled with an elitist know-it-all attitude – it is the criterion of doubt,……the quest for the contradiction combined with the will to solve it. Therefore, this book contains many questions that have not yet found plausible scientific answers.

The author addresses his colleagues among physicians and other medical professionals as well as healthcare workers and interested medical or scientific lay personnel who not only want to know, but understand. He is looking for critical readers who have the ability to contradict productively.

Rainer-Christian Klopp
July 2007

# The effects of certain low energy pulsed electromagnetic fields on microcirculation

## Current state of research

Remarks:
The research results given in this book are based on the use of the BEMER system (Innomed International AG) and therefore cannot be transferred or applied to other PEMF systems.

Measurement data reported and their interpretation in the following chapters are based on research results acquired based on specific research designs and specific test groups and have to be evaluated in that framework. They can, therefore, not always be seen as a direct recommendation for users, and customers should refer to the manufacturer's user manual for more specific guidelines.

The images created through vitalmicroscopy are selected examples of findings and serve to illustrate certain characteristic behaviors that can be gathered from the measurement data.

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# The impact of certain changing electromagnetic fields on microcirculation, hypotheses on physical effects

---

In analogy to a pharmaceutical substance, we will first look at the physical characteristics of the electromagnetic fields used for therapy and address some important physical laws and terminology.

There is an essential difference between electrical and magnetic phenomena. Electrical charges can be transmitted from one body to another, but no parallel process exists for magnetic fields. Therefore, magnetic charges cannot move through matter in the same way electric charges are transported in electrical conductors. This means that in contrast to electrical phenomena, there are no magnetic charges and no magnetic conductors.

**Comparison of selected electrical and magnetic values:**

Area A (m2), strength of current I (Ampere A), Time t (s), voltage U (Volt V)

| Electrical Values | Magnetic Values |
|---|---|
| Existence of an electrical charge | There is no magnetic charge |
| Framework electrical point charge $Q = I \times t$ Unit Coulomb C: 1C = 1Axs | Framework magnetic pole |
| Electrical field strength $E = \frac{F}{q_p}$ Units: volt per meter V/m | Magnetic induction (flux density) $B = \frac{F}{p_p}$ Units: Tesla T: 1T = 1Wb/m² = 1V s/m² |
| Electric Displacement $\int D \times dA = q$ | Magnetic field strength $\int H \times dA = p$ |
| Electric Flux $\int E \times dA$ | Magnetic flux $\Phi = \int B \times dA$ Unit Weber Wb: 1Wb = 1v s |
| Electric energy density $w_{el} = \frac{E \times D}{2}$ | Magnetic energy density $w_m = \frac{B \times H}{2}$ |
| Dielectric constant $\varepsilon$ $D = \varepsilon \times E$ Relative permittivity $\varepsilon_r = \frac{\varepsilon}{\varepsilon_0}$ | Reciporcal permeability $\mu^{-1}$ $H = \frac{1}{\mu} B$ Reciporcal permeability value $\frac{1}{\mu_r} = \frac{\mu_0}{\mu}$ |

Für die Übertragung einer Kraft von einem Körper auf einen anderen ist erfahrungsgemäß ein unmittelbarer Kontakt zwischen den beiden Körpern nicht erforderlich, sondern es treten Experience shows that to transfer a force from one body to another, it is not necessary for the bodies to be in direct contact, but force action also occurs when the bodies are separated from each other and the space between them is empty or free of substance. An example would be the force action between electrically charged or magnetic bodies. FARADAY assumed that through the presence of a body the surrounding space becomes a carrier of physical characteristics that are dependent on the nature and condition of the body as well as the distance from it. Seen in this way, the force actions on a body are generated by the local changes the space around it experiences through the presence of another body. This is called a **field**.

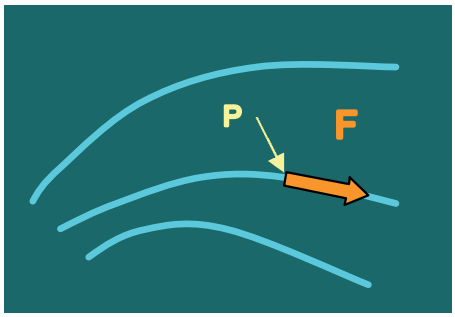
We can express the force F on a point-shaped electrical charge q within the field of another charged body as follows:

$$F(r) = qE(r)$$

The force on a (imagined point-shaped) magnetic pole with the pole strength Φ within the field of another magnetic body can be expressed as follows:

$$F(r) = \Phi H(r)$$

E(r) and H(r) are the vectors of the electrical and the magnetic field strength respectively. They specify the force that is exerted on the unit charge or the magnetic unit pole respectively at the location (r) of the field according to value and direction.
A force field can be illustrated through the lines of force or flux lines . Flux lines or lines of force are the space curves that are aligned in such a way that the direction of their tangent corresponds with the direction of the field vector, that means with the direction of the force action on all points P.




**The flux line pattern of a force field**

The flux lines specify the direction of the force field on all points P. The flux lines are plotted in such a way that the relative density of the field pattern (flux density), that is the number of flux lines that pass vertically through a plane of specified size aligned in the space, depicts a measurement for the field force. The more densely the flux lines are arranged, the higher the field force.

The electrical and magnetic force actions are expressed in the terms COULOMB-force and LORENTZ-force. MAXWELL'S equations form the basis for our understanding of electromagnetic processes. They describe the interaction of electrical and magnetic phenomena; through them the reciprocal relationship between electrical and magnetic fields are made apparent.

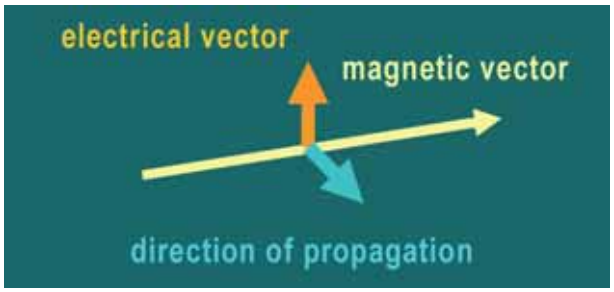
The first of Maxwell's equations expresses the physical science fact that a dielectric current (surrounded by a circular magnetic field) is created wherever the vector of the electric displacement field D or the vector of the electrical field intensity E respectively experiences a temporal change.

$$\int H \cdot dr = \int (j + \dot{D}) \cdot dA$$

According to FARADAY'S law of induction, an electric field Eind is created in a conductor loop as a consequence of a time variation of the magnetic field it surrounds. Maxwell made the assumption that this electric field is present even without the presence of the conductor loop. The conductor loop merely serves to prove the presence of the emerging electric field or the induction voltage.

This means that a magnetic field with a time variation produces a non-conservative electric field. This is the content of the 2nd Maxwell equation, which shows a remarkable analogy to the 1st Maxwell equation.

$$\int E \cdot dr = -\frac{\partial}{\partial t} \int B \cdot dA = -\int \dot{B} \cdot dA$$




In electromagnetic waves electric and magnetic field strengths swing in coinciding phases. The electric and magnetic field vectors are vertical to each other and at a right angle to the direction of the propagation. Electromagnetic waves are transverse waves.

In each electric field an amount of energy is stored that corresponds to the energy necessary for the creation of the field (separation of charges). The electric field thus is the carrier of electrostatic energy.

For further information please refer to the following technical literature on physics:
**Gerthsen Physik, H.Vogel: 19. Auflage, Springer.**

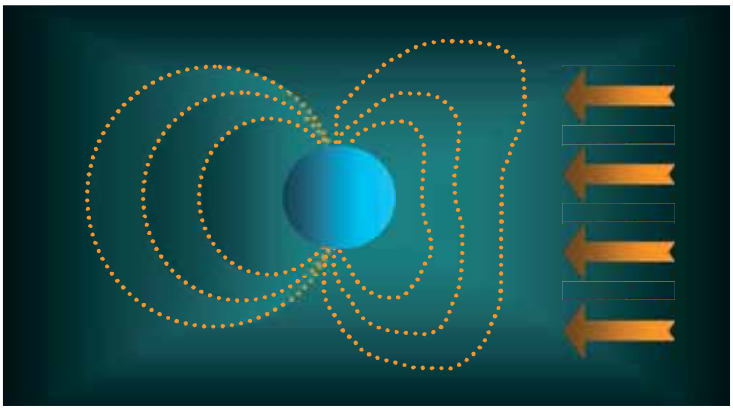
We know from a number of preliminary studies that for therapy-related effects a time variation or local change of the flux density of weak electromagnetic fields is of significance.

When using weak static magnetic fields we can determine changes in the blood distribution in the micro-vascular network of the sub-cutis in the immediate vicinity of biological boundary layers (transition to another skin layer); these changes, however, are extremely minute and of very short duration, and no therapeutic effect can be attributed to them. In the same way, when using “constant” weak electromagnetic fields we can merely determine very small microcirculatory effects in the vicinity of boundary layers (local impact on the flux line). Therapy modalities that are based only on a local change of the flux density of applied fields are therefore not suitable. Similarly, efforts to achieve improved biological effectiveness by increasing the intensity of constant fields are unsuccessful as well.

The main criterion for therapeutically effective properties of weak electromagnetic fields, according to most recent knowledge, is much more the **time variation** of the flux density than the value of the flux density itself. The flux density of the magnetic fields used for therapy purposes does not need to be significantly different from that of the earth’s natural magnetic field.

To help us classify changing electro-magnetic fields used for therapy purposes we will digress for a moment to explore the known effects natural and technically created fields have on biological systems, whereby we will limit ourselves to the exploration of the current knowledge on how magnetic fields affect the organism.

Living matter is constantly under the influence of a variety of forces that are contingent on the physical characteristics of our planet. These forces create the background for the environmental conditions to which life forms had to keep adapting over the course of evolution. The most important of these geo-physical conditions are: electromagnetic radiation with the sun as its main source, electric fields in the atmosphere, the earth's gravitational field, varied pressures from surrounding media and the earth's magnetic field.



The earth's magnetic field

Due to the varying effects of the sun's radiation (solar wind), the earth's magnetic field exhibits significant deviations in its field profile in the areas farthest away from the earth.

For the nearly stationary organism, some of these forces, like gravity, are almost constant in value and direction (e.g. intensity). Others experience relatively minor periodic or non-periodic fluctuations, such as the earth's magnetic field. In addition, some change primarily in daily or yearly cycles, such as radiation, and in conjunction with them a number of meteorological factors.
If we examine the effect of a certain factor on the organism, a two-fold qualification is necessary, allowing for physical influences and physiological response characteristics. For many of these influences we already have documented research results.

A guide to understanding the dimension of natural and technical fields exerting influence:
The static electric field (electrical field strength) of the atmosphere close to the ground is ~100 V/m. In a storm front the electrical field strength can reach thousands of V/m.
The circadian rhythm of human body functions is influenced by low frequency electromagnetic fields (~10 Hz), which have a constant impact on us from the atmosphere with a distinctive daily rhythm.
The normal electrical activity of the nervous system is accompanied by magnetic fields that can measure 10-12 to 10-11 Tesla and are in the 8-12 Hz range of the alpha rhythm of the EEG or MEG.
Temporary variations of the natural magnetic field change its intensity only in an amount below 100 ( ~8 -4 A/m). Only in rare cases will there be a change of up to 1% maximum ("magnetic storm").
Compared to natural magnetic fields (magnetic field strength ~80 A/m), technically created magnetic fields are often extremely intensified (up to ~8 6A/m).
It is well known that technically created magnetic fields with extremely high field strengths can have numerous damaging effects: disturbance of metabolic and cell division activities as well as growth processes, impact on the rate of mutations and neuro-physiological phenomena (e.g. EEG). Currently under discussion is the influence of very strong magnetic fields on molecules with dipole characteristics (proteins), radical dissociation, certain cellular activities, and more.

> During a clinical MRI the magnetic field strength impacting the patient's body is up to 200,000 times higher than that of the earth's natural magnetic field. In addition to a strong static magnetic field, the procedure employs a changing magnetic field and a radiofrequency field. Animal studies have shown reversible EKG changes like disturbances in the formation and conduction of impulses under the influence of static magnetic fields up to 1 Tesla. Based on further research results about direct and indirect effects on the visual system, the heart muscle, endoprostheses (hip replacement) and other structures, the possible damaging effects of this procedure have been defined and appropriate contraindications have been identified.

When we review the current knowledge about the biological effects of different electric/magnetic fields from the lowest field intensities of the earth's magnetic field all the way to extremely strong technically created fields with their harmful effects, we gain an open window for possible therapeutic applications in the range of a few µT to the mT range. As previously mentioned, it is not only the flux density that is important for therapy purposes but especially the corresponding time change (changing magnetic field). Similar to pharmacological substances, the question about appropriate signal characteristics arises in order to achieve optimal therapeutic effects of the applied changing magnetic field. This question is inseparably tied to the clarification and understanding of how magnetic fields work and valid evidence of their effectiveness.

Best suited to provide such evidence are molecular-biological processes (e.g. stimulating the formation and influencing the activity of proteins) and cellular interactions in the tissues during the regulation of microcirculatory transportation phenomena (e.g. influencing the distribution status of the plasma-blood cell mixture in the microvascular networks and the blood flow in the venules).

It is thanks to W. KAFKA that an optimal signal for therapeutic use was introduced: extremely slow and broadband pulsed electromagnetic fields (WRF-ELF-PEMS) of low energy. Figure 281 illustrates the electromagnetic stimulation signal suggested by W. Kafka, which is utilized in the BEMER® system **(non invasive application of certain changing magnetic fields that are in the range of the geomagnetic field with flux densities of up to 100 micro Tesla).**

Based on a number of experimental studies, W. Kafka was able to substantiate the therapeutic effect of extremely slow and broadband pulsed electromagnetic fields of low energy with proven stimulation of the molecular, intra-cellular and tissue related interactions that are the foundation of regulatory processes in organisms:

> Geared toward the support of the molecular interactions which underlie self-healing mechanisms, the BEMER concept is based on the fact that the beginning and ongoing processes of physical chemical interactions are principally tied to a change of energy in the electron configuration, so in the end to the electromagnetic activation of the nuclear, ional and molecular partners involved.

In detail, the BEMER concept aims at supporting the energy needs of the processes of molecular activation with the non-invasive application of appropriate electromagnetic fields as widely effective as possible – in other words addressing a broad spectrum of varying molecular structures.

*Other current (electro-) magnetic therapies are based on the application of static (permanent magnets) or sinusoidal, trapezoid or saw tooth, pulsed changing electromagnetic fields. The basic requirements for a form of stimulation (stimulation signal) that is suitable for the molecular conditions in the physiological system are usually not mentioned or limited to incomprehensible physical-physiological ideals – without any regard for absolutely necessary test results concerning a specific system.*

Quoted from W. Kafka, Bio-Electro-Magnetic-Energy-Regulation (BEMER): The physical concept and its application for pain producing disorders. In: G. Bernatzky (Hrsg.) Pain therapy without medication, Springer-Verlag Vienna, 2007

According to current knowledge, the biological effects of the BEMER signal are based on a not yet fully clarified influence of its electrical and magnetic energy components on the physical-chemical reactivity of the molecular components (mostly proteins) participating in the regulatory processes. With an appropriate chronological sequence of intensity of the chosen electromagnetic stimulation signal, which is mainly dependent on the molecular mass-charge ratio (similar to the physical-chemical structure-affinity properties of a pharmaceutical agent), the effects of these fields can stimulate regulatory processes and influence transportation phenomena by increasing the likelihood of reactions through "electromagnetic pharmaceuticals", so to speak.

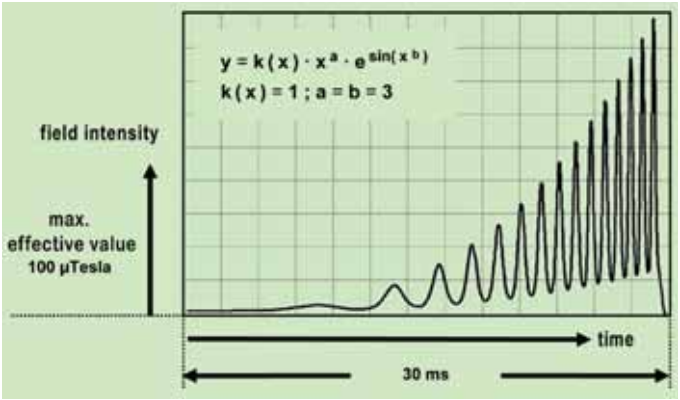
Regarding the importance of genetic factors on the formation of and influence on the activity of proteins, we refer to the differential up- and down regulation of gene-expressed protein amounts on bone marrow stem cells (bone- and cartilage cells). In the framework of comparative gene-chip analyses (Affymetrix) we could demonstrate that the amount of expressed proteins among the individual cell types in part increases, in part decreases and in part remains unchanged compared to those not treated with an electromagnetic field (interestingly so among others with respect to the expression of cancer causing oncogenes). This was interpreted as an influence on the protein production.

With reference to W. KAFKA, N. SCHÜTZE, M. WALTHER: Orthopädische Praxis (2005) 41, 22-24

**Figure 281**

**Electromagnetic stimulation signal according to KAFKA (BEMER ®)**

(reproduced with the kind permission of W. KAFKA)



The above named views regarding molecular mechanisms are, to a large extent, still of hypothetical character. Current experimental and clinical test results regarding the effects of the BEMER system supporting these views are:

In the context of research of the hemoglobin-oxygen affinity of erythrocytes in healthy adults we were able to establish that an 18-day whole body therapy with the BEMER system (2 x 20 minutes per day, 35 µT) led to a significant increase of the ATP content (comparison of measurement data before therapy and on the 18th day of treatment: ~14% change in values). The 2.3-BPG values showed an increase of ~12% in this time frame.

W. KAFKA, K. SPODARYK: Fizoterapia (2003) 11 (3), 24–31

W. KAFKA and K. SPODARYK found a significant decrease of radical induced lipidperoxidation of the erythrocytes (indicated by increased activity of glutathione reductase) in healthy adults after 3 weeks of BEMER whole body therapy (20 min. per day, 35 µT).

In the context of a series of clinical tests, marked improvements were observed in slowing the progression of the disease for patients with cytostatic polyneuropathy (4 week therapy with the BEMER system, 8 min. 3 times per day, 35 µT).

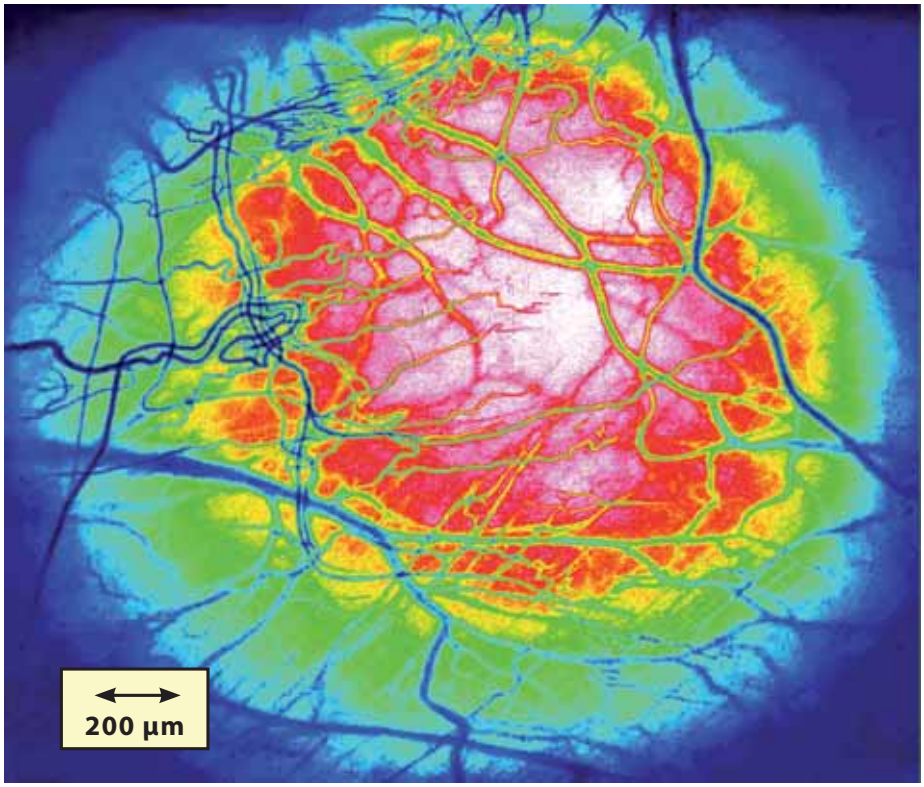
M. GABRYS: Dt. Z. f. Onkologie (2004) 36, 154–156

Clinical findings for treatment of pain, rehabilitation, and for supporting tissue disorders, use of the BEMER system increases physical capacity.

K. SPODARYK: Medizina Sportiva (2002) 6, 19–25

W. KAFKA, N. SCHÜTZE, M. WALTHER: Orthopädische Praxis (2005) 41 (1), 22–24

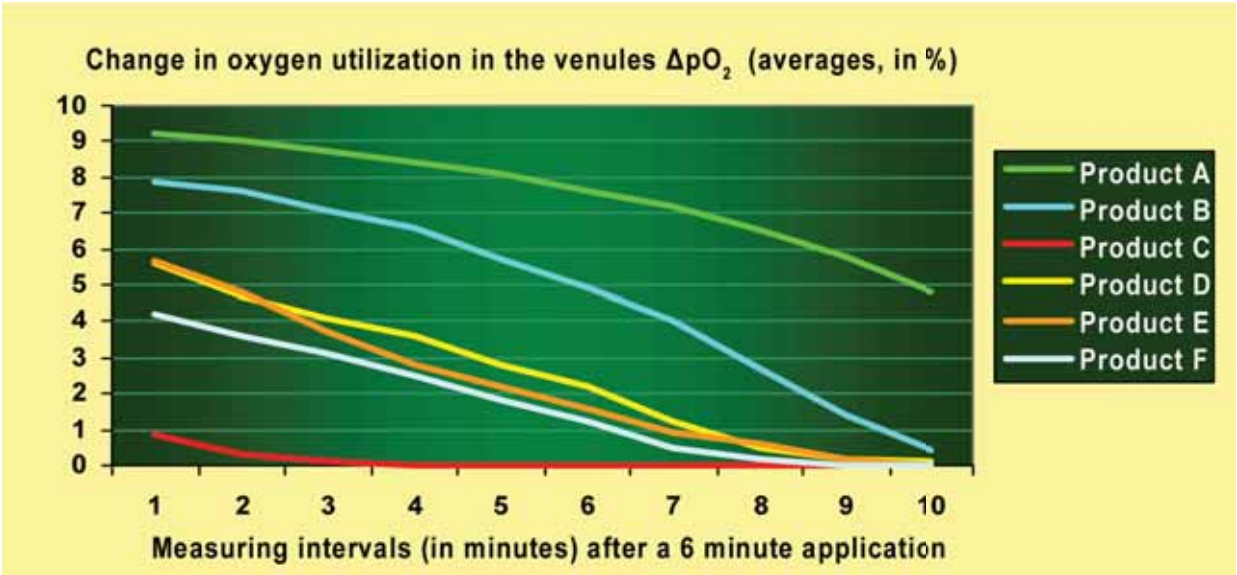
At the center of clinical-pathophysiological interest are the effects of suitable pulsed electromagnetic fields on the functionally most important part of the human circulatory system, the microcirculation.



In the context of comparative research it became evident that the signal used in the BEMER system leads to optimal results in the area of microcirculation.

| | |
|---|---|
| **Test Sample** | Sample Size: $N_{total}$ =12<br>Male test subjects, no pathologic abnormalities detected, under 30 years of |
| **Test System** | 6 standard magnetic or electro-magnetic therapy systems<br>▶ Product A: BEMER 3000<br>▶ Product B: Electromagnetic Therapy System<br>▶ Product C: Therapy System With Static Magnet<br>▶ Product D: Electromagnetic Therapy System<br>▶ Product E: Electromagnetic Therapy System<br>▶ Product F: Electromagnetic Therapy System<br>Products B, D, E, and F are utilizing saw-tooth, square and triangular |
| **Applications** | Each test subject was treated in consecutive intervals of 24 hours under the same basic conditions with all 6 products (randomized) One-time application of 6 minutes for the entire body Comparable intensities of the |
| **Measurement Intervals and Timing** | Observation time – 16 minutes;<br>Equidistant timing of measurement, Initial values were determined before the application, followed by a 6-minute therapy time; subsequent measurements were taken after 1 min., 2 min., 3 min., 4 min., 5 min., 6 min., 7 min., 8 min., 9 min. and 10 min. |
| **Targeted Tissue** | Sub-cutis (left forearm) defined target area. |
| **Measurement Methods** | ▶ Laser-doppler-microflow-measurement and white light spectroscopy. Defined conditions of macro-circulation and temperature regulation. |
| **Parameter** | ▶ Oxygen utilization in the venules ΔpO2 (percentage of change in comparison to the initial measurements before treatment) |
| **Statistical analysis** | Wilcoxon rank-sum test (MWW), a = 5% |

Test results are shown in the following **figure #282**




The measurement data for product A show a statistically significant difference to the data of all other products.

To assess the effects of a suitable changing electromagnetic field on the microcirculation we look at the main characteristics that determine its functional state. First we will focus on the **immediate effects of a suitable changing electromagnetic field on the microcirculatory network close to the surface in the sub-cutis and in the intestine** for a biometrically defined sample test group of subjects exposed to stress and infection of middle age. For the selection of the therapy system the test results from figure 282 above were the deciding factor.

**Research Design**

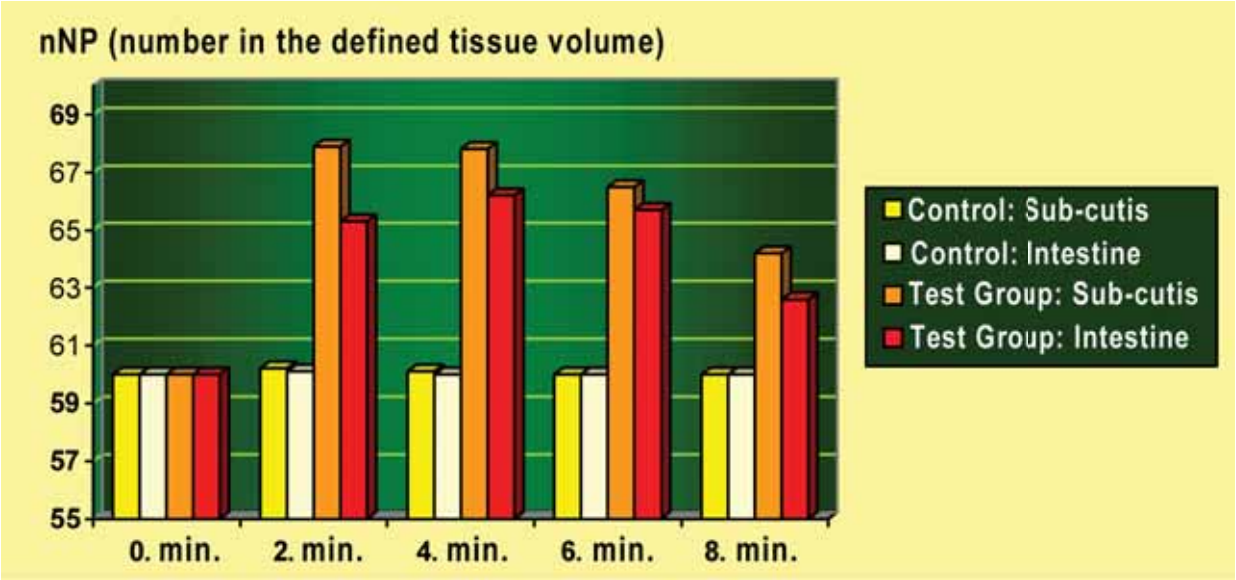
| | |
|---|---|
| **Test Sample** | Test sample size $N_{total}$ =36<br>Male test subjects, age ~30 years of age, no pathological abnormalities<br>Exposure to stress and infection |
| **Partial Test Samples** | 2 equal partial test samples of n=18:<br>▶ Control group: no treatment (placebo)<br>▶ Test Group: treatment with a changing pulsed electromagnetic field |
| **Test System, Application** | Blind study, GCP criteria<br>Pulsed changing electromagnetic field BEMER 3000<br>One-time treatment of 2 minutes (intensity level 3) |
| **Measurement Intervals and Timing** | Observation time of 8 minutes, equidistant measurement intervals:<br>Zero minutes (determination of base values immediately prior to the application), subsequent 2-minute treatment, with data measurements following in the 2nd, 4th, 6th, and 8th minute. |
| **Target Tissue** | Synchronized measurements in two target tissues:<br>Sub-cutis (abdomen, regio epigastr.)<br>Intestine (rectum, lamina muscolaris) |
| **Measurement Methods** | ▶ Intravitalmicroscopy with computer assisted image processing. (documentation of findings: high-speed camera, 35 mm film, high resolution, up to 120 pictures per second).<br>▶ Vitalmicroscopic reflection spectrometry.<br>▶ Laser-DOPPLER-microflow-measurement and white light spectroscopy.<br>Capture of complete interconnected micro-vascular networks with defined tissue volume V=1200µm3 (diameter of vessels d≤200µm). |
| **Parameters** | ▶ Number of blood cell perfused nodal points nNP.<br>▶ Changes in the venular flow rate ΔQven.<br>▶ Area below the envelope of the amplitude-frequency-spectrum of the (spontaneous) arteriolar vasomotion Avm.<br>▶ Oxygen utilization in the venules $\Delta pO_2$.<br>▶ Number of white blood cells adhering to a defined venular wall nWBC/A.<br>▶ Localized change in concentration of ICAM-1. |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), a = 5% |

The measurement results are compiled in the following figures 283 to 287.

## Figure 283

**Measurements for the parameter "number of blood cell perfused nodal points nNP" (mean values) in the target tissues sub-cutis and intestine after 2 minutes of treatment with a certain pulsed electromagnetic field (BEMER) for test subjects exposed to stress and infection compared to a non-treated control group.**

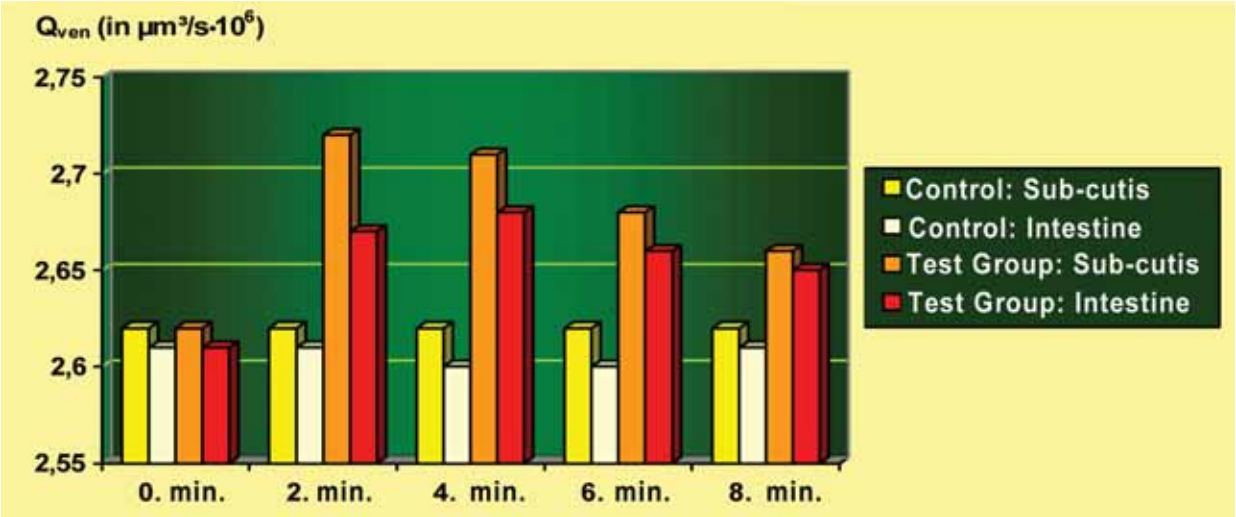
No significant parameter changes in the control group. The measurement data of the test group show a significant change from the base values and from those of the control group after 2 minutes.




## Figure 284

**Measurements for the parameter "venular flow rate $Q_{ven}$" (mean values) in the target tissues sub-cutis and intestine after 2 minutes of treatment with a certain pulsed electromagnetic field (BEMER) for test subjects exposed to stress and infection compared to a non-treated control group.**

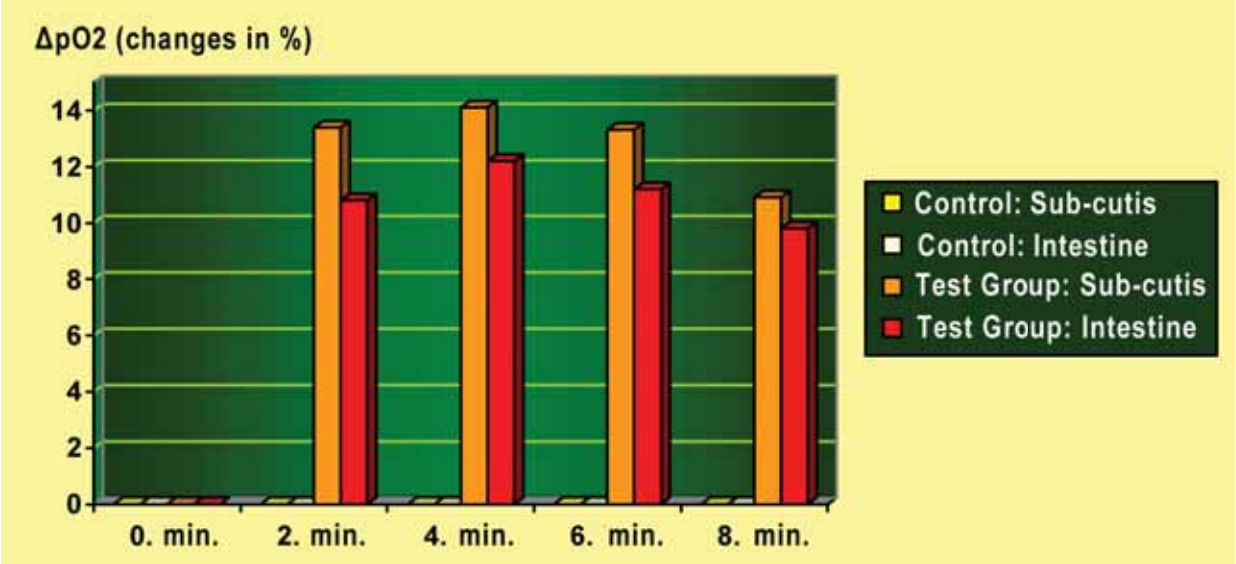
No significant parameter changes in the control group. The measurement data of the test group show a significant change from the base values and from those of the control group after 2 minutes.



## Figure 285

**Measurements for the parameter "area below the envelope of the amplitude-frequency spectrum of the (spontaneous) arteriolar vasomotion $A_{vm}$" (mean values) in the target tissues sub-cutis and intestine after 2 minutes of treatment with a certain pulsed electromagnetic field (BEMER) for test subjects exposed to stress and infection compared to a non-treated control group.**

No significant parameter changes in the control group. The measurement data of the test group show a significant change from the base values and from those of the control group after 2 minutes.




## Figure 286

**Measurements for the parameter "oxygen utilization in the venules $\Delta pO_2$" (mean values) in the target tissues sub-cutis and intestine after 2 minutes of treatment with a certain pulsed electromagnetic field (BEMER) for test subjects exposed to stress and infection compared to a non-treated control group.**

No significant parameter changes in the control group. The measurement data of the test group show a significant change from the base values and from those of the control group after 2 minutes.

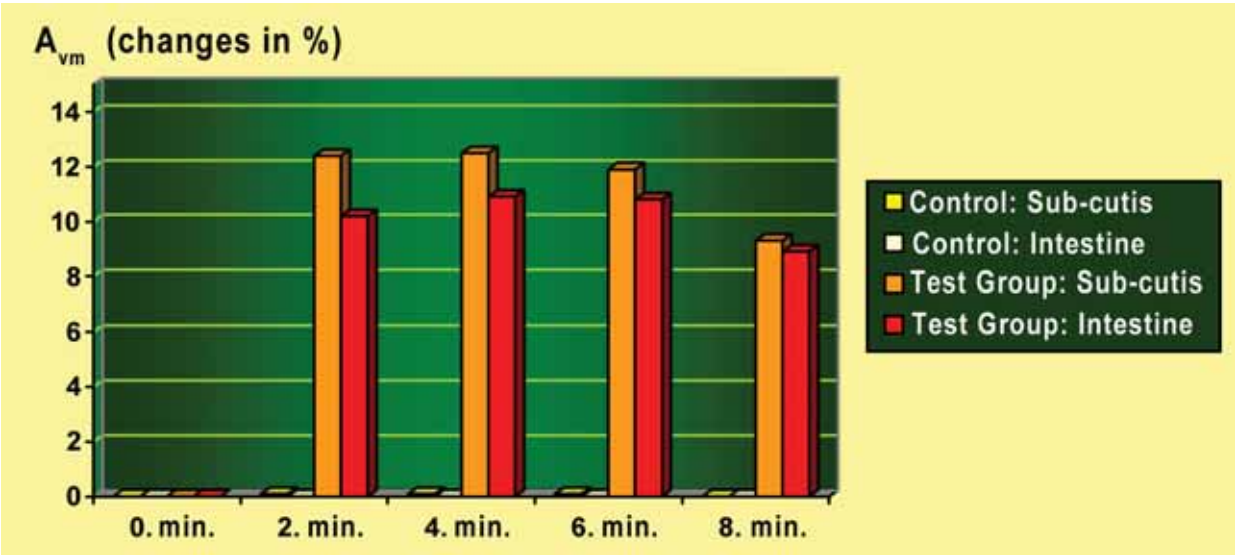
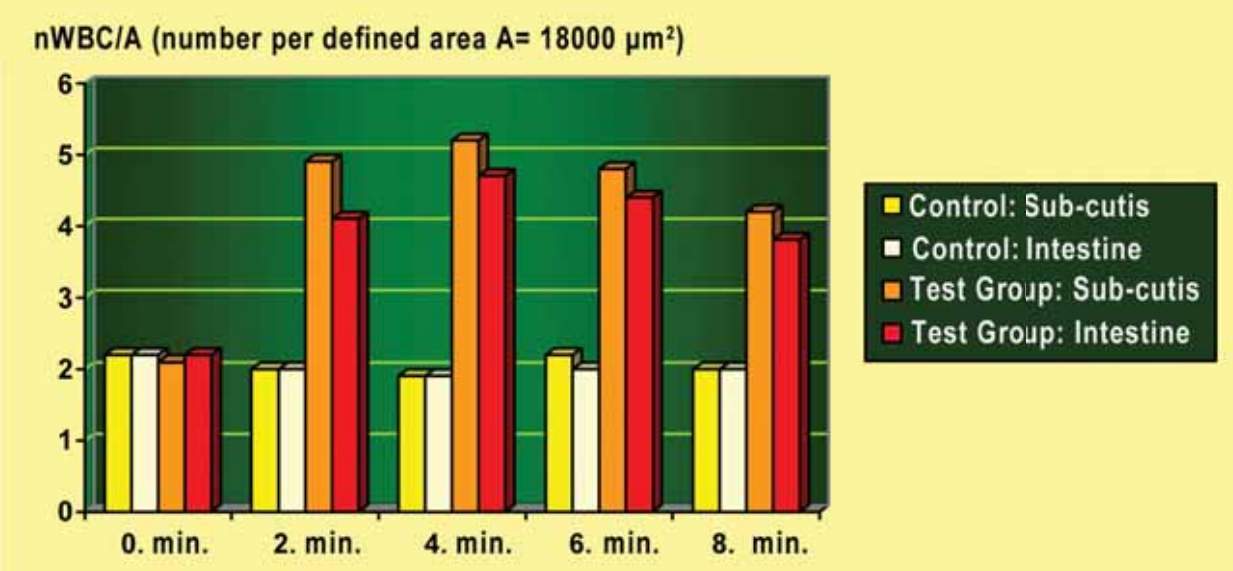


**Figure 287**

**Measurements for the parameter "number of white blood cells adhering to a defined venule wall nWBC/A" (mean values) in the target tissues sub-cutis and intestine after 2 minutes of treatment with a certain pulsed electromagnetic field (BEMER) for test subjects exposed to stress and infection compared to a non-treated control group.**

No significant parameter changes in the control group. The measurement data of the test group show a significant change from the base values and from those of the control group after 2 minutes.




The test sample showed the following behaviors of microcirculatory characteristics in the subcutaneous and intestinal target tissues after the application of a certain pulsed electromagnetic field (BEMER):

>> Complex changes in the functional state of the microcirculation to a biologically relevant degree (increased venular flow rate from the micro-vascular networks, expanded distribution of the plasma-blood cell mixture in the capillary network, increased spontaneous vasomotion in the arterioles). This translates to a localized extension of microcirculatory function, resulting in increased oxygen utilization in the venules.

>> Due to the increased venular flow rate and the perfusion of an increased number of micro vessels, the micro-hemodynamic conditions for an uninterrupted sequence of the first steps of an immune reaction in the test subjects exposed to infection are improved (increased adhesion of white blood cells, corresponding localized changes in concentration levels of ICAM-1 [measurement data not represented here]).

>> Two parallel changes in parameters occur in the sub-cutis and the intestine. This means the criteria changes apply to two organs that are representative of circulation and immunological activity.

They therefore are relevant for the entire organism.

>> The criteria changes are temporary (additional tests show a return to the base values after about 15 minutes).

One considers: The data refer to the investigation (Design) of a certain selected sample (Responder/ Non Responder) and to the research methods here used.

The effects of **varying therapy durations** and **varying intensity levels** within the flux density levels of the therapy system used (see figure 281) on the degree of change in parameters and the time it takes for the changes to subside can be gathered from the following research series.

**Research Design**

| | |
|---|---|
| **Test Sample** | Test sample size Ntotal =30<br>Male test subjects, ~35 years of age, no pathological abnormalties,<br>Exposure to stress and infection<br>Participation in two test series at least 3 days apart |
| **Test Series, Partial Test Samples** | Variation of the length of therapy (one time) with identical intensity level(level 3): 3 equal partial test samples of n=10<br>▶ Therapy time 2 minutes<br>▶ Therapy time 10 minutes<br>▶ Therapy time 20 minutes<br>Variation of the intensity level with identical length of therapy (one time 10 minutes): 2 equal partial test samples of n=15<br>▶ Therapy with intensity level 3<br>▶ Therapy with intensity level 10 |
| **Test System, Application** | Blind study, GCP-criteria<br>Pulsed, changing electromagnetic field BEMER 3000<br>Single therapy session each |
| **Measurement Intervals and Timing** | Observation time of 30 minutes. Equidistant measurement intervals:<br>Zero minutes (determination of base values immediately prior to the application), subsequent treatment, with data measurements following in the 2nd, 4th, 6th, 8th, 10th, 12th, 14th, 16th, 18th, 20th, 22nd, 24th, 26th, 28th, and 30th minute. |
| **Target Tissue** | Sub-cutis (abdomen, region epigastr.) |
| **Measurement Methods** | ▶ Laser-DOPPLER-microflow measurement and white light spectroscopy |
| **Parameter** | ▶ Oxygen utilization in the venules $\Delta pO_2$ |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), a = 5% |

Figures 288 and 289 provide information on the measurement data collected.

Longer therapy times do not result in added contributions to the parameter changes, however, they prolong the time it takes for the changes to subside.

**Figure 288**

**Measurements for the parameter "oxygen utilization in the venules $\Delta pO_2$" (mean values) in the subcutaneous target tissue after treatment with a certain changing pulsed electromagnetic field (BEMER) of varying application times (2 min., 10 min., 20 min.; intensity level 3) for test subjects exposed to stress and infection.**

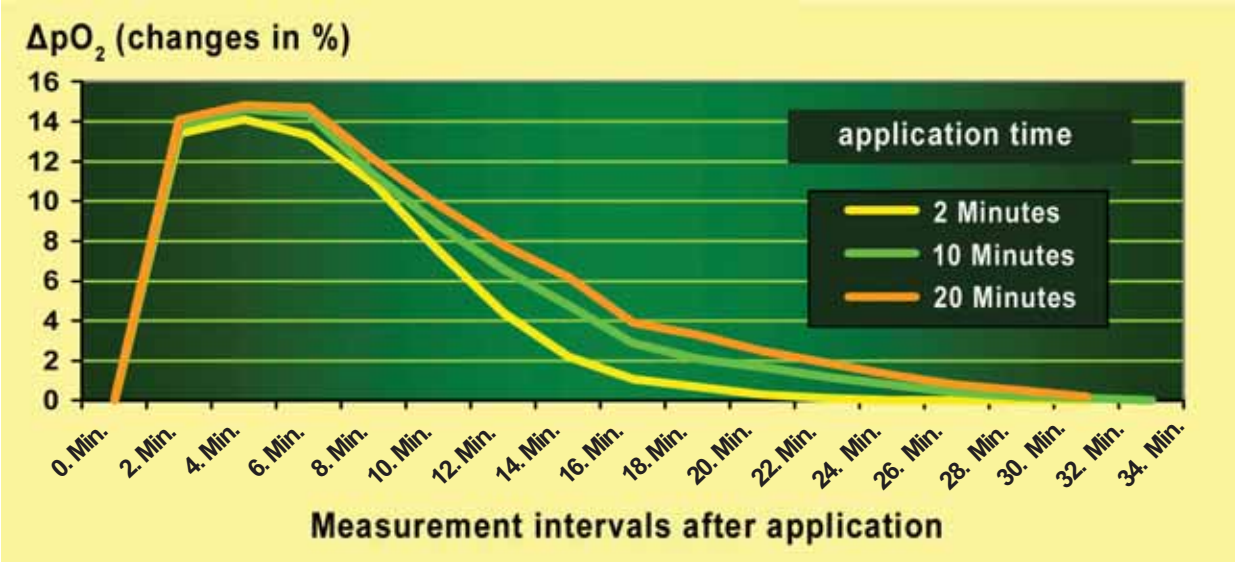
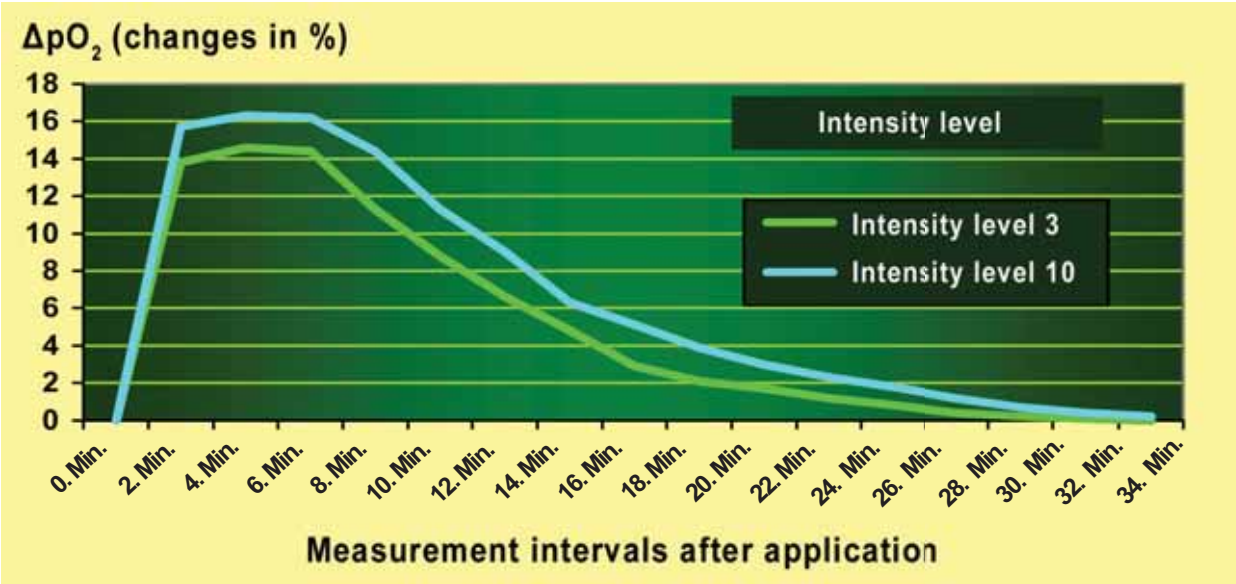



**Figure 289**

**Measurements for the parameter "oxygen utilization in the venules $\Delta pO_2$" (mean values) in the subcutaneous target tissue after treatment with a certain changing pulsed electromagnetic field (BEMER) of varying intensities (10 minute application, intensity levels 3 and 10) for test subjects exposed to stress and infection.**




Please note: The data refer to the research (design) for a specific selected test sample and to the applied research method.

The following figures 290 to 293 display selected vitalmicroscopic findings from the subcutaneous and intestinal target tissues regarding the effects of a certain changing electromagnetic field (BEMER) on the microcirculation.

**Abbildung 290**

**Change in the distribution of the plasma-blood cell mixture in the micro-vascular networks of the sub-cutis after a 10 minute application of a certain changing electromagnetic field (BEMER, intensity level 3).**

**(Example of vitalmicroscopic findings, 1/1000 second; capillaries, arterioles and venules).**

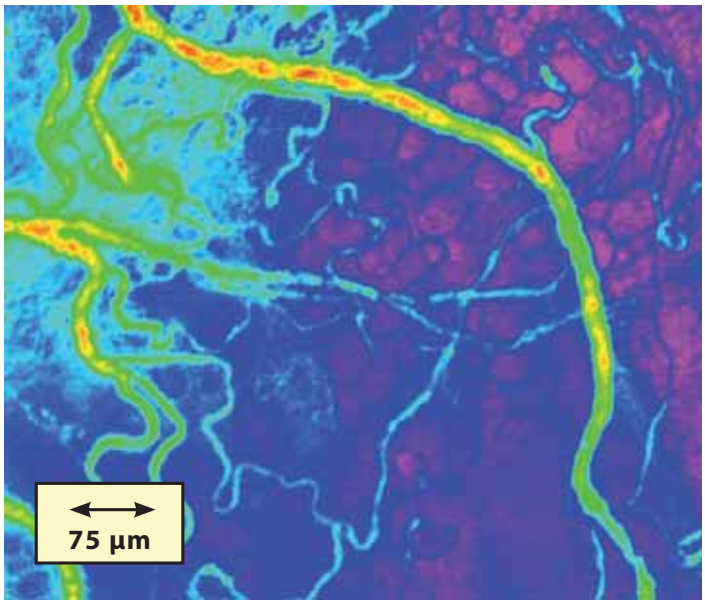
Pseudo-transformation of color of the primary images

**(the blood cell perfused micro vessels are marked in red)**

**a: Distribution before application**

**b: Distribution after 10 minutes of application**

**a**




**b**

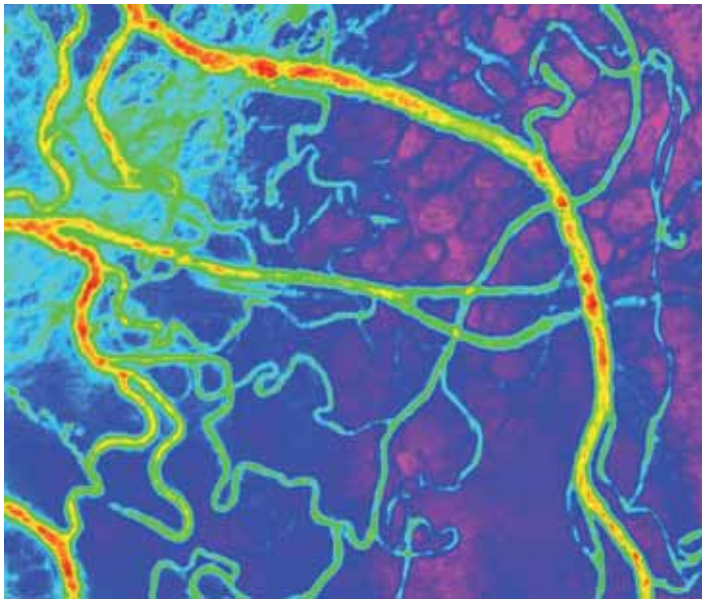
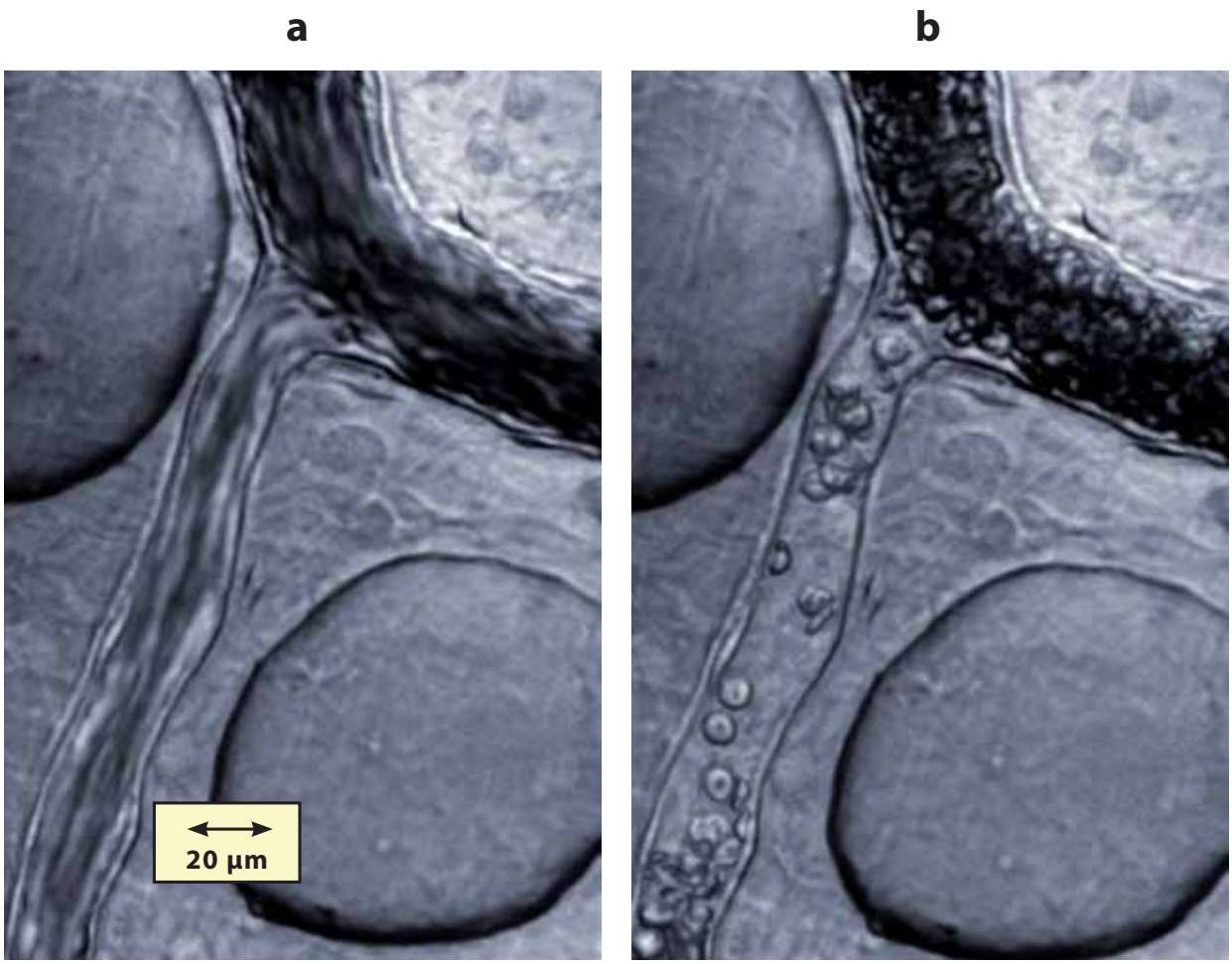


**Figure 291**

**Change in the perfusion level at micro-vascular nodal points in the sub-cutaneous network after a 10 minute application of a certain changing electromagnetic field (BEMER, intensity level 3).**
**(Example of vitalmicroscopic findings, 1/1000 second; capillaries, arterioles and venules).**

**a: Perfusion level before application**
**b: Perfusion level after 10 minutes of application**

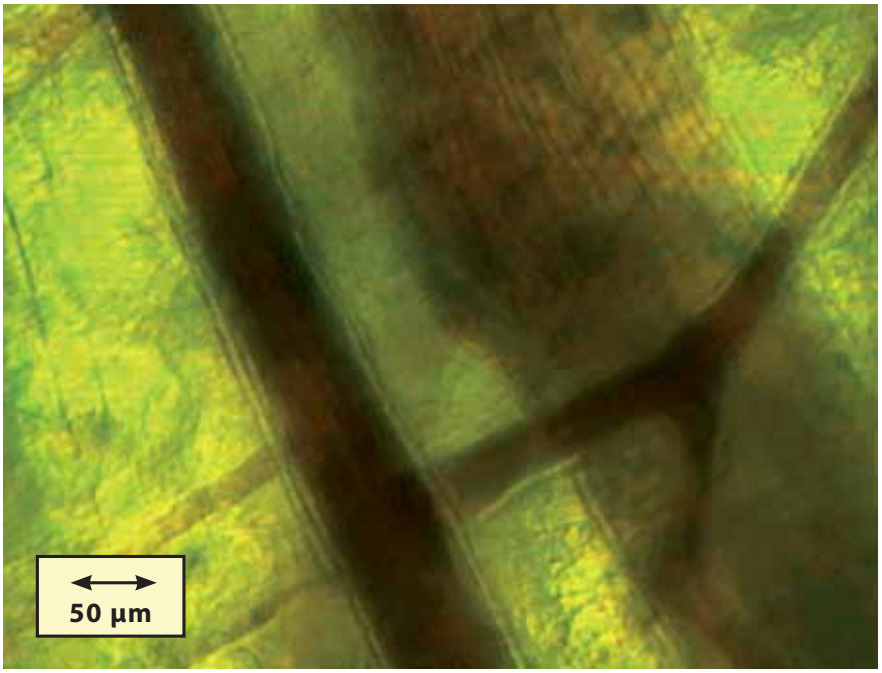


## Figure 292

**Change in the perfusion level at micro-vascular nodal points in the sub-cutaneous network after a 10 minute application of a certain changing electromagnetic field (BEMER, intensity level 3). (Example of vitalmicroscopic findings, 1/1000 second; capillaries, arterioles and venules).**

**a: Perfusion level before application.**
**b: Perfusion level after 10 minutes of application**
One considers the changes of diameter.

**a**




**b**

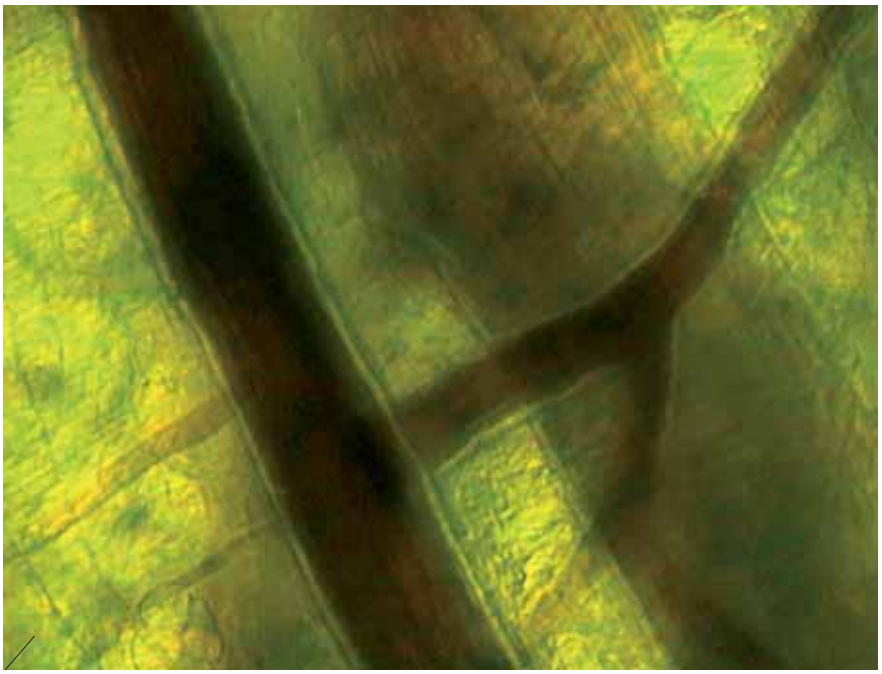
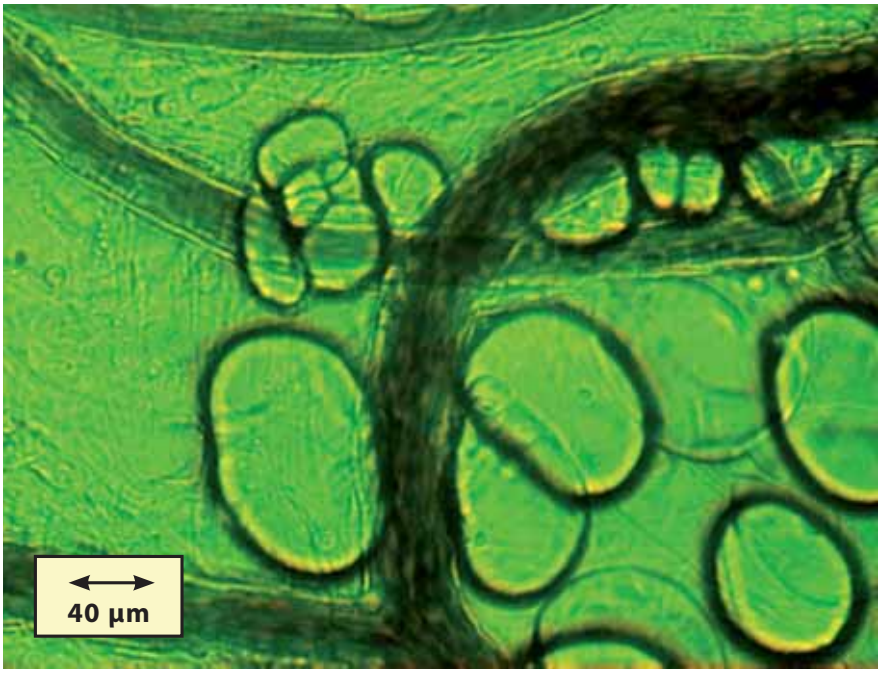


**Figure 293**

**Change in the level of vasomotion and the tonus of intestinal micro vessels after a 10 minute application of a certain changing electromagnetic field (BEMER, intensity level 3). (Example of vitalmicroscopic findings, 1/1000 second; capillaries, arterioles and venules).**

**a: Accumulation of few white blood cells before application.**
**b: Increased accumulation of white blood cells after 10 minutes of application.**

**a**




**b**

We now turn to the question if, and in which way **repeated applications** can result in increased parameter changes.

## Research Design

| | |
|---|---|
| Test Sample | Total test sample $N_{total}$ =36<br>Male test subjects, ~40 years of age, no pathological abnormalities<br>Exposure to stress and infection |
| Test Series, Partial Test Samples | ➡ Test series A<br>One-time application on one day<br>➡ Test series B<br>Three applications 2 hours apart on one day<br>➡ Test series C<br>Two applications per day 2 hours apart, within one week on<br>Two equal partial test sample groups of n=18 for each partial test group<br>► Control group: No treatment (placebo)<br>► Test group: treatment with a changing electromagnetic field |
| Test System, Application | Changing pulsed electromagnetic field BEMER 3000<br>Applications of 2 minutes each (intensity level 3)<br>Blind study, GPC criteria |
| Measurement Intervals and Timing | Observation time of 30 minutes each. Equidistant measurement intervals:<br>Test series A:<br>Zero minutes (determination of base values immediately prior to the application), subsequent 2-minute treatment with data measurements following in the 2nd, 4th, 6th, and 8th minute.<br>Test series B:<br>Zero minutes (determination of base values immediately prior to each application), subsequent 2-minute treatment with data measurements after each application following in the 2nd,4th, 6th, and 8th minute.<br>Test series C:<br>Zero minutes (determination of base values immediately prior to each application on each treatment day), subsequent 2-minute treatment with data measurements following after each application on each treatment day in the 2nd,4th, 6th, and 8th minute. |
| Target Tissue | Sub-cutis (abdomen, regio epigastr.) |
| Measurement Methods | ► Intravitalmicroscopy with computer-enhanced image processing<br>► Vitalmicroscopic reflectionspectrometry<br>► Laser-DOPPLER-microflow measurement and white light spectroscopy<br>Capture of complete interconnected micro-vascular networks with defined tissue volume V=1200µm³ (diameter of vessels d≤200µm). Defined conditions of macro-circulation and |
| Parameters | ► Number of blood cell perfused nodal points nNP<br>► Changes in the venular flow rate $\Delta Q_{ven}$<br>► Area below the envelope of the amplitude-frequency-spectrum of the (spontaneous) arteriolar vasomotion Avm<br>► Oxygen utilization in the venules $\Delta pO_2$<br>► Number of white blood cells adhering to a defined venule wall nWBC/A<br>► Localized change in concentration of ICAM-1 |
| Statistical Analysis | WILCOXON rank-sum test, a = 5% |

Research results:

The data from test series A are used for comparison, they are literally identical to the data of another research series named above (see fig. 283-287).

Test series B (3 applications two hours apart on the same day) displays parallel parameter changes for all applications, however with differing values. After the 2nd application the measurement values were somewhat increased compared to the 1st application; the changes in measurement values after the 3rd application however were slightly lower than after the 1st application. This means the documented (slight) “potentiating effect” occurring after a 2nd application on the same day does not continue with subsequent applications.

Conclusion:

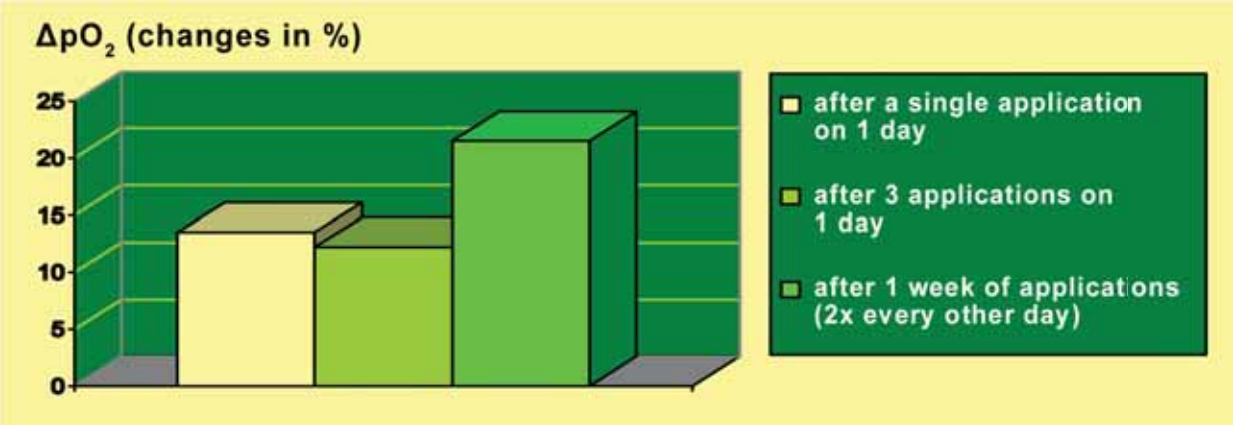
Multiple applications within a short time frame on the same day do not have a positive effect on the behavior of functional parameters of the microcirculation. A “potentiating effect” and a slower subsiding of the parameter changes occur when applications are conducted 2 day apart, twice a day, 2 hours apart, within one week on three different days (test series C).

The measurement data depicted in figure 294 for the parameter “oxygen utilization in the venules ΔpO2” give a visual illustration of how application frequency affects the change in microcirculatory parameters.

**Figure 294**

**Measurements for the parameter “oxygen utilization in the venules ΔpO2” (mean values) in the target tissue sub-cutis for test subjects exposed to stress and infection after applications with varied frequencies.**

**Test Series A:**
Collection of measurements immediately after the 2 minute application.
**Test Series B:**
Collection of measurements immediately after the 3rd application (2 minutes) on the day of treatment.
**Test Series C:**
Collection of measurements immediately after the 2nd application on the last treatment day after 1 week of treatments (2x2 minutes every other day).



The influence of a beneficial therapy frequency on increased and prolonged microcirculatory effects (test series C) can be seen in the data displayed in figures 295 through 298.

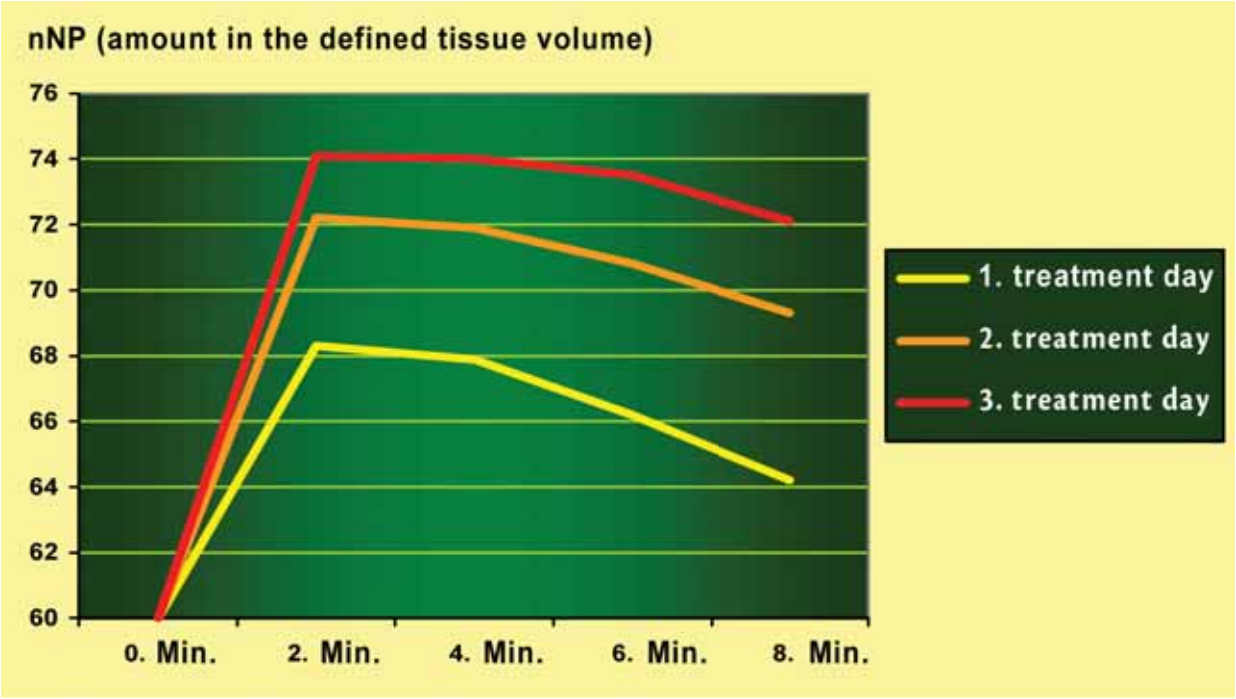
## Files 295

**Measurement data for the parameter "number of blood cell perfused nodal points nNP" (mean values) in the target tissue sub-cutis for test subjects exposed to stress and infection after one week of treatment with a certain pulsed electromagnetic field (BEMER).**

**3 treatment days at intervals of 2 days with 2 applications each (2 min., intensity level 3), 2 hours apart.**

**Measurements on the 1st day of treatment (2nd application):** 0 minutes (base values before the 2nd application), then a 2-minute application, with measurements following in the 2nd, 4th, 6th, and 8th minutes.
**Measurements on the 2nd day of treatment (2nd application):** 0 minutes (base values before the 2nd application), then a 2-minute application, with measurements following in the 2nd, 4th, 6th, and 8th minutes.
**Measurements on the 3rd day of treatment (2nd application):** 0 minutes (base values before the 2nd application), then a 2-minute application, with measurements following in the 2nd, 4th, 6th, and 8th minutes.

No changes in parameters were noticed in the untreated control groups (we therefore forgo listing these data here).
Results of the statistical evaluation:
Significant differences in parameters after the 2nd minute for all 3 days of therapy.



## Files 296

**Measurements for the parameter "venular flow rate Qven" (mean values) in the target tissue sub-cutis after 1 week of treatment with a certain pulsed electromagnetic field (BEMER) for test subjects exposed to stress and infection.**

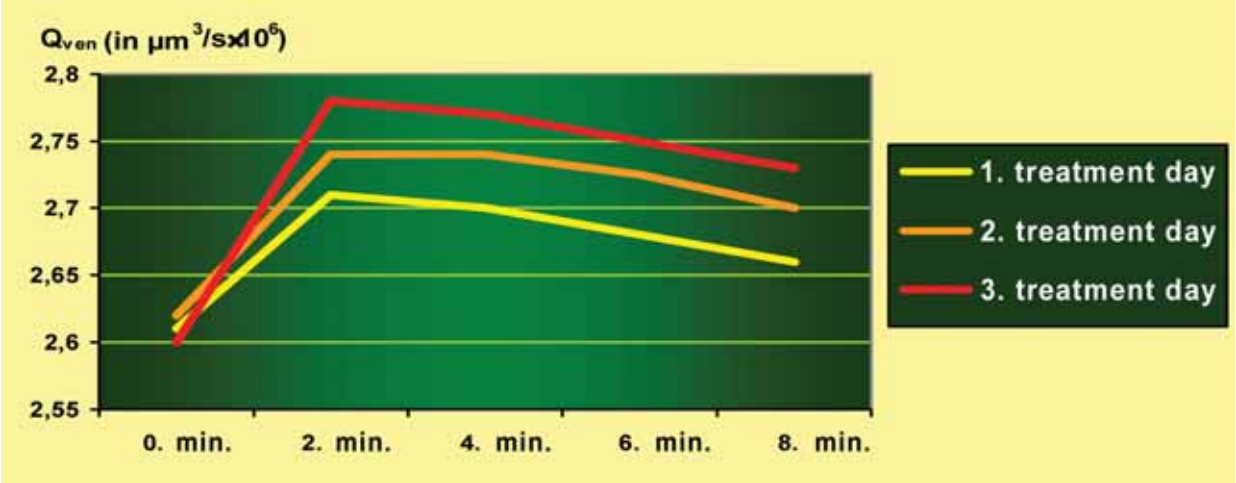
3 treatment days at intervals of 2 days with 2 applications each (2 min., intensity level 3), 2 hours apart.

Measurements taken after the 2nd treatment each day.

**For additional explanation refer to the legend for figure 295.**

Results of the statistical evaluation:

Significant differences in parameters after the 2nd minute for all 3 days of therapy.




## Files 297

**Measurements for the parameter "area under the envelope of the amplitude-frequency spectrum of spontaneous vasomotion in the arterioles Avm" (mean values) in the target tissue sub-cutis after 1 week of treatment with a certain pulsed electromagnetic field (BEMER) for test subjects exposed to stress and infection.**

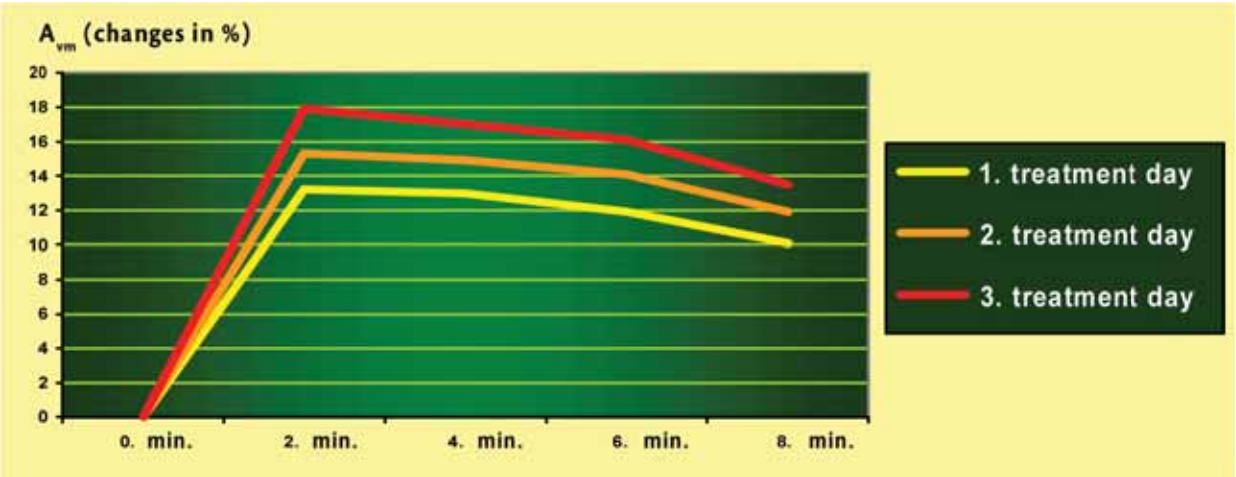
3 treatment days at intervals of 2 days with 2 applications each (2 min., intensity level 3), 2 hours apart.

Measurements taken after the 2nd treatment each day.

**For additional explanation refer to the legend for figure 295.**

Results of the statistical evaluation:

Significant differences in parameters after the 2nd minute for all 3 days of therapy.



## Files 298

**Measurements for the parameter "number of white blood cells adhering to a defined venule wall nWBC/A" (mean values) in the target tissue sub-cutis after 1 week of treatment with a certain pulsed electromagnetic field (BEMER) for test subjects exposed to stress and infection.**

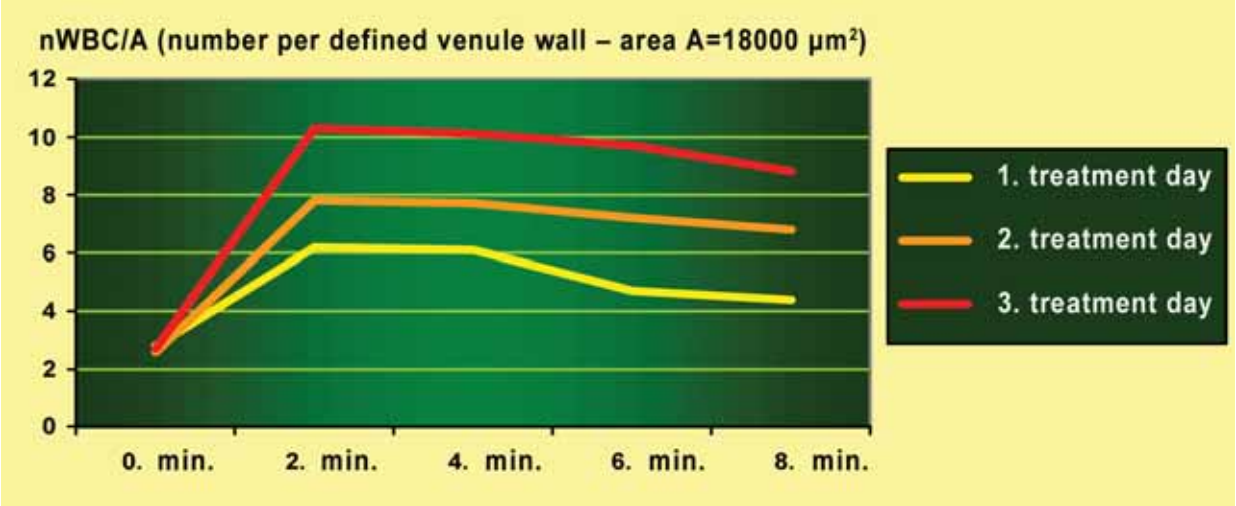
3 treatment days at intervals of 2 days with 2 applications each (2 min., intensity level 3), 2 hours apart.

Measurements taken after the 2nd treatment each day.

**For additional explanation refer to the legend for figure 295.**

Results of the statistical evaluation:

Significant differences parameters after the 2nd minute for all 3 days of therapy.




Up to now we have considered microcirculatory parameter in tissue depths close to the surface. Below we will examine criteria behavior in varying tissue depths (penetration depths).

## Research Design

| | |
|---|---|
| Test Sample | Total sample Ntotal =14<br>Male test subjects, ~30 years of age, no pathological abnormalities |
| Test Series | Simultaneous measurement in two depths of penetration:<br>▶ Depth of penetration 3mm<br>▶ Depth of penetration 8mm |
| Test System, Application | Changing pulsed electromagnetic field BEMER 3000<br>One-time application (2 minutes, intensity level 3) |
| Measurement Intervals and Timing | Observation time 14 minutes. Equidistant measuring intervals:<br>Zero minutes (determination of base values immediately prior to the application), subsequent 2-minute treatment, with data collection following in the 2nd, 4th, 6th, 8th, 10th, 12th, 14th minute |
| Target Tissue | Sub-cutis / infra-cutis (left forearm) |
| Measurement Methods | ▶ Intravitalmicroscopy<br>▶ Laser-DOPPLER-microflow measurement and white light spectroscopy |
| Parameters | ▶ Number of blood cell perfused nodal points nNP<br>▶ Venular flow rate $Q_{ven.}$ |
| Statistical Analysis | WILCOXON rank-sum test, a = 5% |

The measurements show an unexpected result (figures 299 and 300).

**Files 299**

**Measurement data for the parameter "number of blood cell perfused nodal points nNP" (mean values) in sub-cutaneous and infra-cutaneous target tissues at varying tissue depth after a one-time treatment with a certain pulsed electromagnetic field (BEMER, intensity 3, 2 minute application).**

Results of the statistical evaluation:

Significant differences in the parameters after the 2nd minute between the two tissue depths.

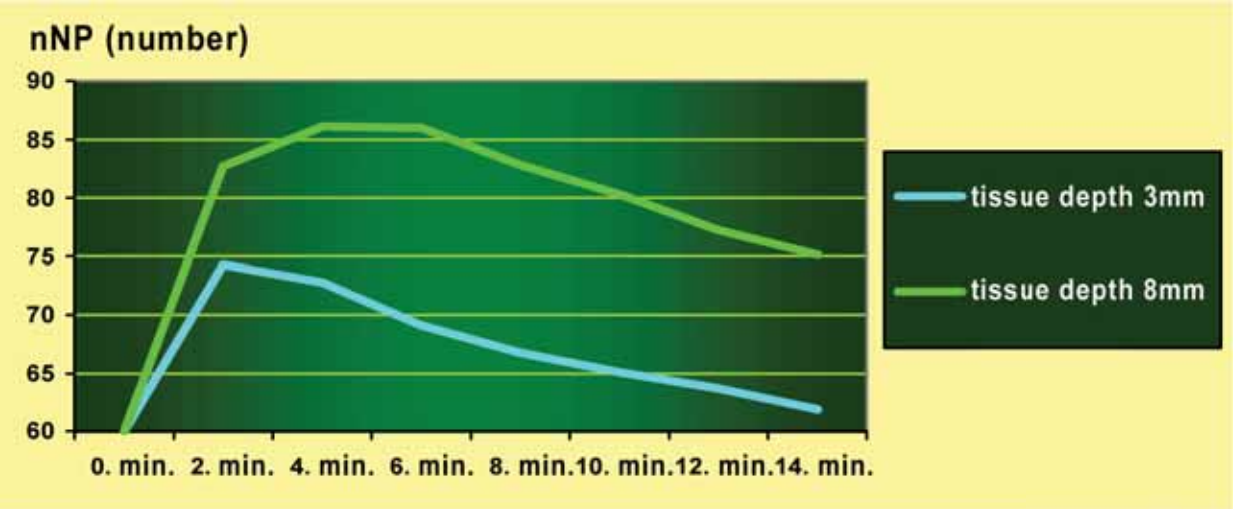
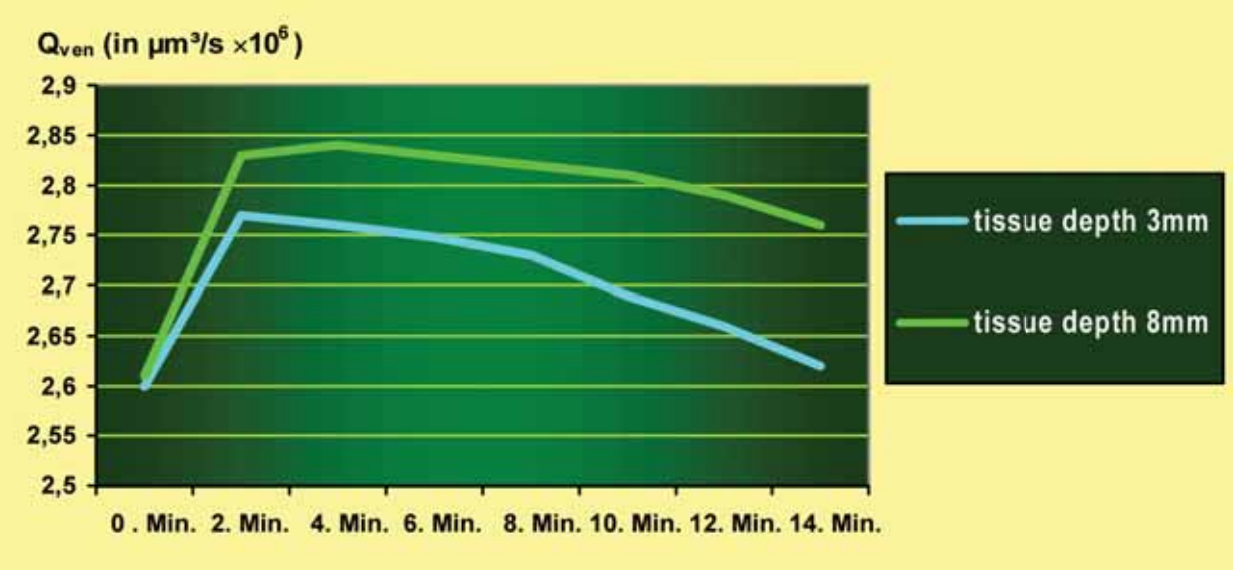



**Figure 300**

**Measurement data for the parameter "venular flow rate" (mean values) in sub-cutaneous and infra-cutaneous target tissues at varying tissue depth after a one-time treatment with a certain pulsed electromagnetic field (BEMER, intensity 3, 2 minute application).**

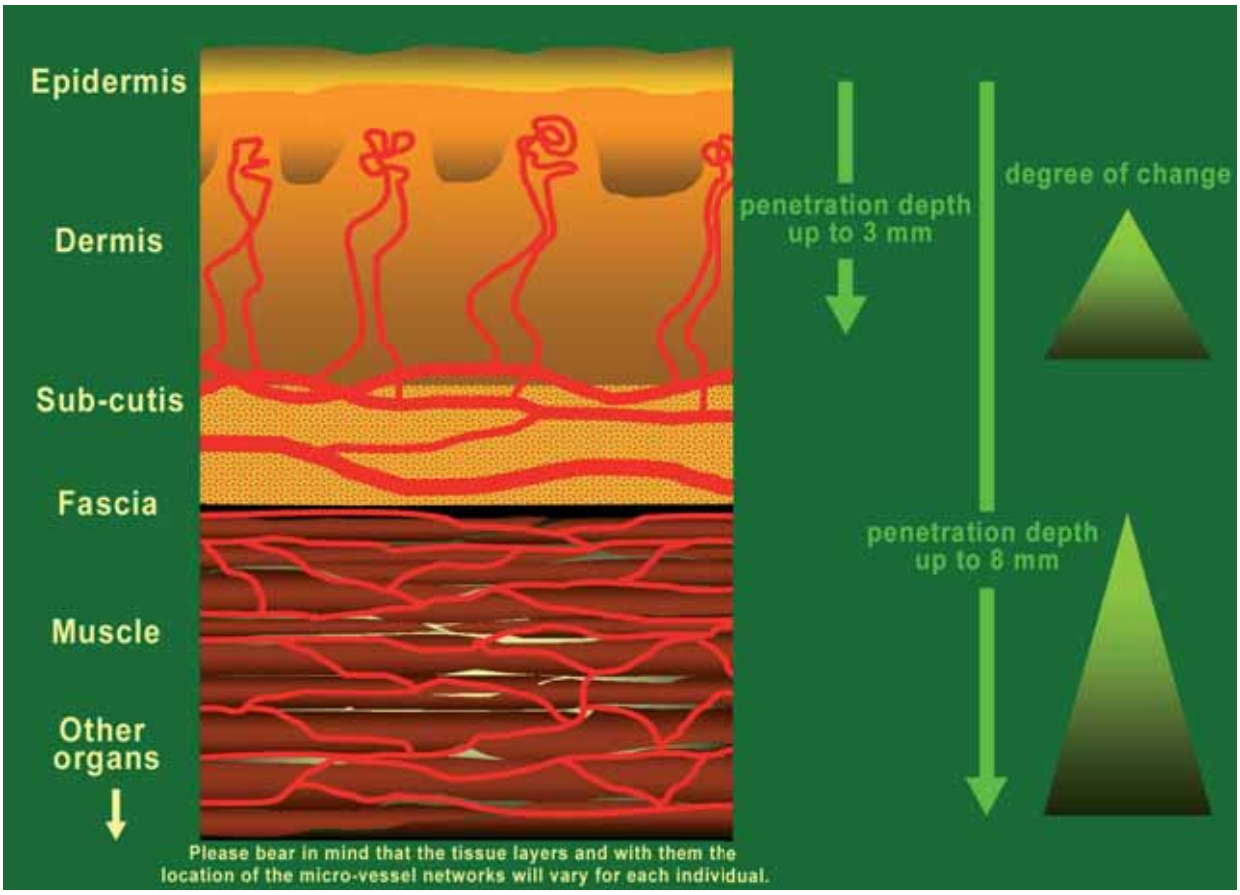
Results of the statistical evaluation:

Significant differences in the parameters after the 2nd minute between the two tissue depths.



The findings lead to the following conclusion:

The micro vessel networks of deeper lying tissues show higher and longer lasting changes in microcirculatory parameters after the application of a certain changing electromagnetic field (BEMER) than areas closer to the surface.




Please bear in mind that the tissue layers and with them the location of the micro-vessel networks will vary for each individual.

At the close of this chapter we would like to pay attention to the effects of a certain changing electromagnetic field on an area of tissue that is distinguished by its extraordinary immunological activity: the gingiva or gums. In the outspread flow pattern of the venules of the gumtissue that borders the teeth, stimulations of immunological behavior of the white blood cells can be observed impressively.

To illustrate this, we introduce the following results and selected vitalmicroscopic findings from two test series conducted.

## Research Design

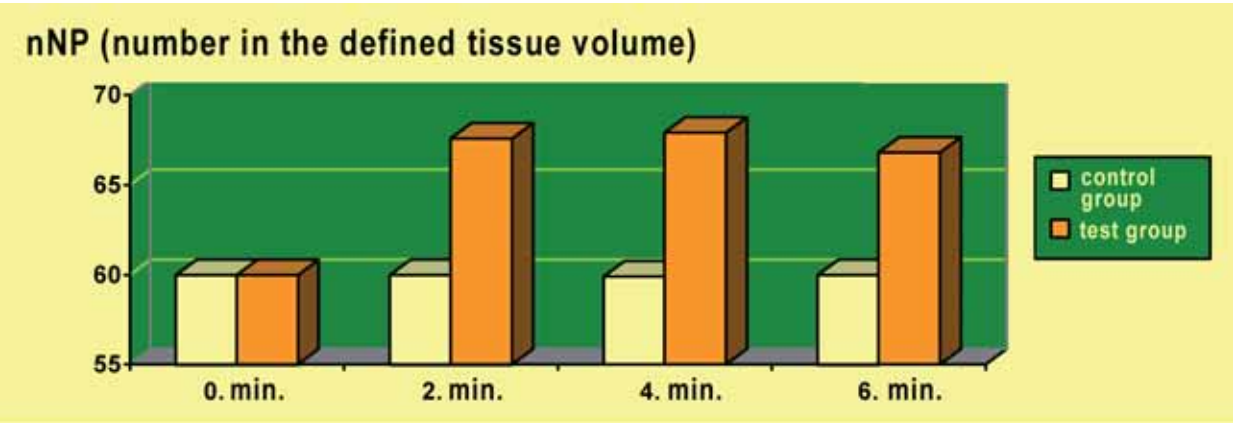
| | |
|---|---|
| **Test Sample** | Total test sample Ntotal =28<br>Male test subjects, ~35 years of age, no pathological abnormalities |
| **Partial Test Samples** | 2 equal partial test samples of n=14<br>► Control group: no treatment (placebo)<br>► Test group: treatment with a changing electromagnetic field |
| **Test System, Application** | Blind study, GPC criteria<br>Changing pulsed electromagnetic field BEMER 3000<br>One-time application of 2 minutes (intensity level 3) |
| **Measurement Intervals and Timing** | Observation time 6 minutes. Equidistant measurement intervals<br>Zero minutes (determination of base values immediately prior to the application), subsequent 2-minute treatment, with data collection following in the 2nd, 4th and 6th minute. |
| **Target Tissue** | Gingiva (upper jaw, labial side, incisor) |
| **Measurement Methods** | ► Intravitalmicroscopy with computer assisted image processing<br>Documentation of findings: high-speed camera, 35 mm film, high resolution, up to 120 pictures per second.<br>► Vitalmiroscopic reflectionspectrometry<br>► Laser-DOPPLER-microflow measurement and white light spectroscopy<br>Capture of complete interconnected micro-vascular networks with defined tissue volume V=1200µm3 (diameter of vessels d≤200µm). Penetration depth 3 mm maximum |
| **Parameters** | ► Number of blood cell perfused nodal points nNP<br>► Changes in the venular flow rate $\Delta Q_{ven}$<br>► Number of white blood cells adhering to a defined venule wall nWBC/A<br>► Localized changes in concentration of ICAM-1 |
| **Statistical Analysis** | WILCOXON rank-sum test, a = 5% |

The results are represented in figures 301 through 303.

**Figure 301**

**Measurements for the parameter "venular flow rate Qven" (mean values) in the target tissue gingiva after a one-time application of a certain pulsed electromagnetic field (BEMER, intensity level 3, 2-minute application).**

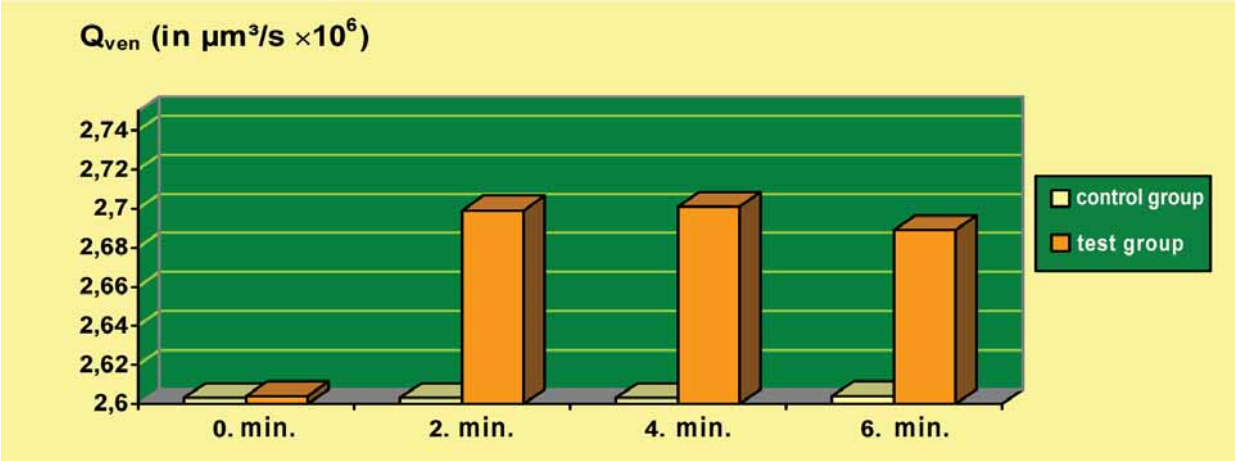
Results of the statistical evaluation:
Significant differences in the parameters after the 2nd minute between the control group and the test group.



## Figure 302

**Measurements for the parameter "number of blood cell perfused nodal points nNP" (mean values) in the target tissue gingiva after a one-time application of a certain pulsed electromagnetic field (BEMER, intensity level 3, 2-minute application).**

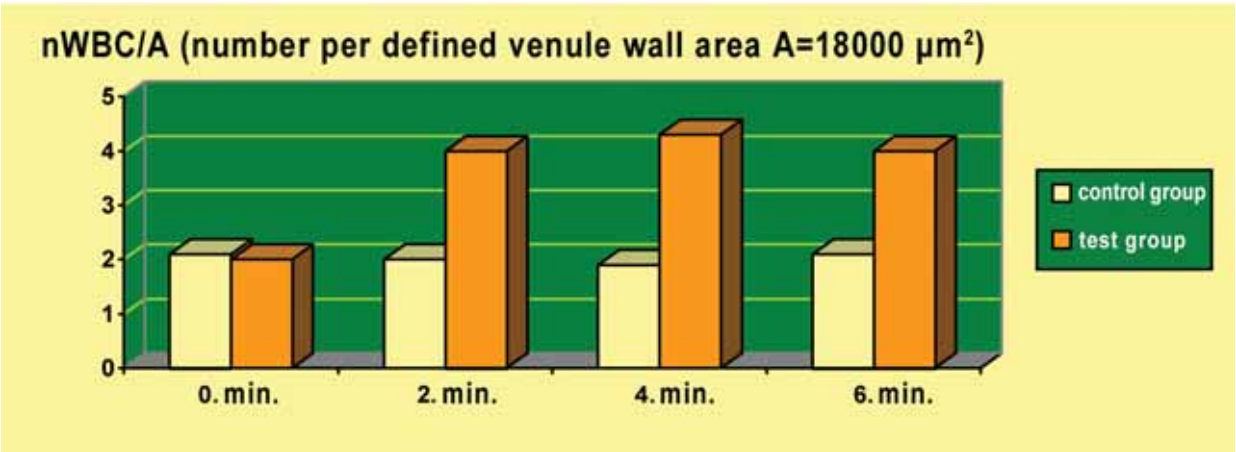
Results of the statistical evaluation:
Significant differences in the parameters after the 2nd minute between the control group and the test group.




## Figure 303

**Measurements for the parameter "number of white blood cells adhering to a defined venule wall area nWBC/A" (mean values) in the target tissue gingiva after a one-time application of a certain pulsed electromagnetic field (BEMER, intensity level 3, 2-minute application).**

Results of the statistical evaluation:
Significant differences in the parameters after the 2nd minute between the control group and the test group.




The heightened adhesion factor of the white blood cells after application of the pulsed electromagnetic field is assumed to be the result of the increased distribution of the blood-plasma mixture in the microvessel network of the gingiva when flow in the venules is increased and regarded as indirect stimulation of the body's own defense mechanisms.

In the larger area of the intestines a parallel change in characteristics is to be expected (rectum, tunica muscularis, see figures 283 through 287). The significance of such an impact on the immunologic properties of white blood cells (e.g. adhesion to the endothelium) becomes apparent when a certain changing electromagnetic field is used for the treatment of experimental gingivitis.

Experimental gingivitis constitutes a reversible, moderately developed acute-inflammatory process in younger, healthy subjects with otherwise healthy teeth. The experimental gingivitis is induced by forgoing all dental hygiene for 3 days.

## Research Design

| | |
|---|---|
| **Test Sample** | **Total test sample $N_{total}$ =24**<br>Male test subjects, ~20-25 years of age, no pathological abnormalities, healthy teeth |
| **Partial Test Samples** | 2 equal partial test samples of n=14<br>► **Control group:** no dental hygiene for 3 days, with standard oral hygiene afterwards (placebo).<br>► **Test group:** no dental hygiene for 3 days, with standard oral hygiene afterwards plus treatment with a changing electromagnetic field.<br>day-3 day -2 day -1 no dental hygiene<br>day-0 day -1 day -2 day -3 day -4 day -5 day -6<br>dental hygiene (control group)<br>dental hygiene plus changing electromagnetic field (test group) |
| **Test System, Application** | Blind study, GPC criteriria<br>Changing pulsed electromagnetic field BEMER 3000<br>**Test group: additional application of a changing electromagnetic field on day 1 and day 3**<br>(2 treatments of 2 minutes each, 2 hours apart, intensity level 3 per treatment day) |
| **Measurement Intervals and Timing** | **Observation time 10 days.** Equidistant **measurement intervals:**<br>Day -3, day -2, day -1 (experimental gingivitis)<br>Day 0 (restart dental hygiene)<br>Subsequent days 1,2,3,4,5,6<br>Starting day 0, data collection 1 hour after treatment (dental hygiene and dental hygiene plus changing electromagnetic field respectively). |
| **Target Tissue** | **Gingiva** (upper jaw, labial side, incisor) |
| **Measurement Methods** | ► Intravitalmicroscopy with computer assisted image processing<br>Documentation of findings: high-speed camera, 35 mm film, high resolution, up to 120 pictures per second.<br>► Laser-DOPPLER-microflow measurement and white light spectroscopy<br>Capture of complete interconnected micro-vascular networks with defined tissue volume V=1200µm3 (diameter of vessels d≤200µm). Penetration depth 3 mm maximum<br>Defined conditions of macro-circulation and temperature regulation. |
| **Parameters** | ► Changes in the venular flow rate $\Delta Q_{ven}$<br>► Number of white blood cells adhering to a defined venular wall area nWBC/A |
| **Statistical Analysis** | WILCOXON rank-sum test, a = 5% |

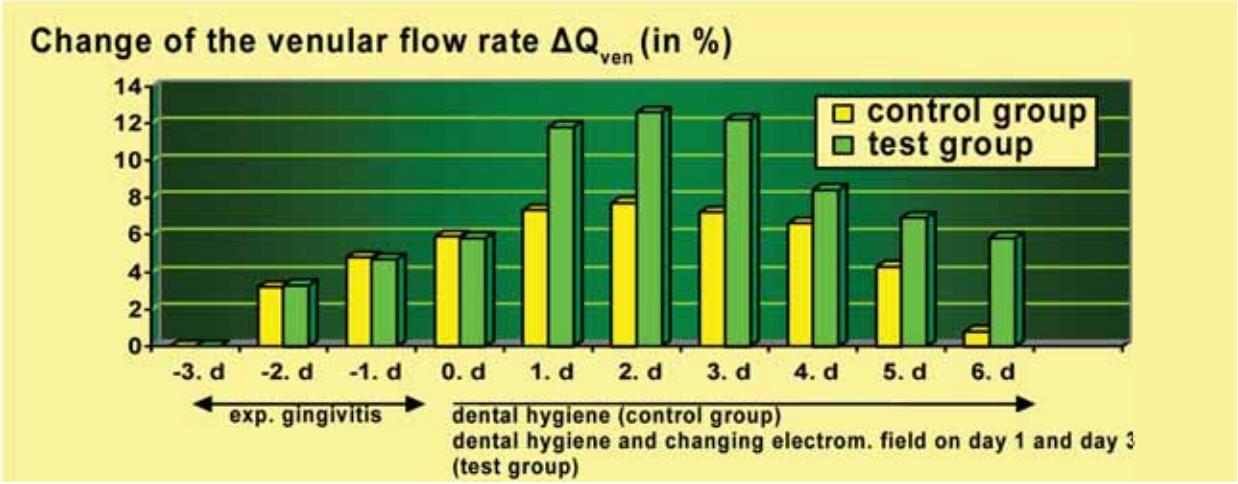
The collected data are displayed in figures 304 and 305.

## Figure 304

**Measurements for the parameter "change in venular flow rate $\Delta Q_{ven}$" (mean values) in the target tissue gingiva for subjects with experimental gingivitis before and after application of a certain pulsed electromagnetic field (test group) in comparison to a control group not treated with the changing electromagnetic field.**

Results of the statistical evaluation:

Significant differences in the parameters after the 1st day between the control group and the test group.

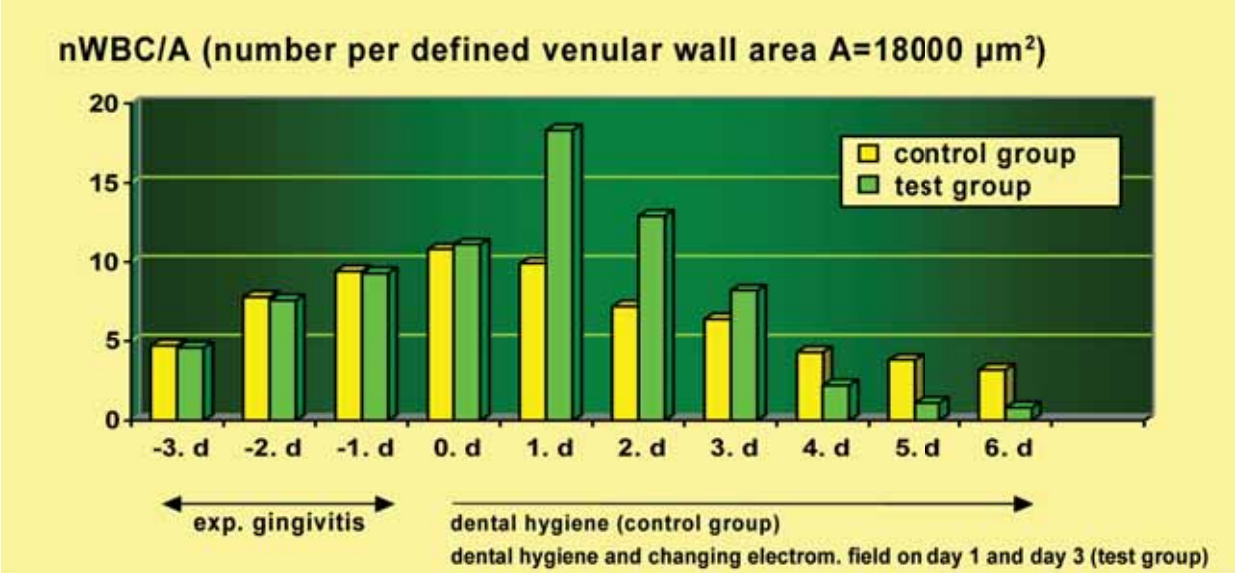



## Figure 305

**Measurements for the parameter "number of white blood cells adhering to a defined area of a venular wall nWBC/A" (mean values) in the target tissue gingiva for subjects with experimental gingivitis before and after application of a certain pulsed electromagnetic field (test group) in comparison to a control group not treated with the changing electromagnetic field.**

Results of the statistical evaluation:

Significant differences in the parameters after the 1st day between the control group and the test group.



Figures 306 through 308 show selected findings from the gingival tissue for (indirect) stimulation of immunological criteria in white blood cells under the influence of a certain changing electromagnetic field.

## Figures 306

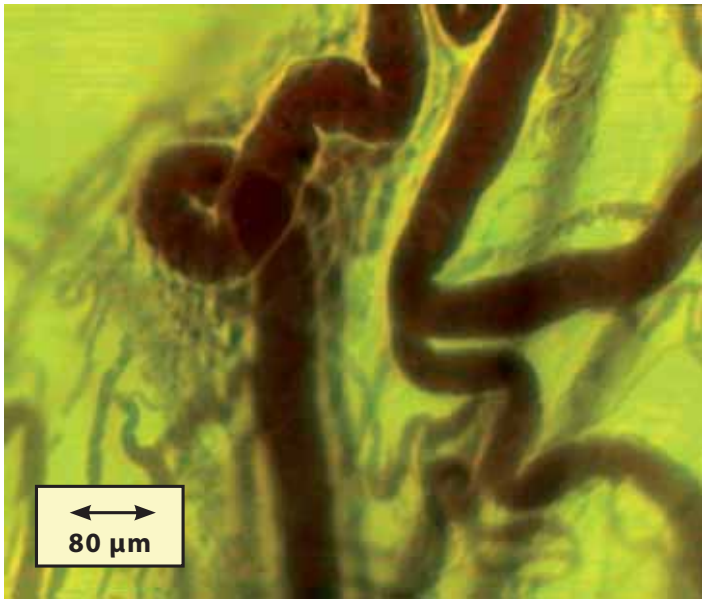
**Changes in the venular flow rate and the blood distribution in the gingival microvessels for a test subject with experimental gingivitis before and after application of a certain changing electromagnetic field (BEMER).**

**Vitalmicroscopic findings, 1/1000 second**

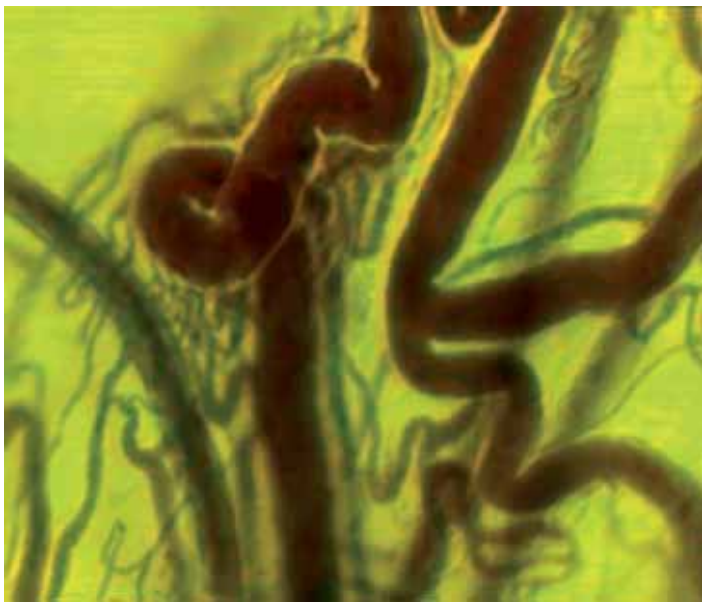
**a: functional state of the gingival micro-circulation on the 3rd day of experimental gingivitis (day -1 in figures 304 and 305).**

**b: functional state of the gingival micro-circulation on the 2nd day of treatment with a certain changing electromagnetic field (day 3 in figures 304 and 305).**

**a**




**b**



## Figure 307

**Changes in the adhesion properties of white blood cells in the gingival micro-vessels for a test subject with experimental gingivitis before and after application of a certain changing electromagnetic field (BEMER).**

**Vitalmicroscopic findings, 1/1000 second, venular flow.**
**a: segment of a venule in the gingival micro-circulation on the 1st day of experimental gingivitis (day - 3 in figures 304 and 305).**
**b: identical segment of a venule on the 1st day of treatment with a certain changing electromagnetic field (day 1 in figures 304 and 305). Numerous white blood cells are aggregated, some of them adhering to the endothelium of the venule.**

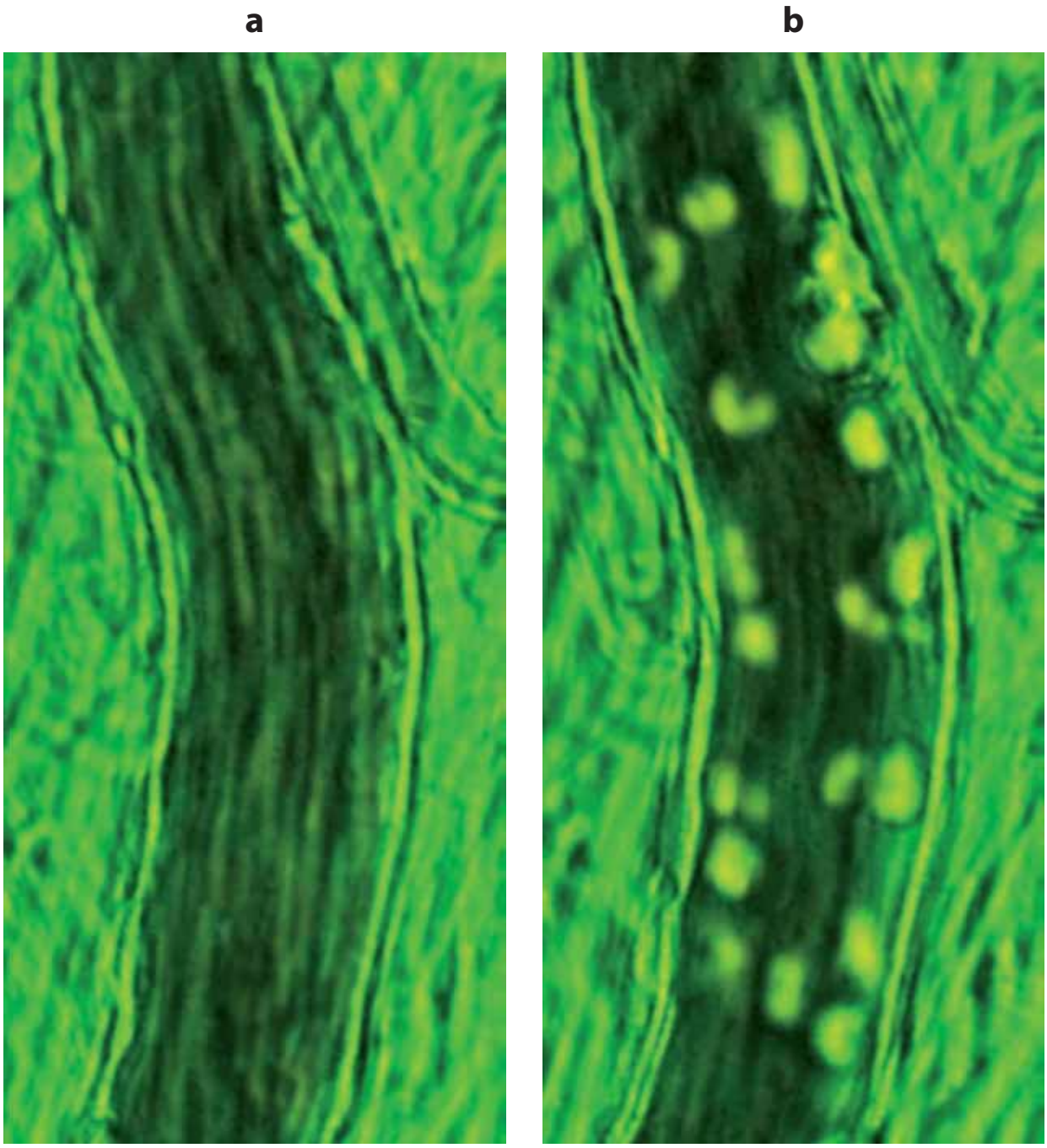
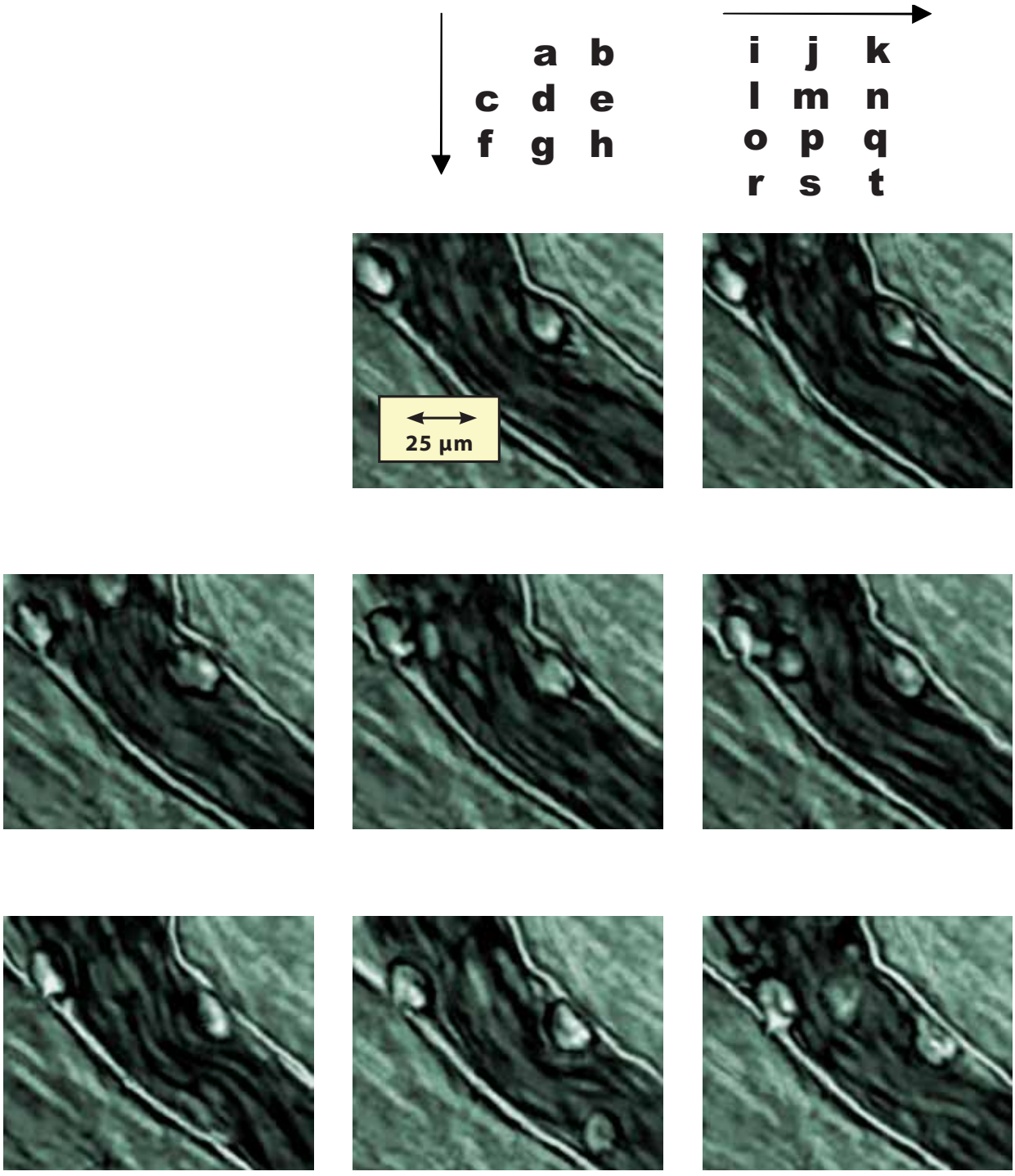


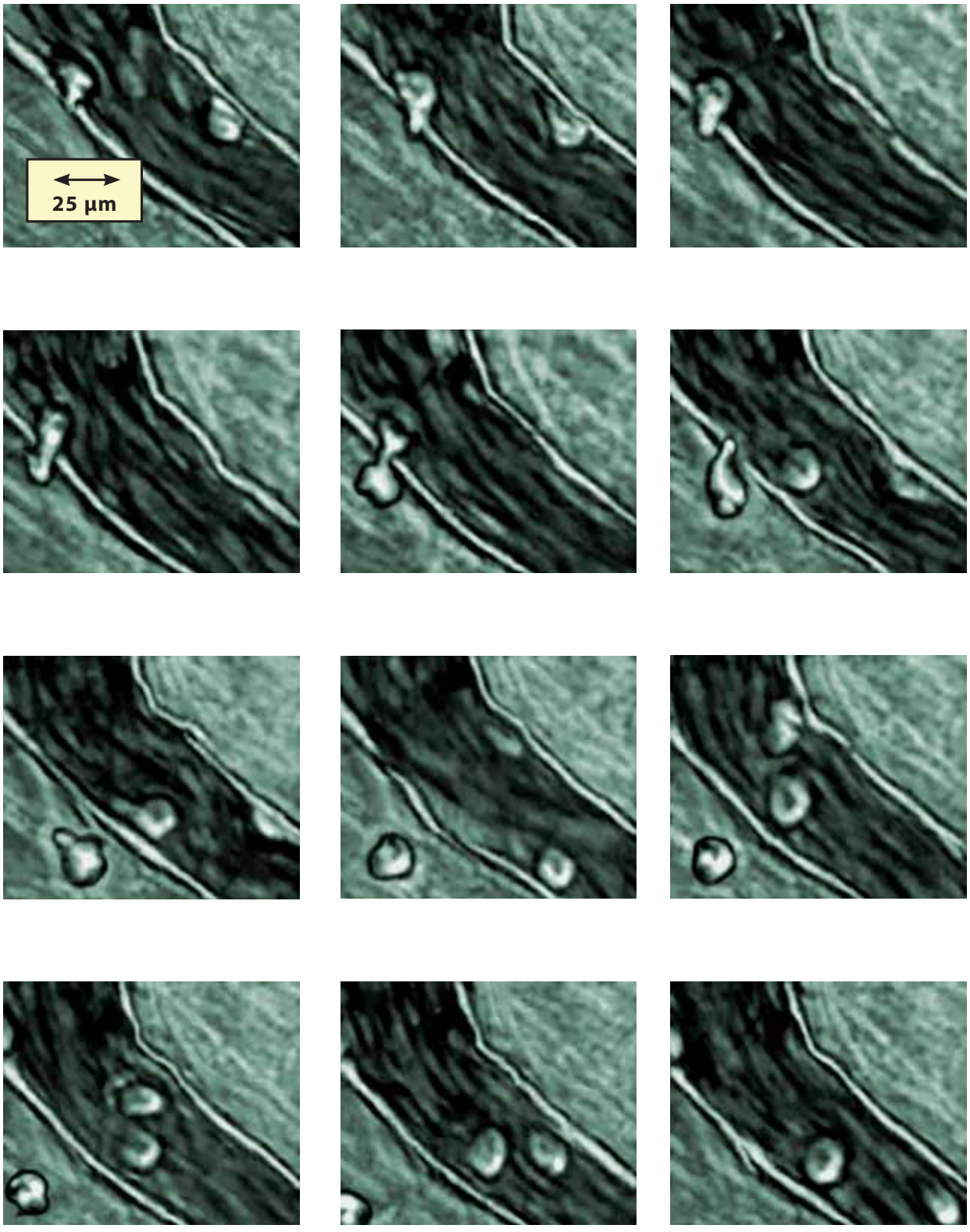
**Figure 308**

**Observations of the transmigration of a white blood cell through the venule endothelium into the interstitial area of the gingival tissue for a test subject with experimental gingivitis after application of a certain changing electromagnetic field (BEMER).**

**Vitalmicroscopic findings, 1/1000 second, venular flow.**

**Sequence of pictures a through j taken about 5 seconds apart.**




25 µm

## Summary of the displayed research results:

With the extremely slow and broadband pulsed electromagnetic field of low energy (BEMER), a physiologically beneficial (temporary) effect on microcirculatory function is achieved after only a 2 minute application (intensity level 3), which can be verified firsthand in the circulatory and immunologically active organs of derma and intestine.

In the deeper tissue levels (about 8 mm) more pronounced effects on microcirculatory function can be seen than in tissue layers closer to the surface. Longer application times (10 to 20 minutes) and repeated applications with appropriate application-free intervals produce higherparameter changes in the microcirculation.

The confirmed (temporary) stimulation effects in the microcirculation are: Increase of the pressure differences between the arterioles and venules. (increase of the venular flow rate from the micro-vascular networks). Expanded dispersion of plasma-blood cell mixture in the micro-vascular networks (improvement of distribution, more nodal points and as a result a larger number of capillaries are perfused with blood cells). As a result of the (temporarily) improved functioning of the microcirculation, the oxygen utilization in the venules increases (tissues are better supplied with nutrients). Intensified spontaneous vasomotion of the arterioles (enhanced ability of the microcirculation to adapt the perfusion rate to changing metabolic requirements in the tissues supplied). More favorable micro-hemodynamic conditions for an unhindered sequence of the first steps of immunological reactions (accumulation and distribution of white blood cells, rolling off behavior at the endothelium, adhesion- and transmigration phenomena).

The proven effects of an extremely slow and broadband pulsed electromagnetic field of low energy (BEMER) on microcirculation speak in favor of a prophylactic and complementary therapeutic application. A comparison of this effectiveness with established therapy options shows that neither the temporary change of parameters nor the size of their values stand in the way of this assessment.

# 26

## The effects of a certain changing electromagnetic field with added vasomotion stimulation on the perfusion of organs

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Among all the proven effects of certain changing electromagnetic fields on microcirculation, the impact on vasomotion deserves special attention. There are two main therapy-relevant reasons:

» **The influence on the balance between capillary filtration and re-absorption (trans-capillary fluid exchange).** This balance is maintained via the lymph drainage and can be impacted by several factors. In addition to the hydrostatic and oncotic pressure this especially concerns the periodic variations of the intra-capillary and transmural pressure because of the rhythmic contractions of the upstream arterioles (vasomotion). The diameters of the arterioles (vasodilation, vasoconstriction) play an important role for the shift in the ratio of filtration and absorption because they alter the transmural pressure being exerted on the capillary walls:
Diameter of arterioles ↑ → transmural pressure ↑ → filtration ↑
Diameter of arterioles ↓ → transmural pressure ↓ → re-absorption ↑.

» **Determination of the standard width of local vessels so the blood supply of an organ tissue can be adapted to meet its respective energy needs.** Aside from normal cardiac function, two main factors are significant for the blood supply of an organ tissue: the distance of the capillaries in the microvascular network (capillary density of the tissue) and the functional state of arteriolar vasomotion.
Arteriolar vasomotion causes rhythmic changes in the perfusion of the capillaries:

Muscle tone of the vessels ↓ → capillary flow rate and amount of blood cell perfused capillaries ↑ → path of diffusion ↓

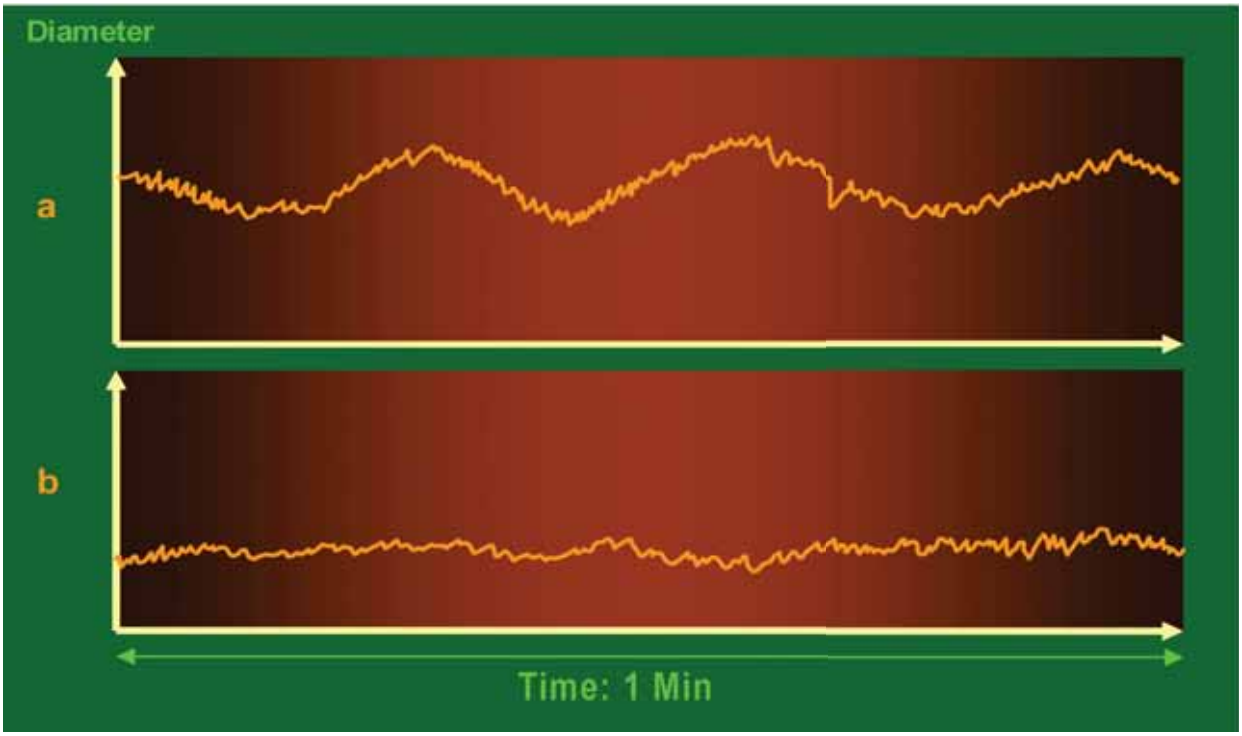
Muscle tone of the vessels ↑ → capillary flow rate and amount of blood cell perfused capillaries ↓ → path of diffusion ↑

**Spontaneous (auto rhythmic) arteriolar vasomotion** plays a prominent role among the vasomotion phenomena, since we now know that it most likely has the largest influence on the functionally important distribution of the plasma-blood cell mixture in the capillary networks.

Spontaneous (auto rhythmic) arteriolar vasomotion is reduced or at times completely disrupted in almost all forms of illness that involve restriction of microcirculation (figure 309).

**Figure 309**

**Schematized path-time diagrams of arteriolar vessel wall movements for spontaneous vasomotion (a) and disrupted spontaneous vasomotion during illness (b).**




We currently assume the a spontaneous vasomotion frequency of the arteriolar vessel wall of about 1 to 3 oscillations per minute corresponds to a physiological condition. Vasomotion frequencies between 0/min and significantly less than 1/min (about 1 oscillation movement in 10 minutes) are considered pathological.

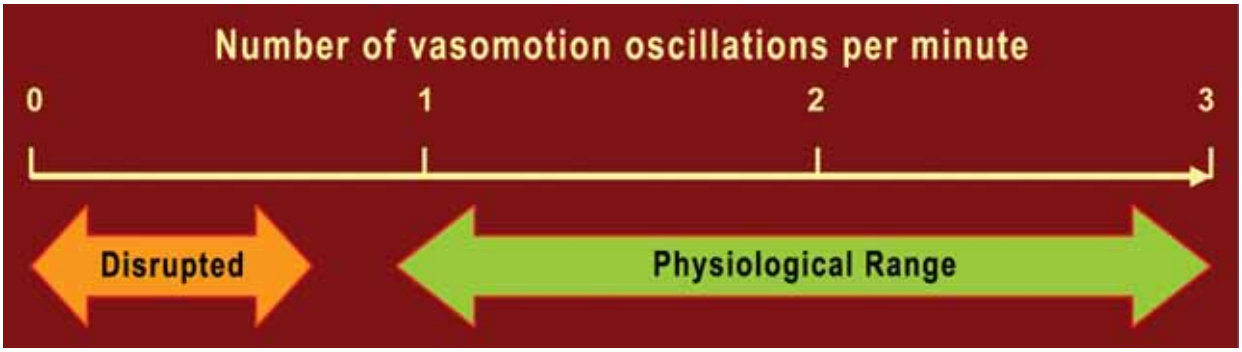
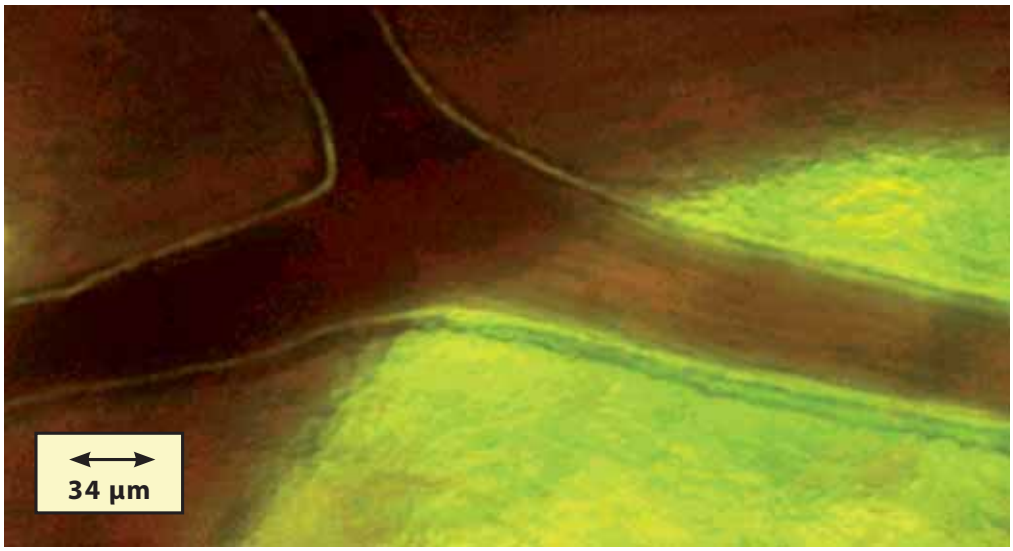


Figure 310 shows an example of vitalmicroscopic findings of spontaneous physiological vasomotion of an intestinal arteriole.

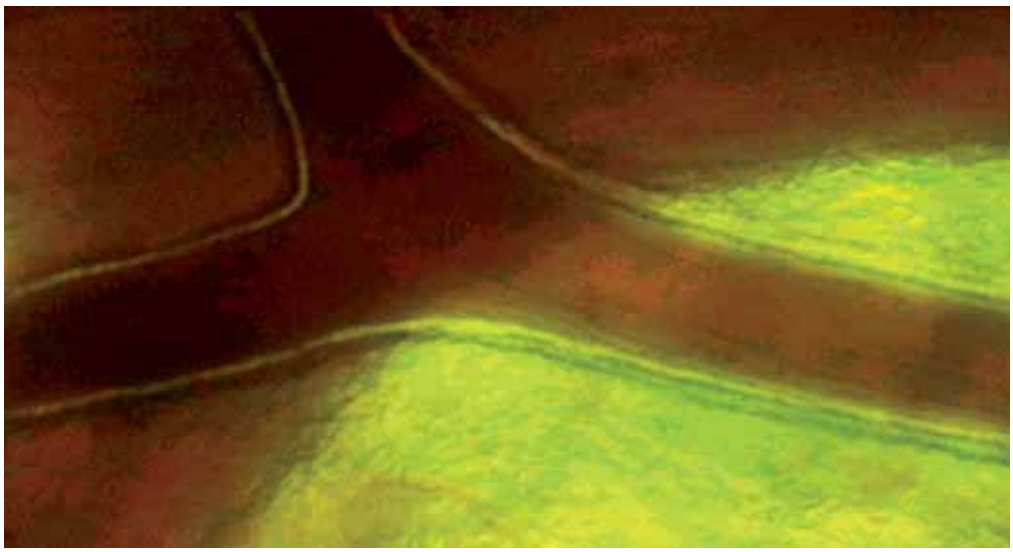
**Figure 310**

**Normal spontaneous vasomotion (vasomotion frequency 1/min) of an intestinal arteriole at several consecutive observation times.**
**Image sequences from a through d are taken 15 seconds apart**
**(Vitalmicroscopic result, 1/1000second, rectum, lamina muscularis)**

a

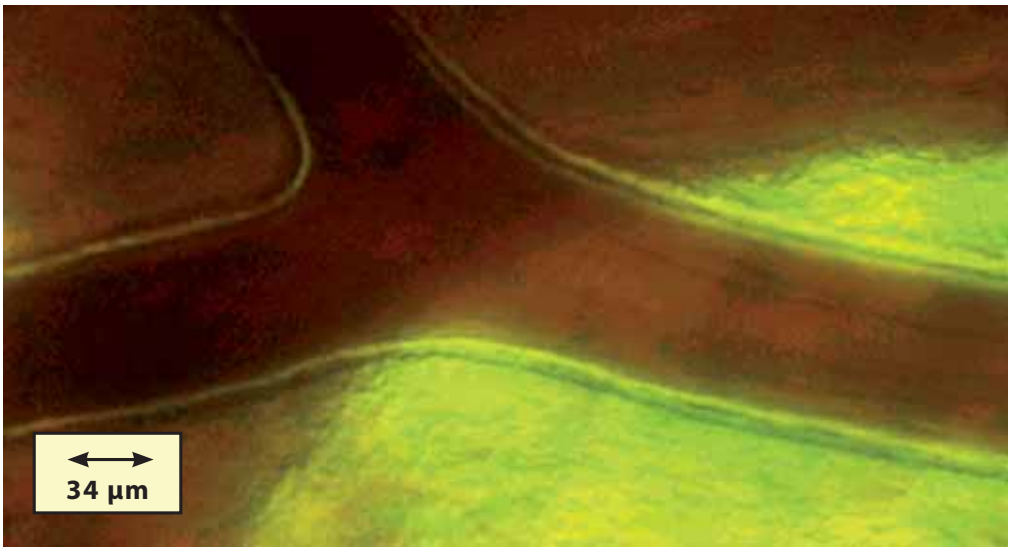



b

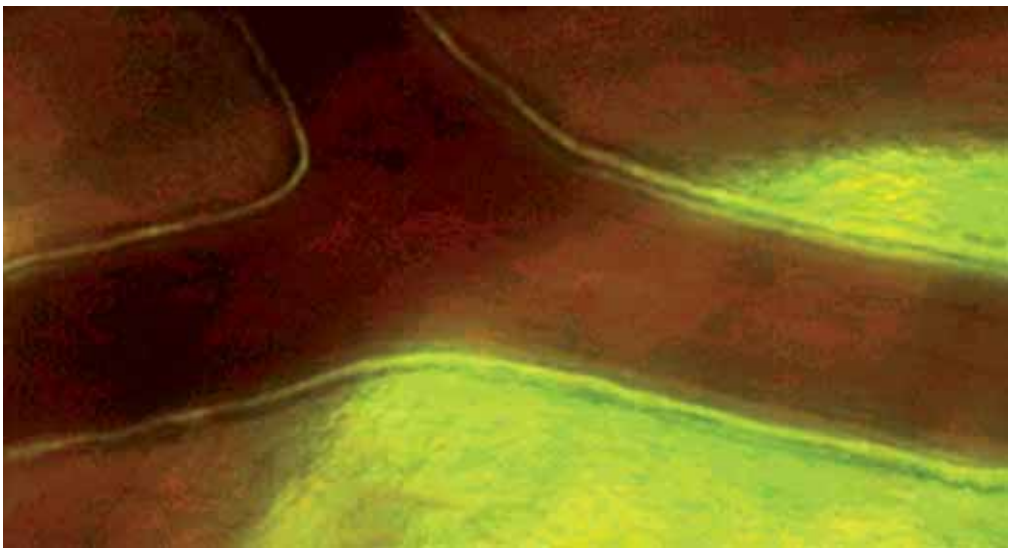


*The lumen changes of the arteriolar micro vessel can be identified; we should also note that the radius enters into the equation for the flow rate in the 4th power (see chapter 2, Law of Hagen-Poiseuille).*

**c**




**d**



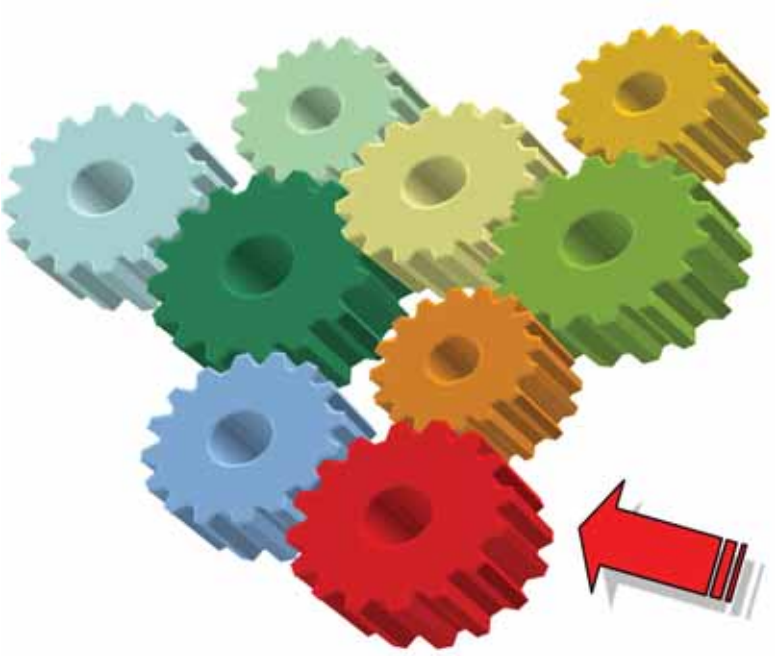
A number of reciprocal influences exist among the many factors that determine the functional state of microcirculation (e.g. local hematocrit, number of blood cell perfused nodal points, venular flow rate, spontaneous arteriolar vasomotion). The phenomenon of vasomotion is perceived as playing a particular role.

The effects of a certain changing electromagnetic field on microcirculation and thereby especially on spontaneous vasomotion (as described in chapter 25) as well as the results of several other exploratory research series, which we will not discuss in detail here, raise the following questions:

» The phenomenon of spontaneous vasomotion is an active process and therefore dependent on a certain supply of energy. Since each electric field is a carrier of certain amount electrostatic energy (see chapter 25), the question arises about a relevant interaction of electromagnetic waves of low energy and (molecular-) biological structures. Is it conceivable, within reason, that there is a (probably indirect and possibly small) influence on the multifaceted, interconnected enzymatic processes that underlie spontaneous vasomotion?

» Important functional characteristics of microcirculation follow the rhythm of the periodically changing arteriolar diameters brought on by spontaneous vasomotion: rhythm of the capillary flow and rhythm of the distribution of the plasma-blood cell mixture in the network among others. We know that in cases of pronounced microcirculatory disturbances (especially in multi-morbid geriatric patients) spontaneous vasomotion is greatly reduced or completely disrupted (see chapter 25). Is it possible to increase the already proven and therapeutically relevant influence on spontaneous vasomotion with the changing electromagnetic field of the BEMER system? Can we normalize a significantly disrupted or extinct rhythm of vasomotion again by adding appropriate electromagnetic stimulation? Can we, in addition, demonstrate increased effects on capillary perfusion after additional stimulation of vasomotion?

» What types of characteristics does this kind of additional stimulus need to have?



All regulatory factors of micro-perfusion are subject to reciprocal influences.

Spontaneous vasomotion is the “impulse generator” of the physiologically necessary rhythm of micro-perfusion.

**Can this “impulse generator” be stimulated more effectively?**

The results of extensive research suggested that vasomotion can be stimulated by adding a certain impulse sequence of signals with higher flux density. We expected an increased treatment success rate in cases of impaired vasomotion with a vasomotion stimulation impulse frequency of 3/minute (see figure 309).

The development of a therapy device that utilizes a certain changing electromagnetic field with added vasomotion stimulation (BEMER PLUS) is an innovative achievement of INNOMED INTERNATIONAL AG in Liechtenstein.

This therapy option makes use of the proven impulse configuration (see chapter 25, figure 281) and provides the possibility of adding a signal that stimulates vasomotion (frequency of the stimulation impulse 3/min.). The configuration of the added signal for vasomotion stimulation follows the principle illustrated in figure 281.

Figure 311 shows a schematic illustration of the signals utilized in the BEMER PLUS system.

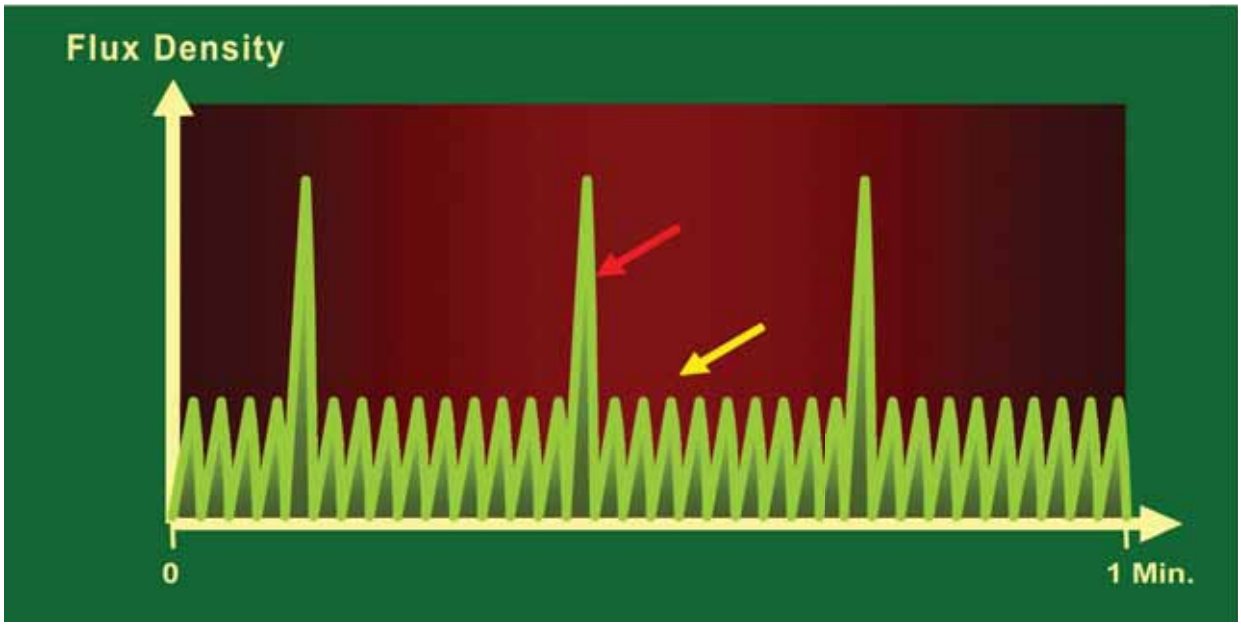
**Figure 311**

**Schematic illustration of the electromagnetic stimulation signals of the BEMER PLUS therapy device:**

**Basic stimulation identical to BEMER 3000 (yellow arrow), pulse width 33ms.**

**Added signals for vasomotion stimulation (red arrow), pulse width 165 ms, consisting of 5 single impulses each. Added signals are 20 seconds apart.**

When using the mat:
Flux densities correspond to an intensity level range of ~5 µT to ~35 µT.



The following test results show confirmation of this concept. We can see that this kind of stimulation is “recognized” by the biological system and elicits increased therapy-relevant results.

**Research Design**

| | |
|---|---|
| **Test Sample** | Total test sample $N_{TOTAL}$=54<br>Multi-morbid male test subject, -70 years of age,<br>no aculte ailments,<br>vasomotion frequency ≤ 0.1/min |
| **Partial Test Sample** | 3 equal partial test samples of n=18; treated with a certain changing electromagnetic field (BEMER).<br>► Additional vasomotion stimulation signal frequency 1/min<br>► Additional vasomotion stimulation signal frequency 2/min<br>► Additional vasomotion stimulation signal frequency 3/min |
| **Test System, Application** | Blind study, GPC criteria<br>Changing pulsed electromagnetic field BEMER 3000<br>One-time treatment of 8 minutes (intensity level 3, on the mat)<br>plus added stimulation signal |
| **Measurement Intervals and timing** | Observation time 8 minutes. Equidistant measurement intervals<br>Zero minutes (determination of base values immediately prior to the application),<br>subsequent 8-minute treatment, with data collection following immedi- |
| **Target Tissue** | Sub-cutis (left forearm) |
| **Measurement Methods** | ► Intravitalmicroscopy with computer assisted image processing<br>► Laser-DOPPLER-microflow measurement in combination with white light spectroscopy<br>Depth of penetration 3 mm maximum. Capture of arteriolar diameters in defined tissue volume |
| **Parameters** | ► Number of vasomotion oscillations per minute<br>► Venular flow rate |
| **Statistical Analysis** | WILCOXON rank-sum test, a = 5% |

The measurement data gathered are displayed in figures 312 and 313.

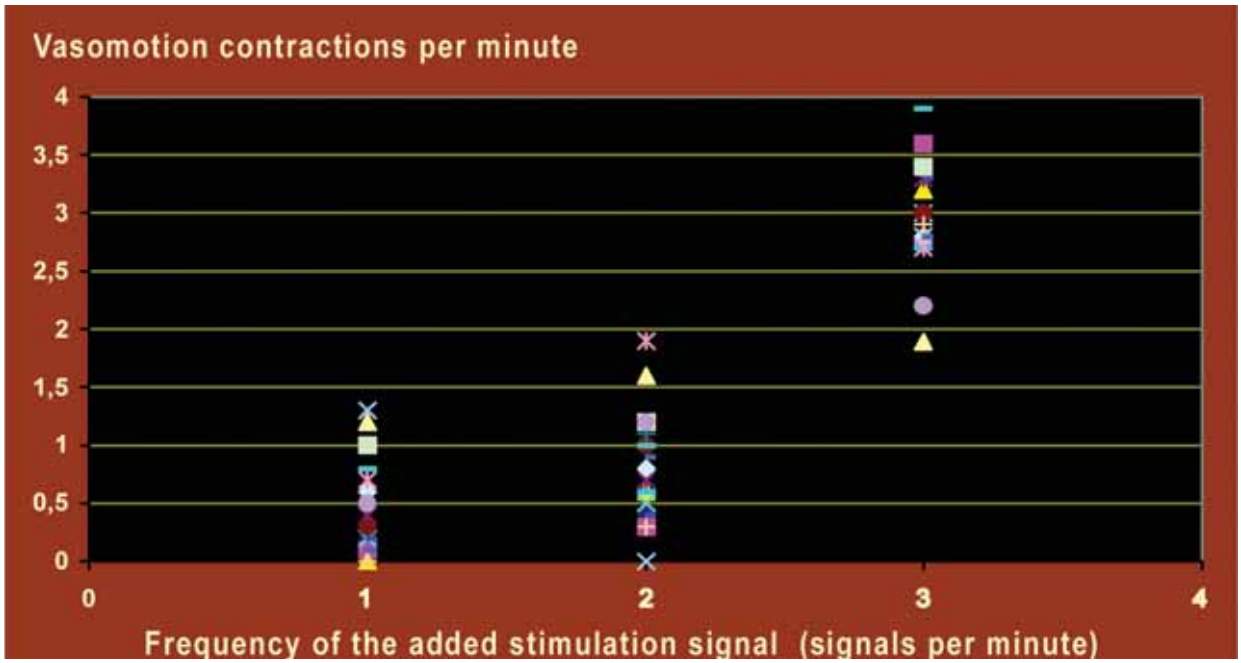
The data displayed in figure 312 indicate that a stimulation of the auto-rhythmic contractions of the smooth muscle cells in the smaller arterioles happens immediately after an 8-minute application of a certain changing electromagnetic field with added vasomotion stimulation in a test sample of persons with almost nonexistent vasomotion. The most significant changes in characteristics occur with a frequency of 3 additional signals per minute. We can gather from figure 313, based on the parameter changes in the venular flow rate, that the effects of stronger stimulation of the vasomotion result in a more pronounced influence on the functional state of the microcirculation.

We can interpret this as a confirmation of the signal configuration with added vasomotion stimulation that is used in the BEMER PLUS therapy system.

## Figure 312

**Stimulated vasomotion contractions after an 8-minute application of a certain changing electromagnetic field with added vasomotion stimulation of varying signal sequence frequency in 3 partial test samples (n=18) of multi-morbid older patients.**

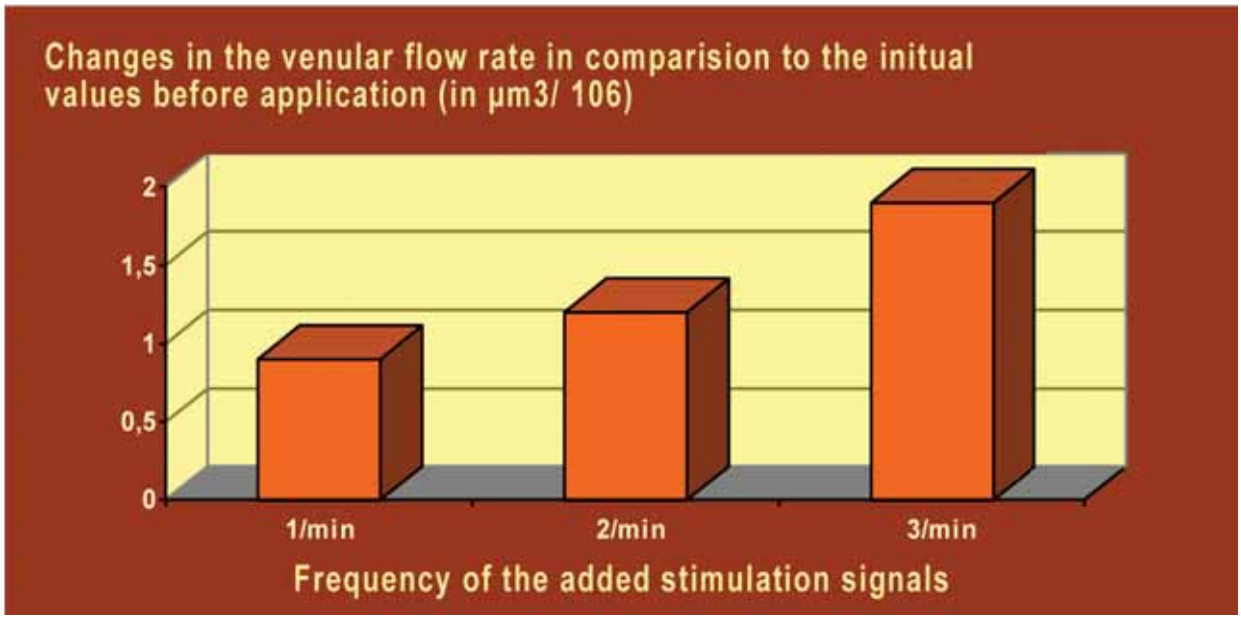
Abscissa: Varying signal sequence frequencies of the added signal used in the 3 partial test samples.
Ordinate: Related, in part overlying data points of the individual vasomotion contractions




## Figure 313

**Changes in the venular flow rate in the sub-cutaneous target tissue subject to the impulse sequence frequency of the added signal immediately after an 8-minute application.**

(Difference of the venular flow rate between the times t=0 before treatment and t= t immediately after an 8-minute application; mean values, significant differences in parameters).



Below we will address the behavior of functional microcirculatory parameters after the application of a certain changing electromagnetic field with added vasomotion stimulation (BEMER PLUS) for two patient samples whose local microcirculation is restricted in differing degrees: a test sample of middle aged individuals exposed to stress and infection, and a test sample of high-risk geriatric with cardio-vascular patients (therapy controls).

**Research Design**

| | |
|---|---|
| **Test** | Test sample size $N_{TOTAL}$=48<br>Male test subjects, 35-45 years of age, no pathological abnormalties<br>Exposure to stress and infection |
| **Partial Test Samples** | 3 equal partial test samples of n=18; treated with a certain changing electromagnetic<br>➡ Partial test sample A<br>Application of a certain changing electromagnetic field without added vasomotion stimulation (BEMER 3000).<br>➡ Partial test sample B<br>Application of a certain changing electromagnetic field with added vasomotion stimulation (BEMER Plus). |
| **Test System,** | Pulsed changing electromagnetic field<br>BEMER 3000 and BEMER Plus<br>Application: 2 application each, 2 hours apart (8 minutes, intensity level 3, on the mat). |
| **Measurement Intervals and** | Observation time of 60 minutes, equidistant measurement intervals:<br>► Zero minutes (determination of base values immediately prior to the 1st application), subsequent 8-minute treatment.<br>► Data collection immediately following the 2nd treatment in the 4th, 8th, 12th, 16th, 20th, 24th, 28th, 32nd, 36th, 40th, 44th, 48th, 52nd, 56th, and 60th |
| **Target Tissue** | Sub-cutis/ infra-cutaneous tissue (abdomen, region epigastr.). |
| **Measurement Methods** | Simultaneous measurements at 2 different tissue depth:<br>Penetration depth 3 mm<br>Penetration depth 8 mm<br>► Intravitalmicroscopy with computer assisted image processing<br>► Vitalmicroscopy with computer assisted image processing.<br>► Laser-DOPPLER-microflow-measurement and white light spectroscopy.<br>Capture of complete interconnected micro-vascular networks with defined tissue volume V=1200µm³ (diameter of vessels d≤200µm).<br>Defined conditions of macro-circulation and temperature regulation. |
| **Parameters** | ► Number of blood cell perfused nodal points nNP.<br>► Changes in the venular flow rate $\Delta Q_{ven}$.<br>► Area below the envelop of the amplitude-frequency-spectrum of the (spontaneous) arteriolar vasomotion $A_{vm}$. |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), a = 5% |

Figures 314 through 316 show a summary of the data collected.

**Figure 314**

**Measurements for the parameter "number of blood cell perfused nodal points nNP" (mean values) in the target tissue sub-cutis after application of a certain pulsed electromagnetic field with and without added vasomotion stimulation for test subjects exposed to stress and infection.**

**Partial test sample A: no added vasomotion stimulation (BEMER)**

**Partial test sample B: with added vasomotion stimulation (BEMER PLUS)**

**Measurement values taken at 2 different penetration depths: 3 mm and 8 mm.**

Two applications of 8 minutes each, 2 hours apart (intensity level 3).

Measurement timing: 0 minutes: initial values prior to the first application. Every four minutes up to 60 minutes after the 2nd application.

Significant differences in measured parameters after the 4th minute between the two partial sample groups.

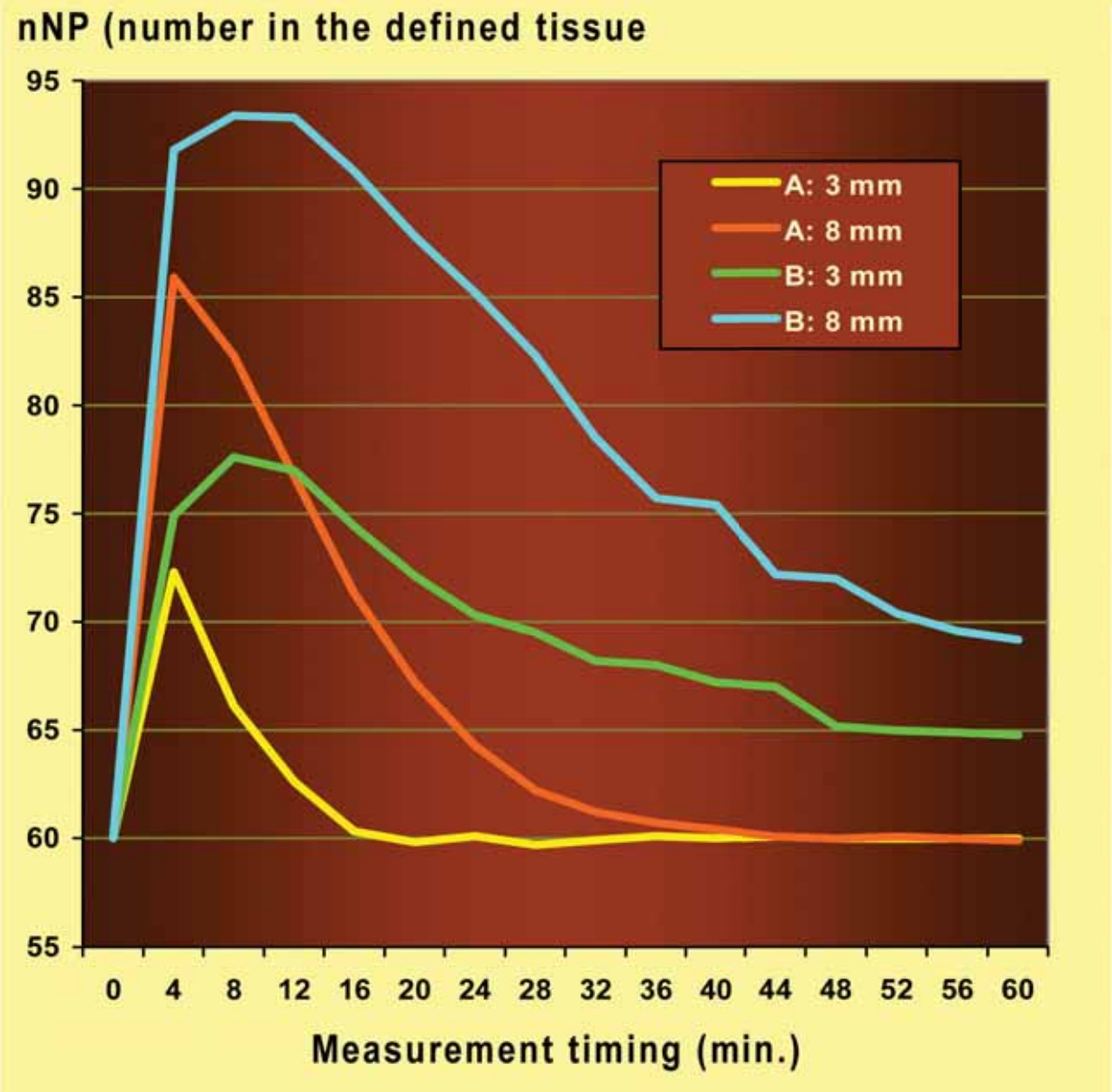


**Figure 315**

**Measurements for the parameter "changes in the venular flow rate ΔQven" (mean values) in the target tissue sub-cutis after application of a certain pulsed electromagnetic field with and without added vasomotion stimulation for test subjects exposed to stress and infection.**

**Partial test sample A: no added vasomotion stimulation (BEMER)**
**Partial test sample B: with added vasomotion stimulation (BEMER PLUS)**

Measurement values taken at 2 different penetration depths: 3 mm and 8 mm.

Two applications of 8 minutes each, 2 hours apart (intensity level 3).

Measurement timing: 0 minutes: initial values prior to the first application. Every four minutes up to 60 minutes after the 2nd application.

Significant differences in measured parameters after the 4th minute between the two partial sample groups.

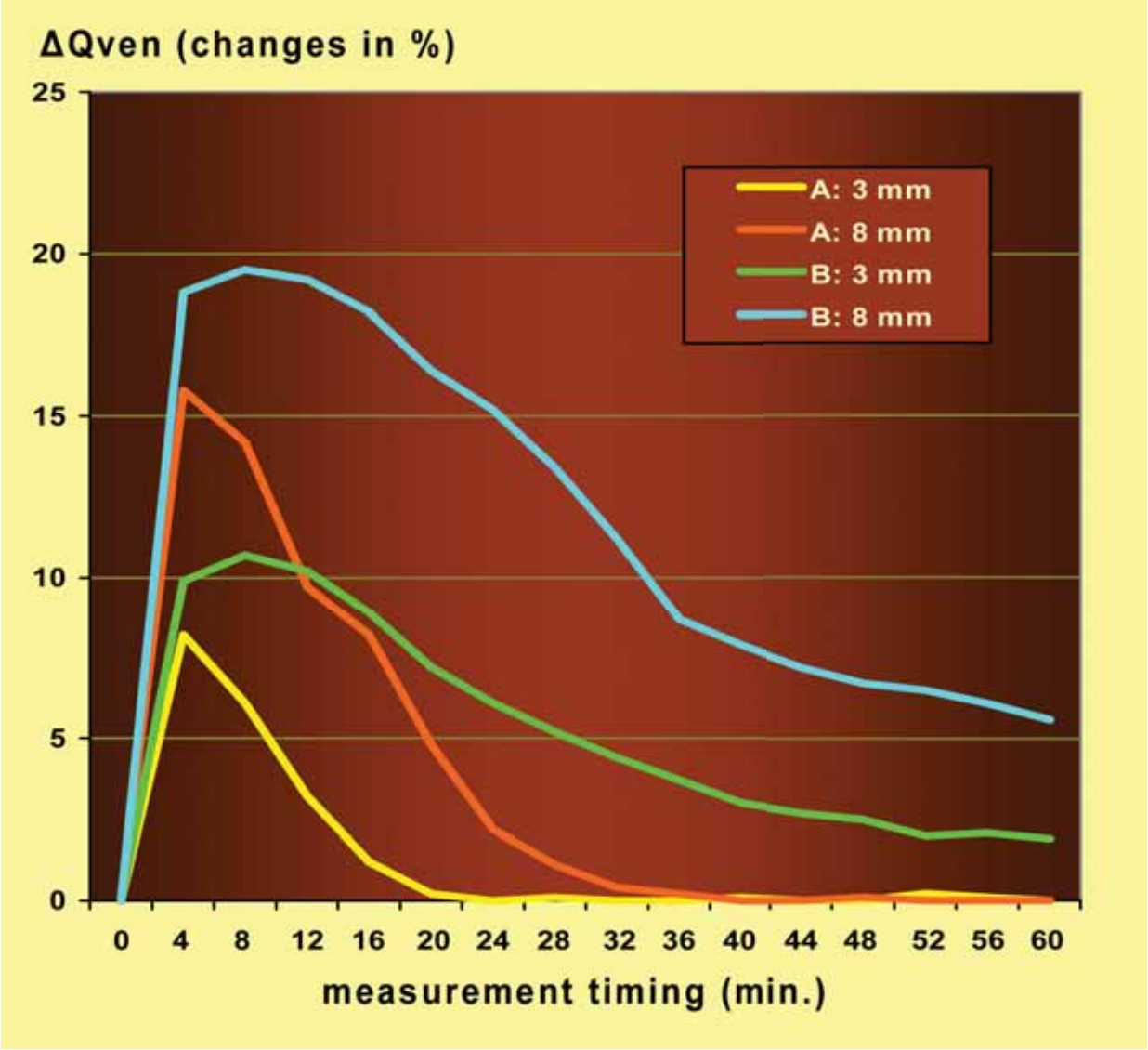


**Figure 316**

**Measurements for the parameter "area under the envelope of the amplitude frequency spectrum of spontaneous arteriolar vasomotion Avm" (mean values) in the target tissue sub-cutis after application of a certain pulsed electromagnetic field with and without added vasomotion stimulation for test subjects exposed to stress and infection.**

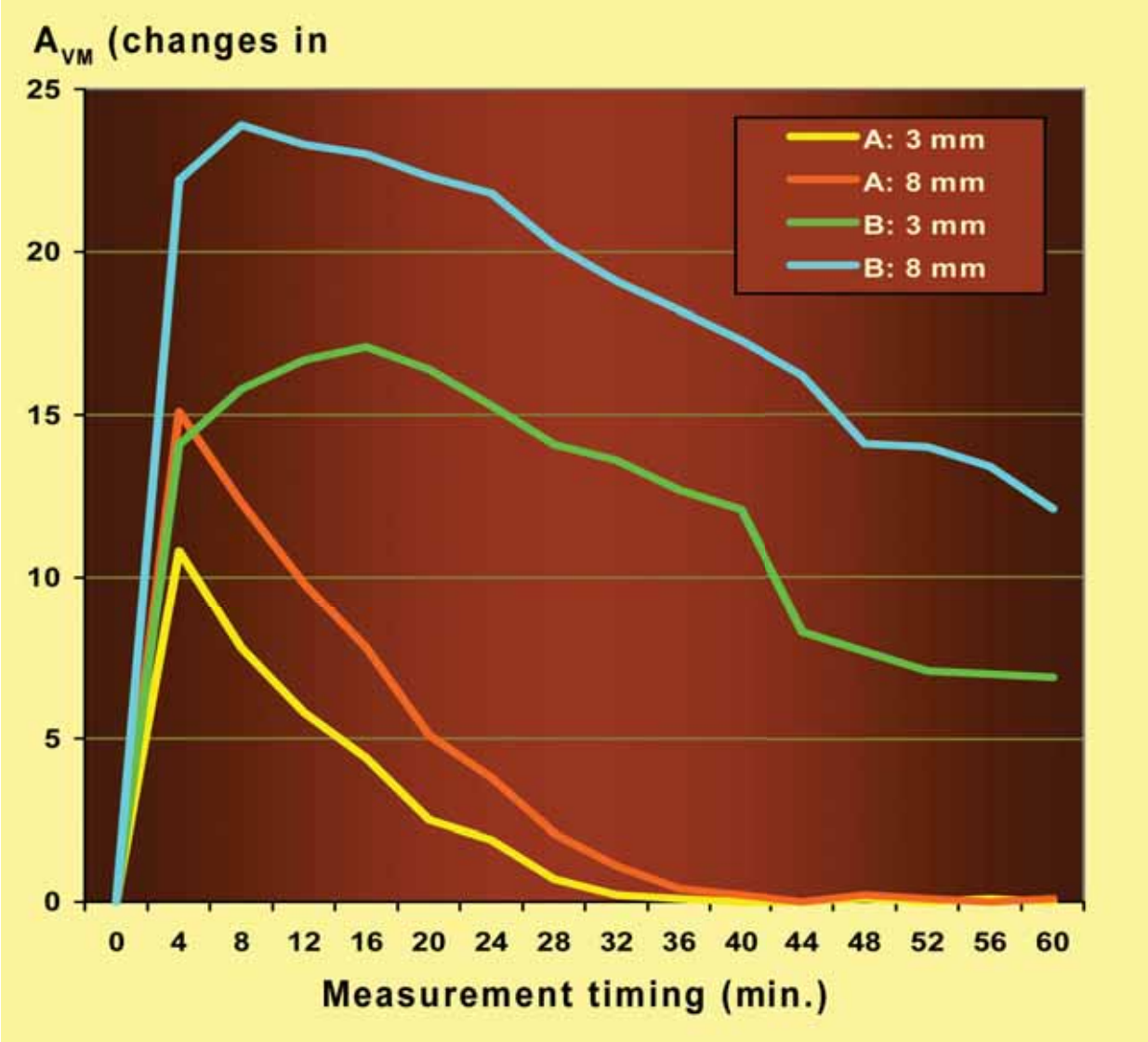
**Partial test sample A: no added vasomotion stimulation (BEMER)**
**Partial test sample B: with added vasomotion stimulation (BEMER PLUS)**

**Measurement values taken at 2 different penetration depths: 3 mm and 8 mm.**

Two applications of 8 minutes each, 2 hours apart (intensity level 3).

Measurement timing: 0 minutes: initial values prior to the first application. Every four minutes up to 60 minutes after the 2nd application.

Significant differences in measured parameters after the 4th minute between the two partial sample groups.



The increased effects of a certain changing electromagnetic field with added vasomotion stimulation become impressively evident in the context of long term therapy for ambulant multi-morbid patients suffering from extensive vasomotion disturbances.

**Research Design**

| | |
|---|---|
| **Test** | Total test sample $N_{TOTAL}$=36<br>Ambulant male and female patients, 69-78 years of age.<br>Multi-morbid geriatric cardio-vascular at-risk patients.<br>No indication for inpatient treatment (adult onset diabetes) |
| **Partial Test Samples** | Two equal partial test samples of n=18<br>▶ Partial test sample A<br>Application of a certain changing electromagnetic field <u>without</u> added vasomotion stimulation (BEMER 3000).<br>▶ Partial test sample B<br>Application of a certain changing electromagnetic field <u>with</u> added vasomotion stimulation (BEMER Plus). |
| **Test System,** | Pulsed changing electromagnetic field<br>BEMER 3000 and BEMER Plus<br>Two applications every other day, 2 hours apart<br>(8 minutes, intensity level 3, on the mat). |
| **Measurement Intervals and** | Observation time of 60 minutes, equidistant measurement intervals:<br>▶ Day zero (determination of base values immediately prior to the 1st application), subsequent beginning of treatment.<br>▶ Data collections 1 day after each application on the 4th, 8th, 12th, 16th, 20th, 24th, 28th, 32nd, 36th, 40th, 44th, 48th, 52nd, 56th, and 60th day. |
| **Target Tissue** | Sub-cutis/ infra-cutaneous tissue (abdomen, region epigastr.). |
| **Measurement Methods** | Simultaneous measurements at 2 different tissue depth:<br>Penetration depth 3 mm<br>Penetration depth 8 mm<br>▶ Intravitalmicroscopy with computer assisted image processing<br>Vitalmicroscopy with computer assisted image processing.<br>▶ Laser-DOPPLER-microflow-measurement and white light spectroscopy.<br>Capture of complete interconnected micro-vascular networks with defined tissue volume $V=1200\mu m^3$ (diameter of vessels d≤200µm).<br>Defined conditions of macro-circulation and temperature regulation. |
| **Parameters** | ▶ Number of blood cell perfused nodal points nNP.<br>▶ Area below the envelop of the amplitude-frequency-spectrum of the (spontaneous) arteriolar vasomotion $A_{vm}$. |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), a = 5% |

Figures 317 and 318 provide information on the measurement data collected. Figures 319, 321 and 322 display examples of vitalmicroscopic findings. In figure 320, we use selected individual diagnostic findings to point to the rhythmic character of the changes in microcirculatory parameters after the application of a certain changing electromagnetic field with added vasomotion stimulation.

**Figure 317**

**Measurements for the parameter "number of blood cell perfused nodal points nNP" (mean values) in the target tissue sub-cutis after application of a certain pulsed electromagnetic field with and without added vasomotion stimulation for multi-morbid geriatric patients with high cardio-vascular risk factors.**

**Partial test sample A: no added vasomotion stimulation (BEMER)**
**Partial test sample B: with added vasomotion stimulation (BEMER PLUS)**

**Measurement values taken at 2 different penetration depths: 3 mm and 8 mm.**

Two applications of 8 minutes each, 2 hours apart, every other day (intensity level 3, on the mat).

Measurement timing: Day zero: initial values prior to the first application.

Day 4 to day 60 of therapy period.

Significant differences in measured parameters after the 8th day between the two partial sample groups.

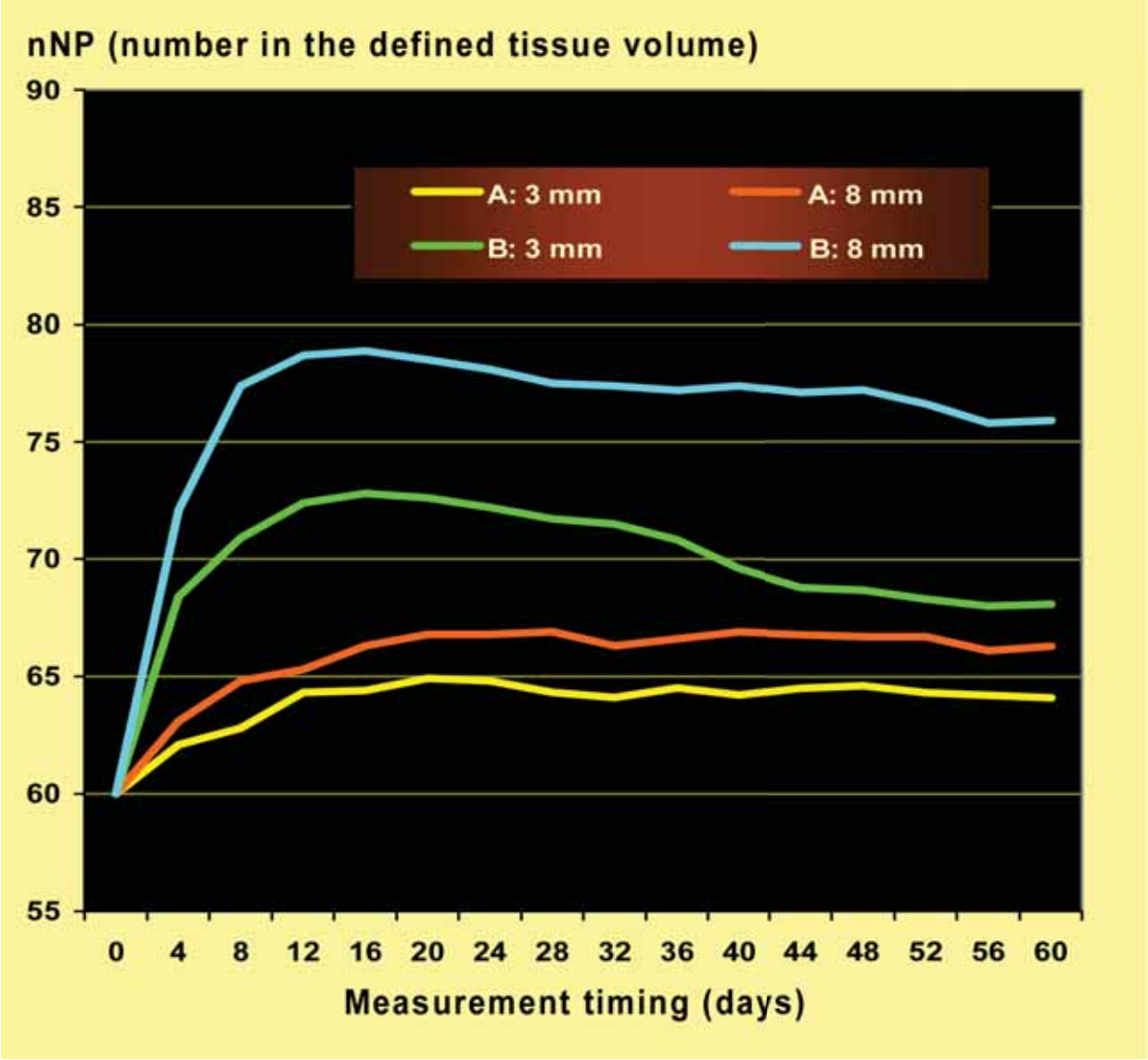
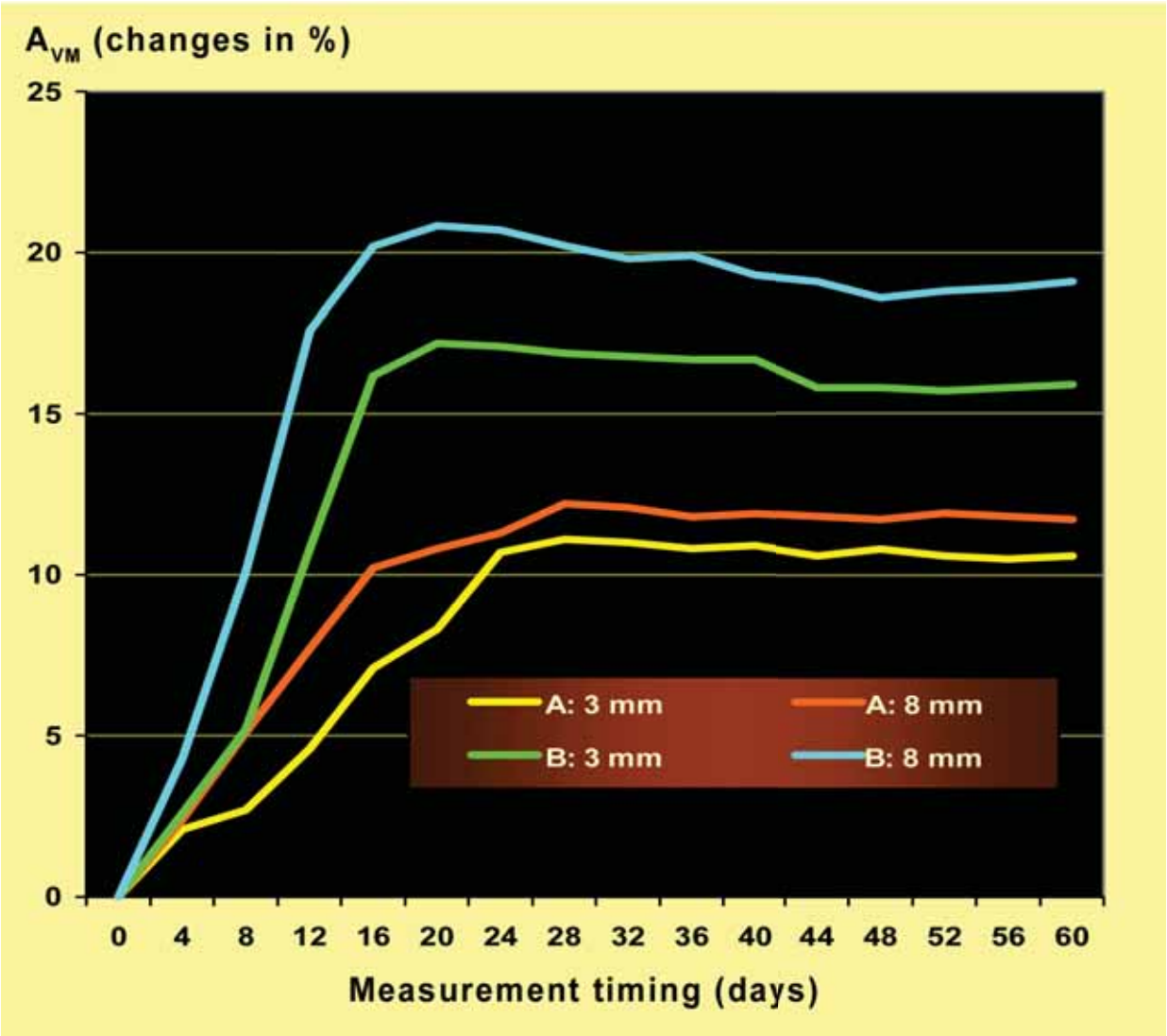


**Figure 318**

**Measurements for the parameter "area under the envelope of the amplitude frequency spectrum of spontaneous arteriolar vasomotion Avm" (mean values) in the target tissue sub-cutis after application of a certain pulsed electromagnetic field with and without added vasomotion stimulation for multimorbid geriatric patients with high cardio-vascular risk factors.**

**Partial test sample A: no added vasomotion stimulation (BEMER)**
**Partial test sample B: with added vasomotion stimulation (BEMER PLUS)**

**Measurement values taken at 2 different penetration depths: 3 mm and 8 mm.**
Two applications of 8 minutes each, 2 hours apart, every other day
(intensity level 3, on the mat).
Measurement timing: Day zero: initial values prior to the first application.
Day 4 to day 60 of therapy period.
Significant differences in measured parameters after the 12th day between the two partial sample groups.



a

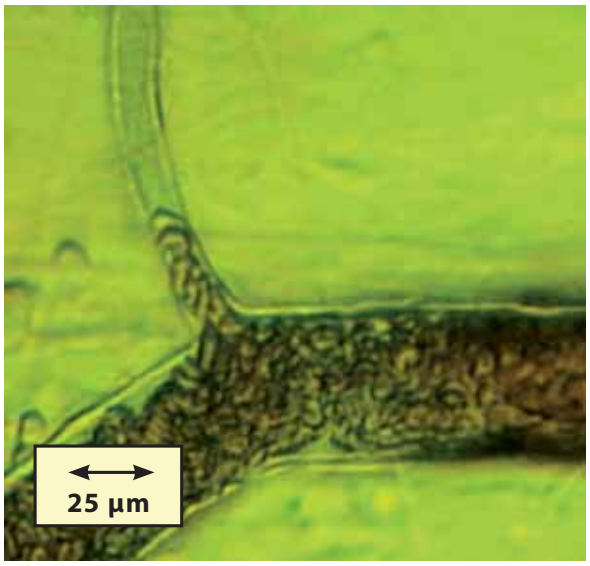


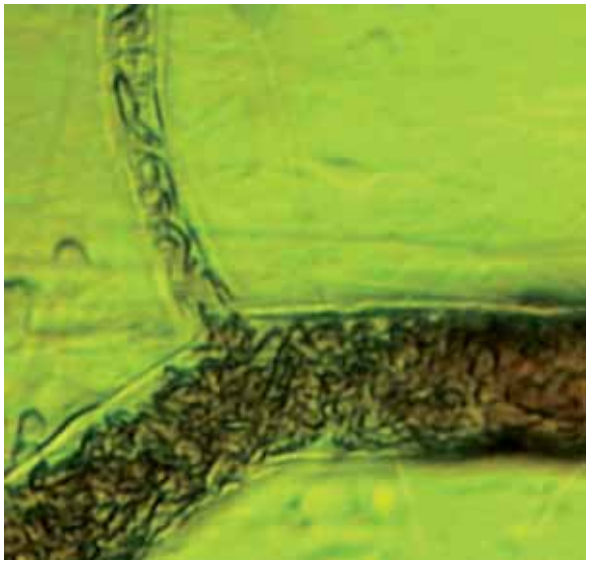

**Figure 319**

**Changes in the perfusion state of a micro-vessel arborization (capillaries, venules) in the target tissue sub-cutis under the influence of a certain changing electromagnetic field with vasomotion stimulation.**

**Example of vitalmicroscopic findings, 1/1000 s.**

**Images a to c taken in 15 second intervals**

b



c

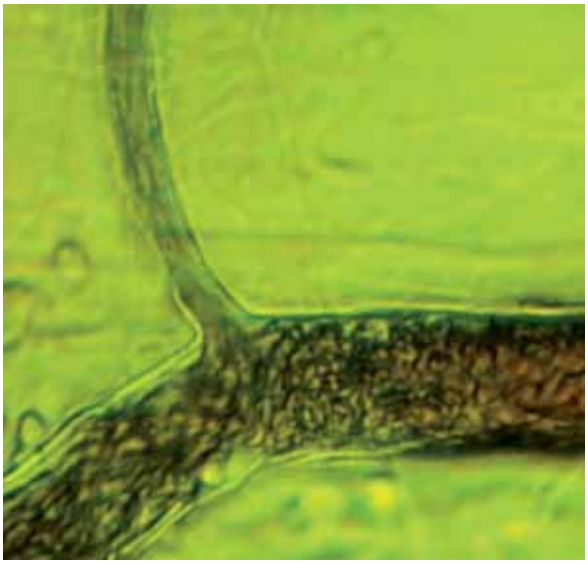


**Figure 320**

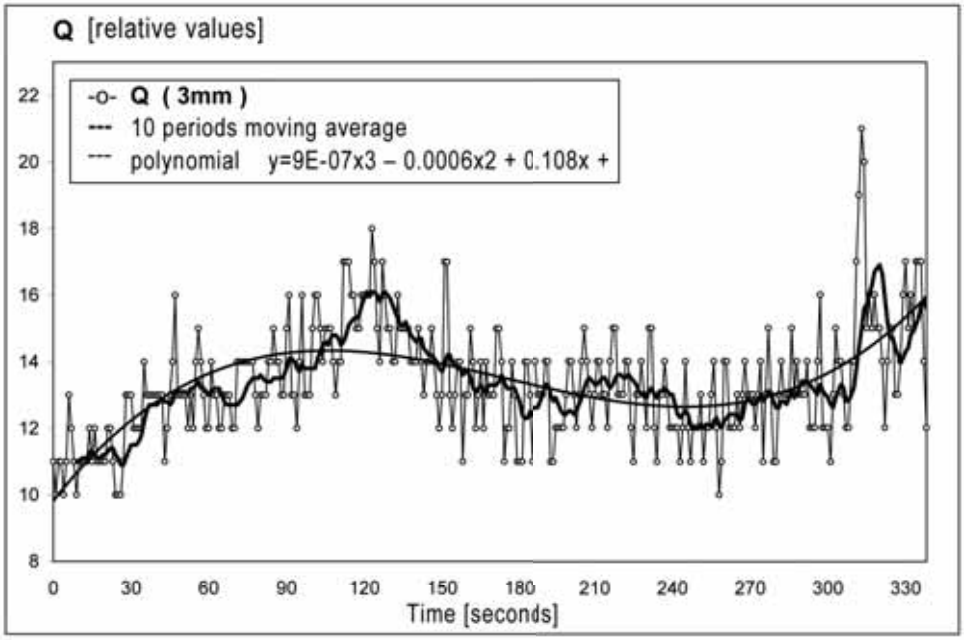
**Changes in the venular flow rate in the micro-vessels of the sub-cutaneous target tissue at varying tissue depths (3 mm and 8 mm) under the influence of a certain changing electromagnetic field.**

**Continuous recording within a defined period (beginning with the 2nd minute of the application of a certain changing electromagnetic field).**

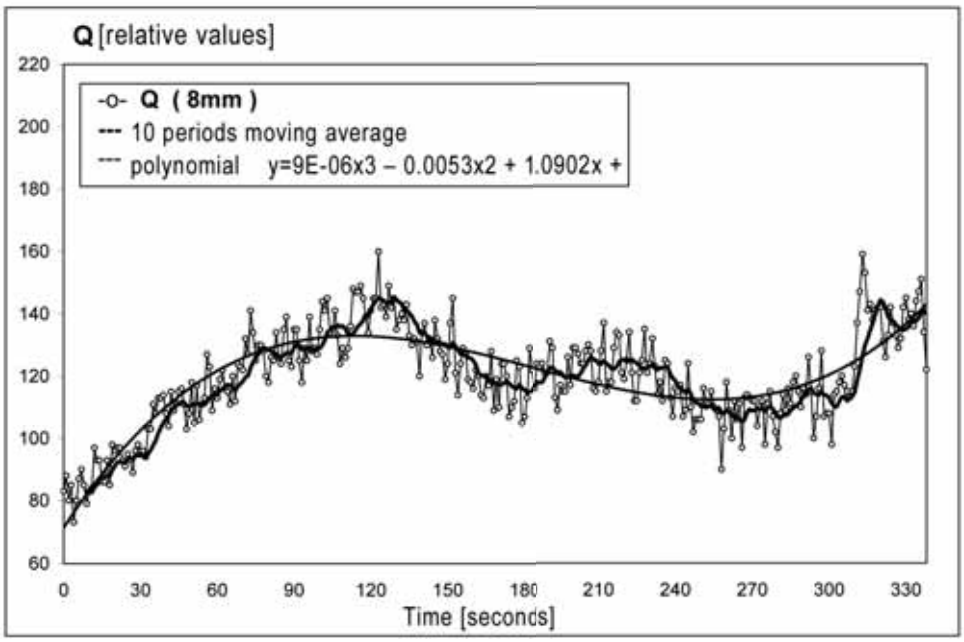
**a, b: application of a certain changing electromagnetic field without added vasomotion stimulation (BEMER).**

**c, d: application of a certain changing electromagnetic field with added vasomotion stimulation (BEMER PLUS).**

**a**



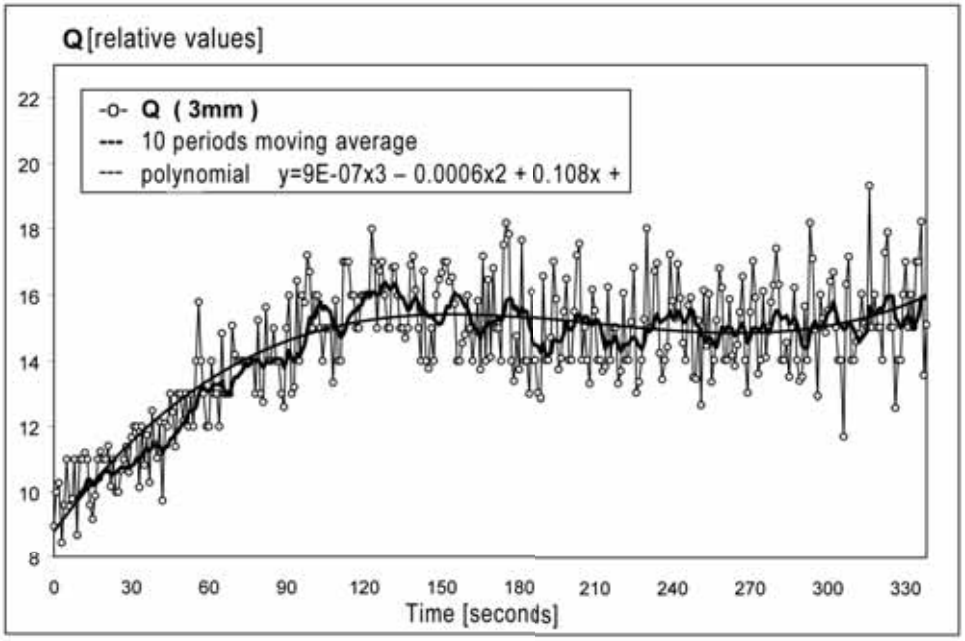

**b**



*Please pay attention to the differing amounts in parameter changes (ordinate scale!) and the rhythmic course of the graphs.*

*Aside from the daily fluctuations of biological rhythms (circadian rhythms) several other variations of biological characteristics occur. The regulatory processes of microcirculation especially are subject to a changing vibration behavior. One example would be the "swing adjustment" of the microcirculatory flow rate to a different regulatory level under the diction of spontaneous vasomotion.*

**c**




**d**

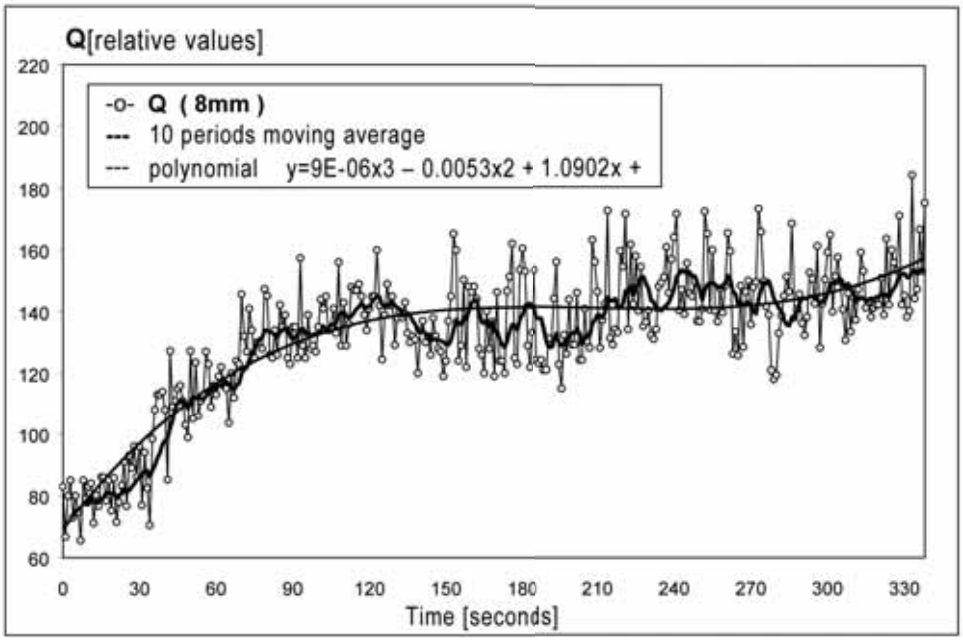


**Figure 321**

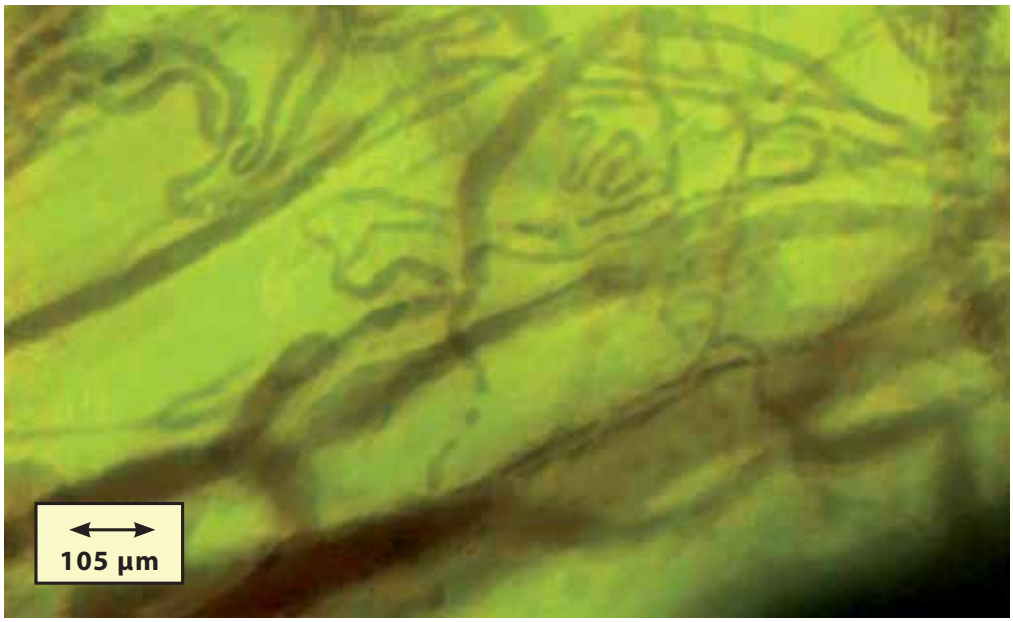
**Distribution of the plasma-blood cell mixture in the micro-vessels of the subcutaneous target tissue before and after the application of a certain changing electromagnetic field with vasomotion stimulation.**

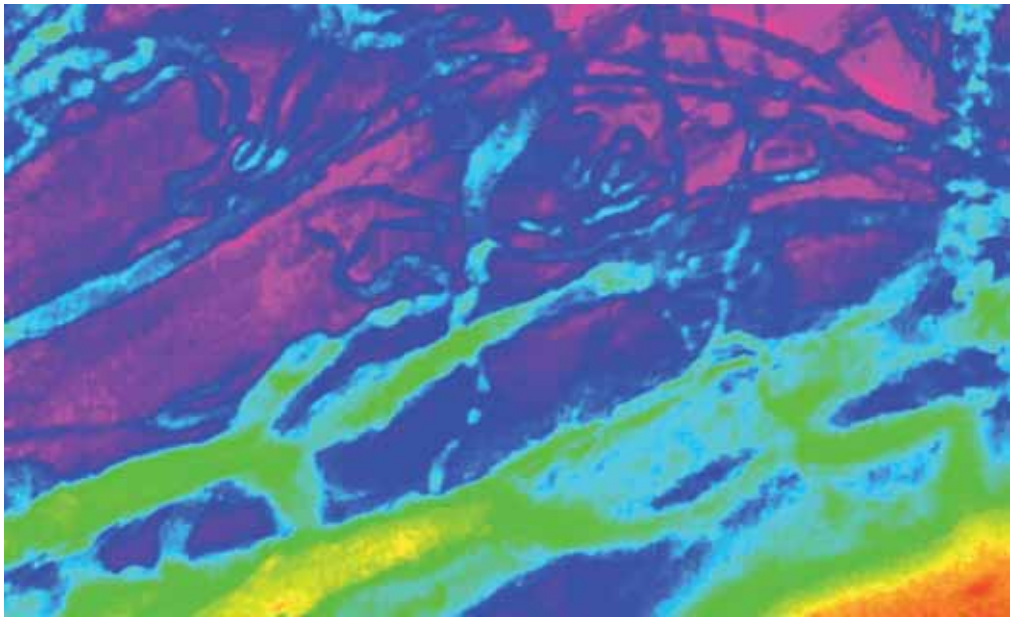
**(Example of vitalmicroscopic findings, 1/1000 second; capillaries, venules, arterioles).**

**a: distribution before application** ⟶

**b: distribution after an 8-muinute application**

**a**

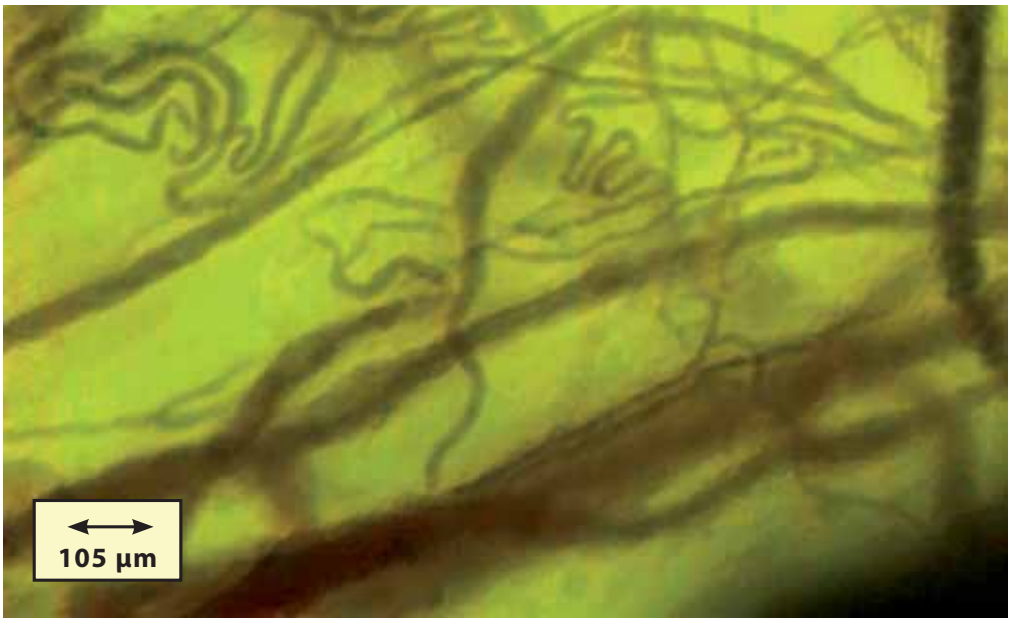


Primary image on top, related pseudo-color-transformation of the primary image below (the blood cell perfused micro vessels are marked in red)

The noticeable increase of blood cell perfused nodal points in the micro-vascular network after the application of a certain changing electromagnetic field with added vasomotor stimulation can be clearly seen.

**b**



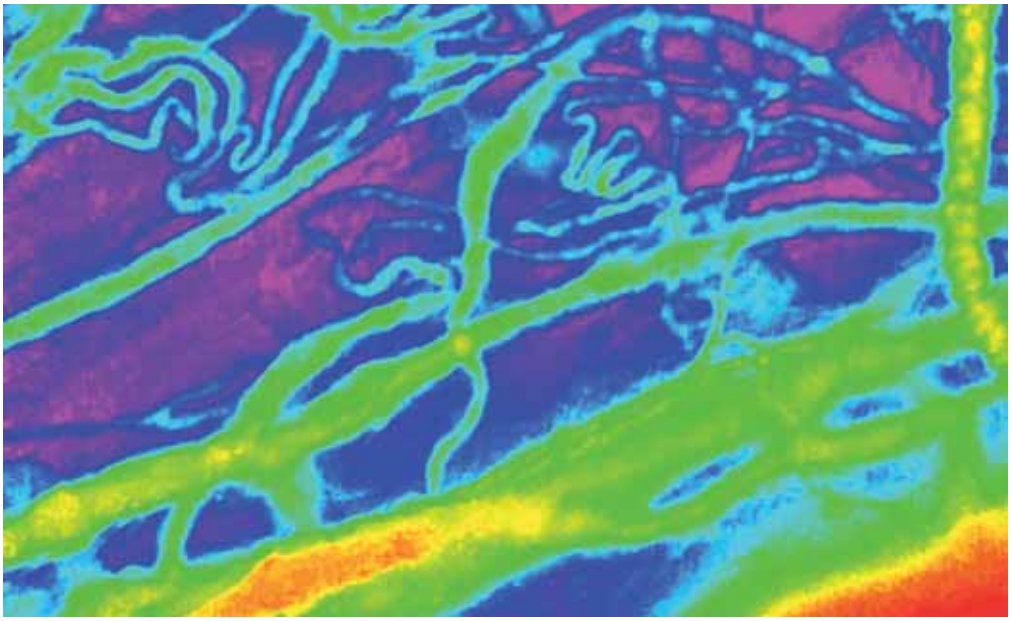



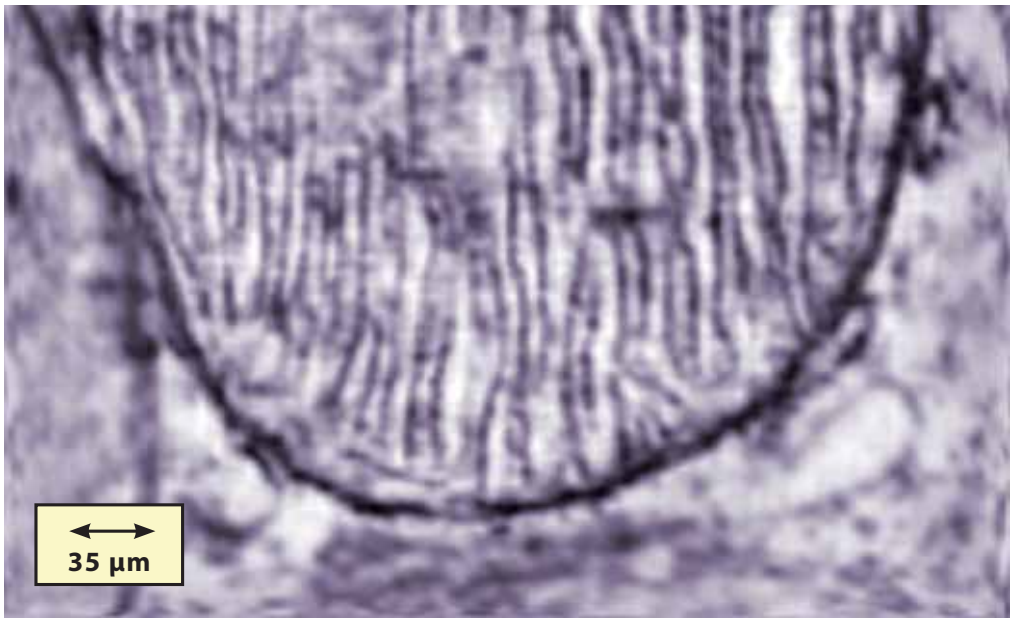
**Figure 322**

**Change of the perfusion level in the micro-vessels of the sub-cutaneous target tissue before and after the application of a certain changing electromagnetic field with vasomotion stimulation.**

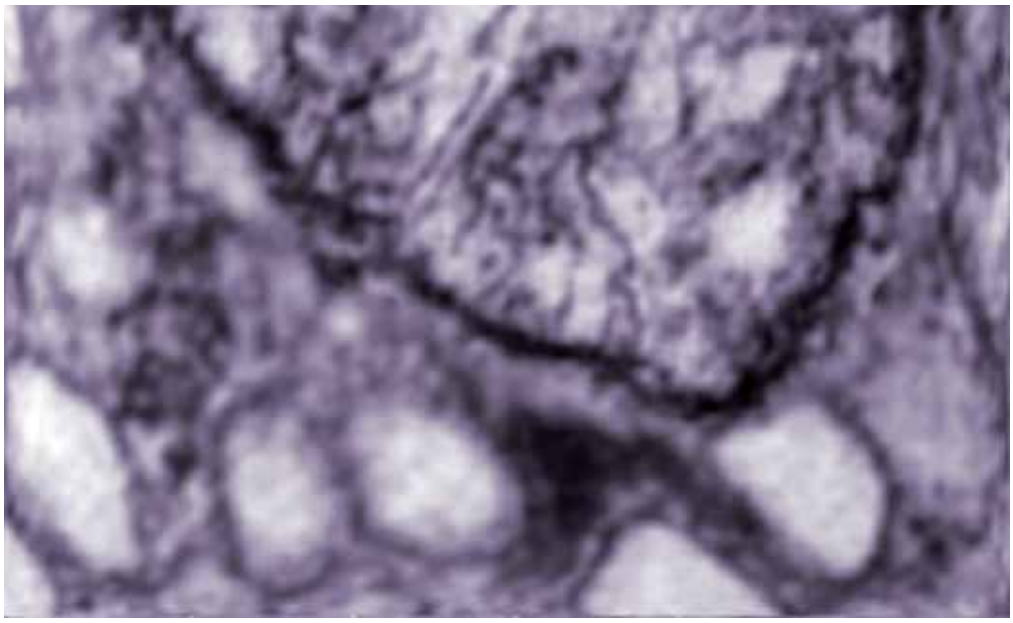
**(Example of vitalmicroscopic findings, 1/1000 second; capillaries, venules, arterioles).**

**Image sequence a to d: identical region of micro-vessels at different observation times (60 seconds apart)** →

**a**



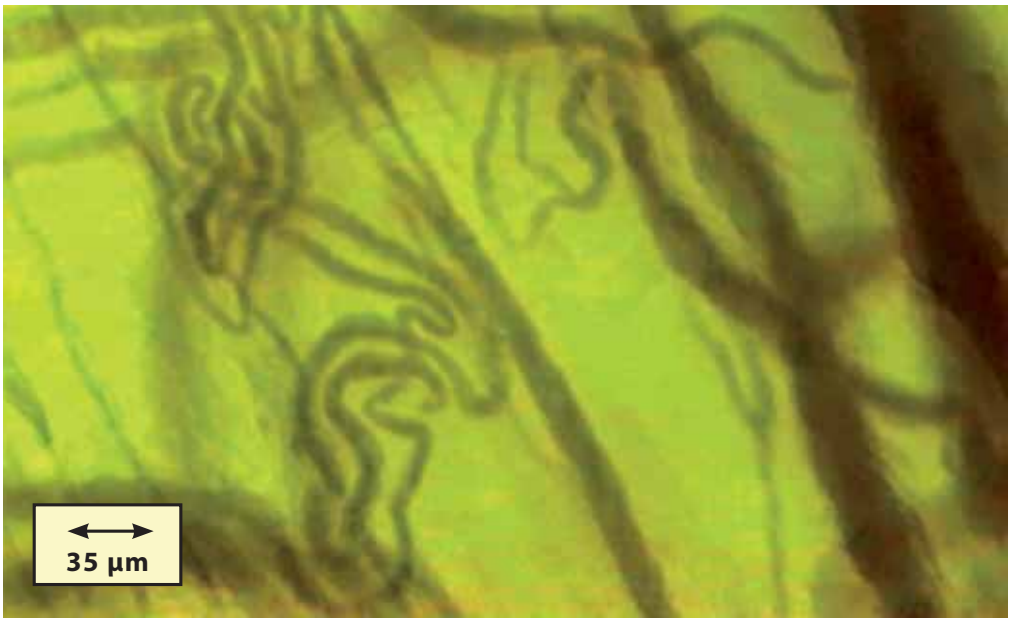

**b**



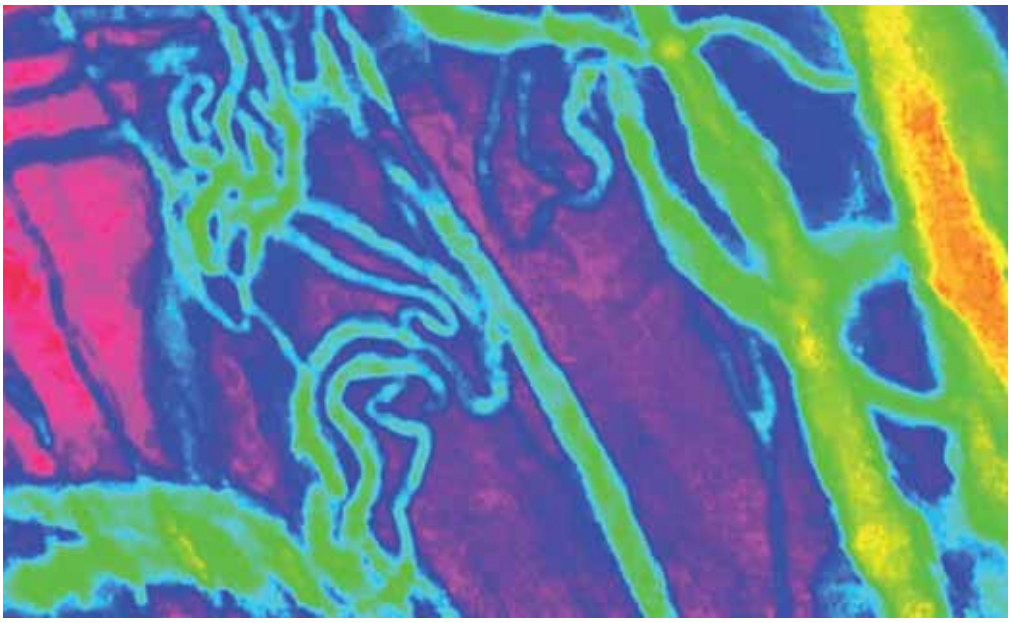
*The functional state of the micro-circulation in this network changes from minute to minute under the influence of the application:*

*Increased speed in the flow of red blood cells, increase of the flow rate in the arterioles and venules, disaggregation of red blood cells, normalized capillary perfusion.*

**c**




**d**



The following summary presents the research results regarding the effects of certain electromagnetic fields with added vasomotion stimulation on microcirculation:

Micro-circulatory function can be influenced to a physiologically relevant degree by the application of certain changing electromagnetic fields.
For conditions of stress and illness that are accompanied by impaired spontaneous vasomotion, added signals for vasomotion stimulation produce increased therapeutic benefits on micro-circulatory function.
A comparison to other therapy option shows that the application of certain changing electromagnetic fields has a valid place in the spectrum of effectual prophylactic and complementary therapy options.

In figure 323 the image sequences shown give an example of stimulated spontaneous arteriolar vasomotion in the intestinal target tissue.

The proven possibilities to influence spontaneous vasomotion have revived scientific discussions regarding **the hypothesis for possible effects** of certain electromagnetic fields in the area of microcirculation. This applies to the following intra-cellular aspects:

- Endothelial factors of the spontaneous vasmotoric functions
- Processes during energy provision in the mitochondria

Even though these newly discovered results still need further critical testing and are provisional working hypotheses, we cannot forgo mentioning them in the context of this book. Below we will address some available data.

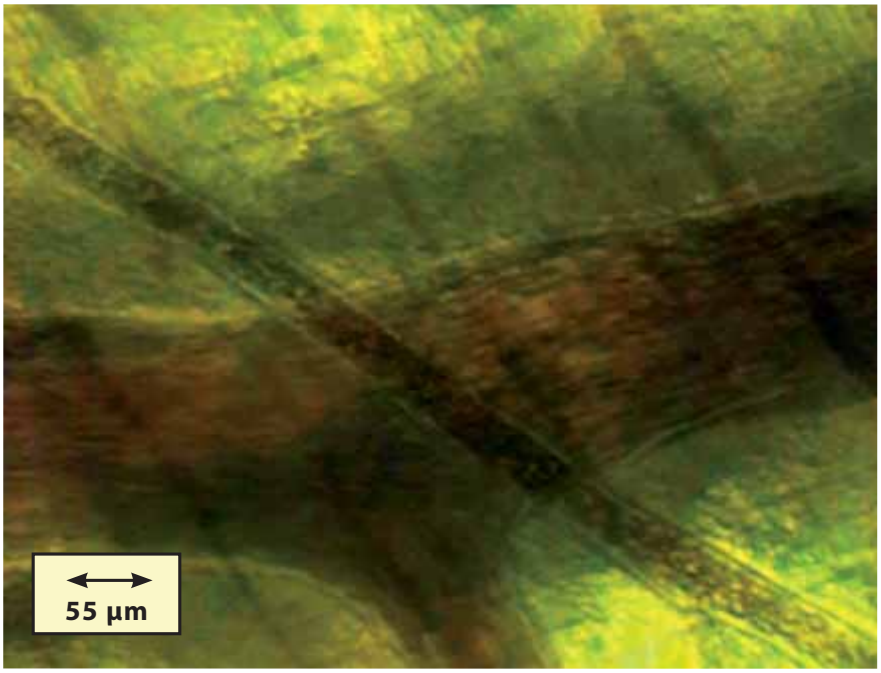
The author expresses his appreciation to the Max-Delbrück-Center for Molecular Biology in Berlin for its advice and assistance.

**Figure 323**

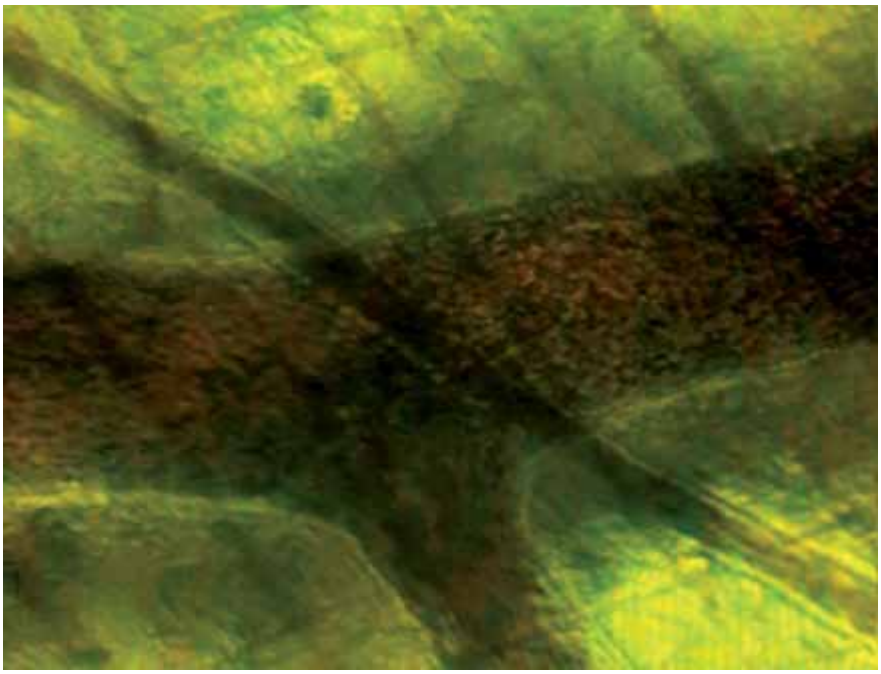
**Spontaneous vasomotion of an intestinal arteriole after stimulation. (Vitalmicroscopic findings, 1/500 second; arteriole in vasomotion diagonally in the picture, venule in the background).**

**Image sequences from a to d taken in ~ 20 second intervals.**

**a**

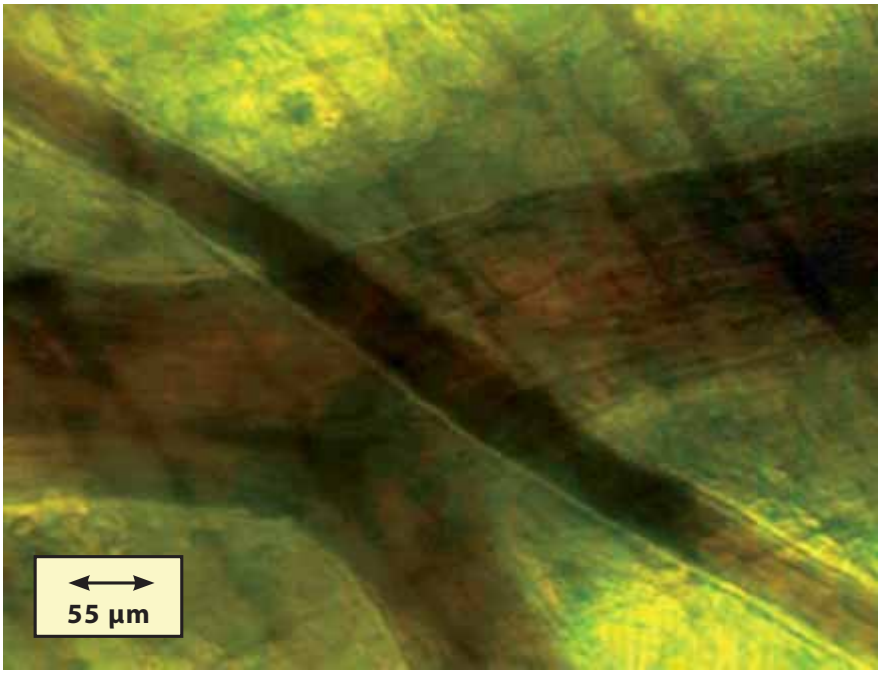



**b**

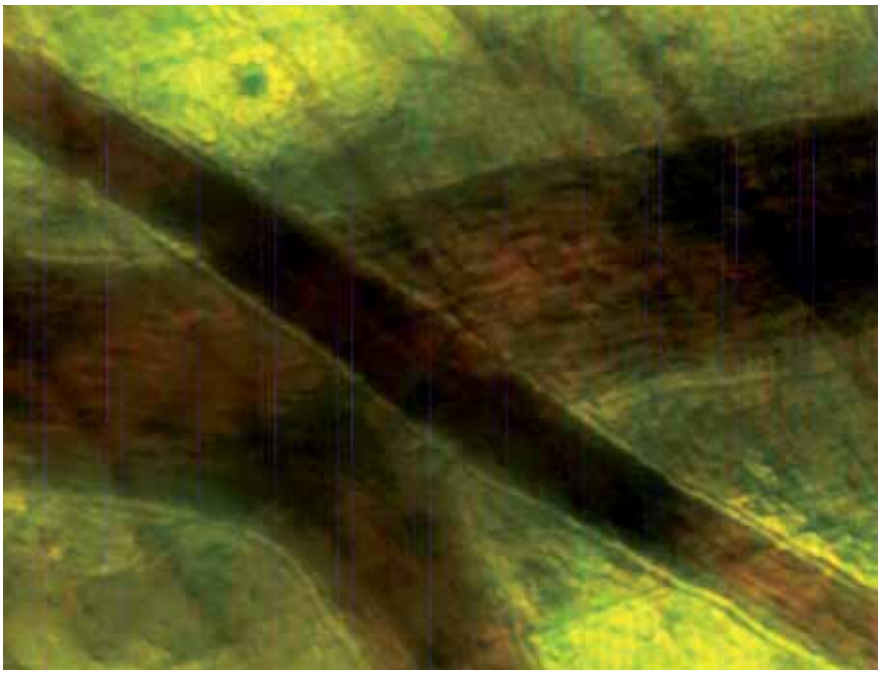


*It is often overlooked that venules also have the ability for vasomotion which is, however, much less pronounced than in the arterioles.*

**c**




**d**



**Which concepts can be drawn upon to explain the stimulation of spontaneous vasomotion? Which measurement data support the working hypothesis?**

Recent experimental data on influencing intracellular processes that are significant in the development of spontaneous vasomotion are available and are being discussed on the condition that further testing be conducted.

Let us first consider the regulatory mechanism of endothelium-mediated modulation of the tone of muscle reinforced (micro) vessels already.

> In addition to active transport of biogenic amines (serotonin, norepinephrine) into the endothelium and their subsequent oxidative deamination, the metabolism of adenine nucleotides (ADP and ATP) circulating in the blood also plays a role in the uptake and metabolism of vasoactive substances. These adenine nucleotides, whose metabolism also occurs via the endothelium, mainly originate from platelets. The metabolism of adenine nucleotides occurs in a cascade-like manner through ectonucleotidases located on the luminal side of the endothelial cell surface. Here, ATP is degraded via ADP and AMP to adenosine, which is transported via a carrier dependent mechanism into the endothelial cell, where most of it is rephosphorylated. Thus, an energy source for endothelium-mediated regulation of tone is provided. The most important process in endothelium-mediated regulation of tone is the formation and release of vasoactive autacoids (especially NO formation and NO release, EDRF reactions).
> For the regulation of endothelial NO formation, endothelial cells express a constitutive NO synthase, whose activity is regulated by phosphorylation and Ca++/calmodulin. The molecular mechanism of NO formation in the endothelial cells is induced by shear stress and has been clarified for the most part. During this process, numerous, multiply linked enzymatic processes occur:
> The effect of a certain shear stress on the luminal side of the endothelial cell surface initiates the phosphorylation of an interendothelial adhesion molecule (PECAM-1), which exerts signaling functions by means of its cytoplasmic portion. As a result, PI3 kinase is activated, which causes enhanced formation of phosphatidylinositide triphosphate (PIP3). This leads to recruiting of protein kinase B/akt to the plasma membrane, which is now phosphorylated by phosphatidylinositide-dependent kinase (PDK) and is thus activated. NO synthase (NOS) is phosphorylated by Akt at a serine residue. This results in an increase in the electron flow at the enzyme and increased enzymatic activity.

These processes affect both the comparatively slow processes involving changes in tone during diameter-dependent flow regulation as well as the (more rapid) periodic changes in diameter that occur after another temporal pattern during spontaneous vasomotion.

Can the aforementioned molecular mechanisms (and other mechanisms which will not be mentioned here) that form the basis of vessel wall motions be influenced by the very low amounts of energy of certain changing electromagnetic fields and be used to explain stimulation of vasomotion?

First it must be established: The idea that any chemical or biochemical reaction can be influenced by the addition of very low energy is absurd in light of the magnitude of energies required for activation.

In enzymatic reactions, however, which occur in a cascade-like manner multiply linked with each other in a chain-like fashion, less and less activation energy is required from one step to the next. In the author's opinion, it is rather unlikely, but cannot be completely ruled out, that the very low energy of certain changing electromagnetic fields are active in the aforementioned molecular mechanisms of shear stress-induced NO formation in the endothelium. Direct evidence that would support the assumption of such an influence on enzymatic reaction processes in the endothelium has not yet been provided.

All of the available experimental data support the idea that the low amounts of energy of certain changing electromagnetic fields cannot solely be used to justify biological effects in the area of microcirculation; rather, certain temporal changes in the stimulation signal (signal configuration of the changing electromagnetic field) are significant.

A more or less two-part constant energy input, such as heat, in and of itself triggers other effects in the area of the microcirculation.

For microcirculation research, another path has recently opened up that further contributes toward clarifying the functional mechanisms of certain changing electromagnetic fields. This pertains to the relaxant effect of NO on smooth vascular muscle cells, which arises through activation of guanylylcyclase.

> In its heme-containing subunit, guanylylcyclase has a bivalent iron onto which NO can bind. This results in a conformational change of the adjacent catalytic center, which induces an increased rate of GTP → cGMP conversion. The result is an increase in the concentration of intracellular cGMP, which leads to activation of cGMP-dependent protein kinases. This activates mechanisms to reduce intracellular calcium in the smooth vascular muscle cells, which permits relaxation of the vessel wall.

In functional endothelial disorders, e.g., arteriosclerosis and diabetes mellitus, NO availability is reduced so that an overbalance of constricting factors act upon the vessel walls. These disorders also affect (with different characteristics) the area of muscle-reinforced micro-vessels, in particular their ability to undergo spontaneous vasomotion. Indicators of these changes are decreasing local concentrations of cGMP.

Unexpected results emerged during treatment monitoring of cardiovascular at-risk patients with marked arteriosclerosis and age-related diabetes.

Local changes in the concentrations of cGMP and PGE2 were determined using a noninvasive spectrometric procedure in a total of 24 outpatient geriatric at-risk patients ~70 years of age in a 60-day observational study (data collection in a time span of 10 days).

Twelve patients were treated according to customary practice (control group), twelve other patients (test group), per their request, were treated with a certain changing electromagnetic field with added vasomotion stimulation (BEMER PLUS, intensity level 3, every other day 2 applications of 10 minutes each, 2 hours apart) in addition to customary medications.

The data collected are displayed in figure 324.

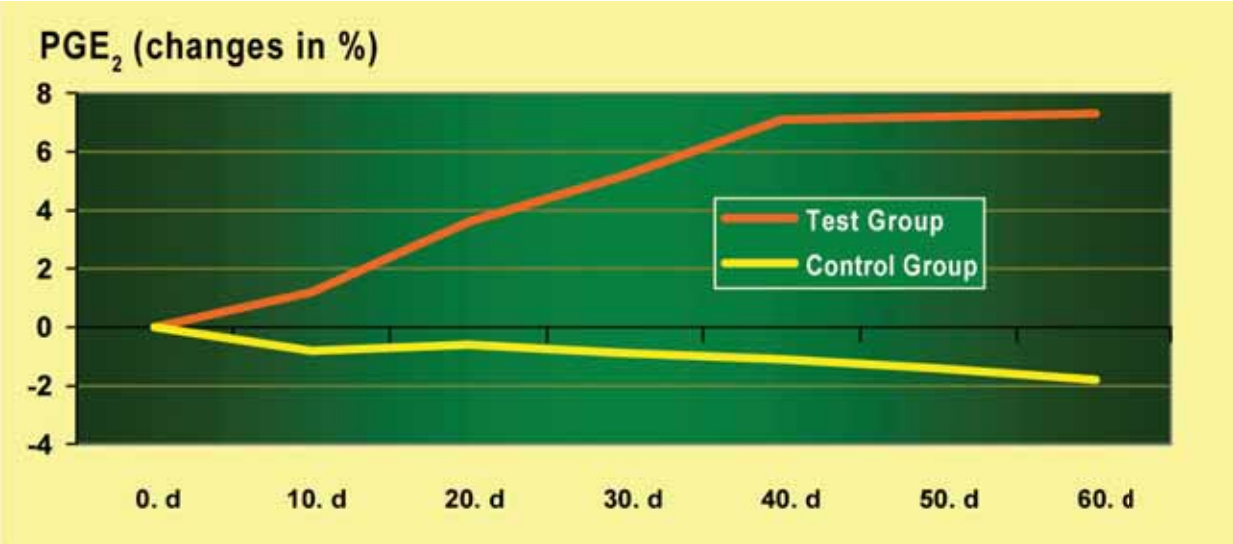
**Figure 324**

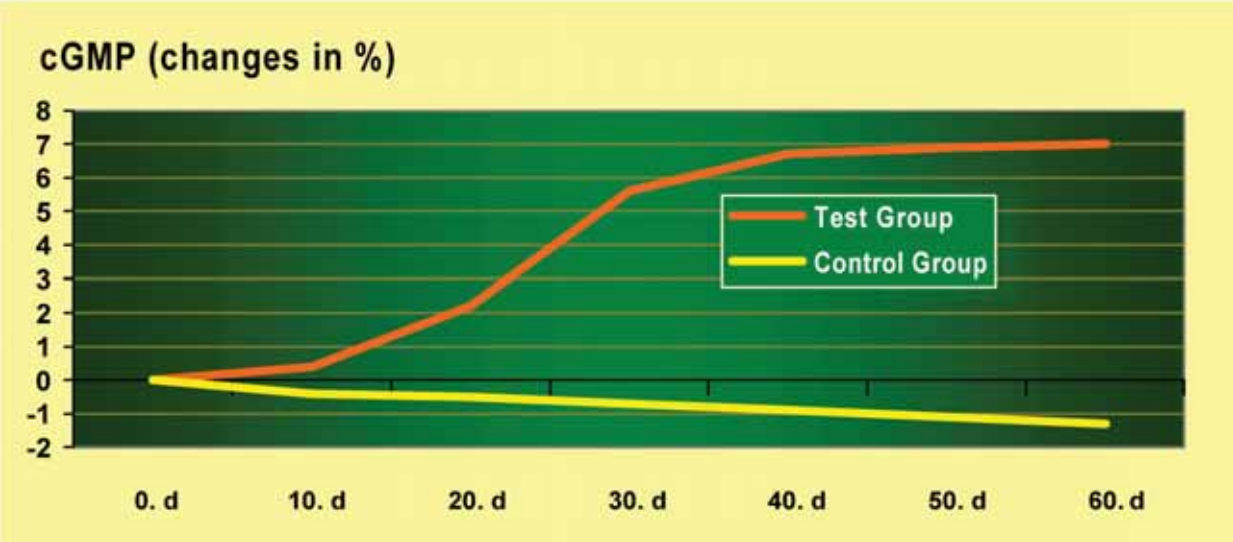
**Local changes in concentration of PGE2 and cGMP (mean values) for outpatient geriatric at-risk patients**

**Control group: customary medications**

**Test group: customary medications plus long term therapy with a certain changing electromagnetic field with added vasomotion stimulation.**

Significant differences in parameters measured between control group and test group beginning on day 30.

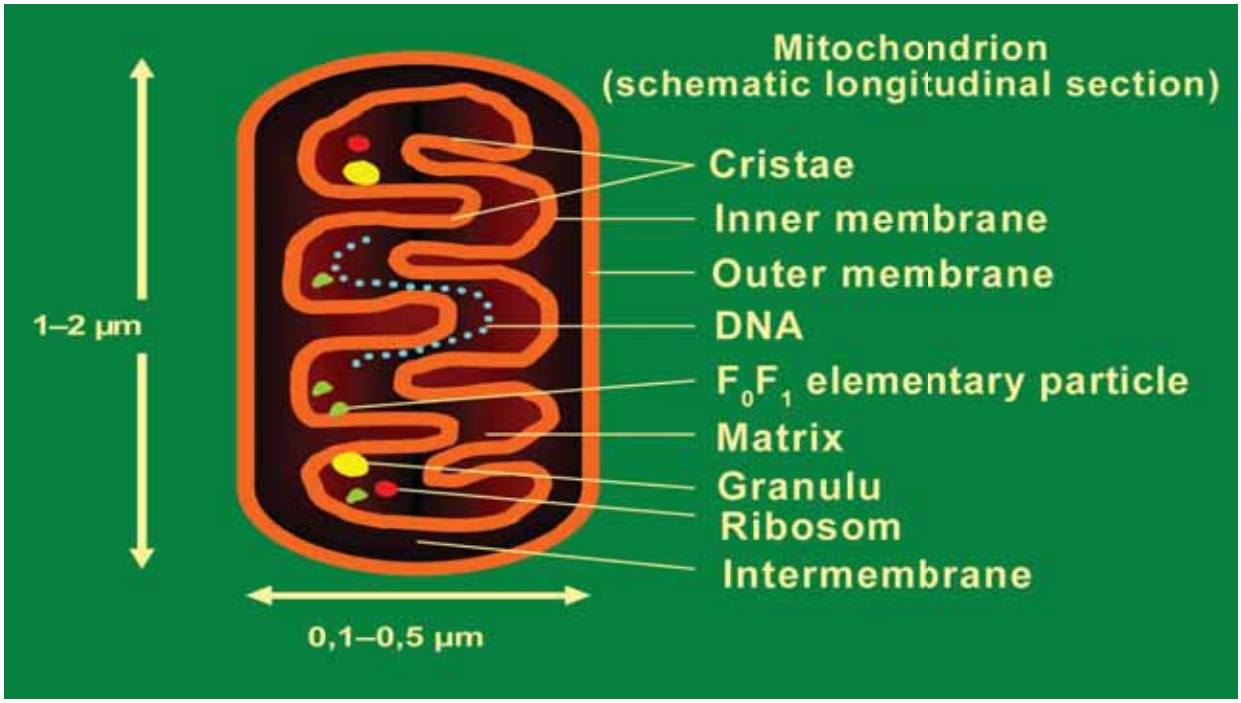


The results of this investigation require additional review. They represent the current status of research concerning the action mechanisms of certain changing electromagnetic fields on the microcirculation. The results of more extensive research will be anticipated with particular interest because the changes in characteristics determined are in opposition to those which occur in the development of arteriosclerotic processes.

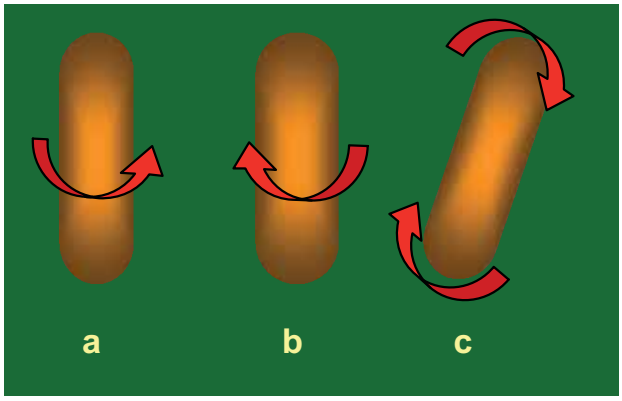
Current research efforts are directed at further questions. Initial experimental data with regard to mitochondrial energy supply under the influence of certain changing electromagnetic fields are available.

Mitochondria are special cell organelles that attend to cell respiration. They serve as the "power plants" of the cell because in them the capacity of the cell to react with oxygen through the respiratory enzymes is concentrated. Furthermore, the entire biochemical system for the final degradation of the carbon skeleton of the various substrates of cell metabolism, as well as the enzymes for fatty acid degradation are located in the mitochondria. In addition to the enzymes of oxidative metabolism, the mitochondria also contain the entire enzyme system for the energy arising during respiration to ADP. During this oxidative phosphorylation, energy-rich phosphate compounds are formed (ATP).




It is known that the enzyme complexes of ATP formation within the mitochondria make very rapid rotational movements (several dozen per second), whose number per time unit is related to the supply of ATP. If the rotational frequency of these enzyme complexes drops, the ATP supply for the cell decreases. It is know that in diabetes mellitus the number of these rotational movements per time unit is decreased, which is associated with reduced ATP provision, which has a direct effect on cell metabolism.

In a cooperative effort between the Institute for Microcirculation in Berlin and the Max Delbrueck Center for Molecular Biology in Berlin-Buch, it was discovered through the use of high resolution imaging techniques (high speed camera with an image sequence frequency >> 120 images per second) that the mitochondrion also performs rotational motions which, however, are considerably slower than those of the enzyme complex. Hypothetically, it is assumed that there is a relationship between the mitochondrial motions and the corresponding substance transport between the cell organelles and the surrounding cell space. Preliminary experimental results indicate a relationship between the mitochondrial rotational motions and the supply of ATP for the cells.




Most probably, the rotation movements around the longitudial axis of the mitochondria (a and b in the adjacent schematic representation) are of significance. Whether there is a preferred right or left spin is still unclear.

Other movements of the cell organelles (c) most probably have their origins in cytoplasmic transport processes.

The mitochondrial ATP supply in the endothelial cells is of particular significance for the regulation of microcirculation. In ambulant geriatric patients with adult onset diabetes and arteriosclerosis, reduced rotational mitochondrial movements were detected in the micro-vascular endothelial cells in comparison with healthy subjects of a younger age. Initial data obtained from various random samples from geriatric patients with diabetes and arteriosclerosis suggest an effect of certain electromagnetic fields on the mitochondrial rotational movements. In agreement with these results, an increased supply of ATP was detected through spectrometry.

> In addition to the commonly used medication, at their request, geriatric patients received a treatment with a certain changing electromagnetic field with additional vasomotion stimulation (BEMER PLUS, intensity level 3, 2 10-minute applications at an interval of 2 hours, every other day) for a treatment period of 60 days.

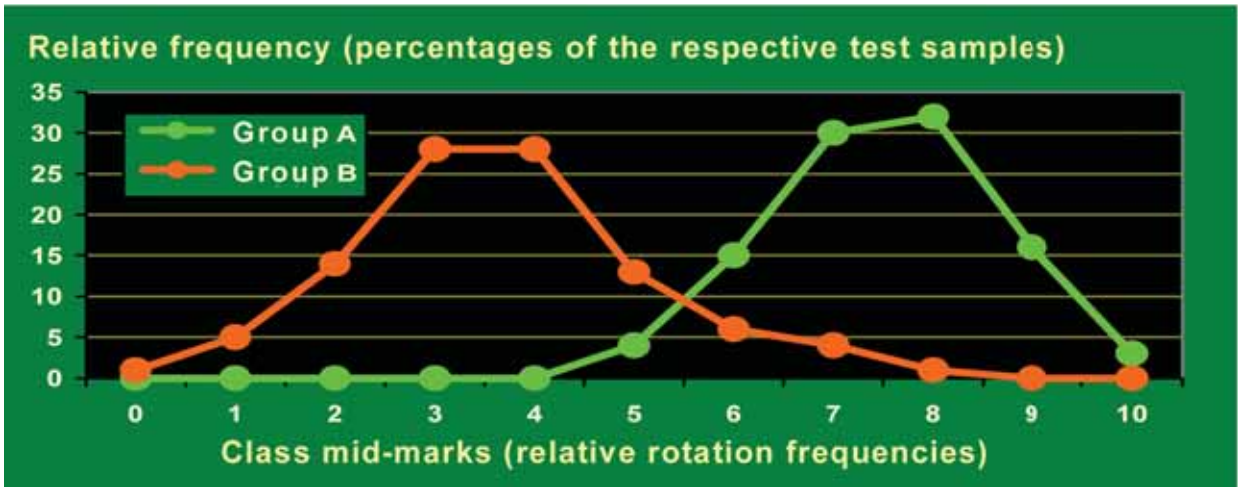
In the context of this book, we will forego the exact description of the design and the complete information of available data. This information is to be published at a later point in time as a joint publication of the Institute for Microcirculation and the Max Delbruck Center for Molecular Biology in Berlin after completion of further investigations.

Preliminary information regarding the current status of several research findings are summarized in figure 325. With them, the author would like to inform the reader about the progress of research projects being conducted.

**Figure 325**

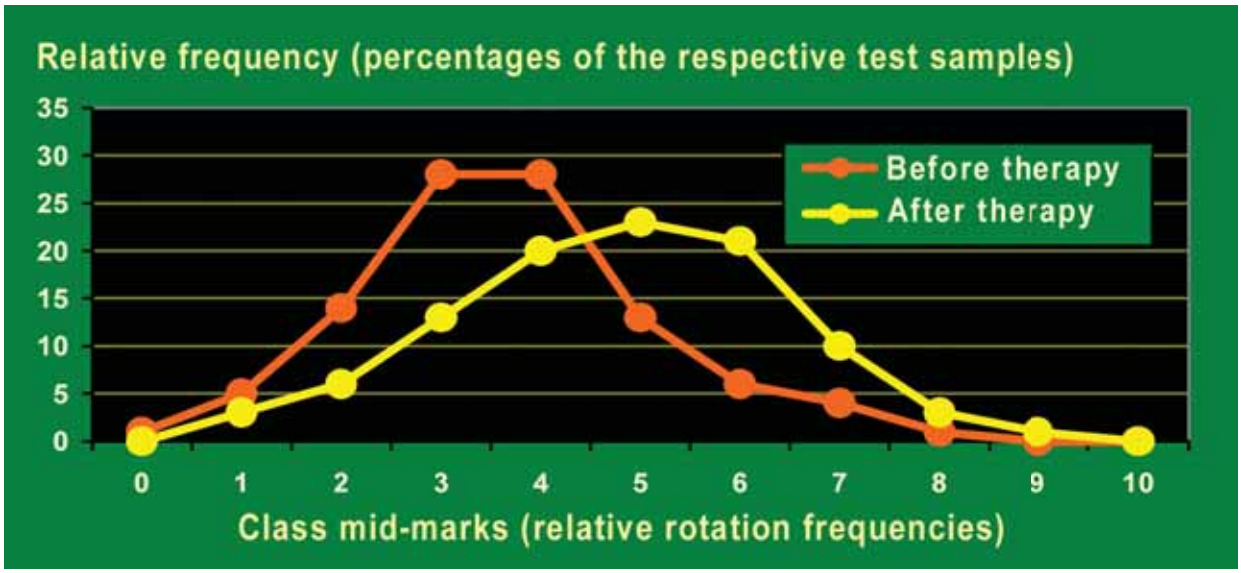
**Frequency polygon (relative frequency) for mitochondrial rotation frequencies (in relative units) for a test sample of healthy subjects ~ 35 years of age (group A) and for a test sample of ambulant multi-morbid geriatric subjects ~ 70 years of age (group B).**

50 individual measurements were taken for each partial test sample (data arranged in classes 0 to 10).




**Frequency polygon (relative frequency) for mitochondrial rotation frequencies (in relative units) for a test sample of ambulant multi-morbid geriatric subjects ~ 70 years of age before and after a 60 day therapy period with a certain changing electromagnetic field.**

50 individual measurements were taken for each partial test sample (data arranged in classes 0 to 10).

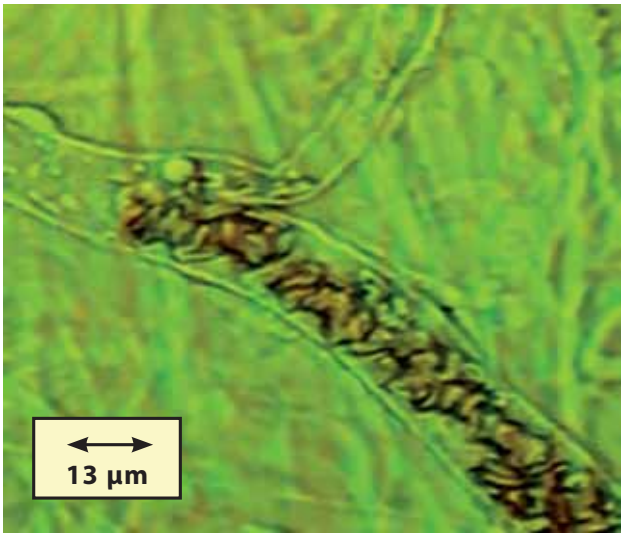


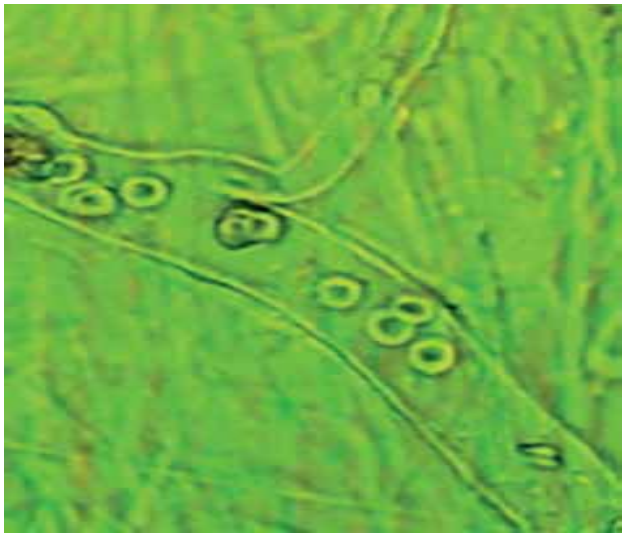
We can gather from figure 325 that an increase of previously reduced mitochondrial rotation frequencies occurred (the frequency polygon shifts to the right in the direction of higher mitochondrial rotation frequency characteristic for the physiological state of younger healthier subjects) in the test sample of multi-morbid geriatric patients after long-term therapy with a certain changing electromagnetic field. Already existing findings regarding ATP provision are consistent with these results.

A final assessment of these research results is currently not possible. The results, however, provide an encouragement for further research regarding the therapy-relevant influence on endothelial factors of spontaneous vasomotion and the energy supply of the mitochondria; this type of research is presently being conducted at the Institute for Microcirculation in Berlin in cooperation with a bio-molecular research institution.

Multi-morbid older patients in particular need effective stimulation of endothelial and spontaneous vasomotoric functions in the area of microcirculation.

We should always remember that the functionality of an organ is determined by the condition of its micro-perfusion.



Both vitalmicroscopic pictures show disturbances in a section of a micro-vessel, which can often be observed in multi-morbid geriatric patients. In most cases, they accompany disruptions in endothelial and spontaneous vasomotoric functions, or are a result of them.

The two images show different disturbances of micro-perfusion in a micro-vessel at two consecutive observation times.

**With investigations to clarify the mechanisms of certain changing electromagnetic fields in the intracellular region of cell organelles, microcirculation research enters the arena of molecular biology.**

For the reader who is especially interested, we examine some additional important state-of-the-art molecular biology aspects of ATP formation in more detail below, which are taken into account as important scientific principles or working hypotheses for further investigations to clarify treatment-relevant effects of certain changing electromagnetic fields.

For all cell activities, energy is required, which mostly originates from hydrolysis of one of the high-energy phosphoric acid anhydride compounds in ATP (adenosine triphosphate; see Chapter 10):

$$ATP^{4-} + H_2O \leftrightarrow ADP^{3-} + P_a^{2-} + H^+$$

ATP = adenosine triphosphate
ADP = adenosine diphosphate
$P_a$ : $HPO_4^{2-}$ (inorganic phosphate)

Under predefined conditions, the change in free energy (free enthalpy) $\Delta W^*$ is:

$$\mathbf{\Delta W^* = -7{,}3\ kcal/mol.}$$

This energy released by hydrolysis of the phosphoric acid anhydride compounds is a prerequisite for enabling many cellular reactions. These include the transport of molecules against a concentration gradient (e.g., Na+/K+-ATPase), the contraction of muscle cells, and endothelial and muscle activities underlying spontaneous arteriolar vasomotion. In addition, the energy released during conversion of ATP is used in a plethora of metabolic pathways (e.g., nucleic acid synthesis, protein synthesis).
The synthesis of high-energy phosphoric acid anhydride compounds in the ATP molecule (ATP formation) occurs in an endothermic reaction, in which free energy W* is "consumed."

$$P_a^{2-} + H^+ + ADP^{3-} \leftrightarrow ATP^{4-} + H_2O$$

Under predefined conditions, the change in free energy (free enthalpy) $\Delta W^*$ is:

$$\mathbf{\Delta W^* = +7{,}3\ kcal/mol.}$$

For ATP formation, the degradation of glucose and fatty acids to CO2 is of utmost significance.
During complete aerobic glucose degradation (to CO2 and H2O), 32 mol of ATP per mol of glucose are formed:

$$\mathbf{C_6H_{12}O_6 + 6O_2 + 3P_a^{2-} + 32ADP^{3-} + 32H^+ \rightarrow 6CO_2 + 32ATP^{4-} + 38H_2O}$$

The energy required for this reaction originates from the membrane potential of the mitochondria as well as the protein gradients, which together are summarized as the proton motor force. In the mitochondria, carbohydrates, fatty acids, and other substances are oxidized by oxygen so that the released energy can then be used to pump protons across the inner mitochondrial membrane and thus to build up proton motor force.

Proton motor force functions in various ways. Proton gradients supply energy for the “uphill” transport of small molecules that are moved across membranes against a concentration gradient. In addition, ATP-consuming proton pumps use the energy released during hydrolysis of a phosphoric acid anhydride compound to move protons against a concentration gradient. This process is hypothetically explained by the assumption of **chemiosmosis:**

> **The energy of a membrane potential and the energy of a concentration gradient of ions (and thus also protons) and the energy supplied in the form of phosphoric acid anhydride compounds in ATP are equivalent forms of chemical potential energy that can be converted into one another.**

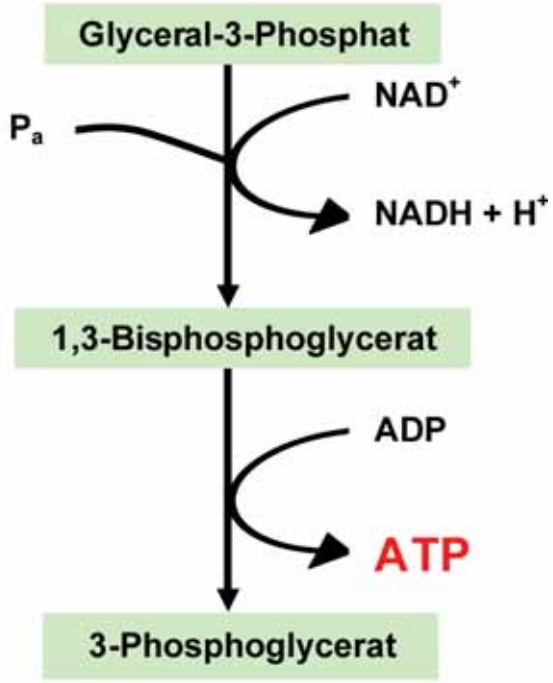
During glycolysis, 2 mol of pyruvate and 2 mol of ATP originate from 1 mol of glucose. Thus, during glycolysis, there is a “net gain” of only 2 mol of ATP per mol of glucose.

$$C_6H_{12}O_6 + 2NAD^+ + 2ADP^{3-} + 2P_a^{2-} \rightarrow 2C_3H_4O_3 + 2NADH + 2ATP^{4-}$$

$NAD^+$ : nicotinamide adenine dinucleotide

In cells, ATP is formed by two fundamentally different reactions:

- Ion gradients in the membranes of mitochondria as energy sources for ATP formation.
- Substances soluble in the cytosol are enzymatically converted by substrate chain phosphorylation; neither membranes nor substance gradients are involved in this process.




**Formation of ATP from ADP after preceding substrate chain phosphorylation**

Note:

ATP regeneration in the respiratory chain coupled with redox reactions (oxidation of H) is known as oxidative phosphorylation. Substrate chain phosphorylation refers to metabolic reactions in which inorganic phosphate is brought to a high conversion potential without simultaneous hydrolysis of a high-energy nucleotide.

Thus, it is understandable why spontaneous arteriolar vasomotor is diminished or can come to a standstill during oxygen deficiency, thereby further enhancing a microcirculatory disorder (vicious circle). For the success of a therapeutic measure, it is important to what extent we can succeed in improving the conditions for increased ATP supply; the focal point of all these considerations are the morphology and functions of the mitochondria.

Mitochondria are present in varying number in all cells. Approximately 100 of these cell organelles are detectable in an endothelial cell; approximately 1000 to 2500 in a hepatic cell. Their life span is very short (probably only about 5 to 10 days), so that continuous new formation is required. Mitochondria are among the larger cell organelles (approximately 1-2 µm) and comprise up to 25% of the cytoplasmic volume. Under the optical microscope, structural details of the mitochondrial are visible to only a limited extent; for more accurate morphological representations, the use of electron optical methods is essential (see below).

In cases of disease, the following morphological changes in the mitochondria can be observed, which are closely correlated with parallel reductions in the ATP supply for the cell.

Delayed new formation, reduction in the number per cell
Dissolution of matrix substance and vesicular conversion of the cristae
Intramitochondrial vacuole formation
Membrane ruptures
Lamellar transformations
Various changes in the cristae, reduction in the number of cristae
Hyperplasia or coalescence of the mitochondria, etc.

Mitochondria have two very different membranes, the outer membrane and the inner membrane. These delineate two submitochondrial compartments: the intermembrane space, which is located between the outer and inner membrane, and the mitochondrial matrix.
The outer membrane contains transmembrane channels consisting of a certain protein, through which protons and small molecules can move freely. The influx of metabolic intermediates through the outer membrane probably limits the rate of mitochondrial oxidation.
The mitochondrial inner membrane is the actual permeability barrier between the cytosol and the matrix of the mitochondrion. It contains molecular structures that are involved in electron transport of NADH or FADH2 to O2 as well as ATP synthesis. In other structures there are transport molecules that enable ADP, Pa and other compounds to pass from the cytosol into the matrix or that catalyze the transport of ATP from the matrix into the cytosol. A certain lipid probably influences the permeability for protons, which enables the buildup of proton motor force.

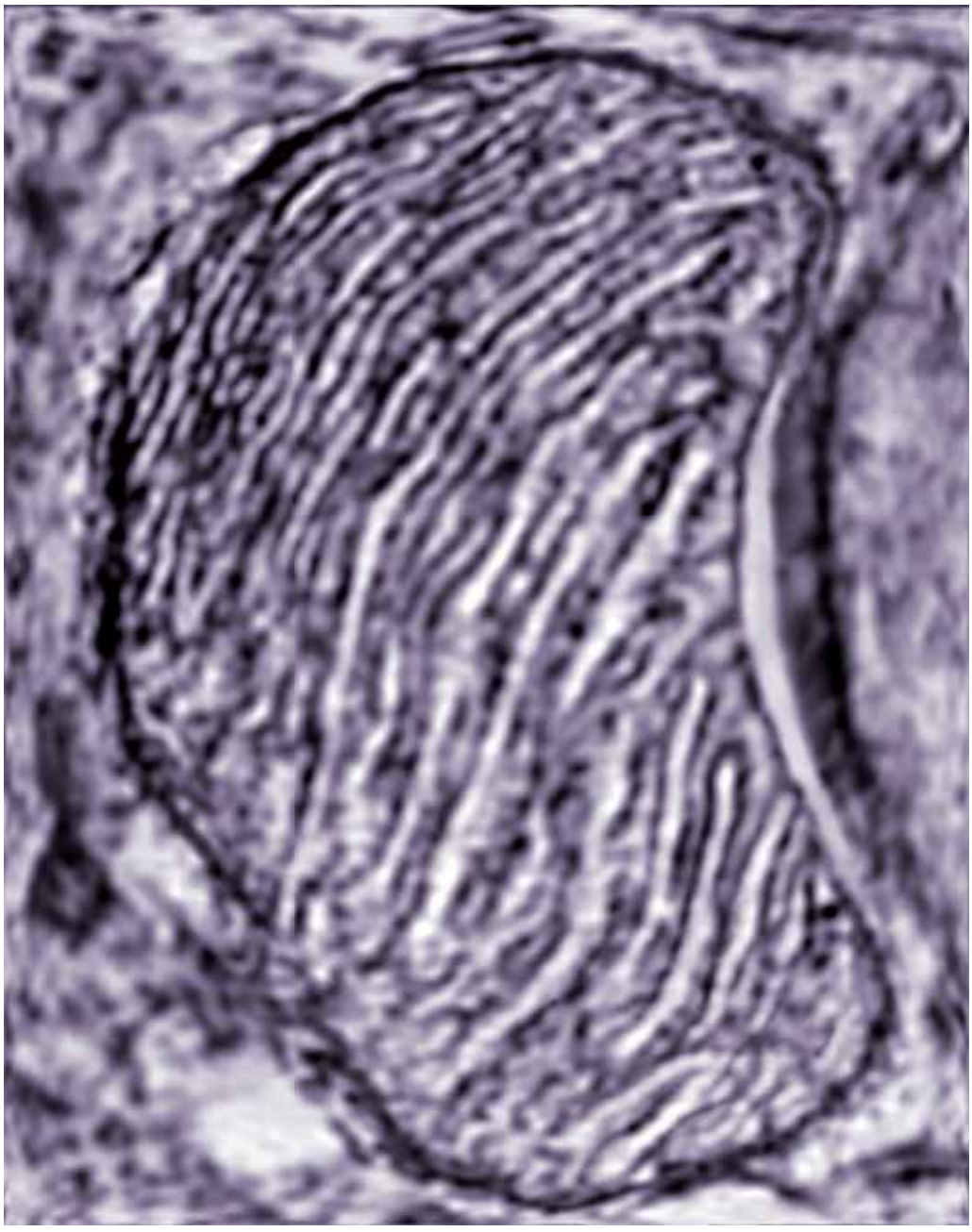
Both in the inner membrane and in the matrix, a plethora of reactions occur, during which pyruvate and fatty acids are oxidized to H2O and CO2 and ATP is synthesized simultaneously. These processes take place in various stages, with each occuring in a certain membrane region or certain mitochondrial space:

- Oxidation of pyruvate or fatty acids to CO2 (associated with a reduction in the electron acceptors NAD+ and FAD during formation of NADH and FADH2). These reactions occur on the matrix or on proteins of the inner membrane facing the matrix.
- Electron transfer from NADH and FADH2 to O2.
- These reactions occur in the inner membrane (coupled with the buildup of proton motor force).
- Using the energy supplied from the proton gradients, ATP formation occurs on the F0F1-ATP complex of the inner membrane.

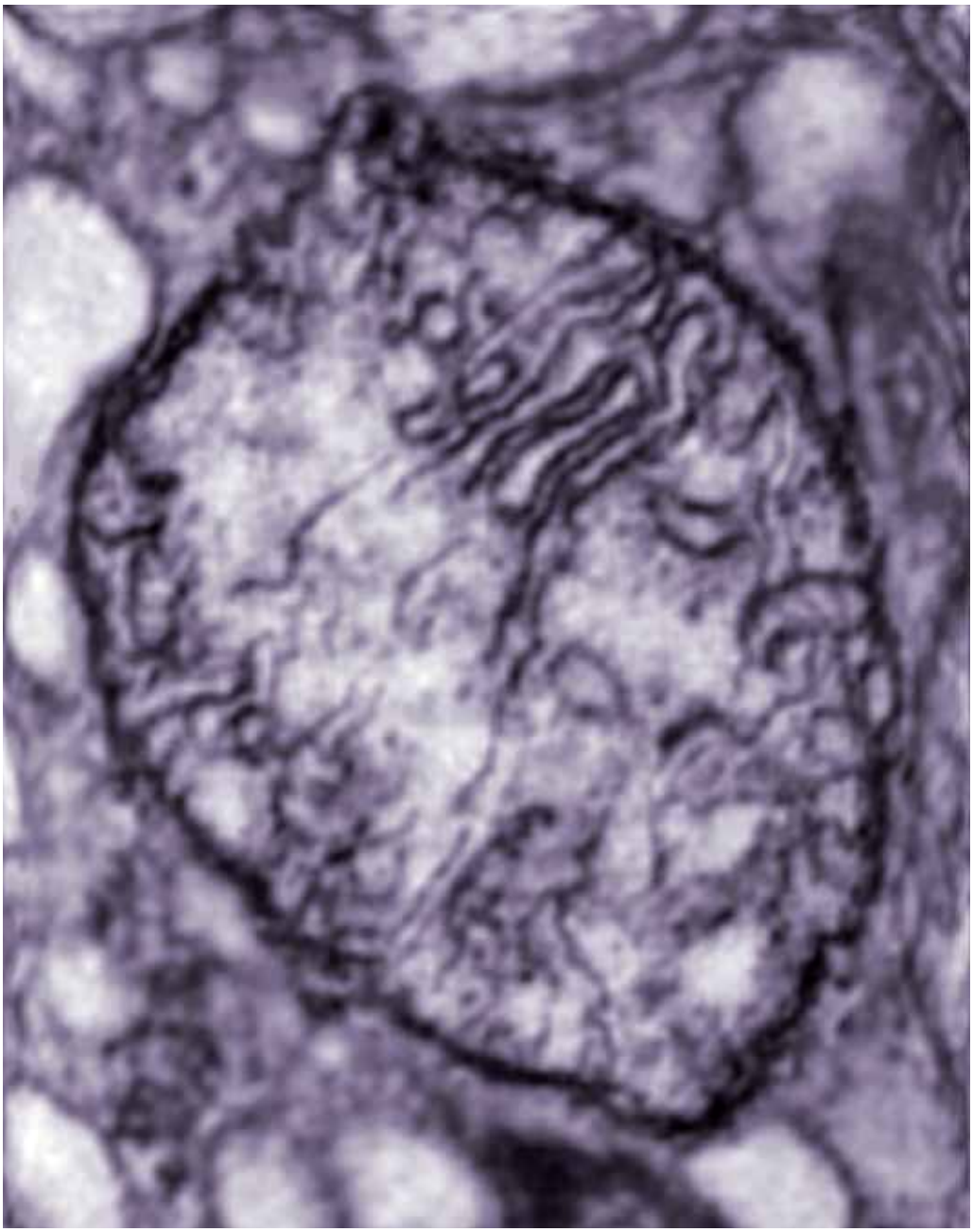
The folded inversions of the inner membrane (cristae) help to achieve an enlarged surface and thereby increased capacity for ATP formation.

**Electron-optical picture of a well functioning mitochondrion. (animal research, liver cell, dog)**

Electron-optical picture of a well functioning mitochondrion.
(animal research, liver cell, dog)



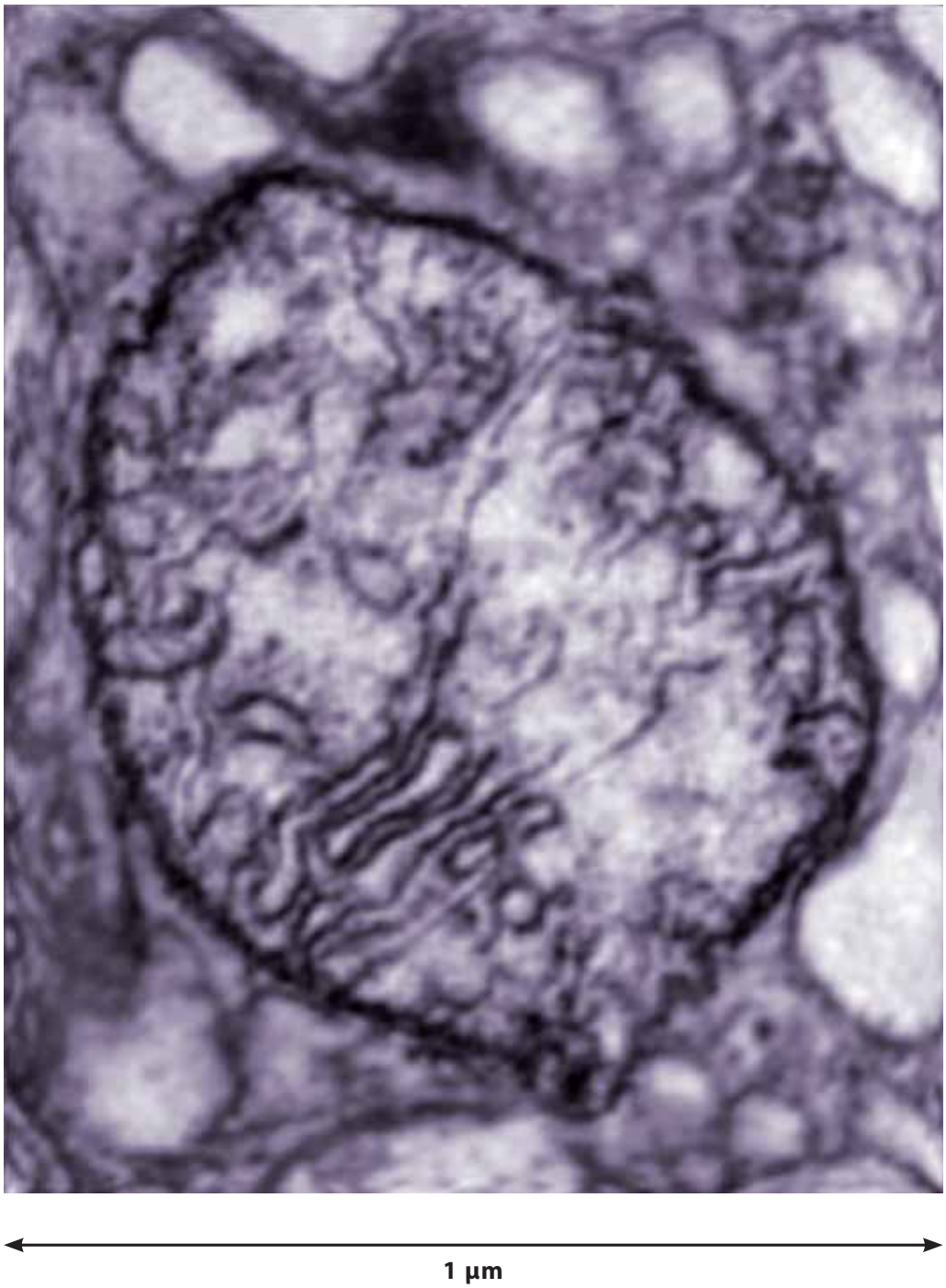
**Electron-optical picture of a well functioning mitochondrion.**
**(animal research, liver cell, dog)**



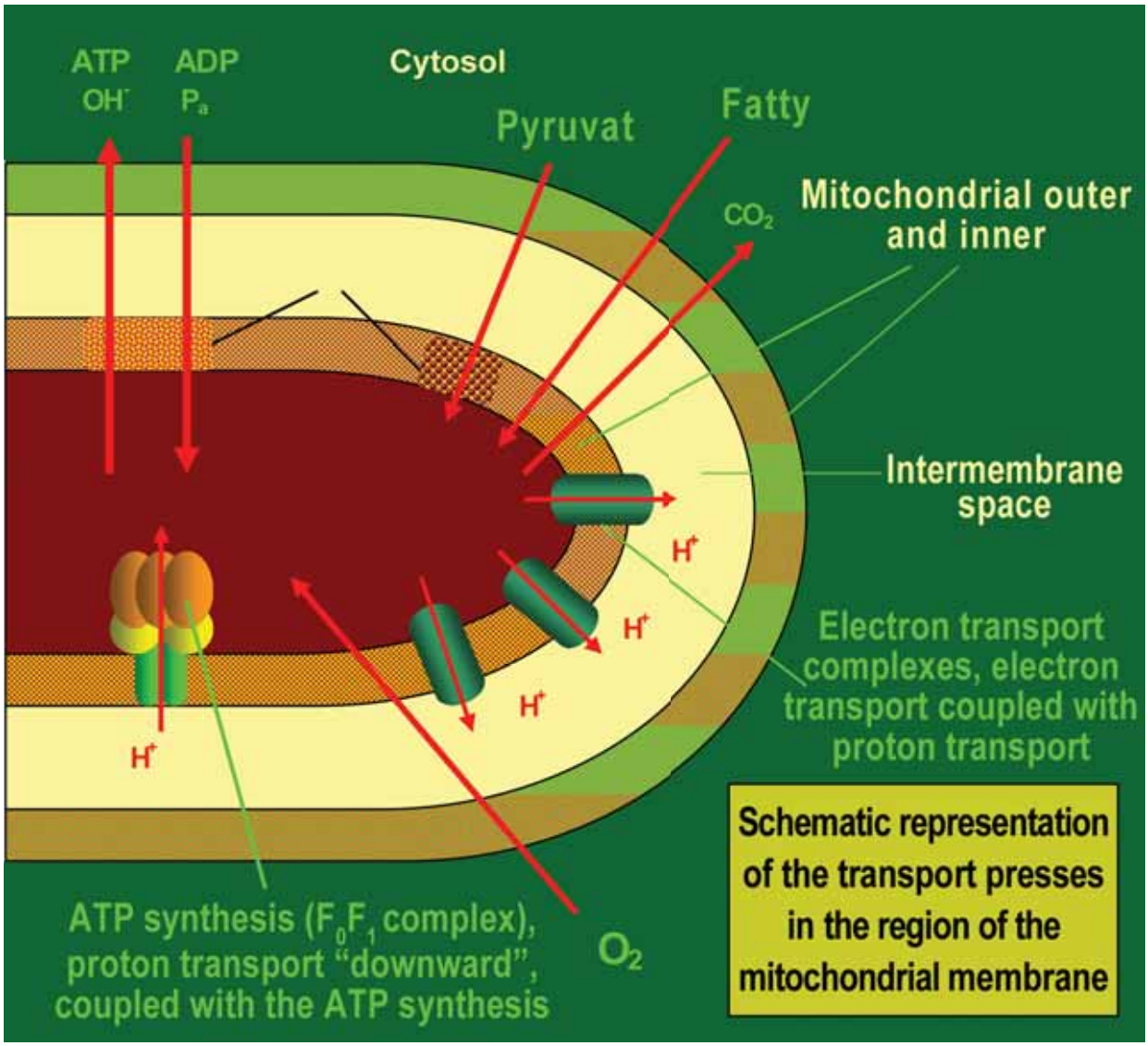
1 µm

**Electron-optical picture of a pathologically altered mitochondrion.**
**Condition of manifest ischemia**
**(animal research, endothelial cell, dog)**

A reduced number of cristae and damage to the membranes can be seen.



In connection with the investigation of possible action mechanisms of certain changing electromagnetic fields, the realization of ATP provision in the area of the inner mitochondrial membrane is of utmost importance:



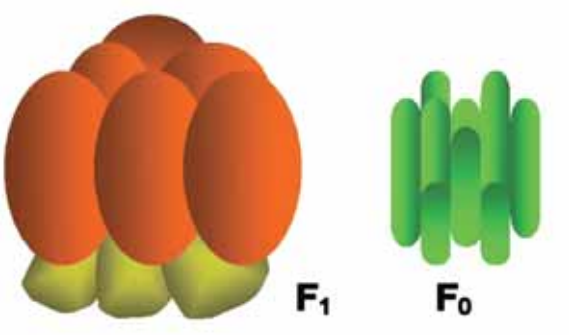

Important reactions in the matrix are:

During degradation of pyruvate and fatty acids, acetyl-CoA arises as an intermediate compound.

In the citric acid cycle, the acetyl group of the acetyl-CoA molecule is oxidized to CO2 and simultaneously, the reduction of NAD+ and FAD to NADH and FADH2 occurs.

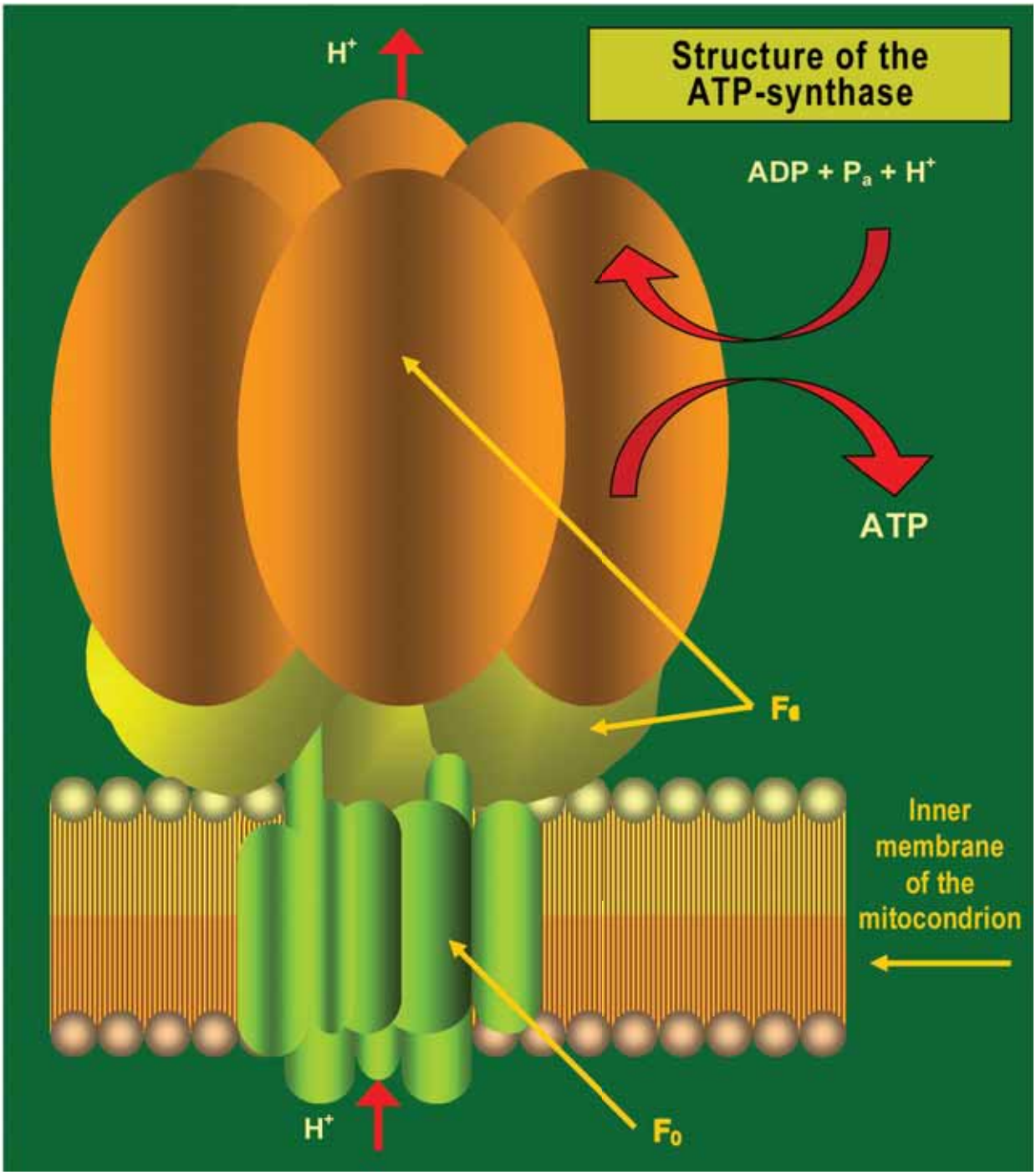
The electrons are transferred from NADH and FADH2 to molecular O2 through electron transport proteins.

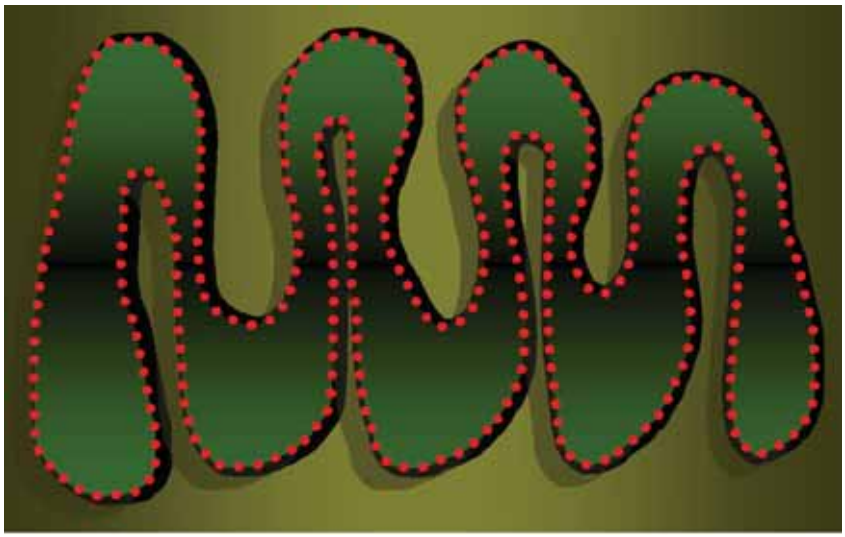
As already mentioned, the mitochondrial NADH and FADH2 oxidation and the ATP synthesis are coupled via proton gradients which are built over the mitochondrial inner membrane. In the presence of O2 and pyruvate, mitochondria only synthesize ATP when their **inner membrane is undamaged**. If this prerequisite is not met, the substrates are still oxidized, however, ATP is no longer synthesized. Under these conditions, neither the proton gradient nor the electrical potential across the membrane can be maintained.




A certain enzyme complex is responsible for ATP synthesis: the $F_0F_1$-ATPase-complex couples the proton movement along the electrochemical gradient with the ATP synthesis.

The enzyme complex consists of the two components $F_0$ und $F_1$.



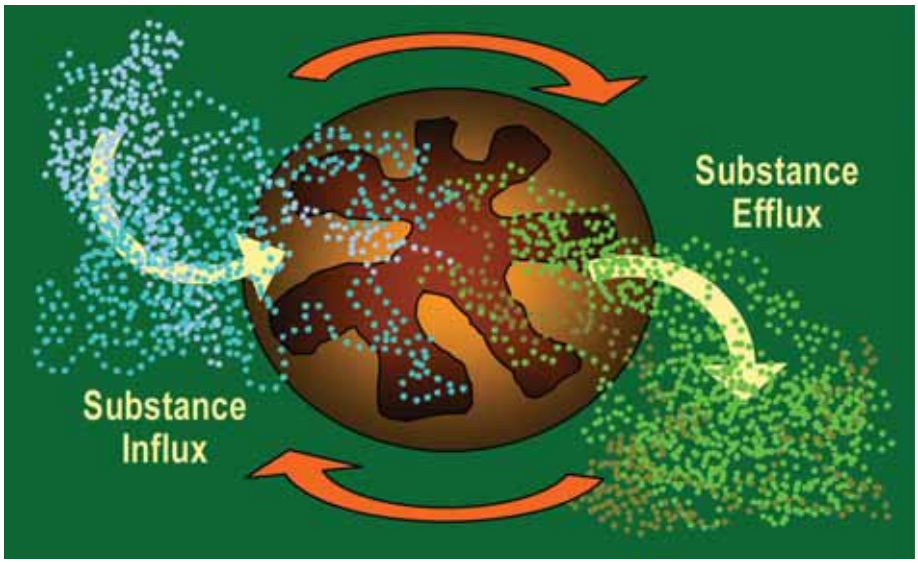


This illustration depicts the arrangement of the $F_0F_1$-complexes in the folds of the inner membrane of mitochondria.

The $F_0F_1$-complexes are marked as red spots.

The membrane complex (F0) contains three different subunits that cross through the membrane with different frequencies. F0 contains the membrane canal through which the protons flow to complex F1. It is very probable that this process can be stimulated or inhibited by physiochemical means. The water soluble complex F1 sticks to F0 which contains various polypeptides. This complex can be separated from the membrane by shear force. The separated complex can then hydrolyze only ATP and because of this, it is referred to as F1-ATPase. Although F1 is not a membrane protein, this subunit behaves like a barrier to proton flow. If F1 is detached from the mitochondrial inner membrane, the membrane becomes permeable to protons.

As already mentioned, preliminary measurements have shown that mitochondria in the cytoplasm perform movements around their longitudinal axis, which exhibit a dependence on the amount of ATP released. In diabetes mellitus, these movements are reduced (lower provision of ATP). Preliminary investigational results indicate the rotational movements of the mitochondria as well as the ATP provision can be increased, within limits, through the use of certain changing electromagnetic fields. The actual cause of these mitochondrial movements is still unclear.




Schematic cross-section through a mitochondrion (normal to the longitudinal axis).

It is conceivable that an uneven influx and efflux of substances results in rotation of the mitochondrion in the cytoplasm.

It is known that the release of ATP in the mitochondrion does not occur in an evenly distributed pattern. This probably also applies to the substance influx and efflux. Whether certain preferential directions for substance transport exist and, based on this, the movements of the mitochondria in the cytoplasm can easily be explained (dependent on the ATP release) has not yet been definitively established. It is conceivable that in this way concentration gradients are maintained as high as possible for the in- and out flowing substances. It should also be taken into consideration that possibly all (or the majority) of the F0F1 complexes of a mitochondrion (or of a region of its inner membrane) perform synchronized movements in such a way that, depending on the biochemical reactions during ATP synthesis, a resulting force of more or less strength has an effect on the mitochondrial corpus.

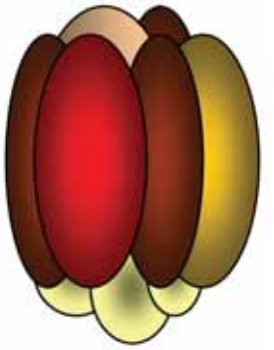
The observation of mitochondrial movements in the cytoplasm does not surprise the author of this book. This phenomenon is already recognized in other cell organelles, in particular, in the cell nucleus.

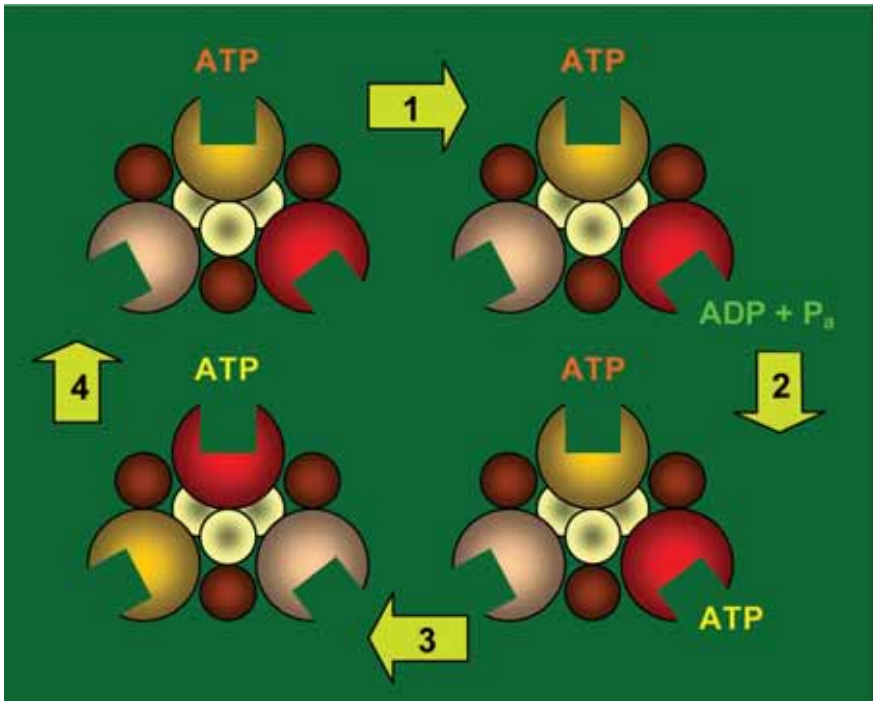
The established movements of the enzyme complex, F0F1-ATP synthase during ATP synthesis can be explained in that the molecular subunits alternate between the three conformations which vary with regard to their affinity to ATP, ADP and Pa.

> In what way the proton transport from the intermembranespace through the F0F1 complex into the matrix is coupled with the ATP formation is presently the subject of intense investigation. According to the hypothetical assumption of a mechanism of binding alteration (rotational model), the proton flow generates a rotation in the molecule complex (see also Chapter 10, in particular figure 78).

Schematic representation of the rotational model for ATP synthesis.

Cross-section through an F1 complex. ⟶






1: ATP and $P_a$ are bound.
2: ATP formation from ADP and $P_a$ with the release of $H_2O$.
3: Due to the rotation driven by the flow of protons, released of ATP, conformational change in the molecular subunits.
4: Reorganized subunits which are chemically idential with the status of $F_0F_1$ prior to ATP synthesis.

The preceding analyses reveal that in the attempt to find a molecular-biological explanation of the measurements available so far regarding the effects of certain electromagnetic fields on the mitochondria, a series of very complicated questions arise, which fundamentally pertain to the following aspects:

Proton motive force, the formation of ATP and transport of metabolites.
NADH, electron transport and proton pumps.
Effect of mitochondria on metabolic regulation (regulation of respiration through the formation of ATP as well as through the proton motive force, dependence of the speed of glycolysis on cellular ATP requirements, among others).

Current experimental research is concentrated on the following questions:

- Can the currently available data regarding the effects of certain changing electromagnetic fields on mitochondria (see above) be confirmed in the context of more extensive research? Can a definite relationship between altered ATP supply and correspondingly altered spontaneous arteriolar vasomotion be proven?
- Is direct or indirect proof of a therapeutically relevant effect on the mitochondrial ATP release through certain changing electromagnetic fields experimentally possible using suitable fluorescing import substances?
- Will valid experimental evidence of changes of certain ATP dependent cellular functions under the influence of certain changing electromagnetic fields be successful?

In the pursuit of this, the following research methods were employed: confocal laser scan microscopy, fluorescence microscopy, various spectrometric techniques and molecular biological laboratory methods. Target structures for the experimental investigations are: various cell cultures, ex-vivo compounds, etc. The system BEMER PLUS (intensity level 3) was used for stimulation.

The current molecular-biological knowledge level is a decisive factor in the selection of suitable target cells for the investigation of the effects of certain changing electromagnetic fields on the mitochondrial ATP supply:

ATP serves as “energy currency” in the cells of all living things. It can therefore be assumed that ATP was already available to the earliest forms of life at the start of the evolutionary process.
Among other things, the energy released by hydrolysis of the phosphoric acid anhydride compounds is used in animal cells to enable certain cell functions, for example, the movement of cilia and flagella, as well as the contraction of muscle cells. The ATP dependent cilial frequencies and cilial amplitudes of the ciliated epithelium in a defined cell culture can be considered to be a characteristic of mitochondrial stimulation.
In plant cells, ATP is generated during photosynthesis in the chloroplasts (transformation of light energy into chemical energy of a phosphoric acid anhydride compound). At first glance, there seems to be little similarity between photosynthesis and aerobic oxidation. Consequently, it was an almost revolutionary discovery that bacteria (which do not possess mitochondria), as well as mitochondria and the chloroplasts of plant cells, fundamentally

make use of the same mechanism for the formation of ATP from ADP and Pa (chemiosmosis, similar use of an electrochemical proton gradient for ATP formation).
Consequently, chloroplasts are suitable target objects for molecular biological research on the effects of certain changing electromagnetic fields.

During experimental investigations of ATP formation it should be noted that plant and animal cells do use the same mechanisms, however, they exhibit differences with regard to the amounts and the temporal behavior of the bio-molecular responses (characteristic changes) to a stimulus.
The morphological structure of the mitochondria is a function of the corresponding organ or tissue-specific requirements of metabolic regulation:
In the mitochondria of the hepar, the surface of the inner membrane is approximately five times larger than the surface of the outer membrane. The total area of the inner membrane of all mitochondria of a single liver cell is actually approximately 17 times greater than that of the plasma membrane. Mitochondria from muscle cells (in particular cardiac muscle cells) possess approximately more than three times as many cristae as liver cells due to the greater ATP requirement.

Fluorescence microscopic observations of cell cultures support the assumption that the molecular biological processes in the release of ATP are of a periodic nature. On the other hand, the results currently available from preliminary investigations indicate that during the stimulation of ATP formation, not only the energy but also the temporal changes of the electromagnetic field are of significance (signal rhythm, signal configuration). For experimental research regarding the stimulating effect on ATP production in the cells, the application of the electro-magnetic fields of the BEMER PLUS system has proven to be of value, as the following examples demonstrate.

Evidence of the stimulating effect of a certain changing electro-magnetic field on the movements of chloroplasts, which is closely related to the synthesis of ATP in plants.

A (reduced) production of ATP is present in plant cells even when there is only a minute amount of light energy. The measurements of an exploratory analysis show that even electro-magnetic fields with low energy can stimulate the production of ATP to a certain extent.

## Research Design Table

| | |
|---|---|
| Test Object | Ginako biloba, small healthy potted plant (daylight in the shade) |
| Test Equipment, Application | BEMER Plus (mat, level 3)<br>3 applications for 3 minutes, 7 minutes apart |
| Measurement Intervals and Timing | Observation time of 30 minutes.<br>Equidistant timing of measurements<br>Intitial values were determined before the first application;<br>subsequent measurements one minute apart, up to 30 minutes. |
| Target Structure | Gingko leaf (middle section) |
| Measurement Methods | Microscopy with computer assisted image evaluation,<br>reflection spectrometry. Defined conditions. |
| Parameters | ► Movement of cloroplasts<br>► Release of ATP |
| Statistical Analysis | WILCOXON rank-sum test (MWW), a = 5% |

The following illustration shows selected measurement results.

**Changes in the movement of chloroplasts in a Gingko leaf under the influence of a certain changing electromagnetic field.**

(Mean values from 80 individual measurements for each measurement point)

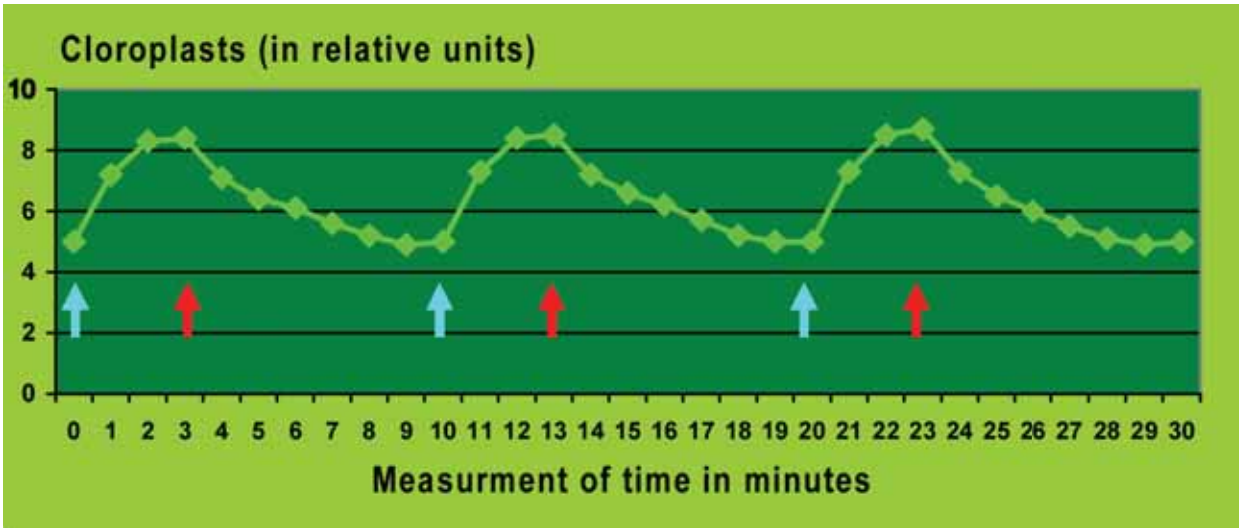
Ordinate: movement of chloroplasts in relative units

Abscissa: measurement points in minutes

3 applications of a certain changing electro-magnetic field, 3 minutes in duration

Blue arrow: beginning of application

Red arrow: end of application




Under the influence of a certain changing electromagnetic field an increase in movement of the chloroplasts becomes evident, corresponding with an increase in measurement values for ATP release.

Verification of the stimulation effect of a certain changing electromagnetic field on the cilial beat frequency and cilial beat amplitude of respiratory epithelium cells in cell culture as well as on ATP-synthesis.

## Research Design Table

| | |
|---|---|
| Test Object | Ciliated epithelium, cell culture (defined laboratory conditions) |
| Test Equipment, Application | BEMER Plus (mat, level 3)<br>3 minute applications |
| Measurement Intervals and Timing | 0 minutes (initial values are determined prior to the first application), subsequent measurements immediately following the 3 minute application. |
| Target Structure | Ciliated epithelium cell |
| Measurement Methods | Intravitalmicroscopy with computer assisted image evaluation, reflection spectrometry. Defined conditions. |
| Test Parameters | ▶ Cilial beat frequency, cilial beat amplitude<br>▶ Release of ATP |
| Statistical Analysis | WILCOXON rank-sum test (MWW), a = 5%<br>Descriptive statistics (definition of classes and class ranges, frequency |

The measurement data are captured in the following graphics.

**Changes in the cilial beat frequency of respiratory epithelium cells in a cell culture under the influence of a certain changing electromagnetic field.**

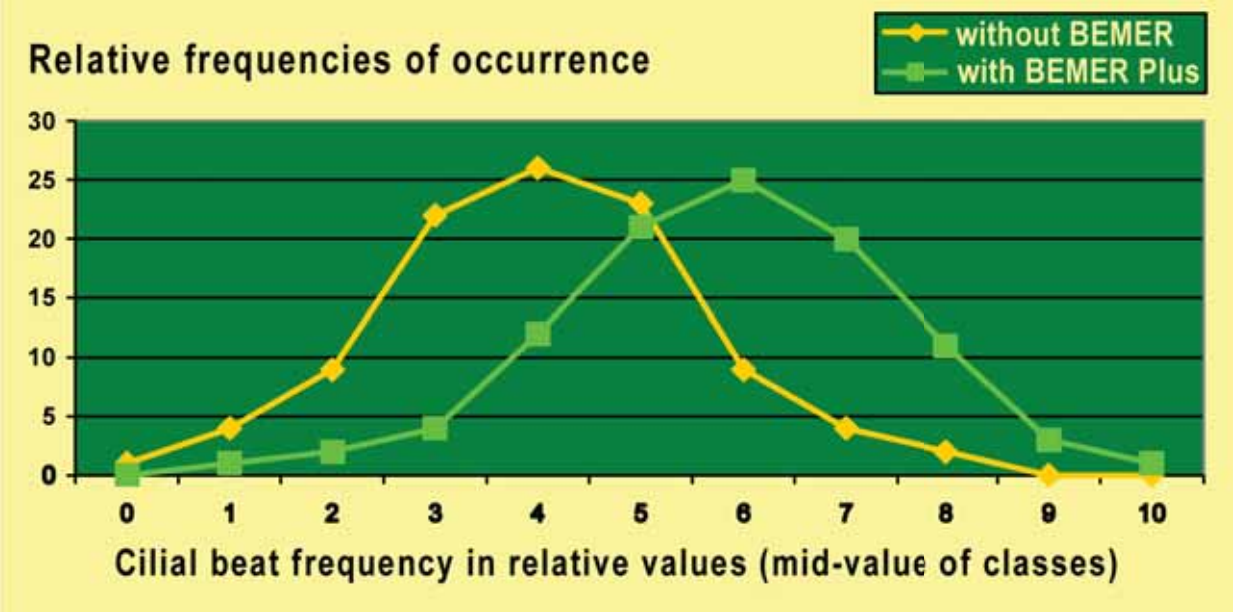
Measurement data collected prior to the application of the changing electromagnetic field (without BEMER PLUS) and immediately after a 3-minute application of a certain changing electromagnetic field. (BEMER PLUS).

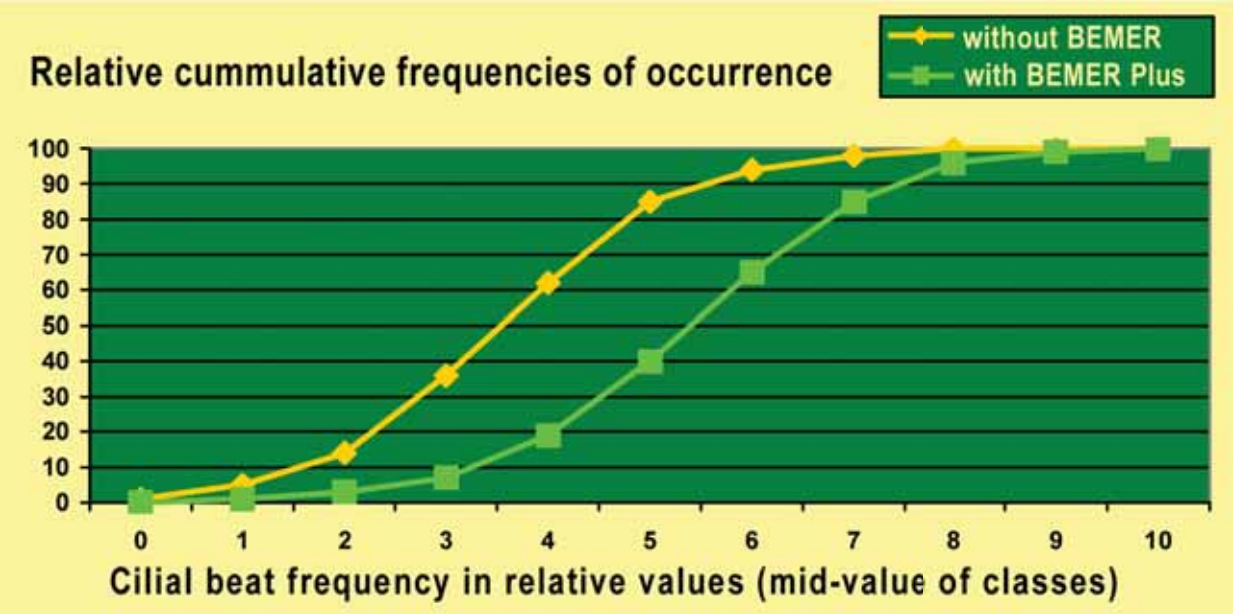
(Mean values of 100 individual measurements)

Celial beat frequency in relative values assigned to classes.

Top: relative frequencies of occurrence

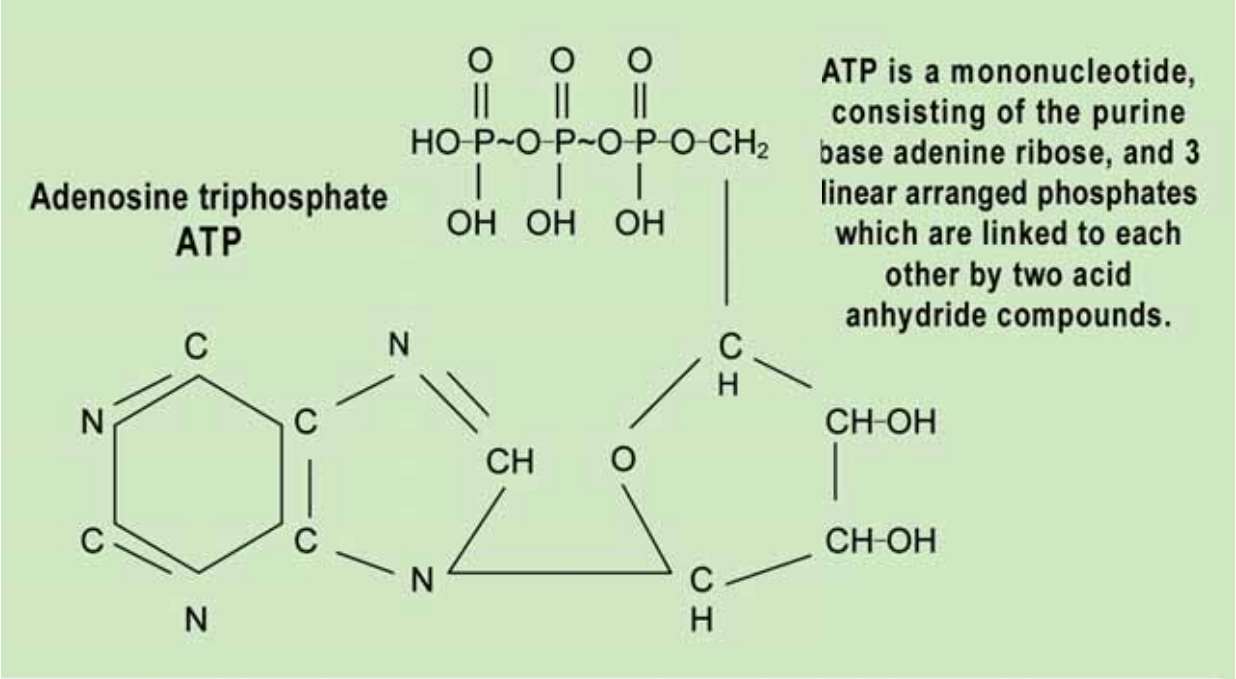
Bottom: related cumulative frequencies of occurrence



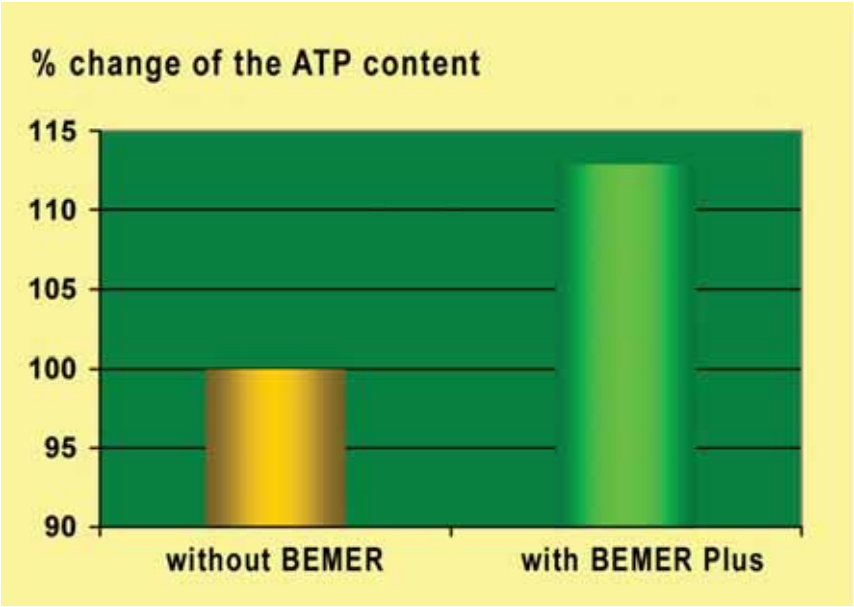

The polygons show an increase of the cilial beat fequency as a sign of heightened cellular activity under the influence of a certain changing electromagnetic field. We can see a shift in the distribution of frequency occurrences to the higher cilial beat fequency values.
Parallel parameter changes can be observed for the cilial beat amplitude.

Corresponding changes in the concentration of adenosinetriphosphate (ATP) in the cells of the ciliated epithelium can be observed virtually simultaneously to the increased cilial activity after the application of the electromagnetic field. As the structural formula shows, ATP is a substance that can be activated, and therefore can be measured with spectrometry or reflectionspectrometry respectively.




**Changes in the provision of ATP in the ciliated epithelium cells of a cell culture under the influence of a certain changing electromagnetic field.**

Measurement data before application of the changing electromagnetic field (without BEMER PLUS) and immediately following a 3-minute application of a certain changing electromagnetic field (BEMER PLUS). (Mean values of 100 individual measurements)



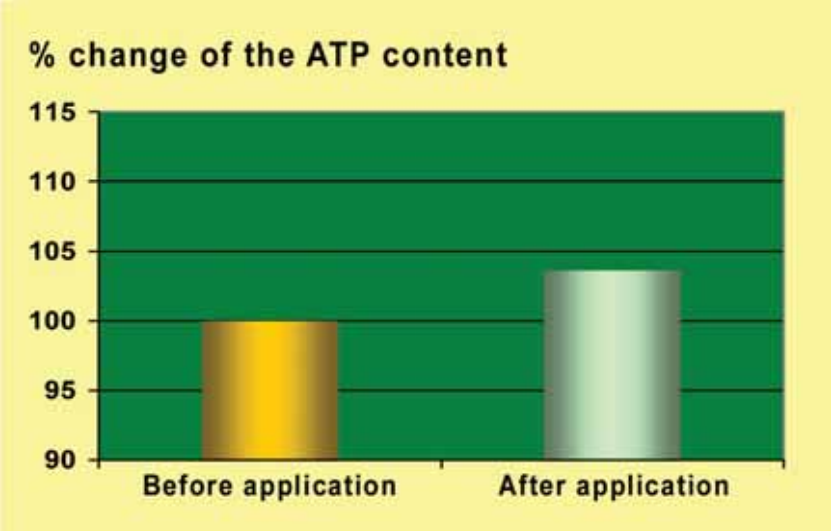

The ATP concentration established before application of the changing electromagnetic field is equal to 100%.

After a 3 minute application of a certain changing electromagnetic field a significant increase of cellular ATP concentration occurs.

In the context of supplemental studies, the culture of ciliated epithelium cells was treated according to the above mentioned research design with a changing electromagnetic field whose signal configuration for comparable flux densities differed noticeably from the BEMER signal (customary device from a different manufacturer). The data collected are outlined in the following graph.

**Changes in the provision of ATP in the ciliated epithelium cells of a cell culture under the influence of a changing electromagnetic field with a signal configuration that differs noticeably from the BEMER signal.**

Measurement data before application of the changing electromagnetic field and immediately following a 3 minute application of the changing electromagnetic field.
(Mean values from 100 individual measurements)




The ATP concentration established before application of the changing electromagnetic field is equal to 100%.

After a 3 minute application of a certain changing electromagnetic field a minor increase of cellular ATP concentration occurs.

When we view these results in connection with the research findings described in chapter 25 (figure 282), which were collected from healthy subjects after the application of various therapy devices (oxygen utilization in the venules), we can regard them as further evidence that the temporal changes of the electromagnetic field which are necessary for therapy-relevant effects cannot be achieved by arbitrarily chosen signal configurations.
Caution is recommended for the interpretation of currently available (experimental) research findings. Further tests are needed before a final assessment can be made. By presenting data analysis of experimental research, the author merely intends to inform the reader about the status of current research, which has further clarification of the possible therapeutic effects of changing electromagnetic fields as its goal. Numerous questions need to be addressed, even though we have already learned from unexpected research results that an overly dogmatic and narrow point of view resulting from a healthy skepticism towards new ideas does not appear to be appropriate here. It certainly should not take the place of a willingness to take seriously and scientifically discuss well documented findings, even (or especially) if they do not appear to be in complete or partial agreement with traditional views.

**As complementary literature for theoretical foundations we recommend:**

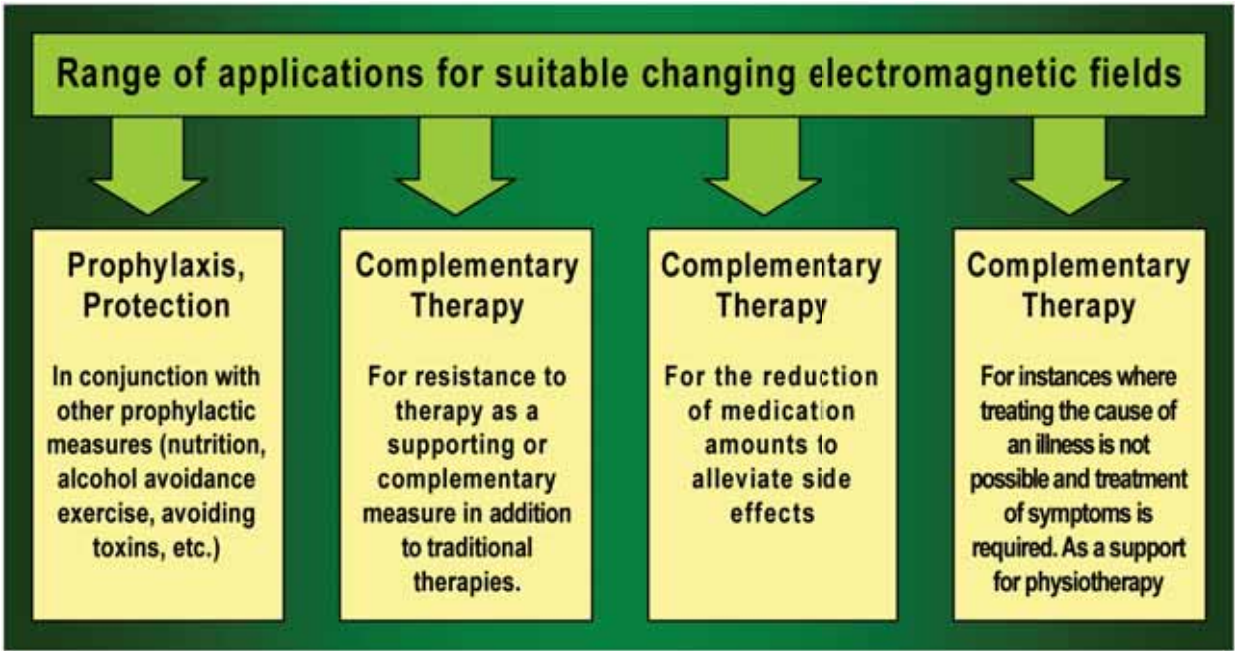
Lodish H., D. Baltimore, A. Berk, S.L. Zipursky, P. Matsudaira and J. Darnell: MOLECULAR CELL BIOLOGY.
3rd edition (1995 ff.), W.H. Freeman and Company, New York, Basingstoke

Now let us shift our focus once again to clinical research results.

# 27

# Research results regarding the application of certain changing electromagnetic fields with added vasomotion stimulation

Considering the research results presented in chapters 25 and 26 regarding the effects of certain changing electromagnetic fields (BEMER and BEMER PLUS) on microcirculation, a range of possible applications emerges.




In this chapter we will introduce therapy results that were the subject of microcirculation research as part of an examination of **prophylactic and complementary therapy effects** of certain changing electromagnetic fields with added vasomotion stimulation.

The research questions addressed conformed to clinical standards and pertained to the following main points:

- Prophylactic therapy for exposure to stress and infection, increase of physical capacity, complementary therapy with multi-morbid geriatric patients.
- Complementary therapy for peripheral circulatory disorders, diabetes-related polyneuropathy and fatty liver due to alcohol.

» Complementary therapy for impaired healing of wounds and bones and for chronic-degenerative arthropathy, for chronic pain and geriatric rehabilitation patients.

» Complementary therapy for therapy-resistant chronic inflammatory processes and for rheumatic diseases.

The need for effective **prophylactic measures**, especially in older patients, has already been documented in chapters 12 and 13 of the german microcirculation book. In the previous chapters 25 and 26, research results indicated that the application of certain changing electromagnetic fields (BEMER and BEMER PLUS) in younger or middle-aged subjects exposed to stress and infection causes relevant changes in micro-hemodynamic and (indirect) immunological characteristics in the realm of microcirculation. The importance of effective prophylactic measures increases with age, since disposition toward infection increases and an intolerance to stress occurs.

After the application of certain changing electromagnetic fields (BEMER and BEMER PLUS), changes in microcirculatory characteristics occur more pronounced in older multi-morbid patients than in younger patients at times, but also subside more quickly. As a result, longer therapy periods (weeks, months) may be required for older patients.

In the context of using certain changing electromagnetic fields with vasomotion stimulation for complementary therapy purposes, many promising possibilities for the support of established treatment concepts are developing. This applies especially to (chronic) illnesses where disturbances of microcirculation develop into a separate condition over time and often unfold their own dynamic independent from the course of the original illness.

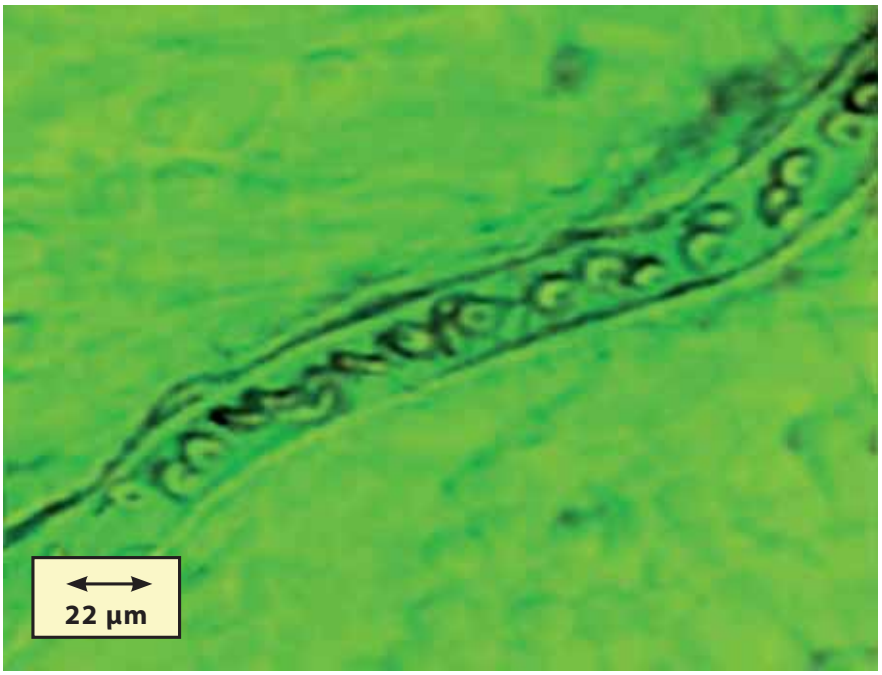
Not infrequently, the causes of **therapy resistance** can be found in the realm of microcirculation. We must remember that disturbances of microcirculation are also disturbances of diffusion. Based on the limited drug therapy options for microcirculatory disturbances, the use of effective complementary therapy methods is highly recommended.

Figures 326 through 328 present examples of vitalmicroscopic findings and display the problem of self-activating microcirculatory disturbances in (chronic) therapy-resistant illnesses.

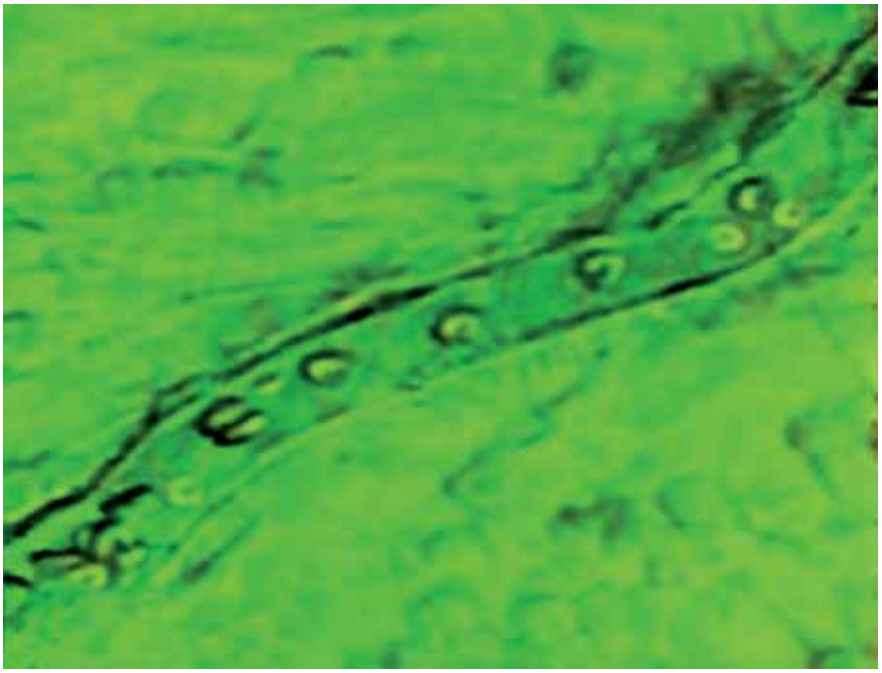
**Figure 326**

**Example of vitalmicroscopic findings of self-activating microcirculatory disturbances in cases of therapy resistance.**
**(1/2000 second; section of micro vessel in the subcutis, sequence of photographs from a to d at an interval of 15 minutes).**

a

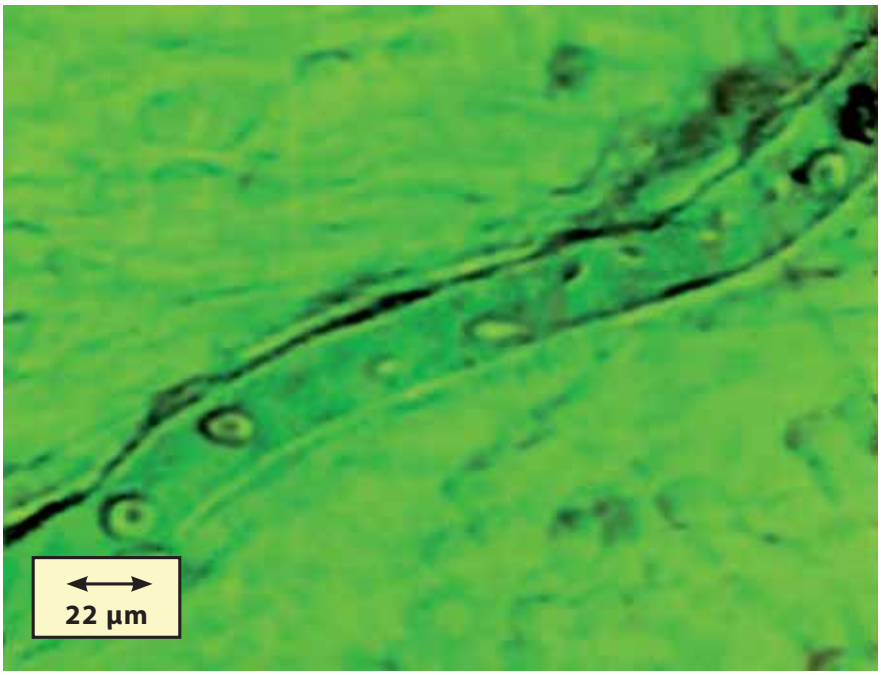



b



*Continued decrease of the flow rate of the red blood cells until the micro vessel is only perfused with plasma.*

**c**




**d**

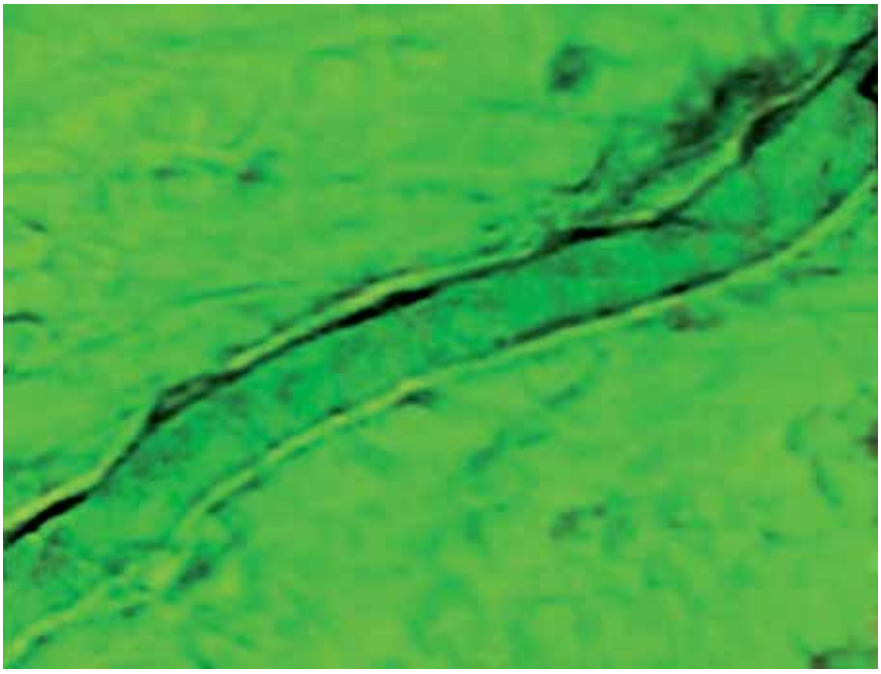
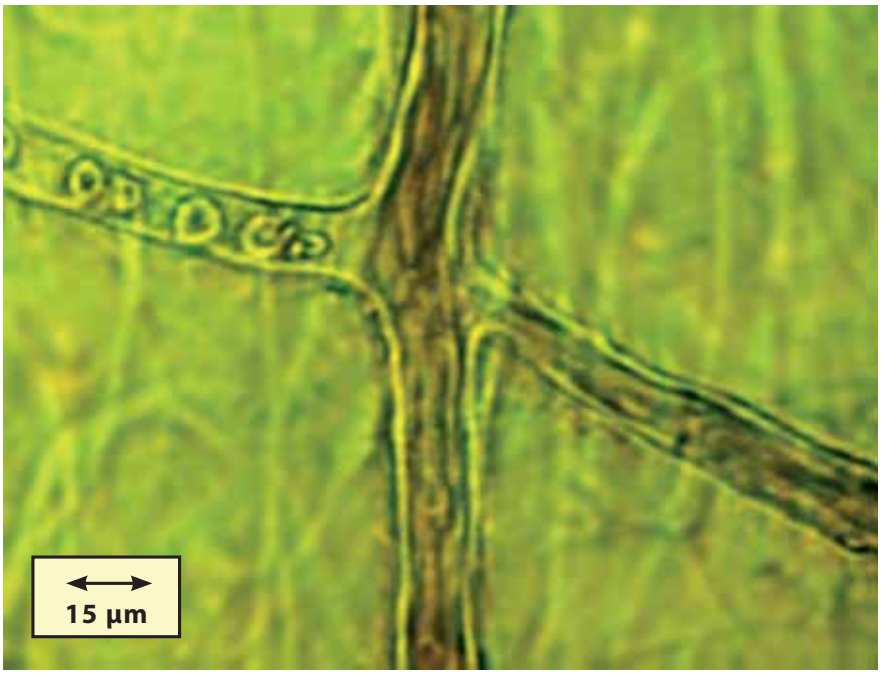


**Figure 327**

**Example of vitalmicroscopic findings of self-activating microcirculatory disturbances in cases of therapy resistance.
(1/2000 second; section of micro vessel in the subcutis, sequence of photographs from a to b at an interval of 25 minutes).**

*A nodal point is no longer perfused with blood.*

**a**




**b**

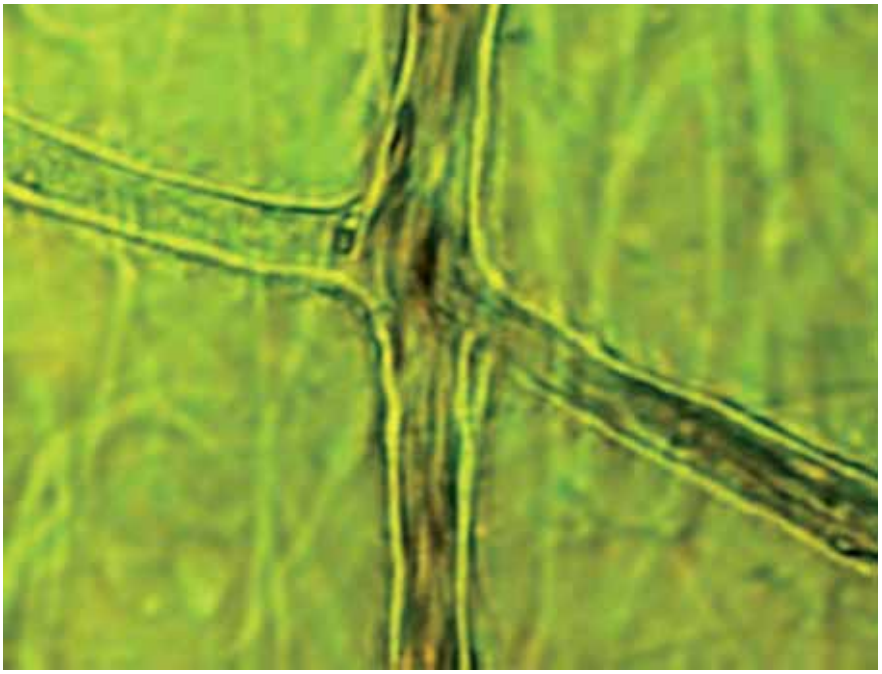
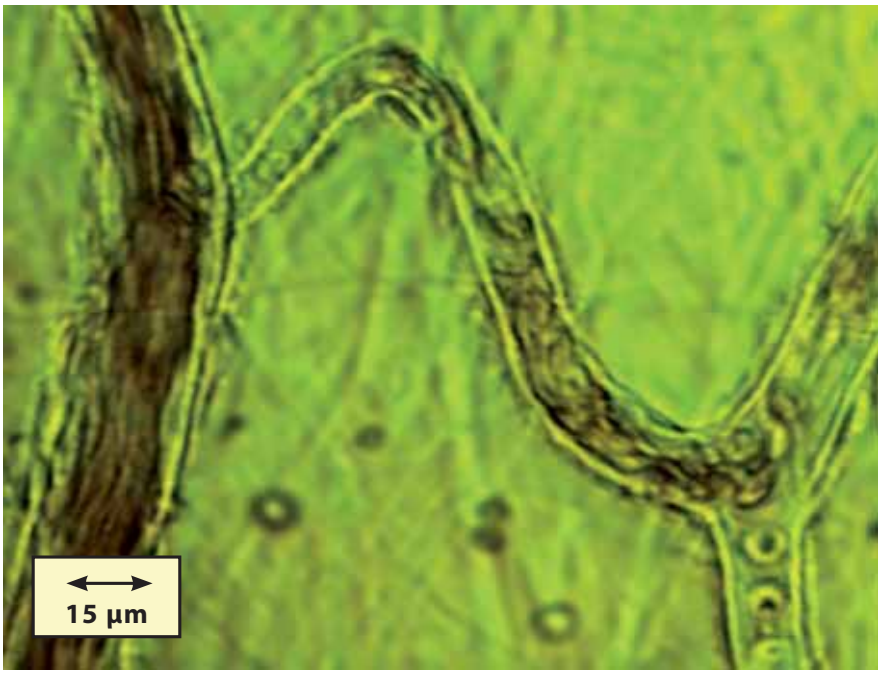


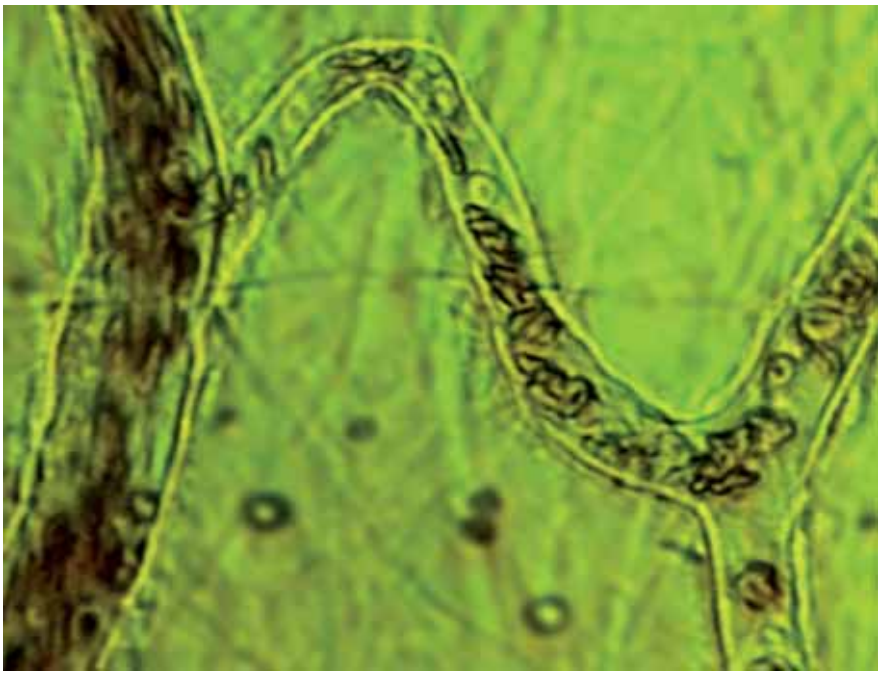
**Figure 328**

**Example of vitalmicroscopic findings of self-activating microcirculatory disturbances in cases of therapy resistance.
(1/2000 second; section of micro vessel in the subcutis, sequence of photographs from a to b at an interval of 20 minutes).**

**a**




**b**



An example for effective support of mainstream therapy concepts is the use of a certain changing electromagnetic field with added vasomotion stimulation for the **postoperative rehabilitation (physiotherapy) of geriatric patients.**

## Research Design

| | |
|---|---|
| **Test Sample, Partial Test** | Total test sample $N_{TOTAL}$=36<br>Geriatric rehabilitation patients, 70-79 years of age, male and female<br>Condition after completion of surgical treatment (femoral neck fracture (hip), femoral fracture, tibia-, fibula, and metatarsal fracture)<br>Two equal partial test samples of n=18<br>► Control Group:<br>Outpatient physiotherapy without application of a certain changing electromagnetic field.<br>► Test Group:<br>Outpatient physiotherapy with additional application of a changing electromagnetic |
| **Test System, Application** | Therapy device: changing electromagnetic field with added vasomotion stimulation (BEMER Plus)<br>Test Group: 2 times a day, 10 minutes each, lying on the mat (level 3), for a duration of 27 days. |
| **Measurement Intervals and Timing** | Observation period 27 days, equidistant measurement intervals:<br>Data collection 1 hour after the 2nd application on day of measurement.<br>Day zero (determination of base values prior to the 1st application, control group accordingly), subsequent data collections on days 3, 6, 9, 12, 15, 18, 21, 24 and 27. |
| **Target Tissue** | Simultaneous measurements in tow target tissues:<br>Subcutis<br>(lower extremity or hip area, close to the fracture)<br>Intestine<br>(rectum, lamina, muscularis, penetration depth approx. 60mm) |
| **Measurement Methods** | ► Intravitalmicroscopy with computer assisted image processing (documentation of findings: high speed camera, 35 mm high resolution film, image sequence 60 and 90 pictures per second).<br>► Vitalmicroscopy reflectionspectrometry<br>► Laser-DOPPLER-microflow-measurement and white light spectroscopy<br>Penetration depth: 3 mm to 8 mm<br>Capture of complete interconnected micro-vascular networks with defined tissue volume V=1200 µm³ (diameter of vessels d≤200µm).<br>Defined conditions of macro-circulation and temperature regulation. |
| **Parameters** | ► Oxygen depletion in the venules ΔpQ2.<br>► Number of blood cell perfused nodal points nNP.<br>► Venular flow rate $Q_{ven}$.<br>► Arteriolar vasomotion status $A_{vm}$.<br>Subjective evaluation of the treatment success on day 27 by the patients (interview by the physician). |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), a = 5% |

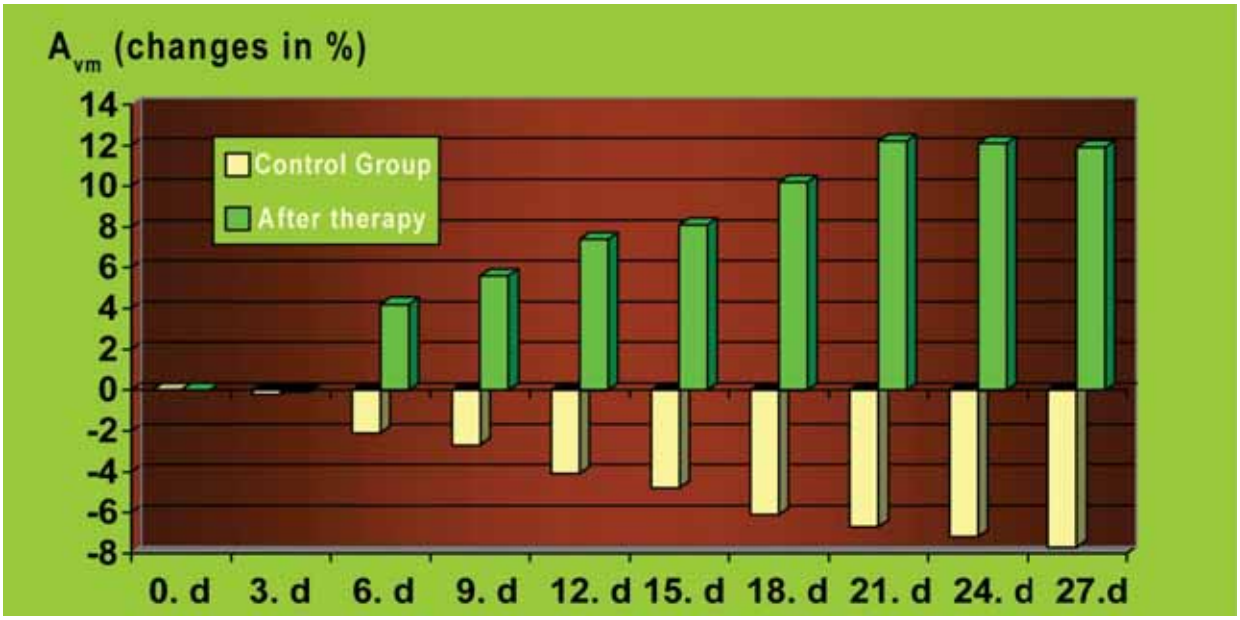
Figures 329 and 330 provide information on the behavior of selected characteristics during the observation time period.

**Figure 329**

**Behavior of the parameter "area under the envelope of the amplitude frequency spectrum of the spontaneous arteriolar vasomotion $A_{VM}$" (mean values) over a 27-day observation period in the subcutaneous target tissue of geriatric rehabilitation patients.**

**Control group: conventional physiotherapy without complementary use of a changing electromagnetic field.**
**Test group: conventional physiotherapy + complementary use of a changing electromagnetic field.**

Statistical examination results: Significant differences in characteristics - control versus test group beginning on the 6th day.




Parallel behaviors of characteristics were determined in the venular flow rate $Q_{ven}$ and in the distribution status of the plasma-blood cell mixture in the microvascular networks (number of blood cell perfused nodal points nNP). The impact of the behavior differences of the microcirculatory perfusion characteristics in the control and verum groups on the nutrition of tissue comes to light in the characteristic "oxygen depletion in the venules $\Delta pO_2$". The data collected in the subcutaneous and intestinal target tissues exhibited no significant differences.

The (temporary) slight deterioration of the microcirculatory function in the rehabilitation patients of the control group is not surprising at the beginning of physiotherapeutic rehabilitation measures.

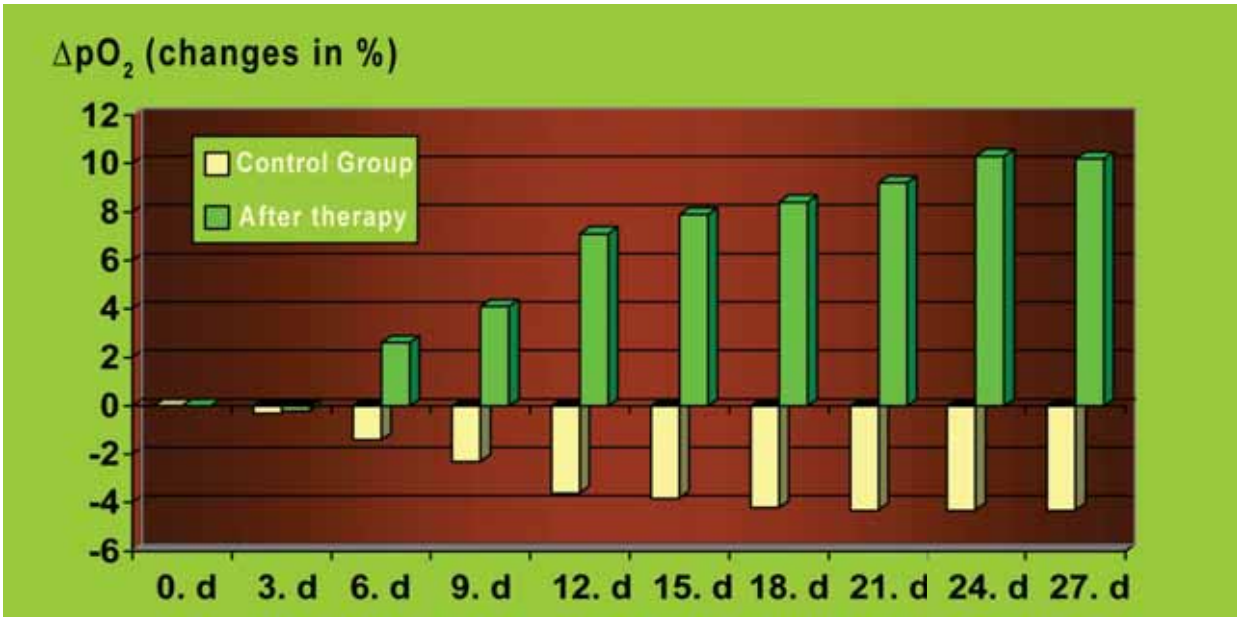
**Figure 330**

**Behavior of the parameter "oxygen depletion $\Delta pO_2$ in the venules" (mean values) during a 27-day observation period in the sub-cutaneous target tissue in geriatric rehabilitation patients.**

**Control group: conventional physiotherapy without complementary use of a changing electromagnetic field.**

**Test group: conventional physiotherapy + complementary use of a changing electromagnetic field.**

Statistical examination results: Significant differences in characteristics - control group versus test group beginning on the 6th day.




The subjective evaluation of the treatment success by the rehabilitation patients on the 27th day of the observation corresponded to the behavior of microcirculatory characteristics determined in both partial samples.

In summary, it was determined:
The success of physiotherapeutic rehabilitative measures (at least in the beginning of therapy) is dependent on whether and to what extent microcirculatory functional characteristics can be altered. This applies to the endothelial functions, spontaneous vasomotion, and the extra-vascular fluid movements in the interstitium and in the initial lymph flow. The therapeutic success in the treatment of geriatric rehabilitation patients can be increased through effective complementary treatment options such as the use of a certain changing electromagnetic field with added vasomotion stimulation.

Figures 331, 332 and 333 illustrate the effects of the changing electromagnetic field with added vasomotion stimulation through examples of vitalmicroscopic findings from the subcutaneous and intestinal target tissue.

## Figure 331

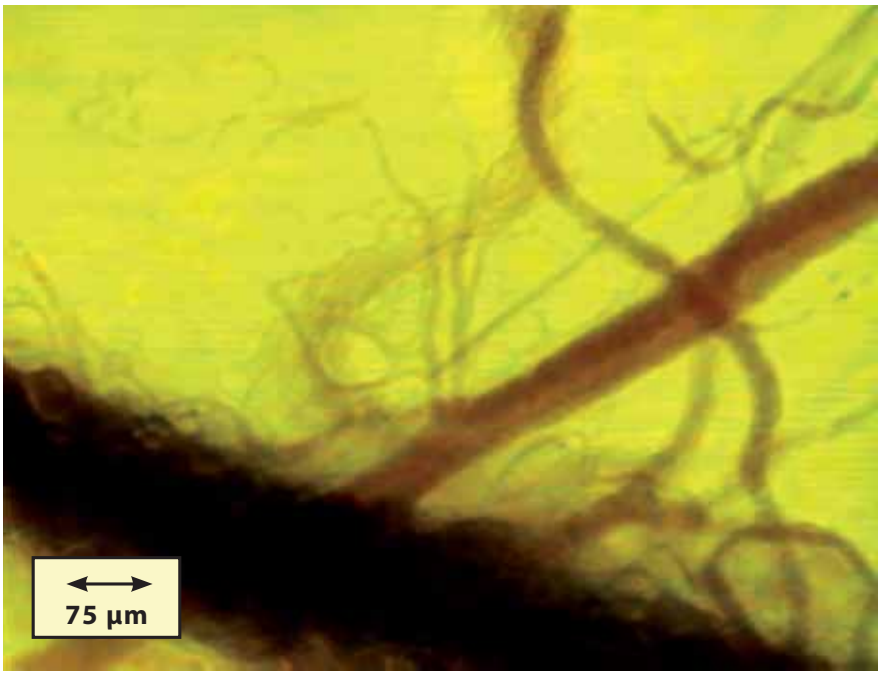
**Functional state of the microcirculation in a geriatric rehabilitation patient before and after 27 days of therapy with a certain changing electromagnetic field with added vasomotion stimulation**

**(Example of vitalmicroscopic findings, 1/1000 second, target tissue intestines).**

**a: prior to therapy**

**b: after a therapy period of 27 days**

**a**




**b**

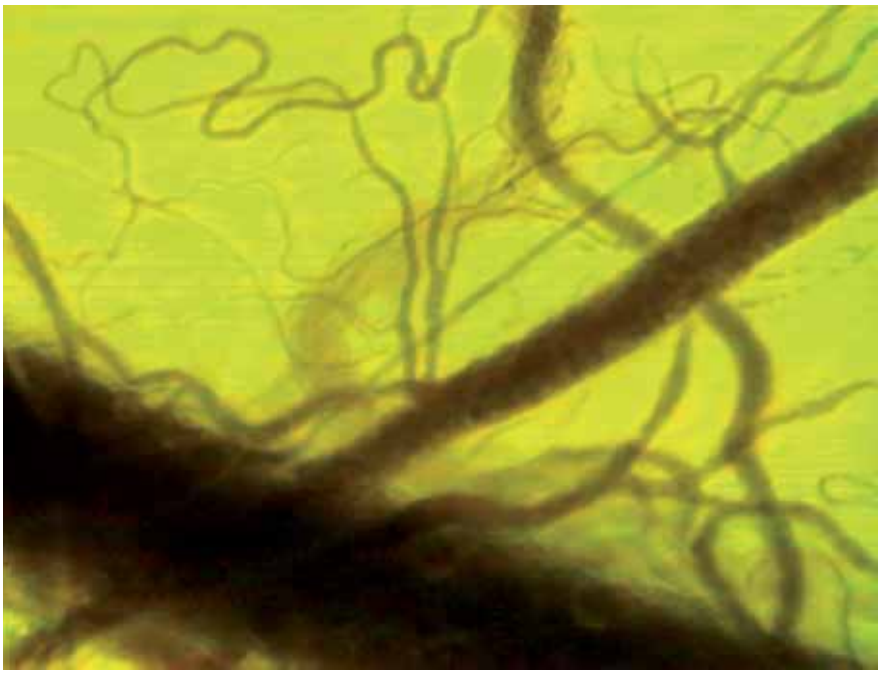
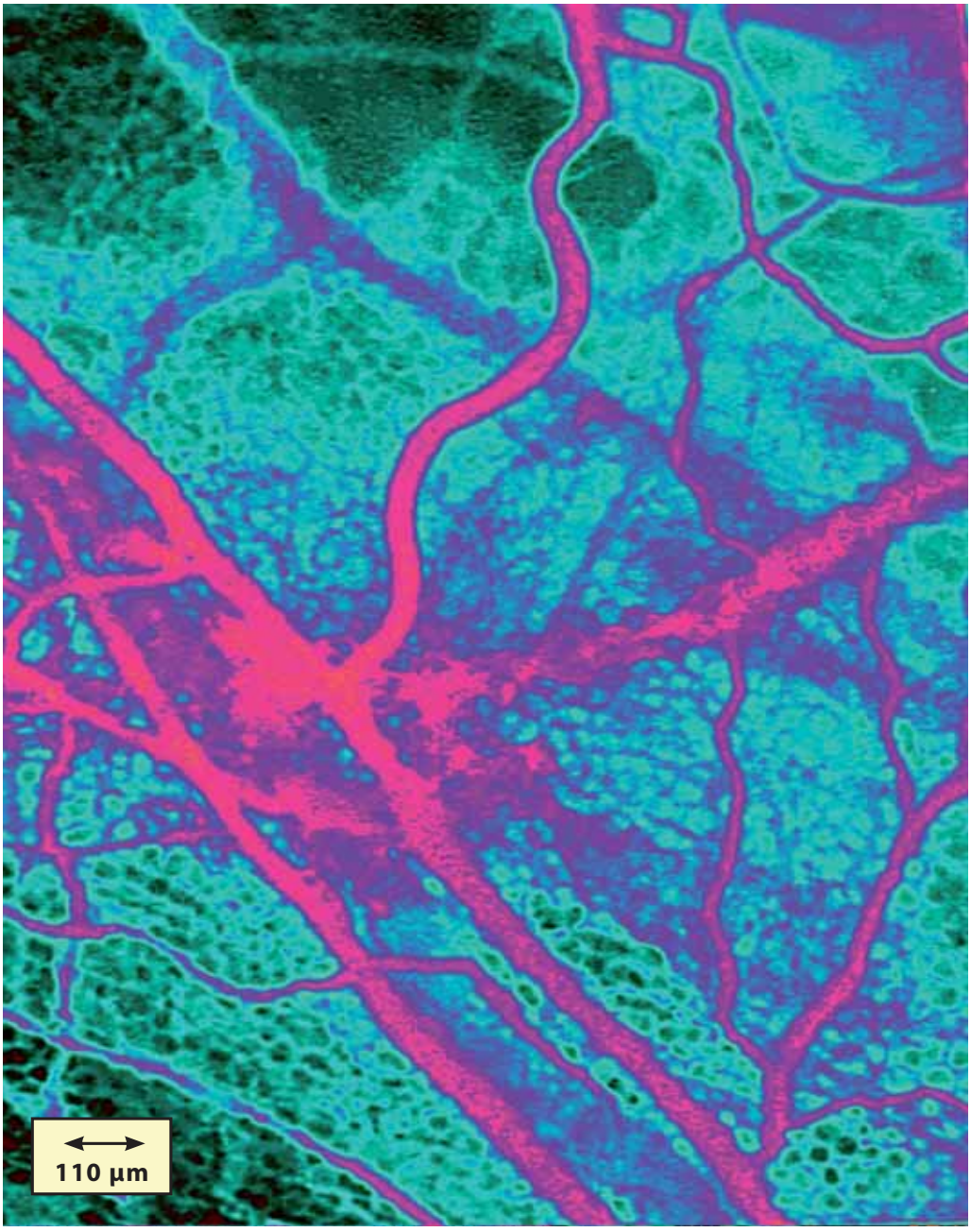


**Figure 332**

**Functional state of the microcirculation in a geriatric rehabilitation patient before and after 27 days of therapy with a certain changing electromagnetic field with added vasomotion stimulation**

**(Example of vitalmicroscopic findings, 1/1000 second, target tissue subcutis).**
**Pseudo color transformation of the primary images:**
**The blood cell perfused micro vessels are marked in red.**

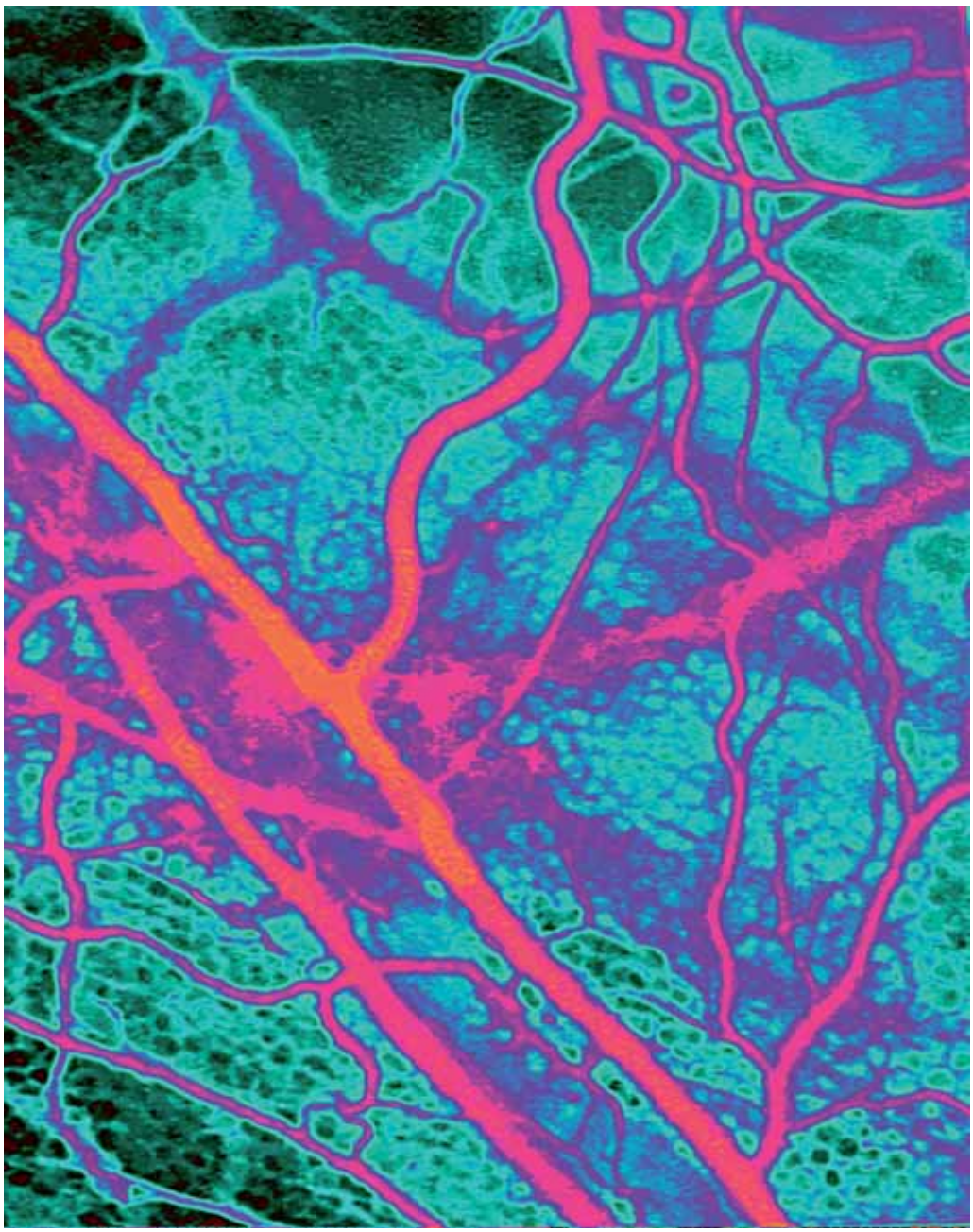
**a**



**a: prior to therapy**

**b: after a therapy period of 27 days**

**b**



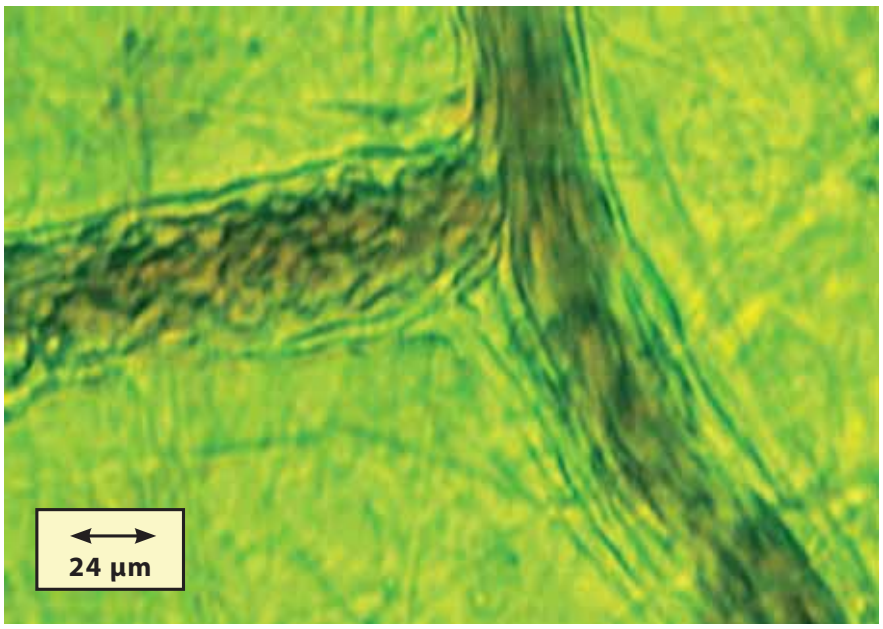
## Figure 333

**Functional state of the microcirculation in a subcutaneous venule section for a geriatric rehabilitation patient before and after 27 days of therapy with a certain changing electromagnetic field with added vasomotion stimulation**

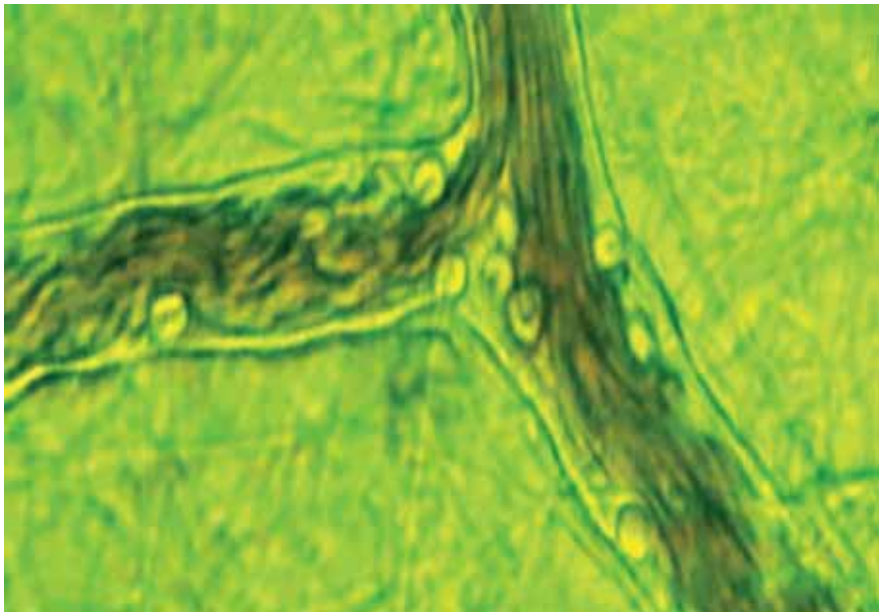
**(Example of vitalmicroscopic findings, 1/1000 second, target tissue subcutis).**
**a: prior to therapy**
**b: after a therapy period of 27 days**

*Due to the changed flow mechanical boundary conditions in the microcirculation at the end of the treating time numerous white blood cells are angeflutet and well distribute the microvascular networks to happen to be able.*

**a**



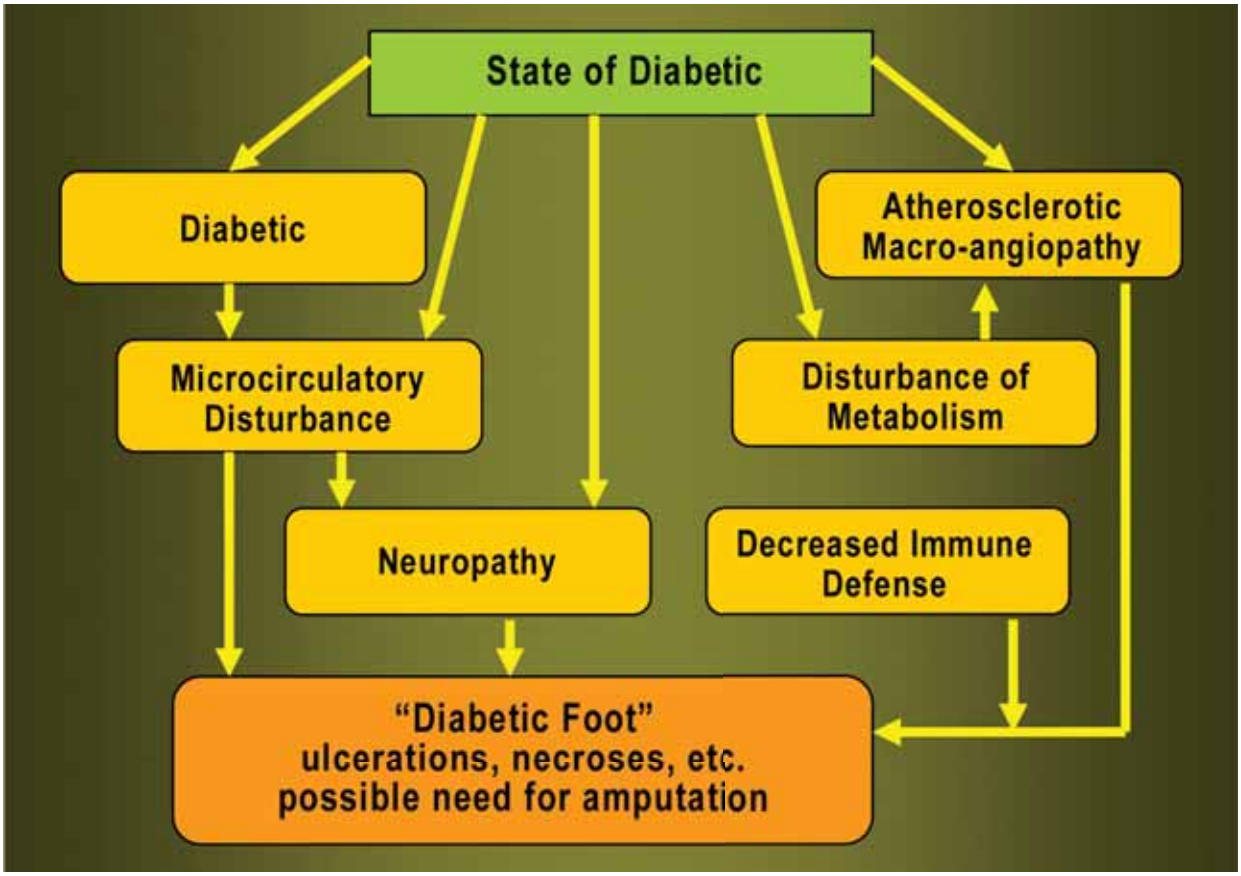

**b**



**Diabetes-related polyangioneuropathy** and its consequences ("diabetic foot") is one of the chronic complications of diabetes mellitus. The diabetic foot is an after-effect of diabetes-related polyneuropathy in conjunction with diabetic microangiopathy and a weakness to stave off infection. In many cases, "diabetic foot" and arterial occlusive disease occur concurrently, creating a therapeutic dilemma. Figure 334 schematically displays the pathogenesis.

**Figure 334**

**Pathogenesis of chronic complication with diabetes mellitus**




A review of figure 334 reveals that therapeutic success can be increased by adding complementary therapy options to established clinical therapies that focus on positively affecting microcirculation and improving micro-hemodynamic conditions for the first steps of an immunological reaction to process unhindert. The results of clinical observations reveal that for this purpose the application of certain changing affecting microcirculation and improving micro-hemodynamic conditions for the first steps of an immunological reaction to process unhindert. The results of clinical observations reveal that for this purpose the application of certain changing electromagnetic fields with added vasomotion stimulation can be considered.

**Research Design**

| | |
|---|---|
| **Test Sample, Partial Test** | Total test sample $N_{TOTAL}$=36<br>Geriatric diabetic patients, 66-77 years of age, male and female<br>Diabetes-related polyangioneuropathy<br>Ulceration, indication for amputation<br>Two equal partial test samples of n=18<br>▶ Control Group:<br>Customary clinical treatment without application of a certain changing electromagnetic field.<br>▶ Test Group:<br>Customary clinical treatment without application of a certain changing electromagnetic field. |
| **Test System,** | Therapy device: Changing electromagnetic field with added vasomotion stimulation (BEMER Plus)<br>Test group: 2 times a day every other day, 2 hours apart, 10 minutes each lying on the mat (level 3) for a therapy duration of 60 days. |
| **Measurement Intervals and** | Observation period 60 days, equidistant measurement intervals.<br>Data collection 1 hour after the 2nd application on day of measurement.<br>Day zero (determination of base values prior to the 1st application, control group accordingly), subsequent data collections on days 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, and 60. |
| **Target Tissue** | Subcutis and infracutaneous<br>(lower extremity, ~20 mm away from the ulceration) |
| **Measurement Methods** | ▶ Intravitalmicroscopy with computer assisted image processing (documentation of findings, high speed camera, 35 mm high resolution film, image sequence 60 and 90 pictures per second).<br>▶ Laser-DOPPLER-microflow-measurement and white light spectroscopy.<br>Penetration depths: 3 mm to 8 mm<br>Capture of complete interconnected micro-vascular networks with defined tissue volume V=1200µm3 (diameter of vessels d≤200µm).<br>Defined conditions of macro-circulation and temperature regulation. |
| **Parameters** | ▶ Number of blood cell perfused nodal points nNP.<br>▶ Arteriolar vasomotion status $A_{vm}$. |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), a = 5% |

The research results are summarized in figures 335 and 336.

We will forego the illustration of the data collected from the control group, which displayed an increasing deterioration of microcirculatory function in the sub-cutis over the 60 day observation period.

Figure 337 illustrates a selected example of vitalmicroscopic findings regarding the effects of the changing electromagnetic field with added vasomotion stimulation used as complementary therapy.

**Figure 335**

**Measurement data for the parameter "number of blood cell perfused nodal points" (mean values) in the subcutaneous and infracutaneous target tissues of geriatric diabetics with polyangioneuropathy over a 60-day treatment period (complementary application of a certain changing electromagnetic field with added vasomotion stimulationfield with added vasomotion stimulation).**

**Simultaneous collection of measurement data in two tissue depths: 3mm and 8 mm**

*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field with added vasomotion stimulation occur after the 8th day of measurement.*

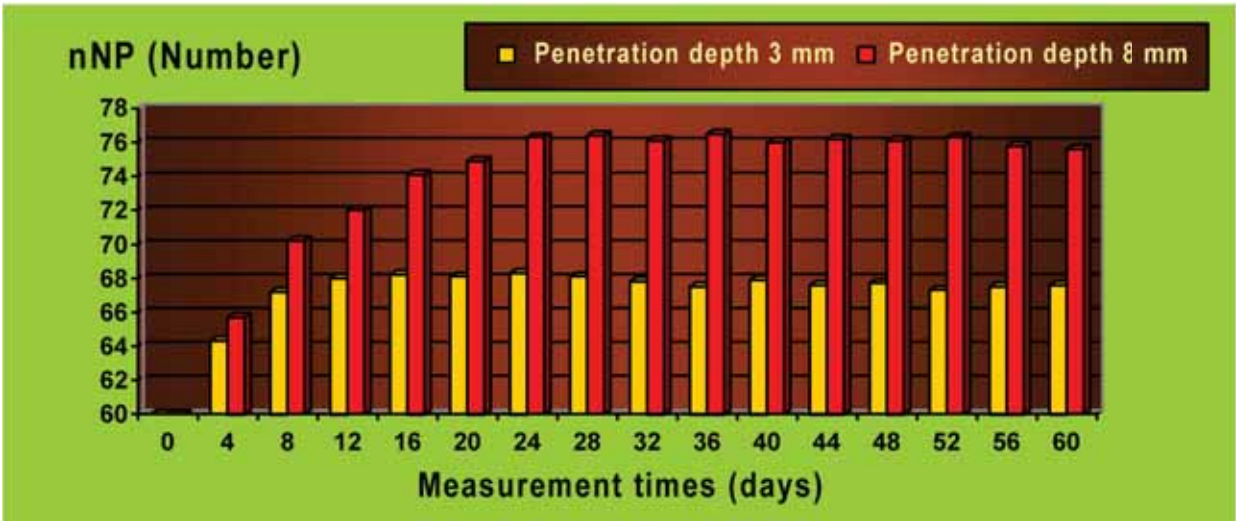
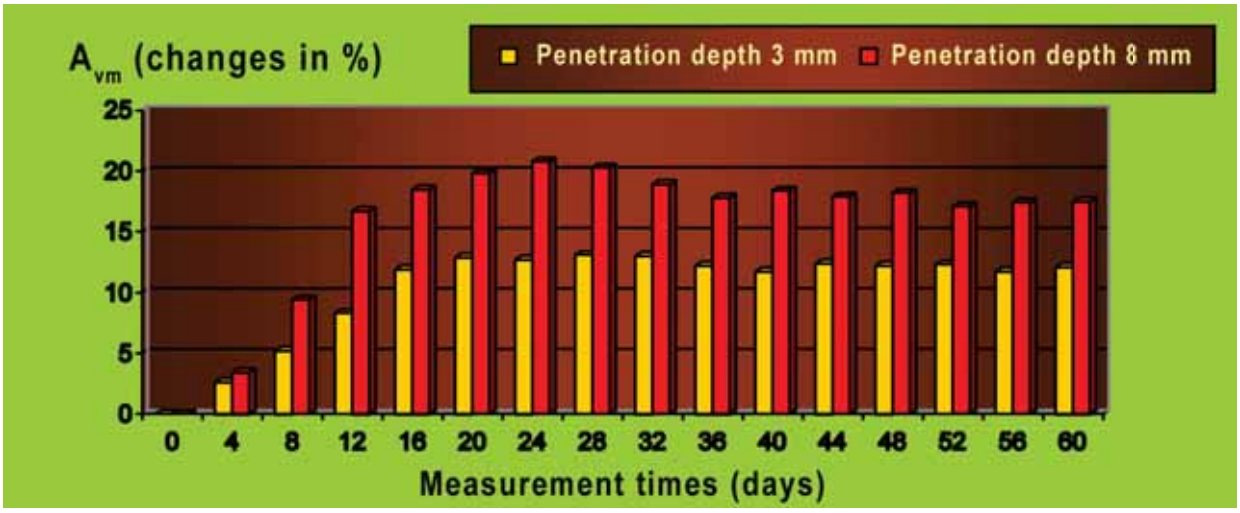



**Figure 336**

**Measurement data for the parameter "area under the envelope of the amplitude frequency spectrum of the spontaneous arteriolar vasomotion AVM" (mean values) in the subcutaneous and infracutaneous target tissues of geriatric diabetics with polyangioneuropathy over a 60-day treatment period (complementary application of a certain changing electromagnetic field with added vasomotion stimulation).**

**Simultaneous collection of measurement data in two tissue depths: 3mm and 8 mm**

*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field with added vasomotion stimulation occur after the 8th day of measurement.*

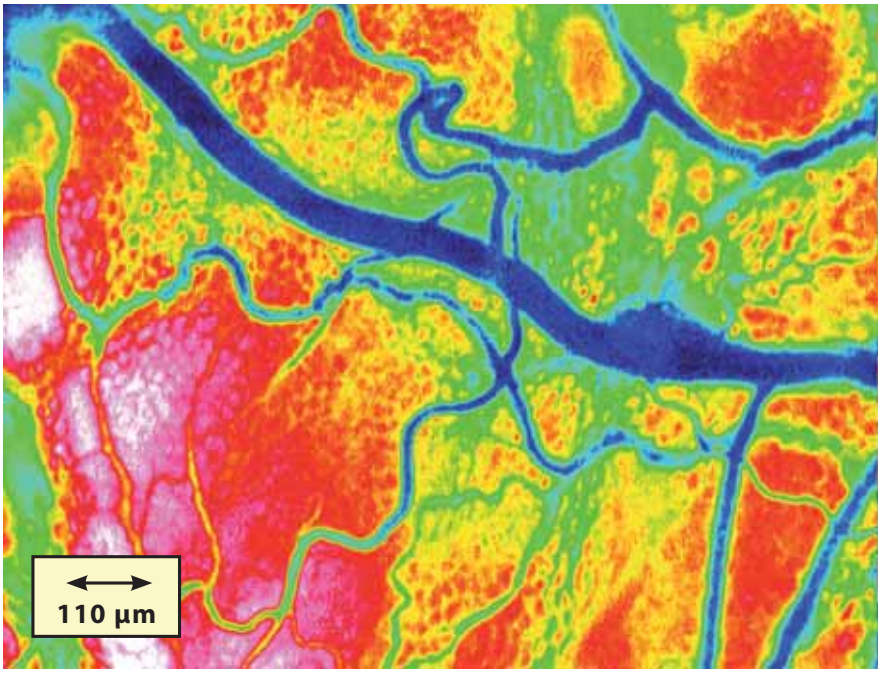


## Figure 337

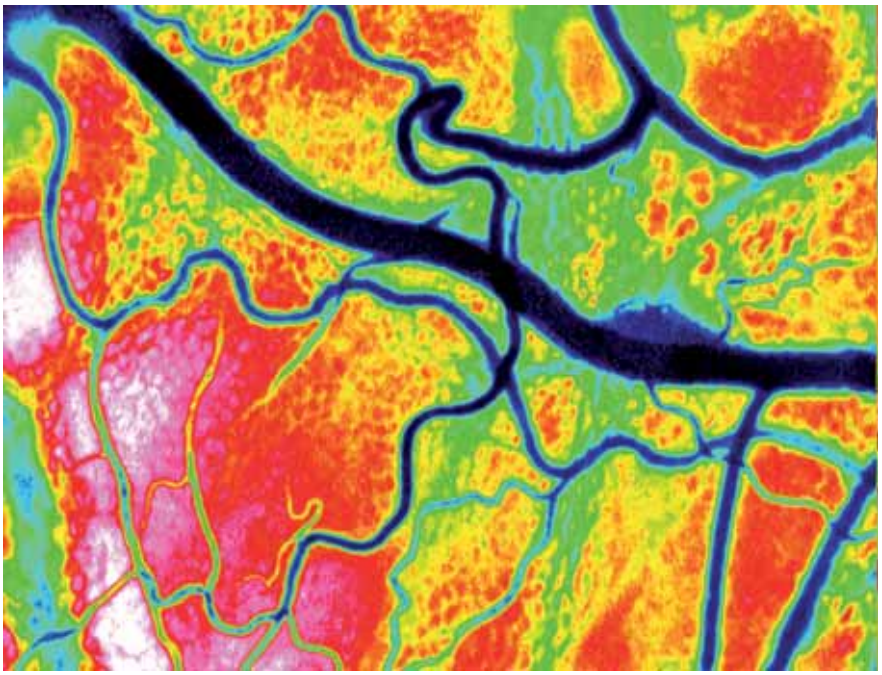
**Changes in the distribution state of the plasma-blood cell mixture in the subcutaneous micro vessels (penetration depth 3 mm) for a patient with diabetes-relates polyangioneuropathy before and after application of a certain changing electromagnetic field.**
**Vitalmicroscopic findings 1/250 second; pseudo color transformation of the primary image: the blood cell perfused micro vessels are marked in blue.**

**a: before additional therapy**
**b: after additional therapy over a 60 day period**

**a**




**b**



In the context of further research on a comparable patient group using the same research design, the following parameters were captured in the subcutaneous target tissue (penetration depth 3 mm) in addition to the parameters “number of blood cell perfused nodal points nNP” and “area under the envelope of the amplitude frequency spectrum of the spontaneous arteriolar vasomotion AVM”:

- Venular flow rate Qven
- Flow rate of the initial lymph fluid QL
- Number of white blood cells adhering to a defined area of venule wall A=18000µm2, nWBCA

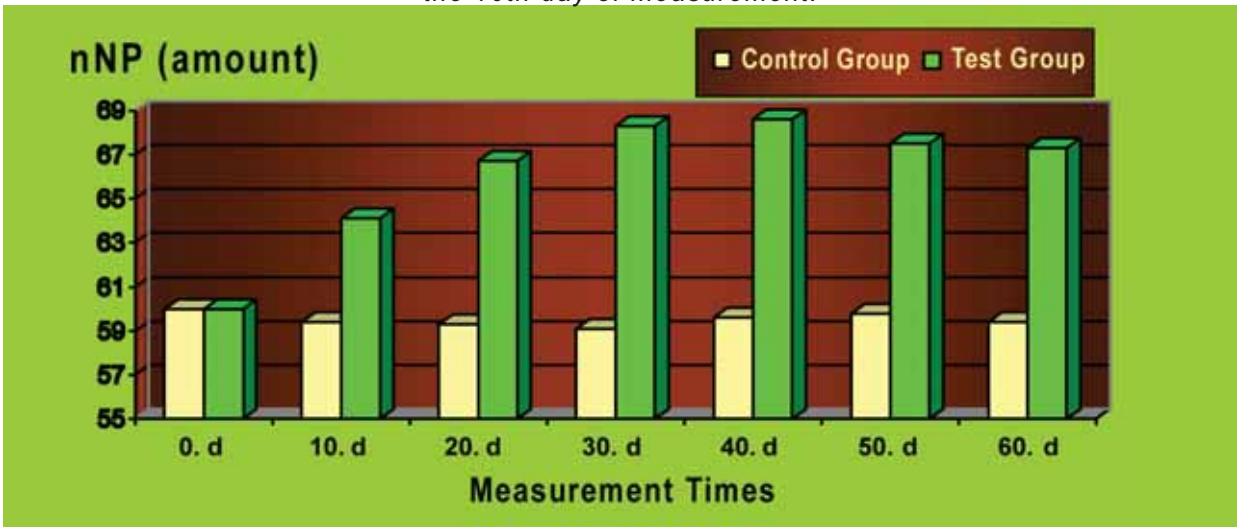
Measurement data for the parameter “number of blood cell perfused nodal points nNP” (mean values) in the sub-cutaneous target tissue over a 60 day therapy period for a test sample of geriatric diabetic patients with polyangioneuropathy, who received complementary therapy with a certain changing electromagnetic field with vasomotion stimulation in addition to the standard clinical therapy (test group), in comparison to a test sample who did not receive complementary therapy (control group).

Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field occurred after the 10th day of measurement.

**Figure 338**

**Measurement data for the parameter “number of blood cell perfused nodal points nNP” (mean values) in the sub-cutaneous target tissue over a 60 day therapy period for a test sample of geriatric diabetic patients with polyangioneuropathy, who received complementary therapy with a certain changing electromagnetic field with vasomotion stimulation in addition to the standard clinical therapy (test group), in comparison to a test sample who did not receive complementary therapy (control group).**

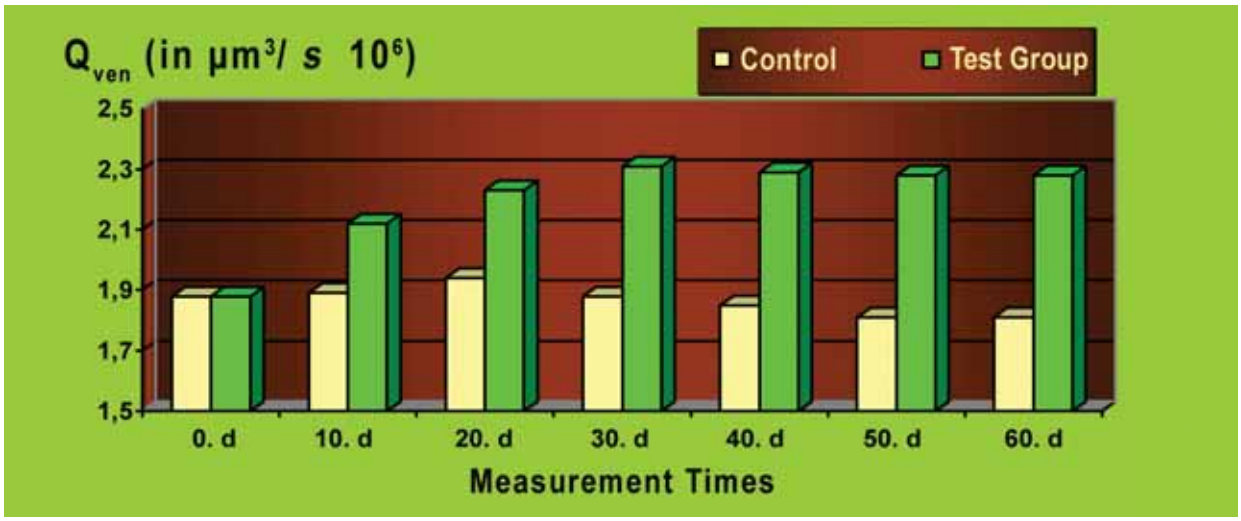
*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field occurred after the 10th day of measurement.*



## Figure 339

**Measurement data for the parameter "venular flow rate Qven" (mean values) in the sub-cutaneous target tissue over a 60 day therapy period for a test sample of geriatric diabetic patients with polyangioneuropathy, who received complementary therapy with a certain changing electromagnetic field with added vasomotion stimulation in addition to the standard clinical therapy (test group), in comparison to a test sample who did not receive complementary therapy (control group).**

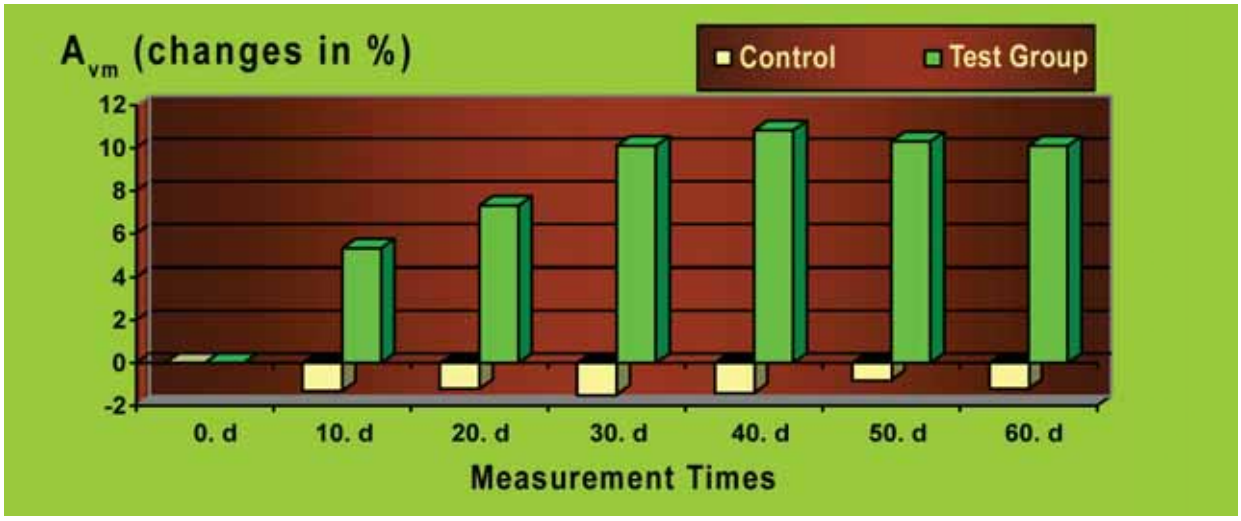
*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field occurred after the 10th day of measurement.*




## Figure 340

**Measurement data for the parameter "area under the envelope of the amplitude frequency spectrum of the spontaneous arteriolar vasomotion AVM" (mean values) in the sub-cutaneous target tissue over a 60 day therapy period for a test sample of geriatric diabetic patients with polyangioneuropathy, who received complementary therapy with a certain changing electromagnetic field with vasomotion stimulation in addition to the standard clinical therapy (test group), in comparison to a test sample who did not receive complementary therapy (control group).**

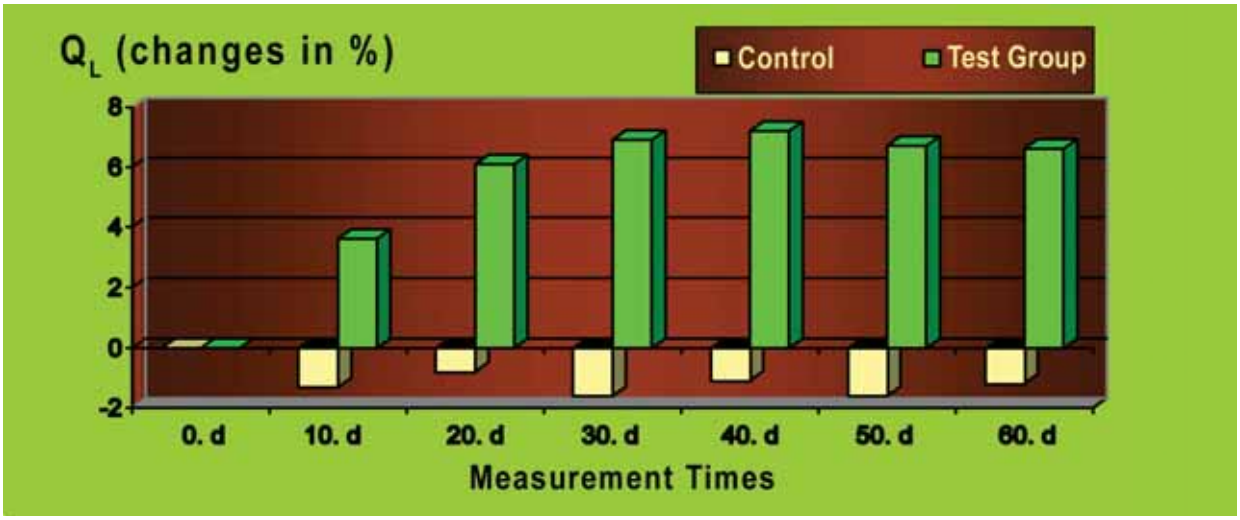
*Significant differences in characteristics between the data of a control group and the group receiving additional treated with a certain changing electromagnetic field occurred after the 10th day of measurement.*



## Figure 341

**Measurement data for the parameter "flow rate of the initial lymph fluid QL" (mean values) in the sub-cutaneous target tissue over a 60 day therapy period for a test sample of geriatric diabetic patients with polyangioneuropathy, who received complementary therapy with a certain changing electromagnetic field with vasomotion stimulation in addition to the standard clinical therapy (test group), in comparison to a test sample who did not receive complementary therapy (control group).**

*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field occurred after the 10th day of measurement.*




## Figure 342

**Measurement data for the parameter "number of white blood cells adhering to a defined venule wall nWBC/A" (mean values) in the sub-cutaneous target tissue over a 60 day therapy period for a test sample of geriatric diabetic patients with polyangioneuropathy, who received complementary therapy with a certain changing electromagnetic field with vasomotion stimulation in addition to the standard clinical therapy (test group), in comparison to a test sample who did not receive complementary therapy (control group).**

*Significant differences in characteristics between the data of a control group and the group receiving additional treated with a certain changing electromagnetic field occurred after the 10th day of measurement.*

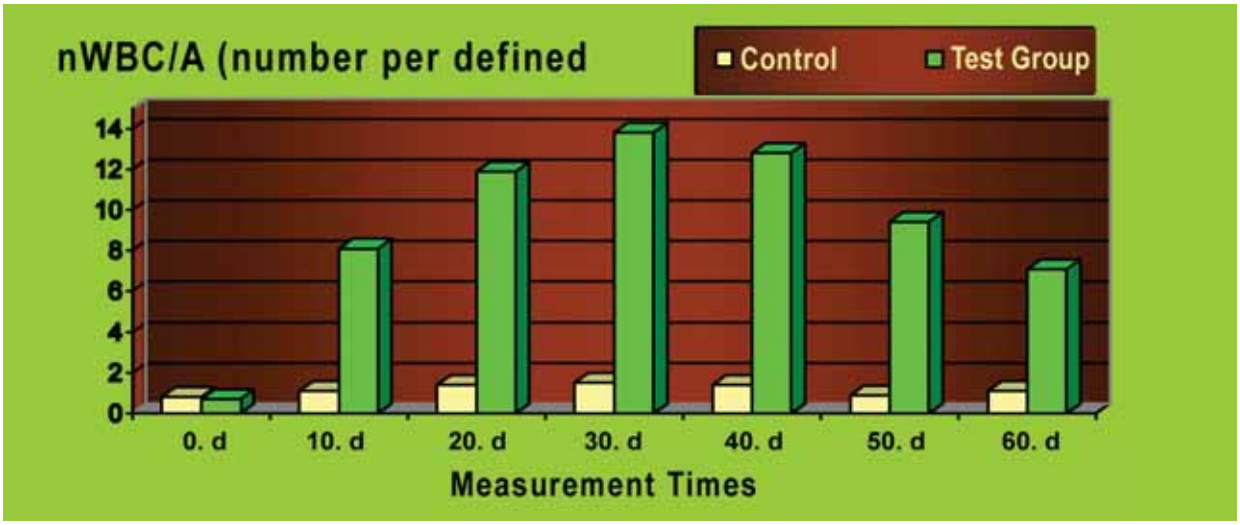
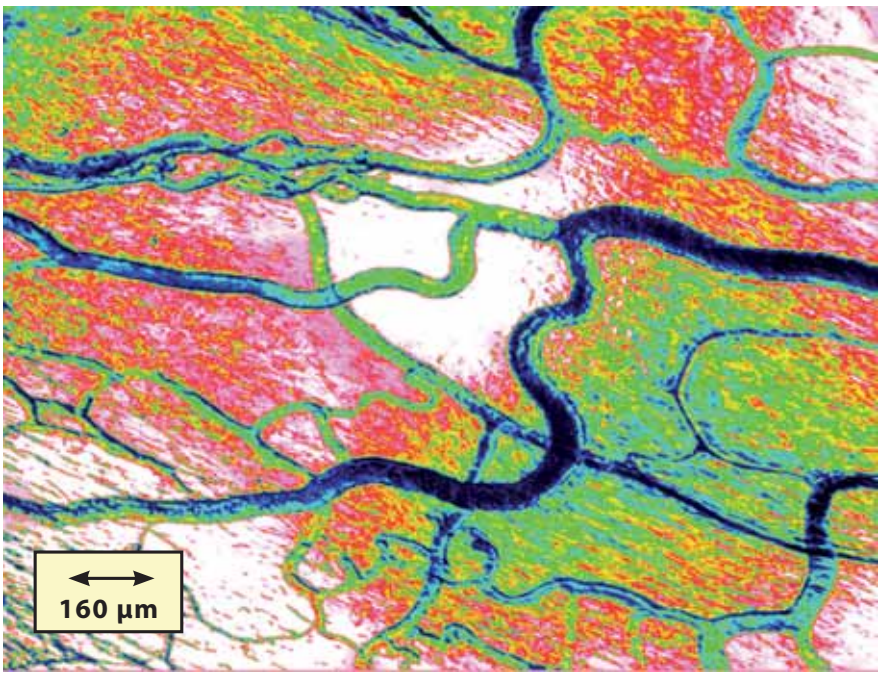


**Figure 343**

**Changes in the distribution of the plasma-blood cell mixture in the subcutaneous micro vessels (penetration depth 3mm) for a patient with diabetes related polyangioneuropathy before and after 60 days of therapy with a certain changing electromagnetic field.**

**(Vitalmicroscopic findings 1/200 second)**
**a: before additional therapy**
**b: after 60 days of therapy**

**a**




**b**

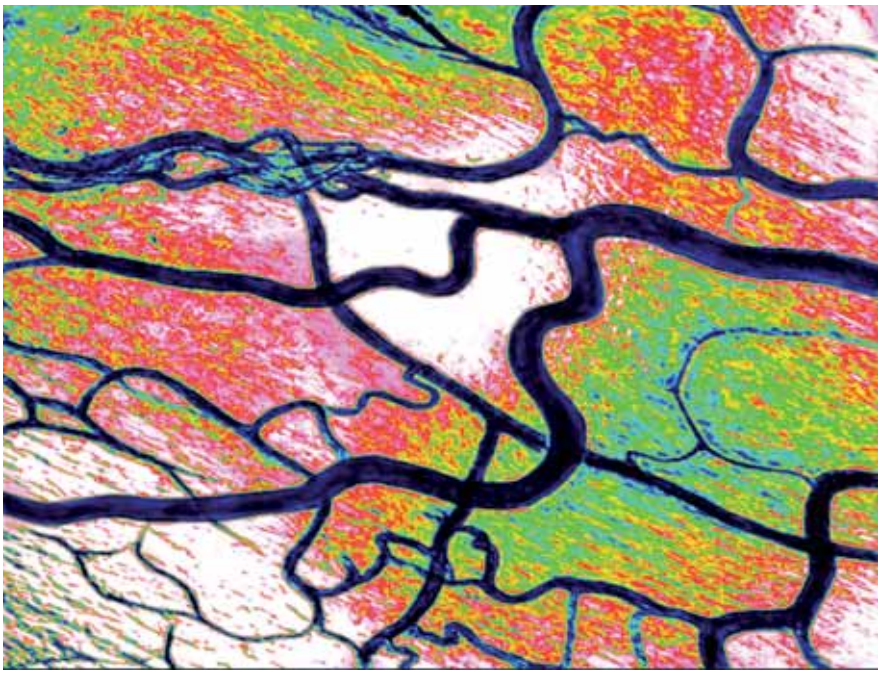
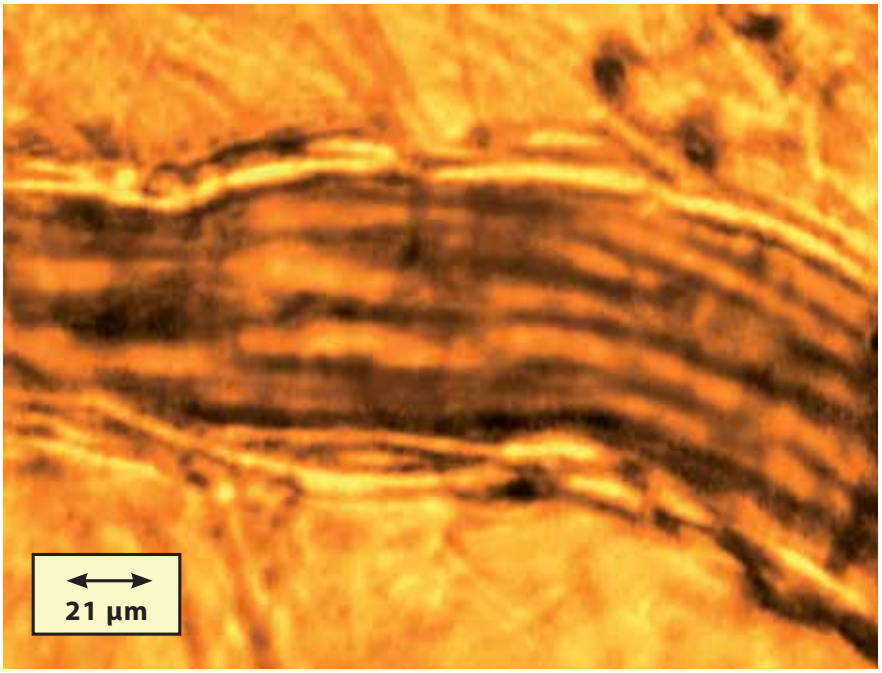


**Figure 344**

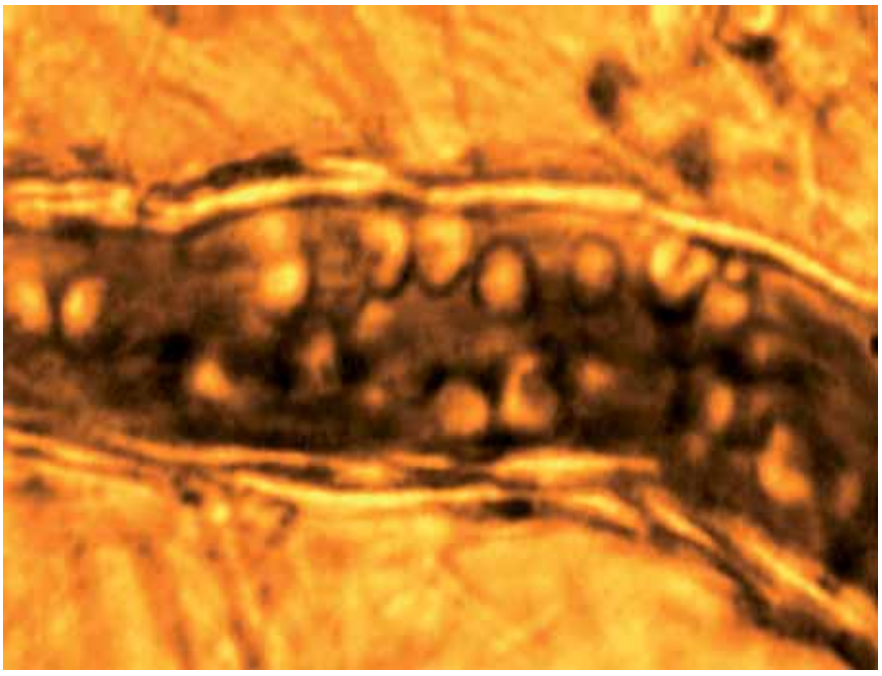
**Immunological behavior characteristics (aggregation and adhesion) of white blood cells in a subcutaneous venule for a patient with diabetes related polyangioneuropathy before and after 60 days of therapy with a certain changing electromagnetic field.**

**(Vitalmicroscopic findings 1/100 second)**
**a: section of a venule before additional therapy**
**b: identical section of a venule after 60 days of therapy**

**a**




**b**



A summary of the research results shows:

For illnesses accompanied by significant disturbances of the microcirculation for which the causes cannot be treated directly, like diabetes-related polyangioneuropathy for instance, complementary application of certain changing electromagnetic fields with added vasomotion stimulation displays promising results for increasing the success rate of established therapy concepts.

Examples of research results for the complementary therapeutic application of certain changing electromagnetic fields with added vasomotion stimulation on patients with alcohol-related fatty liver clarify that the microcirculatory effects of the therapy options described up to now are not limited to the stimulation of the blood flow in the organs derma and intestine, but also affect the “inner” organs, for instance the liver, an important metabolic organ. We also want to call attention to an intracellular redox system and its stimulation: the reduced and oxidized form of glutathione.

Reduced glutathione protects certain enzymes against oxidation and reduces constantly forming peroxides (one of the important intracellular protection mechanisms toward free radicals). Glutathione is present especially in the red blood cells and is concentrated in the liver and in the brain.

**Research Design**

| | |
|---|---|
| **Test Sample, Partial Test** | Total test sample $N_{TOTAL}$=36<br>Male patients with alcohol-related fatty liver, age ~ 60 (diagnosis: echosonography, transaminases)<br>Two equal partial test samples of n=18<br>► Control Group: Customary clinical treatment (strict abstinence)<br>► Test Group: Customary clinical treatment with additional application of a changing electromagnetic field with vasomotion stimulation. |
| **Test System,** | Therapy device: Changing electromagnetic field with added vasomotion stimulation (BEMER Plus)<br>Test group: 2 times a day every other day, 2 hours apart, 8 minutes each lying on the mat (level 3) for a therapy duration of 30 days. |
| **Measurement Intervals and** | Observation period 60 days (30 days of therapy and 30 days of follow-up), equidistant measurement intervals.<br>Data collection 1 hour after the 2nd application on day of measurement.<br>Day zero (determination of base values prior to the 1st application, control group accordingly), subsequent data collections on days 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, and 60. |
| **Target Tissue** | Marginal hepatic tissue (beneath the right costal arch) |
| **Measurement Methods** | ► Intravitalmicroscopy measuring device<br>► Intravitalmicroscopic reflectionspectrometry<br>► Laser-DOPPLER-microflow-measurement and white light spectroscopy. |
| **Parameters** | ► Flow rate in the sinusoids of the liver parenchyma $Q_{sin}$<br>► Local changes in concentration of reduced glutathione in the liver parenchyma $cGl_{red}$ |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), a = 5% |

The data collected are summarized in figures 345 and 346.

**Figure 345**

**Measurement data for the parameter "sinusoidal flow rate $Q_{sin}$" (mean values) in the liver parenchyma over a 30 day therapy period (30 day follow-up) for a test sample of patients with alcohol-related fatty liver, who received therapy with a certain changing electromagnetic field with vasomotion stimulation in addition to the customary clinical therapy (test group), compared to a sample that did not receive complementary therapy (control group).**

*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field occurred after the 10th day of measurement.*

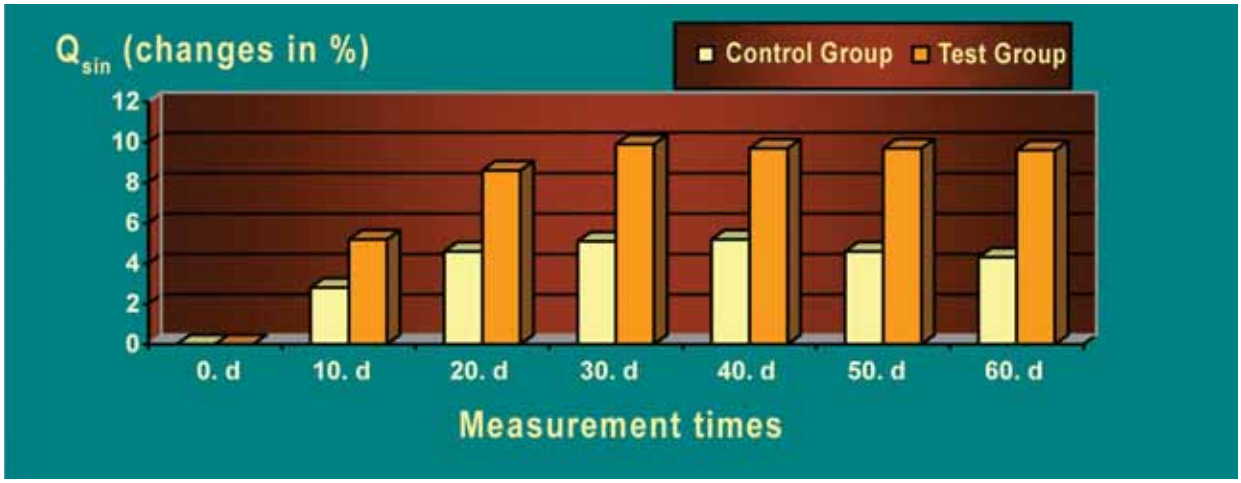
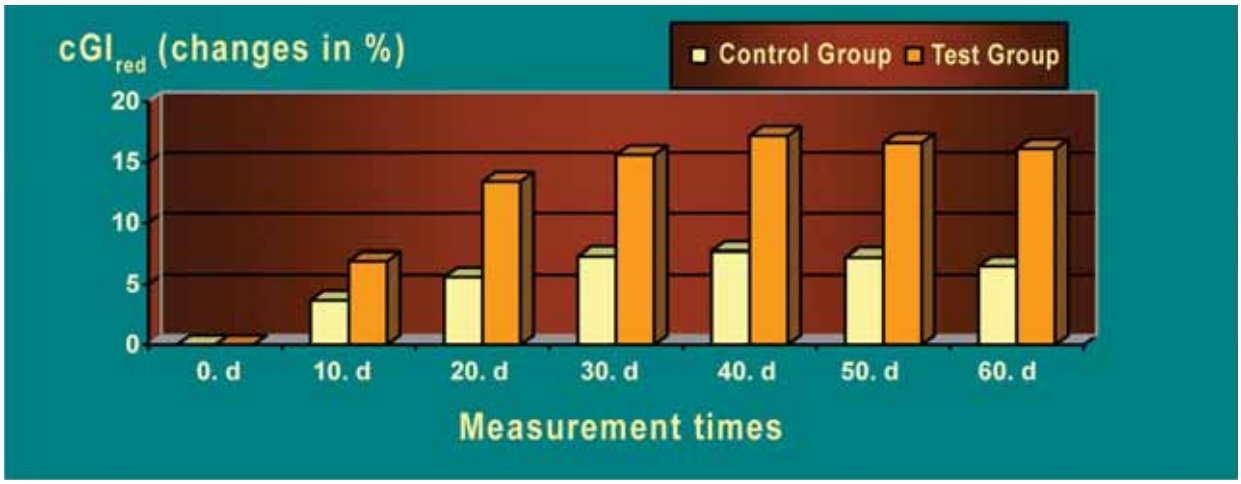



**Figure 346**

**Measurement data for the parameter "changes in concentration of reduced gluthatione cGlred" (mean values) in the liver parenchyma over a 30 day therapy period (30 day follow-up) for a test sample of patients with alcohol related fatty liver, who received therapy with a certain changing electromagnetic field with vasomotin stimulation in addition to the customary clinical therapy (test group), compared to a sample that did not receive complementary therapy (control group).**

*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field occurred after the 10th day of measurement.*



Through the complementary application of a certain changing electromagnetic field with vasomotion stimulation therapy results can be increased and achieved in a shorter time frame. Even though echosonographic examinations demonstrated the beginning of a decrease of the fatty tissue of the liver in the patients of the test group as well as in the patients of the control group as of the 20th day, the process proceeded more pronounced and more quickly in the patients of the test group in subsequent weeks.

In cases of chronic illnesses that can only be treated symptomatically, the complementary application of certain changing electromagnetic fields with vasomotion stimulation can support the clinical therapy.

The complementary treatment of patients with **rheumatoid arthritis** provides a good example.

The clinical picture of rheumatoid arthritis is a system disease of unknown etiology and manifests itself primarily in the joints. Initial chronic inflammation of the synovial membrane leads to the destruction of articular cartilage, affecting the areas near the joint as well. The disease progresses in phases, leading to painful swelling and restricted function of the affected joints. In more advanced stages this leads to complete destruction of the joint structures.
There is no known therapy for treating the causes of rheumatoid arthritis. Established therapies focus on reducing inflammation of the joints and easing discomfort as well as on improving joint functions and preventing joint deformation. Heat application and moor kneading are among the more widely used therapy methods.

**Research Design**

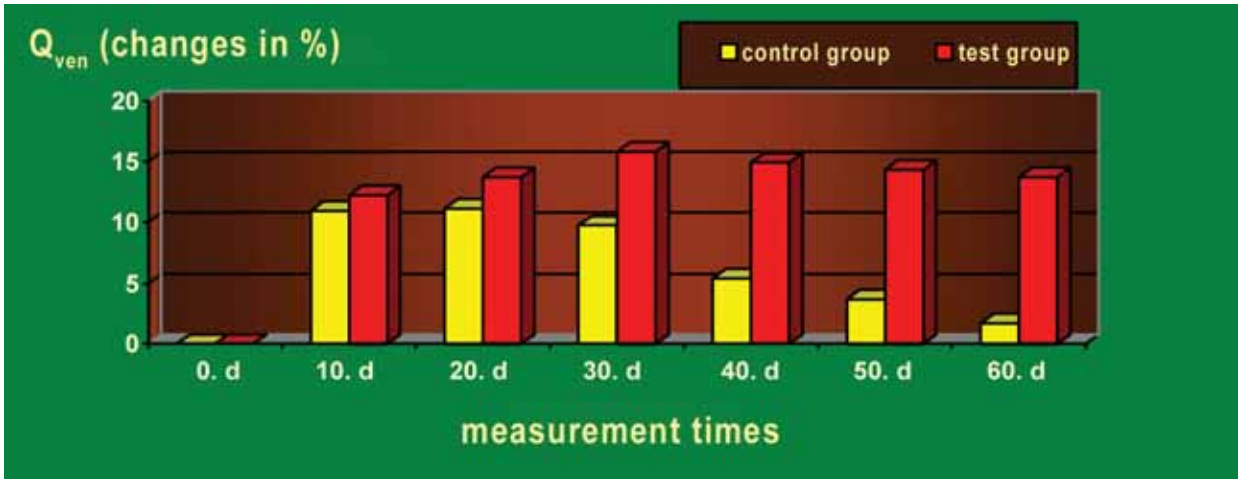
| | |
|---|---|
| **Test Sample, Partial Test Samples** | Total test sample $N_{total}$ = 36<br>female patients with rheumatoid arthritis,<br>age ~ 60, finger joints are affected<br>2 equal partial test samples of n=18<br>▶ Control group: Customary clinical treatment (heat, moor kneading)<br>▶ Test Group: Customary clinical treatment with additional application of a changing electromagnetic field with vasomotion stimulation. |
| **Test System, Application** | Therapy device: Changing electromagnetic field with added vasomotion stimulation (BEMER PLUS)<br>Test group: 2 times a day every other day, 2 hours apart, 10 minutes each lying on the mat (level 3) for a therapy duration of 30 days. |
| **Measurement Intervals and Timing** | Observation period 60 days (30 days of therapy and 30 days of follow-up), equidistant measurement intervals.<br>Data collection 1 hour after the 2nd application on day of measurement.<br>Day zero (determination of base values prior to the 1st application, control group accordingly), subsequent data collections on days 10, 20, 30, 40, 50 and 60. |
| **Target Tissue** | Subcutis (close to the affected joints) |
| **Measurement Methods** | ▶ Intravitalmicroscopic measuring device<br>▶ Intravitalmicroscopic reflectionspectrometry<br>▶ Laser-DOPPLER-microflow-measurement combined with white light spectroscopy. |
| **Parameters** | ▶ Venular flow rate $Q_{ven}$<br>▶ Oxygen depletion in the venules $\Delta pO_2$ |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), α= 5% |

The measurement data collected are summarized in figures 347 and 348.

## Figure 347

**Measurement data for the parameter "venular flow rate $Q_{ven}$" (mean values) in the sub-cutaneous target tissue over a 30 day therapy period (30 day follow-up) for a test sample of patients with rheumatoid arthritis, who received therapy with a certain changing electromagnetic field with vasomotin stimulation in addition to the customary clinical therapy (test group), compared to a sample that did not receive complementary therapy (control group).**

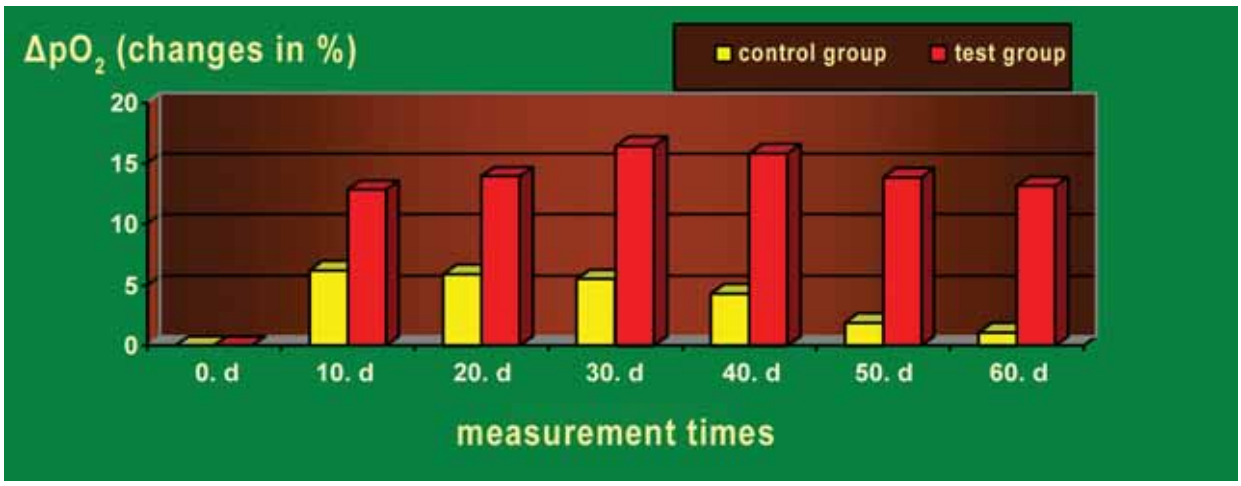
*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field occurred after the 30th day of measurement.*




## Figure 348

**Measurement data for the parameter "oxygen depletion in the venules $\Delta pO_2$" (mean values) in the sub-cutaneous target tissue over a 30 day therapy period (30 day follow-up) for a test sample of patients with rheumatoid arthritis, who received therapy with a certain changing electromagnetic field with vasomotin stimulation in addition to the customary clinical therapy (test group), compared to a sample that did not receive complementary therapy (control group).**

*Significant differences in characteristics between the data of a control group and the group receiving additional treatment with a certain changing electromagnetic field occurred after the 10th day of measurement.*



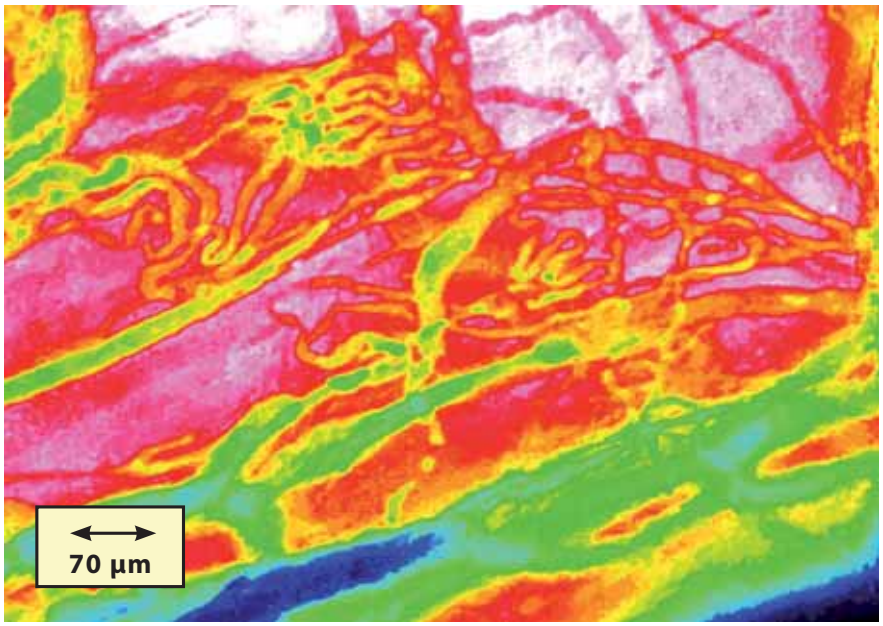

The subjective evaluation of the therapy success by the patients at the end of the observation time is consistent with the changes in characteristics determined in both test samples.

## Figure 349

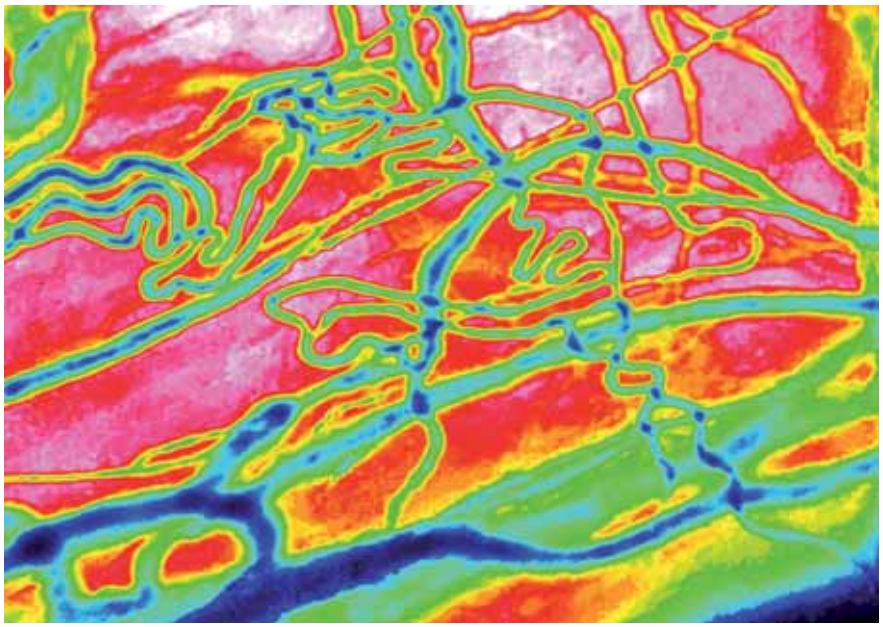
**Impact of a 30-day complementary therapy with a certain changing electromagnetic field on the distribution of the plasma-blood cell mixture in the microvascular networks of a joint-near subcutaneous tissue area in a female patient with rheumatoid arthritis.**
**Example of vitalmicroscopic findings 1/200 second.**
**Pseudo color transformation of the primary image (the blood cell perfused microvessels are marked in blue-green).**

**a: distribution status before therapy**
**b: distribution status in the same network after 30 days of complementary therapy.**

**a**




**b**



In conclusion we will again examine the organ of the **skin**, from the "cosmetic" aspects as well as the medical aspects.
Most recently, the combination of a certain changing electromagnetic field with vasomotion stimulation and a light signal that follows the temporal pattern of the changing electromagnetic field (known as soft laser within the wave lengths of a red light) is being recommended as an enhanced therapy option. Such a combination is expected to further increase the already documented effects of certain changing electromagnetic fields in the cutaneous and sub-cutaneous microcirculation.

The organ of the skin has three different functional components:

- The epidermis and the papillary dermis with the near-surface capillary networks.
- The reticular dermis
- The subcutis (sub-cutaneous fatty tissue).

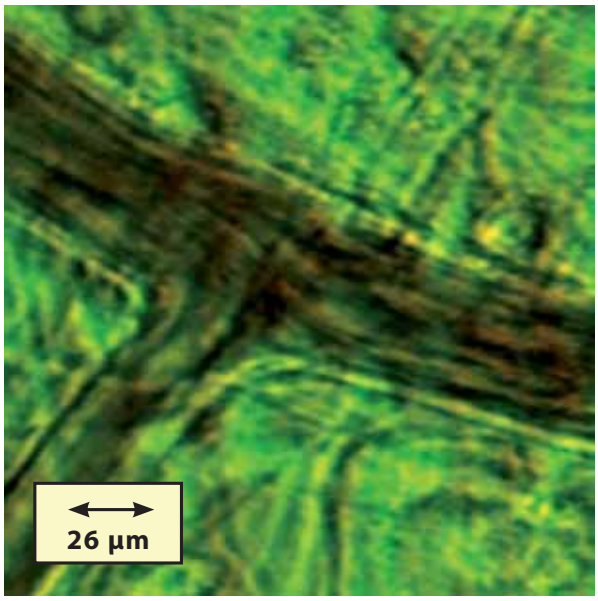
Each of these components responds to the influence of noxes and stimuli with their own respective, typical reactions. Thereby, noxes and stimuli can act "from the inside" via the bloodstream or "from the outside" via the environment.

The main arena of the aging processes is the **papillary dermis**. The comparatively high tissue turgor (plumpness) during the infantile age is based on correspondingly high concentrations of hyaluronic acid in the fundamental substance of the connective tissues, whereby a high viscosity and a large storage capacity for water and electrolytes is provided. After birth, the content of hyaluronic acid falls abruptly, and continues to decrease slowly in subsequent years. Therefore, the skin of an aging person appears more lined and saggy. This effect can be compounded by UV related degeneration of the elastic fibers and other influences.
This natural progression cannot be stopped or reversed. We can, however, effectively influence the acceleration of aging processes (avoiding harmful noxes, implementing measures that promote health, stimulating the microcirculation).
We must remember that the dermis also is a "disposal" and storage organ. Molecular and small corpuscular waste products (of endogenous and exogenic origin) are phagocytized by histiocytes and stored virtually indefinitely. The reactions of the **reticular dermis** are rather slow due to its function as a basic mechanical framework of the skin. The basic reaction patterns are: scar formation, fibrosis, sclerosis, atrophy.
The **sub-cutaneous fatty tissue** displays a simple reaction pattern. It reacts to the influence of mechanical, inflammatory or enzymatic noxes with the demise of fatty cells and the release of fatty acids. These in turn provoke an increased inflammatory stimulus, whereby a chain reaction is triggered: Destruction of more fatty cells →lipogranulomatosis→sclerotization.

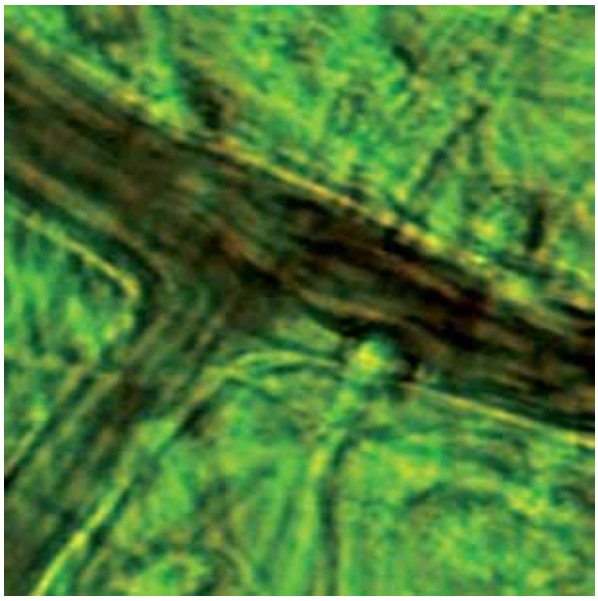
For medical purposes, the most significant organ function of the skin is the homeostasis of the total organism: The dermis is representative of circulation and, together with the intestine, is one of the most immunologically active organs of the organism.

**The beginning of an immunological reaction in the skin:**
Initiation of the transmigration of white blood cells in a subcutaneous venule
(example of vitalmicroscopic findings)
Image sequence from a to d in a timespan of ~ 15 seconds.

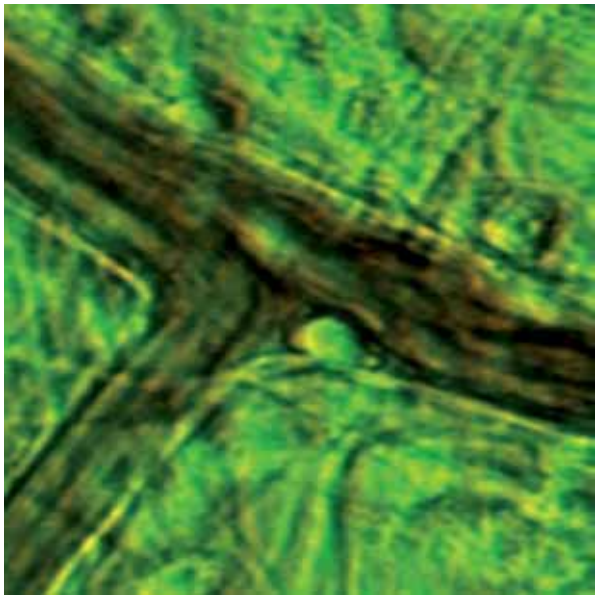
**a**



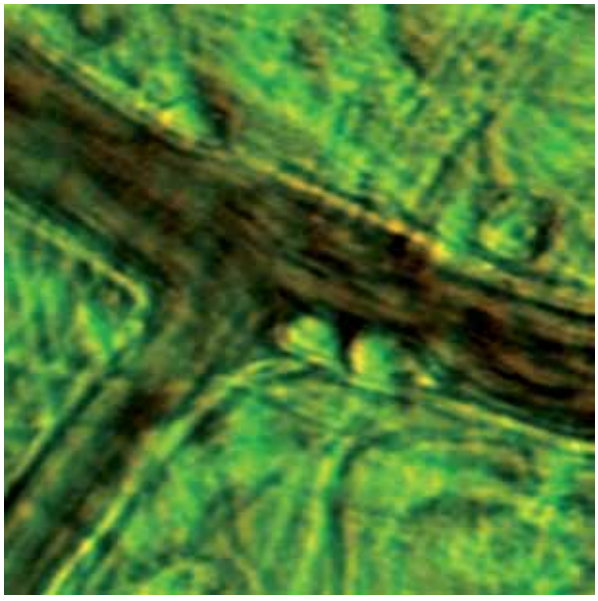

**b**



**c**



**d**



From the perspective of microcirculation research, the combination of soft laser and a changing electromagnetic field is seen as a stimulus modulation with the goal of a heightened effect on microcirculation. This achieved increase (within a certain extent) of the stimulation effect should neither be overestimated nor negated, as demonstrated by the following examples of clinical research.

**Research Design**

| | |
|---|---|
| **Test Sample, Partial Test Samples** | Total test sample N = 54<br>female patients, age ~ 50, no pathological abnormalities, normal skin type, no skin diseases.<br>3 equal partial test samples of n=18<br>▶ Control group: no treatment<br>▶ Test Group 1: treatment with a changing electromagnetic field<br>▶ Test Group 2: treatment with a changing electromagnetic field + soft laser |
| **Test System, Application** | Therapy device: Changing electromagnetic field with added vasomotion stimulation (BEMER PLUS/BEMER PLUS and SLT).<br>Test group: 3 times a day every other day, 2 hours apart, 10 minutes each, lying on the mat (level 3), for a therapy duration of 70 days. |
| **Measurement Intervals and Timing** | Observation period 70 days, equidistant measurement intervals.<br>Data collection 1 hour after the 3rd application on day of measurement.<br>Day zero (determination of base values prior to the 1st application, control group accordingly), subsequent data collections every 7th day up to the 70th day. |
| **Target Tissue** | Subcutis (area of the forehead) |
| **Measurement Methods** | ▶ Specific reflected-light microscopy, computer-assisted image interpretation<br>▶ Laser-DOPPLER-microflow-measurement combined with white light spectroscopy. |
| **Parameters** | ▶ Oxygen depletion in the venules $\Delta pO_2$<br>▶ Maximum depth of roughness Rmax (defined in a target area A=1200µm2), for definition see chapter 24 |
| **Statistical Analysis** | WILCOXON rank-sum test (MWW), $\alpha = 5\%$ |

The measurement data collected are summarized in figures 350 and 351. Figures 352 and 353 display selected examples of findings.

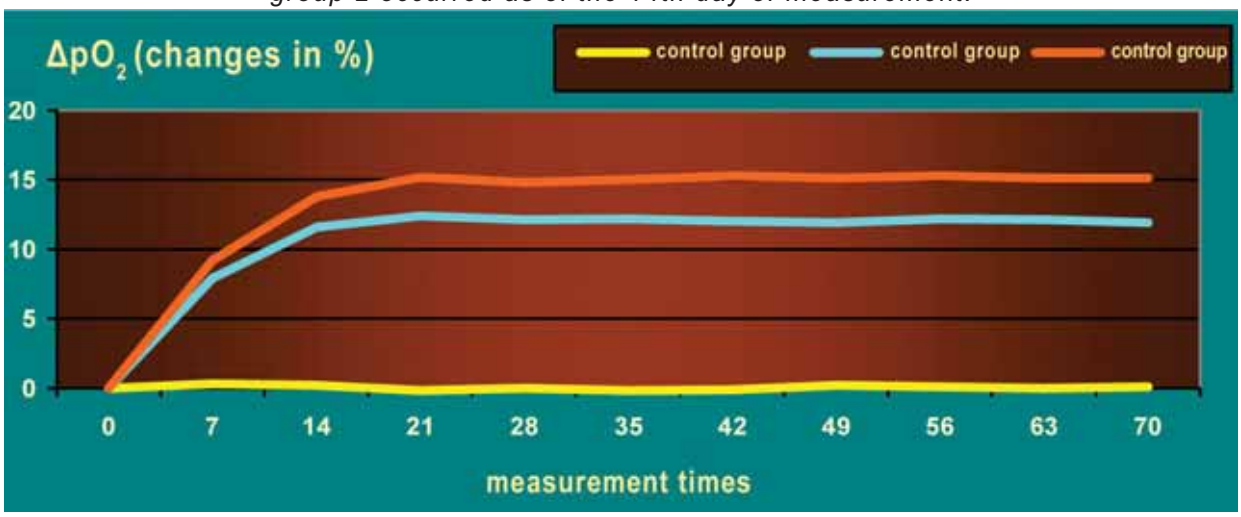
From the displayed data we can gather that intensified effects (increased oxygen depletion in the venules, higher surface quality of the skin) can be achieved through the combined application of a certain changing electromagnetic field with vasomotion stimulation (BEMER PLUS) and an appropriately pulsed soft laser (SLT).

Please note: The effects of the pulsed soft laser light in the wave range of a red light do not relate to the well-known effects after exposure to UV light (e.g. the conversion of the melanocytes from the “dormant” to the “active” stage).

## Figure 350

**Measurement data for the parameter "oxygen depletion in the venules $\Delta pO_2$" (mean values) in the sub-cutaneous target tissue over a therapy duration of 70 days for a test sample of female subjects ~ 50 years of age, who were treated with a certain changing electromagnetic field with vasomotion stimulation (test group 1) or a certain changing electromagnetic field with vasomotion stimulation combined with a pulsed soft laser (test group 2), compared to a test group that did not receive any type of treatment (control group).**

*Significant changes in characteristics between the measurement data of test group 1 and test group 2 occurred as of the 14th day of measurement.*




## Figure 351

**Measurement data for the parameter "maximum depth of roughness Rmax" (mean values) in the sub-cutaneous target tissue over a therapy duration of 70 days for a test sample of female subjects ~ 50 years of age, who were treated with a certain changing electromagnetic field with vasomotion stimulation (test group 1) or a certain changing electromagnetic field with vasomotion stimulation combined with a pulsed soft laser (test group 2), compared to a test group that did not receive any type of treatment (control group).**

*Significant changes in characteristics between the measurement data of test group 1 and test group 2 occurred as of the 14th day of measurement.*

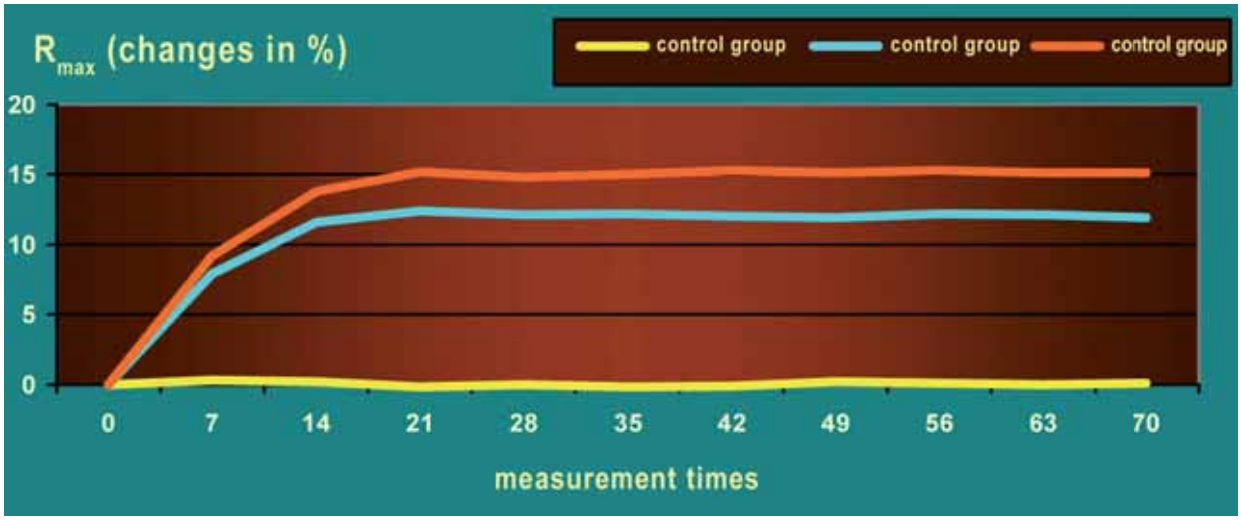


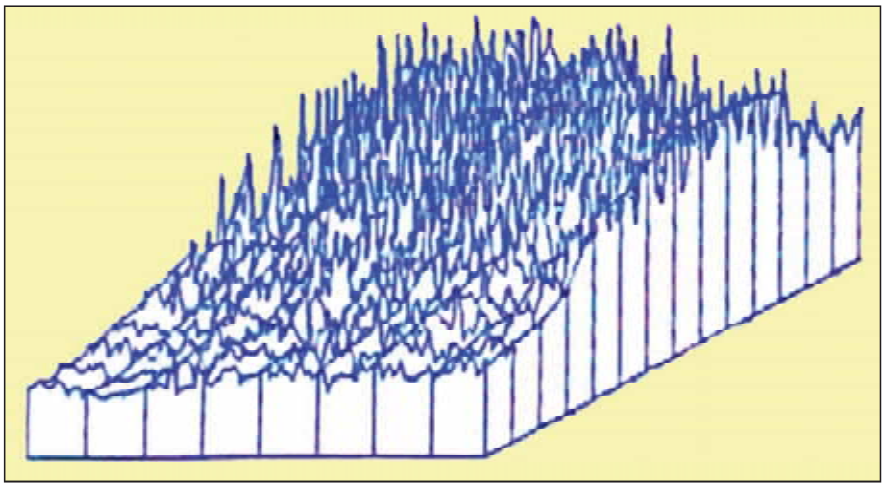
**Figure 352**

**Surface condition of the forehead skin before and after 70 days of treatment with a certain changing electromagnetic field with vasomotion stimulation for a 50 year old female test subject (selected example of findings).**

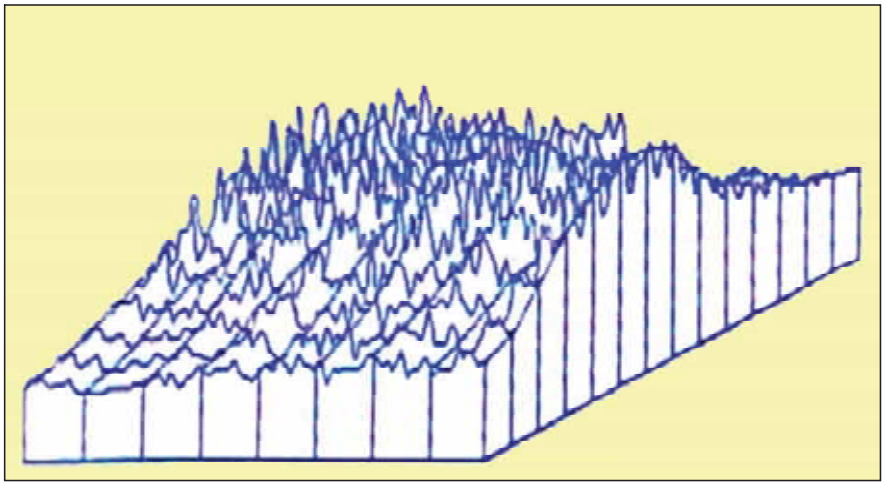
Computerized depiction of the surface texture:
The roughness profiles along the defined measurement lines have been combined for a spatial depiction of the measured surface area.

**a: surface condition before treatment**
**b: surface condition after 70 days of treatment**

**a**



**b**



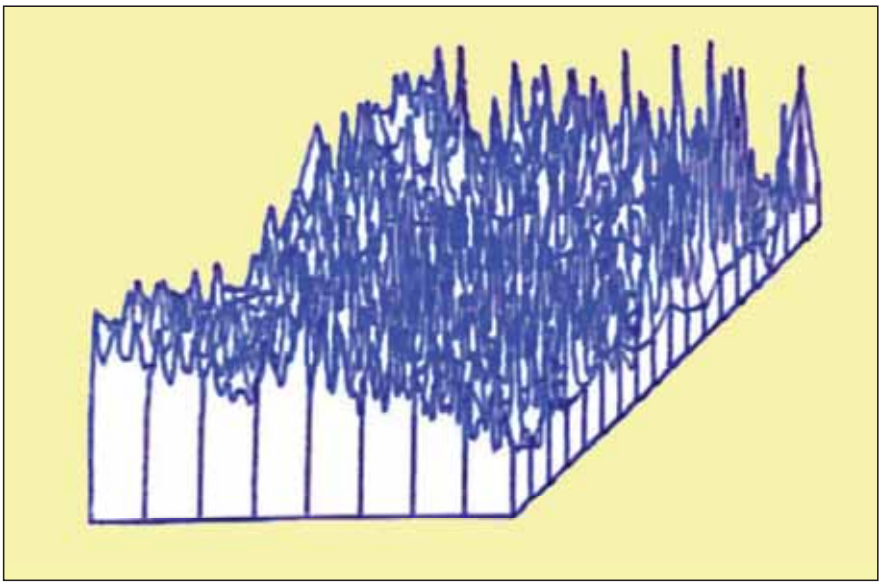
## Figure 353

**Surface condition of the forehead skin before and after 70 days of combined treatment with a certain changing electromagnetic field with vasomotion stimulation and a soft laser (SLT) for a 50 year old female test subject (selected example of findings).**

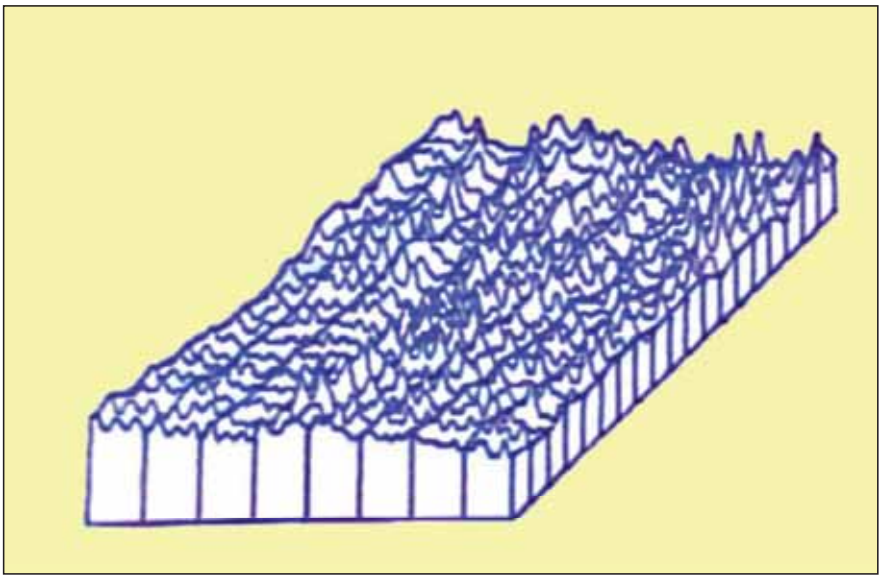
Computerized depiction of the surface texture:
The roughness profiles along the defined measurement lines have been combined for a spatial depiction of the measured surface area.

**a: surface condition before treatment**
**b: surface condition after 70 days of treatment**

**a**



**b**



For a comparison with commercially available skin care products refer to chapter 24.

Please note that the areas of the fields measured to determine the surface quality of the target tissue after application of the changing electromagnetic field and the soft laser amounted to 1200 µm2. The changes identified in the maximum depth of roughness are an expression of the changes in microcirculatory function as a result of the therapies applied.

In addition to general health-promoting measures and the use of appropriate skin care products, the additional application of certain changing electromagnetic fields and soft laser is a promising measure to achieve “visual cosmetic effects” for the skin and the stimulation of its function as an organ.

Additionally, in case of illness, the combined application of certain changing electromagnetic fields with vasomotion stimulation and soft laser can be beneficial within the framework of a complementary therapeutic concept (examples would be: diabetes-related polyangioneuropathy, a variety of chronic inflammatory and degenerative processes, chronic venous insufficiency with ulcus cruris (leg ulcer), and more). The application of certain changing electromagnetic fields and the soft laser during an illness is always meant to be a complementary therapy method and the primary method should always be an established therapy concept.

In conclusion, we would like to address 2 questions which are directed to researches occasionally by individual users and medical practitioners:

Should we be concerned with undesirable effects of certain changing electromagnetic fields of low energy?

> According to current research, no undesirable effects are known. The author does recommend, however, that individual users consult their physician prior to intended application in the case of an illness.

Does the application of certain changing electromagnetic fields have an effect on the growth of tumors?

> There is currently no concrete evidence that substantiates such an assumption. According to current beliefs, the growth of a tumor is dependent on its capacity for neoangiogenesis, which is activated by the appearance of hypoxic zones in its tissue.

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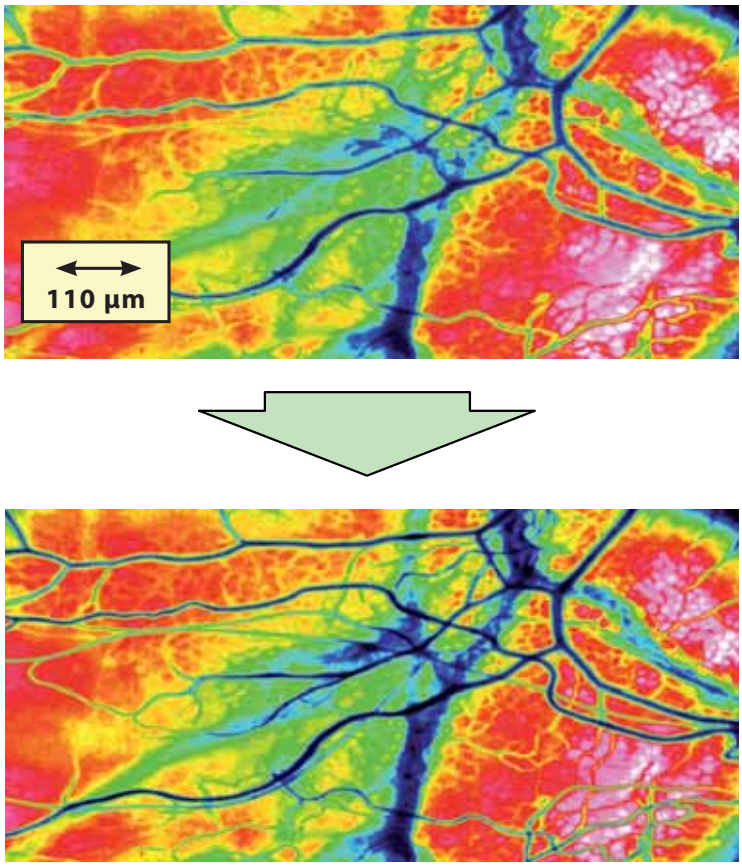
## CONCLUSION

Microcirculation is at the center of clinical pathophysiological considerations. The focus of research should be on healthcare-related counseling and advice for persons who are exposed to stress and infection, the chronically ill and, above all, multi-morbid older individuals whose impaired microcirculation will inevitably lead to a vicious circle in case of illness without effective therapeutic measures.

**The goal of all therapeutic measures should be to strengthen the body's own regulatory mechanisms in order to enable them to transform any limitation or disruption of the microcirculation back to its normal physiological state.**




This book covers research results regarding the effects of a variety of therapy methods on a limited or disrupted microcirculation.

We cannot, however, derive therapy guidelines directly from these results. The behaviors of metabolic, nerval, varied immunological, cellular and intracellular, interstitial characteristics, among others, are being mentioned only in the context of their close affiliation to the object of the research, the microcirculation.
The interpretations and evaluations in this book, and the measurement results in particular, require additional verification in the context of further studies.
We must consider the significance of the ranking of complementary therapeutic measures (as defined by traditional medicine) within the accepted spectrum of mainstream, established treatment concepts, and we cannot only contemplate their possible effects but must also take into account the limits of their effectiveness. Complementary therapy measures can supplement proven therapy concepts effectively, but can never be a substitute for them. The primary areas for the application of (effective) complementary therapeutic measures are in the field of prophylaxis and the support of treatment plans with or without medication (possibly, the dose of prescription medications can be reduced and thereby alleviate the side effects).
This book presents a number of vitalmicroscopic images. These are selected and particularly impressive examples of findings and serve the purpose of illustration only. They can therefore not be considered proof for a certain statement. Statements can only be substantiated by statistically evaluated data.
Scientific research examines the characteristics of a certain test sample. The research results and their evaluations represented in this book are based on the characteristics assessed for a certain test sample group. According to experience, each test sample contains a certain number of test subjects or patients whose parameter changes digress from that of the total test group (non-responders).
Scientific research serves to gain vital new knowledge. Therefore, a certain format of research design must be adhered to for reasons of comparability and reproducibility. This applies to dosages, application times, application locations, etc. In individual cases, this can digress from the conventional approach. It is conceivable that a different approach will produce differing values and response times of the characteristics described.

**The book at hand presents a compendium of current knowledge in the field of microcirculation observed through vitalmicroscopic and spectrometric research. It also contains information regarding up-to-date experimental research that has not yet been completed. To what extent these results and their preliminary interpretations will receive confirmation, differentiation or restatement in the context of further studies and scientific discussions will be available to our readers in the 2nd edition of this book.**

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# Index of Abbreviations

**Abbreviations (according to international. standards) of bio-molecular and functional diagnostic terms**

**Abbreviations of measurements and units**

# Abbreviations of measurements and units

| | |
|---|---|
| **ADP** | **∫ adenosine diphosphate** |
| **AMP** | **∫ adenosine monophosphate** |
| **ATP** | **∫ adenosine triphosphate** |
| **cGMP** | **∫ cyclic guanosine monophosphate** |
| **DNA** | **∫ deoxyribonucleic acid** |
| **EDRF** | **∫ endothelium-derived relaxing factor (identical with NO)** |
| **EEG** | **∫ electroencephalogram** |
| **GTP** | **∫ guanosine triphosphate** |
| **ICAM** | **∫ intracellular adhesion molecule** |
| **MEG** | **∫ magnetoencephalography** |
| **NAD** | **∫ nicotinamide adenine dinucleotide** |
| **NADP** | **∫ nicotinamide adenine dinucleotide phosphate** |
| **NO** | **∫ carbon monoxide** |
| **NOS** | **∫ NO synthetase** |
| **PDK** | **∫ phosphatidylinositol dependent kinase** |
| **°C** | **∫ degrees Celsius** |
| **A** | **∫ ampere** |
| **A** | **∫area** |
| **AVM** | **∫ area under the envelope of the amplitude-frequency spectrum of spontaneous arteriolar vasomotion** |
| **B** | **∫ magnetic flux density (magnetic induction)** |
| **C** | **∫ Coulomb** |
| **cw** | **∫ resistance factor** |
| **d** | **∫ diameter, day** |
| **D** | **∫ electric displacement field** |
| **E** | **∫ electrical field strength** |
| **f** | **∫ frequency** |
| **F** | **∫ force** |
| **I** | **∫ electrical current** |
| **l** | **∫ length** |
| **m** | **∫ mass, meter** |
| **n** | **∫ number, amount** |
| **nBC/V** | **∫ number of transmigrated white blood cells in a defined tissue volume** |
| **nNP** | **∫ number of blood cell perfused nodal points** |
| **nWBC/A** | **∫ number of white blood cells adhering to a defined area of venule wall** |
| **Q** | **∫ electrical charge, flow rate** |
| **QL** | **∫ flow rate of the initial lymph** |
| **r** | **∫ radius** |
| **R** | **∫ roughness** |
| **s** | **∫ second** |

# Technical index