

June 23 to 27, 2002, Québec City, Canada

24th Annual Meeting of the Bioelectromagn

Report by Roland Glaser

The meeting was mainly focused on two topic areas: the protection of the environment against technical fields, and the application of these fields in therapy and diagnostics. Aspects of the use of electric and magnetic fields in biotechnology, which doubtlessly is a field of future potential, were covered only by a few studies from Japan. The magnetic sense of animals played no part during this meeting and was mentioned only in passing. Probably due to sponsor interests, but perhaps also reflecting a general trend, this time medical applications slightly outweighed other issues. This even showed in topics covered by plenary lectures. Out of four sessions, two dealt with this issue – „Transcranial Magnetic Stimulation“ and „Pain – Etiology and Treatment“.

Obviously, even the organisers of the meeting found it difficult to subdivide the approximately 110 short lectures and 130 posters regarding their contents, as well as connect them to the 12 plenary lectures. As can be seen, there were several overlapping criteria used for subdividing contributions which, in turn, could not always be clearly classified as basic in vitro or in vivo research or papers investigating radiation protection or the medical aspect; moreover, the categories „medical applications“, „emerging therapies“, „therapies“, or „diagnostics“ introduced by the organisers were difficult to separate from each other. In addition, there were sessions which did not refer to certain subject matters but to organisational criteria like, for example, the presentations of the REFLEX program or the two Mary Ellen O'Connor Memorial Student Sessions.

This report necessarily mirrors the difficulties emerging in systematising contributions. Regrettably, we could not borrow a given subdivision. Besides, the rapporteur only could attend one of two parallel events at a time, despite trying to jump between sessions. Thus, this report necessarily is limited. The contributions focusing on technical aspects of dosimetry, for example, were left out, as well as the reports on the REFLEX program.



etics Society (BEMS)

Medical applications

With two plenary sessions, two sections and posters, the application of electric, magnetic and electromagnetic fields in diagnosis and therapy this time received a lot of attention. The first main focus with three plenary lectures was the Transcranial Magnetic Stimulation (TMS).

Shoogo Ueno, president of the Magnetic Society Japan and author of numerous publications on this topic, initially talked about physical and biophysical basics of this method where eddy currents induced by short (0.1 to 0.2 ms), partially periodic magnetic pulses with flux densities of several Tesla lead to local stimulation of certain brain areas. Through use of specially designed coils, mostly double coils, the excitation areas in the brain can be reduced to perimeters of 5 mm. Apart from this spatial focusing achieved by field distribution, there is a specificity of excitation determined by form and orientation of neurons in the different brain areas and their communication. As a non-invasive method for nerve stimulation with a high degree of localisation, TMS thus opens up new possibilities both for neurobiologic research and in therapy. To illustrate neurophysiological effects which can occur, the lecturer presented studies on the effect of TMS on the associative memory of test subjects. A continuation of this

method, the „repetitive“ TMS (rTMS), applies pulse sequences of about 25 per second. The hope is not only to achieve neuronal stimulation but additionally to be able to excitate the process of nerve regeneration based upon the idea that processes of gene expression in nerve cells may be induced either directly, by the magnetic field, or indirectly, by induced eddy currents. Pretests in rats have already begun.

The lecture was supported by a number of posters from the lecturer's laboratory thus presenting a good overview of the concept followed at the University of Tokio. The authors of the student posters P-12 (Sekino et al.) and P-13 (Matsumoto et al.) presented dosimetric studies as well as values for conductivity distribution in the rat brain. The posters P-21 (Iwasaka and Ueno), P-18 (Eguchi et al.) and P-64 (Takeuchi et al.) demonstrated effects of strong magnetic fields (up to 14 T) on actin components of cells, on nerve excitation and/or orientation phenomena in a fibrin gel. Poster P-22 (Iwasaka and Ueno) depicted effects of strong magnetic field gradients on the shape of diamagnetic organisms, for example biologic tissues. The possibility to directly affect the process of damaged neuron regeneration by pulsed electric fields (10 Hz, 2.2 kV/m) was demonstrated in an in vitro study by



poster P-84 (Ogiue-Ikeda et al.). According to this study, TMS – and especially rTMS – is not only seen as a method for local nerve stimulation, but this research group also pays attention to long-term biological effects both of the magnetic fields themselves as well as of induced current bursts.

The second plenary lecture on transcranial magnetic stimulation was held by J.C. Rothwell from the Institute of Neurology, London. Here, too, the subject was TMS as well as rTMS focusing on neurological and psychological aspects of this method. What do we actually know about this new non-invasive method? Test subjects immediately experience only the stimulation of optical or motoric centers in the brain: light perception, limb twitching. Responses in other areas can not be perceived immediately. Methods like positron emission tomography (PET), functional magnetic resonance imaging (fMRI), or the EEG are able to elucidate this issue, too. Particularly emphasized and demonstrated by examples was the role of PET which allows not only to demonstrate responses at the site of stimulation itself but also indirect effects at more distant sites of the brain. However, apart from spatial resolution methods, we need real-time measurements which can provide clues, at a millisecond level, to the time course of the biological response after stimulation, like, for example, on the virtual lesion effect, a short-term disruption of cortical activity following the stimulus. This can be done, for example, by the EEG. The lecture made obvious that many related processes occurring here are unclear, despite the generally plausible biophysical mechanism underlying TMS effects. The drawbacks of this method, i.e. possible undesired side effects, still are far from being fully known,

though clinical application of TMS in neurological practice has proven successful many times.

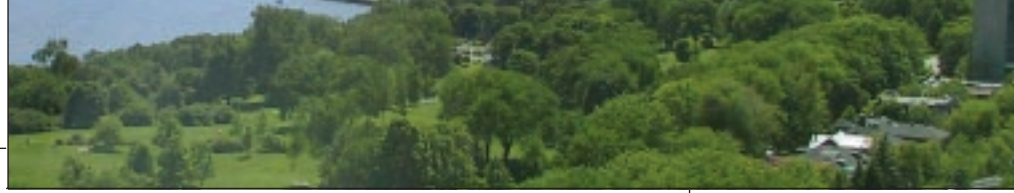
E. Wassermann of the NIH, Bethesda, concluded this plenary section with a lecture on „Transcranial Magnetic Stimulation and Functional Imaging“. This more methodically oriented contribution began with the issue of designing coil systems for optimising TMS magnetic field focusing, especially by accounting for differences of conductivity between different brain areas when calculating occurring eddy currents. The result of such efforts is functional imaging. For Wassermann, this term stands for the pictorial description of brain areas according to their physiological activity. This activity is expressed by blood flow and is visualised – as was mentioned before by the other lecturers – by positron emission tomography (PET) through use of the oxygen isotope ^{15}O (applied as H_2^{15}O). But neither Wassermann could prove that TMS partially activates brain areas being located far from the focus of the magnetic field impulse.

The plenary section of the second morning was also devoted to a neurological issue: „Pain – Etiology and Treatment“. R.S. Menon of the Laboratory for Functional MR Research, John P. Robarts Research Institute (Canada), reported on a study performed by him and other authors of the same institute, as well as by co-workers of the Center for Functional MRI of the Brain, University of Oxford (UK). The subject of the study was the application of functional magnetic resonance imaging (fMRI) for visualising brain areas where pain perception is located. This method is based upon hemoglobin changing from diamagnetic (oxygenated) to paramagnetic (desoxygenated) state dependent on the oxygen charge. Since blood

flow of a given brain area is distinctly enhanced when the area is activated, visualisation is possible at a spatial resolution in the millimeter or even submillimeter range. Comparisons between fMRI measurements and those of the PET method showed no artefacts caused by the 4-T magnetic field of the magnetic resonance tomograph and/or the applied gradient field of 40 mT/m. The lecturer reported experiments in test subjects examining chronic headache localisation as well as acute pain perception caused by thermal or other peripheral stimuli. In the case of chronic headache, subjective pain localisation is nearly, but not completely identical with objectively localised pain. Interestingly, in the case of thermal stimulation, thermal pain perception activates other areas of the brain than the thermal stimulus itself. The authors hope to find clues of possible new therapeutic methods based upon insights gained from pain perception localisation, pharmacological effects, as well as from measurements of local blood flow alterations.

The second lecture on this topic was held by S. Lauterbacher of the University Bamberg. He spoke about the role of pain perception in chronic pain etiology, and its gender-specificity from a medical point of view. After introducing methods for pain perception quantification, he dealt with the different brain areas being responsible for pain perception. He, too, identified PET and fMRI as the methods of choice for examining these processes. He underlined that activity patterns of acute muscle pain have been shown to be different from those of chronic headache. Obviously, women are distinctly more susceptible to chronic pain than men.

The first two lectures on pain, except where dealing with the MRI method, were



physiologically oriented and showed no direct relation to the focus of the BEMS. Probably, they were thought of as a sort of introduction into the key topic of pain treatment with magnetic fields. This topic was covered by A.W. Thomas of the Lawson Health Research Institute (London, Canada) in the third lecture of the second plenary section, which he had written together with F.S. Thomas from the University of Western Ontario (Canada). Unfortunately, this lecture was felt to be highly speculative, particularly compared to the preceding high-quality contributions. Pain treatment certainly is a hot topic both for the general public and for health insurance agencies; pharmacological agents are not always effective and besides have too many side effects. However, the lecturer did not convince where he suggested therapies with extremely low-frequency electromagnetic fields or static magnets as an alternative. He pointed to the problem of finding the right pulse sequence frequency, spoke about light dependence of therapeutically successful use of magnetic fields, and emphasized the importance of magnetic field gradients in treatment with static magnets, for example those sold by the Magnabloc™ company. However, the speaker could not present proper and convincing clinical studies with sufficient test subject numbers. Moreover, it is very difficult to perform double blind tests with static magnets where magnetic properties of an applicator can easily be identified by the patient. The lecturer explicitly pointed to the placebo effect as a non-negligible factor.

When looking at the list of the meeting's sponsors, the huge number of companies producing devices for electrostimulation, magnetic therapy, electro-orthopedics, etc., strikes the eye. This may ex-

plain why in special symposia 16 contributions on emerging therapies and five lectures on „medical applications“ were presented. Some contributions on this subject additionally were part of other sections (1-1, 3-3, 5-1, 5-2, 5-3). Contrary to its strong presence in the lecture program, only five posters dealt with this topic.

The spectrum of medical applications presented by this sections, was wide both regarding physical parameters (static magnetic fields of a few millitesla up to 10-T strength, pulsed magnetic fields, alternating fields from ELF to MHz range, electrostatic fields), as well as medical indicators (pain and cancer therapy, avoidance of hair loss, bone formation stimulation).

Kotani et al. (Japan) (8-7) reported on long-term effects (60 h) of a 8-T magnetic field on proliferation, orientation, differentiation and subsequent matrix and/or bone formation of osteoblasts. This response is logical considering the orientation effect of strong fields and field gradients on diamagnetic molecular structures with a high degree of orientation and diamagnetic anisotropy. The attempt to make use of this phenomenon in favor of possible medical applications was based upon research featuring a clear, comprehensible perspective, an approach unfortunately missing in most other contributions of the section „emerging therapies“.

There should be general agreement on the idea of R. Cadossi (Italy) who claimed in his lecture (8-1) that physical therapies in contrast to chemical methods are easier constrained to certain body regions. However, to date overall convincing successful reports are lacking. Regrettably, Cardoso is absolutely right when claiming that the clinical application of fields is far ahead of the corresponding basic research. However, this is quite a sophisticated way to

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describe a deplorable state of affairs: Devices are produced, sold, and clinically applied without any prior research into their interaction mechanisms; unfortunately, their application is not justified by appropriate clinical tests either.

The superficial nature of clinical tests performed on these methods was made particularly clear by the lecture of Meakin et al. (USA) who presented a pilot study on the application of pulsed electric fields (8 Hz, 5 V/cm air-coupled) for avoiding hair loss of women after chemotherapy for breast cancer. The method was tested in 14 patients. There were no controls. Instead, the quantity of lost hair and photos of the exposed women were compared with statistical data and pictures taken from other publications on hair loss after chemotherapy for breast cancer. However, the corresponding device with the corporate name „electrotrichogenesis“ (ETG) is already on the market. Incidentally, it was already introduced by a poster during the 22nd BEMS meeting in 2000 taking place in Munich. Is this simply an attempt to make money on the grief of sick women? In his lecture (10-2) on lung cancer therapy with static magnetics, J.A. Salvatore (USA) pleaded for not classifying electromagnetic therapy as a so-called „alternative“ method since, after all, it is based upon physics. Instead, we should use the term „adjunctive“, i.e. „supporting“ method. According to him, this would correspond better with the spectrum of application. They could play an „adjunctive“ role, for example, in combination with chemotherapeutical methods. But for the time being, the author could only demonstrate that the application of magnets at least does not lead to toxic side effects.

Following the lecture of Brown et al. (8-3) on a study on pain treatment with

static magnets referred to as a „double-blind pilot clinical study“ and performed in 15 placebo and 17 actively treated patients, in discussion the lecturer had to concede that the study actually cannot be called „blind“, and much less „double blind“.

In this context, there was a detailed discussion on the possibility to perform real double-blind tests with static magnetics, i.e. to exclude the possibility that the patient himself can distinguish the magnet from non-magnetic metal. As yet, McLean (8-5) only could find that the magnetic effect is a little stronger than the equally distinct placebo effect of non-magnetic iron devices. Is this because the patient more strongly believes in the effect if he convinced himself of the magnetic properties of the applied „magnet“? It was recommended to not apply non-magnetic metal devices as a placebo but magnets with non-effective small flux density. But where would the threshold be?

Typical of this topic area was the following circular argument: Lecturers, though not very convincingly, attempting to explain the mechanism of therapeutical effects (Brown et al. 3-8, Sisken et al. 8-6, Pilla 10-1) claimed that there would have to be a mechanism since the clinical success has been demonstrated. Reversely, clinicians with great certainty would rely on allegedly scientifically proved elementary responses which subsequently should have therapeutical effects. However, the influence of static magnetic fields on cellular reactions in the millitesla range is only postulated, not convincingly proved. McLean et al. (8-5) began their lecture on pain treatment with magnets of the company Magnabloc™ claiming that there is proof that magnetic fields of this type block nerve Na channels. (If this is true, this



would be a most effective method for local anesthesia!)

Unlike sessions 8 and 10 dealing with the topic of emerging therapies, session 12 on medical applications, consisted of only four, but far more substantial contributions. Two lectures referred to therapies using high-frequency fields: Radziewsky et al. (12-1) spoke about pain treatment by multiple radiation with microwaves (61.22 GHz) in experiments in mice. Bernardi et al. (12-3) presented an antenna for application of 2.45-GHz fields, which may be used as a catheter for exposure in minimally invasive hyperthermia therapy. Contribution 12-2 (Plank et al.) demonstrated the possibility to make gene transfer more effective by means of paramagnetic particles. Contribution 12-4 (Ryan et al.) showed convincingly small, but significant effects of muscular development in children with congenital myelomeningocele or other neurodegenerative diseases after nocturnal treatment with transcutaneous electric stimulation (TENS).

As mentioned above, there were medically oriented contributions in other sections, too. Logani et al. (5-1), for example, disproved the idea that exposure to millimeter waves (44.2 GHz) protects the immune responses of T-cells against detritous effects of cancerostatics (cyclophosphamide). The lecture of Gordiienko et al. (5-3) equally referred to interaction mechanisms of millimeter wave therapy. The pain-soothing effect of field exposure with 61.22 GHz was shown to result from the release of endogenous opioids both of delta 1 and kappa receptors. The lecture was based upon a recent publication of the group (Radziewsky et al., Life Sciences 68, 2001, 1143).

A contribution of Okano et al. (5-2) dealt with the much-discussed effect of static

magnetic fields on blood flow. In recent years, the authors had published animal tests with different results on this issue (Okano et al., Bioelectromagnetics 20, 1999, 161; Okano and Ohkubo, Bioelectromagnetics 22, 2001, 408; Xu et al., Bioelectrochemistry 53, 2001, 127; Gmitrov et al., Bioelectromagnetics 23, 2002, 224). The tests in rabbits presented at the meeting neither could show more than a weak hypotensive effect of a long-term (12 weeks) magnetic field exposure (10 to 25 mT) without convincing significance.

When looking at successful medical applications of electric, magnetic and electromagnetic fields presented at the meeting as a whole, it becomes clear that there has been made visible progress on a solid scientific basis, especially in the area of imaging techniques as well as magnetic stimulation. The tests mostly performed in Japan using extremely high field strengths are interesting and worthwhile, too, though the application of such fields in therapy, for purely technical reasons, will be possible only in a more distant future. Doubtlessly useful, and certainly showing much more potential for the future are the various applications of electrostimulation and, of course, of hyperthermia. The long-standing hope that pulses or alternating fields could promote bone healing is still uncertain, and despite several contributions devoted to this topic, reports on therapeutic effects of static magnets in the millitesla range seem extremely uncertain.

Epidemiology

Participants were introduced into this topic by three plenary lectures on epidemiology held on the third day of the event. The starting point was a lecture of Mrs. Maria Feyching on epidemiologic methods, their strengths and limitations when

investigating health effects of electromagnetic fields. The lecture began with cohort studies and case-control studies as the most important types of epidemiologic investigations, first describing inherent error sources. For example, in cohort studies examining the incidence of a certain disease in a cohort living in the vicinity of a high-voltage powerline or a transmitter compared to a control group without such an influence, difficulties emerge above all in dosimetry, that is, in the determination of the intensity of the actual influence of the examined agent. This is more easy to do in case-control studies for example examining whether brain tumor patients have made more calls than a control population, or whether they lived nearer to a high-voltage powerline, because the number of examined persons is smaller. This advantage, however, quickly becomes futile considering that small numbers are the main obstacle to drawing reliable epidemiologic conclusions. Another uncertainty or error source is found in how affiliation with a certain cohort is defined, as well as in what is meant by „exposure“. If these definitions are affected by the study subject itself, its objectivity suffers. Examples of such misclassification were presented in the lecture. In this context also the „recall bias“ was mentioned as a misclassification breaching objectivity by subjectively overestimating exposure and underestimating non-exposure. The main source for errors in epidemiologic studies are so-called confounders, side factors characterising the cohort of exposed subjects compared to controls, as well as the examined electromagnetic fields themselves. It was interesting to hear about possible error sources of epidemiologic studies from a scientist who has played a leading role in such investigations herself that were mostly per-

formed in Sweden. The speaker concluded that, though epidemiology in general may provide the clearest evidence for health-damaging effects of a given environmental influence, it is a widespread misapprehension to believe that epidemiological studies are easy to conduct and generally applicable.

The second lecturer, Mrs. Leeka I. Kheifets, addressed the topic from the perspective of the WHO: „Epidemiologic Studies on Low-frequency Fields and their Contribution to Risk Assessment.“ She pointed to the statements of the International Agency for Research of Cancer (IARC) and the National Radiological Protection Board in the United Kingdom (AGNIR) on the association between NF exposure and child leukemia. Though, according to the author, uncertainties and provisional character of to-date available studies are known, in 2001 the WHO put low-frequency fields into the category 2b („possibly carcinogenic to humans“) regarding child leukemia. This is the lowest of three categories defined by the IARC („is carcinogenic to humans“, „probably carcinogenic to humans“, „possibly carcinogenic to humans“). All other cancer types and age groups, regarding NF as well as static fields, in general are seen as „not classifiable“. This provisional classification shall be reviewed in 2003, when the international ELF project initiated in 1996 by the WHO (see also „Fact Sheet N° 263“ from October 2001 on the web, via the WHO site) will be finished. In this context, the speaker pointed to the psychological difference between voluntary and involuntary exposure made in discussion about precautionary and safety measures. Of course, this mainly concerns the high-frequency range on which the WHO plans to issue a statement later on.

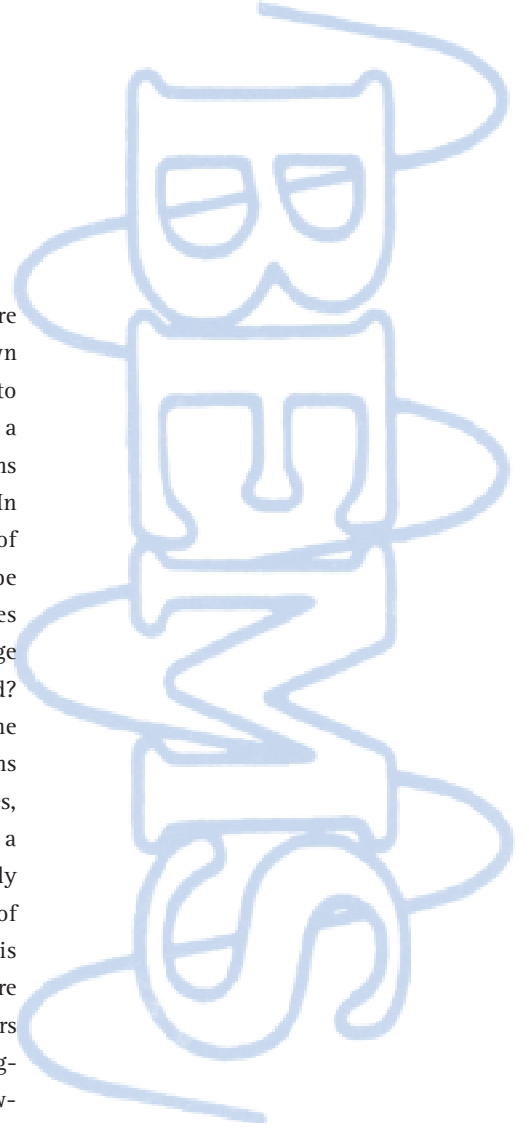
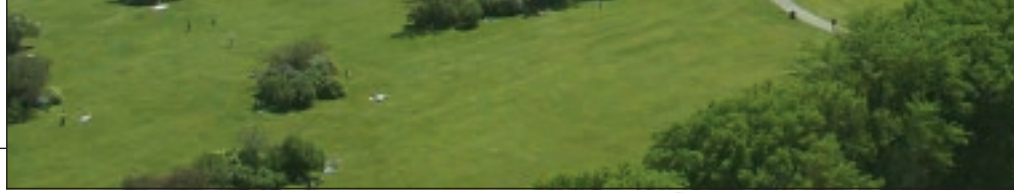
Finally, a third plenary lecture on epidemiologic studies discussed investigations of potential health hazards from radiofrequency and microwave fields produced by wireless communication devices. This lecture was held by M.L. Bride from the British Columbia Cancer Agency (Canada). The speaker emphasized that to date there are only few useful studies examining effects of high-frequency fields on public health under the perspective of statistic safety, dosimetric reliability, and performance accuracy. There is also the mostly short duration of the observed exposure. According to the speaker, studies from the area of military HF applications for different reasons rarely shed light on this issue. However, despite all these limitations, the current result is that there are no proven health effects. Here, the speaker basically referred to the studies of R.W. Morgan et al. (*Epidemiology* 11, 2000, 118) and C. Johansen et al. (*J. National Cancer Institute* 93, 2001, 203) including 200,000 and 420,000 subjects. The speaker emphasized the necessity to perform further studies, but also demanded that conclusions always should be drawn on the basis of experimental studies on possible underlying mechanisms that alone can shed light on causal relations.

Besides, section 17 included three short lectures on epidemiology. Out of these, only one contribution directly referred to an epidemiologic study. T. Tynes (17-1) presented a survey of the Norwegian Radiation Protection Authority which, in cooperation with the Cancer Registry of Norway, searched for correlations between a 50-Hz exposure in the vicinity of high-voltage power lines and different types of hematological cancer. As in the recent publication of the same group (Blaasaas et al., *Occupat. Environ. Med.* 59, 2002, 92)

which investigated congenital risks after parental exposure, no significant correlations could be found.

The two other lectures of section 17 dealt with methodical aspects. In the view of Bowman et al. (17-2), epidemiologic studies wrongly draw a relation between magnetic flux densities in the low-frequency range and diseases. According to them, this is the reason for inconsistencies between the surveys of different authors. Instead, the speaker suggested three other measurement quantities derived from hypotheses on mechanisms like, for example, the temporal alteration of the magnetic flux density (dB/dt) as a quantity for current induction in the body, the square sum of flux densities of the static and the ELF field (related to possible effects on radicals), and the so-called Lednev quantity that was not defined in any detail. Certainly, this proceeding would make sense given that underlying hypotheses are validated. Kang and Gandhi (17-3) discussed feasible dosimetric relations for field pulses and other alternating fields deviating from the sinus function.

Dosimetric aspects of epidemiologic surveys also were addressed in the posters. So Morrissey et al. (P-61) showed the dosimeter phone of Motorola already presented at the 23rd BEMS meeting that allows for a better survey of mobile phone user exposure. Gauvin et al. (P-62) added dosimetric measurements to the published studies on differences of melatonin excretion of women related to the distance of their residence from high-voltage power lines (Levallois et al., *Am. J. Epidem.* 154, 2001, 601). They found out that the value in persons living close to high-voltage power lines is three times higher than the average flux density of 0.13 microtesla in



the control group. However, this did not make trends shown by the preceding study any more significant.

The results of the methodically often criticised Australian study (Med. J. Aust. 165, 1996, 601) claiming an increase in child leukemia in the vicinity of transmitters could neither be confirmed by Hocking et al. (p-59) who additionally examined survival rates of the concerned persons.

Dunn et al. (P-60) demonstrated first results of a case-control study on a potential correlation between leukemia and low-frequency fields. Though it was initiated as early as in 1997, to date only 128 cases of children under 16 diagnosed with leukemia or brain tumor from SW England have been registered. In all cases, interviews with the parents and thorough measurements at the children's home were conducted. To date, there is a significant result only with regard to leukemia. However, in the view of the authors, the numbers still are too small to draw valid conclusions.

Interaction mechanisms

The fourth plenary session as well as a section consisting of six short lectures were devoted to the crucial issue of interaction mechanisms regarding protection against electromagnetic fields as well as their medical application.

As an introduction, S. Engström (USA) presented an overview of the overall situation in a lecture titled: „Physical Mechanisms for Electromagnetic Field Transduction in Biology“. Due to the lack of own theoretical work, the author was free to deal with the issue without putting own hypotheses into the foreground. So he reviewed some common theories criticising that to date no experimentum crucis has been proposed and much less performed to exclude a given hypothesis in compari-

son with others. Instead, scientists more or less convincingly tried to verify own concepts. With this, the author referred to an idea he discussed some years ago in a publication together with R. Fitzsimmons (Bioelectromagnetics 20, 1999, 423). In their opinion, there still is a number of unresolved questions which have to be answered: Why is it that resonances claimed to exist in the low-frequency range in theory to date could not be proved? Does it make sense to further discuss the hypothesis of radical-pair recombinations related to environmental exposure issues, if this effect cannot be measured below a flux density of 1 mT? What do we really learn from tests on the magnetic sense of many different animals? Though this mechanism is not understood either, there seem to be amazingly sensitive receptors responding to amplitude and even magnetic field orientation. At least in the low-frequency range, this would have to be relevant for radiation protection, too. Moreover, these experiments show us that there is an interaction of different environmental factors. Especially light seems to be important for magnet reception, at least in some cases. Could synergy of several physical effects not always controlled in experiment perhaps be the reason for divergent results of different authors? The fact that the lecture was characterised more by open questions than by secure knowledge actually shows how much we still are at a loss regarding mentioned biophysical basics.

In this aspect, the lecture differed hugely from the two subsequent ones which cynically could be characterised by an epigram of Wilhelm Busch: „We know for certain only what we believe in.“

M. Blank (USA) spoke about „Biological Transduction Mechanisms“ presenting



his own repeatedly published hypotheses. He started with his „change in ion activation“ model which is based upon low-frequency activation of ion pumps (Na-K-ATPase). Experiments on this were first published by him 13 years ago (*Bioelectrochem. Bioenerg.* 22, 1989, 313), but never could be verified experimentally by other scientists. As elusive in experiment is his hypothesis concerning field impact on intramolecular electron transfer going back to the time of his cooperation with Mrs. Goodman (*Bioelectromagnetics* 18, 1997, 111) and being based upon own experiments on cytochrome oxidase and DNA. Effects on the Belousov-Zhapotinski reaction, the standard demonstration reaction for dissipative structures in non-linear thermodynamics, caused by magnetic fields of flux densities below 1 microtesla were successfully shown only by the author himself, though tests were conducted all over the world. As a good speaker and crafty theorist, Martin Blank well succeeded in plausibly presenting his ideas; experimental verification, however, is lacking.

Slightly different was the case of the next speaker, R.D. Astumian (USA), who talked about „Non-linear Mechanisms as a Response to Weak EM Fields“ (different from the title given in the abstract book). His engaging and moving speech was highly theoretical and only mentioned in passing a ballistic transport phenomenon from solid-state physics as an analogous experiment. The focus was the question how weak interactions can persist against thermal molecular movement. To answer this he used a mechanic model, the „Feynman's ratchet“, sort of a Maxwell's demon consisting of a wheel and a mechanism blocking reverse movement, so it may turn only in one direction. Consequently, it can be

moved by stochastic thermal thrusts. According to the author, such asymmetries could also be effective in biologic transport phenomena, thus outweighing Brownian movement. Unfortunately, in his elucidations he mostly used the subjunctive form, as in his other publications on this topic, including the one published in *Science* (276, 1997, 917).

In section 18, 6 other short lectures were held on this topic. In view of recently introduced technologies with new frequency bands and modulation or pulse forms, M.L. Swicord (18-1) (Motorola, USA) emphasized the need to compare results from experiments with different field parameters for reaching portability of results. For this, according to the author, a deeper knowledge of mechanisms is required. In this context, he reported from last year's workshop on this topic having taken place in Washington; a report can also be found on the web at www.mmfa.org. He pointed to thermal effects possibly including interaction mechanisms caused by temperature gradients.

Though two contributions from the working group of G. D'Inzeo, Rome, referred to mechanisms, they were not very convincing: Mrs. R. Schiavo (18-2) made calculations on the Larmor precession of lipid headgroups, but had to admit during discussion, following a question of R.D. Astumian, that these calculations were performed under idealised conditions, that is, ignoring viscous damping and thermal noise. Thus, her results lose credibility. The contribution of F. Apollonio et al. (18-5) examining ion channel modelling and the influence of electric alternating fields showed a high degree of idealisation as well.

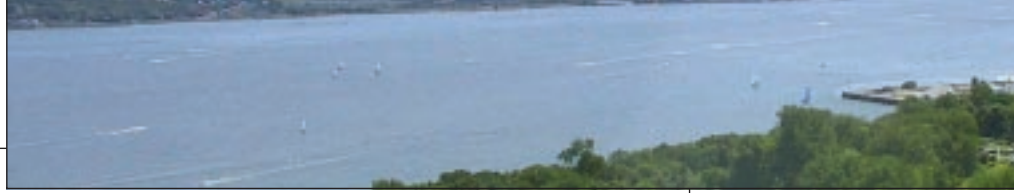
A contribution of Q. Balzano and A. Sheppard (USA) (18-4) dealt with the rele-

vance of non-linearities for possible processes of HF field demodulation caused by the molecular biological system. He provided a theory matching a recently published suggestion of Balzano's for giving experimental proof of such demodulations if existing (*Bioelectromagnetics* 23, 2002, 278).

The activities of Japanese scientists in the area of effects of extremely strong magnetostatic fields in the group around S. Ueno, reflected in a contribution concerning interaction mechanisms. M. Iwasaka et al. (18-3) reported an effect of 8-T fields on catalase activity: hydrogen peroxide decomposition. In contrast to earlier tests where the enzyme was in the solution, the authors could prove an influence on the response if the enzyme was fixed and oriented on a platinum surface. They succeeded in demonstrating the role of molecular orientation at least in magnetic field effects assuming that the response is based upon the radical-pair mechanism.

In a contribution presented in the section on cognitive effects on humans, Adey (4-1) spoke about possible effects of small electromagnetic energies compared to thermal noise. He described examples where such effects are caused without doubt by special mechanisms like, for example, during hearing or in electroreception of some fish. This is made possible by a system of communicating cells, similar to processes where the genetic material of a cell is damaged by an alpha particle which can lead to mutations of adjacent cells.

There were also a few posters, mostly presented by students, on the topic „Interaction Mechanisms“ which, however, did not include any new ideas or insights into the topic, but instead presented cell biological tests which we will discuss later on.



In vitro studies

In vitro studies were the subject of two sections with a total of 12 short lectures. Apart from that, short lectures from other sections as well as 40 posters dealt with this topic, if we extend the meaning of the term from biochemical model studies to experiments performed in tissue and organs. But not only the objects of study were different, but also applied fields and, of course, the goals of experiments varied.

Though the scientific literature currently includes many studies on heat-shock protein expression (HSP), the authors of these publications regrettably were not present at the meeting. Only D. Leszczynski (Finland) (1-2) reported on heat-shock protein (HSP27) expression in human endothelial cells after 1-h exposure to 900 MHz at a SAR of 2 W/kg determined by immunohistochemical methods allowing only qualitative conclusions. According to the author, the response is non-thermal; however, during discussion the determination of the SAR value in the cultures met with certain doubt. The author saw the observed cell shrinkage as being a consequence of HSP expression causing possible effects on blood brain barrier permeability. However, this conclusion somehow seems a little bit daring. For this reason, the announced publication of his research results is quite eagerly anticipated.

While here a mechanism for potential hazards for the organism by HSP is postulated, Sonntag (1-5) and Gottwald et al. (3-4) see possibilities for treatment of ischemia or infarct risk. Isolating hsp72mRNA from HL-60 cells and/or myoblasts of rat, after several hours they found an increase as a consequence of a 15-min exposure to 1 mT (50 Hz). Other investigations that were designed as basic studies on therapeutical applications led

neither to new nor to convincing results (Nindl et al. 1-1, Herbst et al. 1-6, Teng et al. 3-3).

Quite remarkable were some studies on the influence of high-frequency fields on genetic processes. A French group (Perrin et al. 3-1) examined the influence of continuous and pulsed 2.5-GHz fields on mutations of procaryotic fields by means of the Ames-II mutation test performed in salmonella typhimurium. Whereas these fields showed no alteration of growth behavior even after 16-h exposure with SAR values of 3 W/kg, at pulsed (217 Hz) HF fields, though not at unmodulated fields, an influence on chemically induced mutations could be observed which must be called „protective“.

McNamee et al. (3-5) examined cultures of human lymphocytes being exposed for 2 and/or 24 h to a 1.9-GHz field with SAR values up to 10 W/kg. These authors as well applied both continuous and 50-Hz amplitude-modulated fields. 1.5-Gy gamma radiation was used as a positive control. As a test for DNA damages, the alkaline comet assay was used. Additionally, micronucleus formation was examined. However, effects on the genetic apparatus were not found for any exposure type of HF fields. The short lecture was supported by data presented by a poster (McNamee et al. P-90).

A third contribution to this topic area came from a working group from Israel (Mashevich et al. 3-6, lecture held by R. Korenstein). Here, the influence of 830-MHz fields at SAR values between 1.6 and 9 W/kg with an exposure duration of 72 hours was examined in human lymphocyte cultures. At maximum SAR values, a heating of samples occurred which was constrained though to the range from 34.5 to 37.5° C through use of a thermostat. By

means of fluorescent markers (fluorescence in situ hybridisation assay) aneuploid development was examined, i.e. the loss of genetic material in the course of mitosis. Beginning with SAR values of 8.2 W/kg distinct effects could be measured. During discussion it was pointed to the fact that thermostatisation in a water bath is not identical to one using hyperthermia effects.

Finally, two further contributions from a Japanese laboratory should be mentioned, both remarkable because of the fact that they examined effects of uncommonly high field strengths. Nakahara et al. (3-2) showed slight effects of strong (10 T) static magnetic fields on gene expression of human glioma cells. The authors recommended to consider this when setting limit values for these fields in NMR. Miyakoshi et al. (13-1) from the same working group reported genetic alterations in human melanoma cells at strong 60-Hz field exposure. While long-term exposure (6 weeks) had no immediate effect on mutation frequency, in other cells (PC12-VG) 400 mT could induce gene expressions. 2-days exposure of CHO-KI cells with strong 2.45-GHz fields (100 W/kg !) inhibits proliferation.

The contribution of Tattersall et al. (4-2) could have made the section of in vitro studies, too, though it was presented in section 4: „Radiofrequency Fields and Cognition“. Basically, the authors referred to their recent publication (Brain Research 904, 2001, 43) without giving further information. They presented an interesting test design for examining effects of high-frequency fields on the function of the hippocampus. To this end, brain slices mounted on a nylon mesh and in physiological liquid were brought into a waveguide chamber. After electric stimulation, the

collective evoked potential of cells in the slices was determined and used as an indicator for the influence of applied HF fields (700 MHz, 71 V/m). The experiments were well-replicable, however the speaker could give no precise data on SAR value and temperature course. The authors hope to be able to use this model for identifying potential frequency specificities.

In the same section a contribution of the same working group (Green et al. 4-3) was presented elucidating this method and expressing their intention to in future measure calcium metabolism in such brain slices.

In vivo animal tests

This topic was dealt with in two sections, 11 short lectures and 22 posters. The first three lectures (5-1, 5-2, 5-3) were medically oriented and are treated in the corresponding paragraph of this report.

The focus of this section was the issue of possible cancerogenic effects of high-frequency fields. Two contributions dealt with the for some time now discussed question why findings of the group around W. Löscher on cancer-promoting effects of electromagnetic fields could not be verified by other research groups. By example of two genetically different stems of Sprague-Dawley rats, Sasser et al. (5-4) demonstrated differences in sensitivity to the carcinogen DMBS, and also to additional field exposure at 1.6 GHz fields. When examining the same genetic stems, Fedrowitz and Löscher (5-6) found identical results, that is, differences regarding the influence of low-frequency fields matching the recently published results (Fedrowitz et al., Cancer Research 62, 2002, 1356).

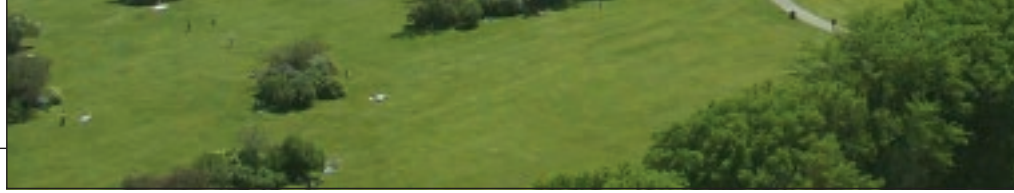
Related to these studies was the contribution of La Regina et al. (11-3) from the Oncology Center, Washington, dealing

with a long-term experiment performed in a total of 480 rats which were exposed to continuous and/or CDMA-modulated 835.62-MHz fields as well as to 847.74-MHz CDMA fields in groups of 80 animals each. Tests began with animals 6 weeks of age and were continued over 2 years. The animals were examined for average survival rate, body weight, tumor incidence and other histopathological alterations of the organs without detecting significant changes.

Buschmann et al. (11-2) presented experiments in rats being exposed from the beginning to 20th day of gestation to a 890-MHz, GSM field (60 W/m²). Again, no significant alterations could be observed, neither in the mother animal nor in the fetus.

In another section, Shirai et al. (13-3) reported on studies investigating possible effects of 900-MHz and 1.5-GHz fields on rat liver carcinogenesis and mouse skin carcinogenesis. In the case of liver cancer, rats were exposed to both frequencies each for 90 min/day, 5 days/week, over 6 weeks. SAR values were between 0.45 and 0.8 W/kg. Liver cancer induced by the application of diethylnitrosamine was not affected by field exposure at all. Negative as well were results of tests where skin cancer was induced in mice by DMBA treatment. Local exposure to 2 W/kg (average whole-body SAR: 0.084 W/kg) applying the same regime as mentioned above over 19 weeks, showed no influence on tumor growth at all.

Masuda et al. (5-5) reported on tests examining blood flow rate in rat brain after long-term exposure to 1.439 GHz reaching peak SAR values in the brain of 6.2 W/kg. After 4-weeks exposure, neither alterations of microcirculation nor alterations of blood vesicles or of the brain could be



found indicating effects on the blood brain barrier. The number of leukocytes stayed the same as well.

Seaman et al. (11-5) presented a study on behavioral effects in rats applying one-off exposure to a 1.25-GHz pulse package (6 microseconds pulselength, 10 Hz, 30 min duration, 0.6 W/kg). By automated measurements, different movement types of the animals were compared to those of control animals, including startle response after pulse application. Only one single movement variable, the total duration of stereotypy activity, was slightly shortened in exposed animals. However, according to the authors, this effect has no biological relevance.

In a contribution presented in the section on cognition processes, Cobb and Adair (4-5) criticised the study already published a few years ago by Lai et al. (Bioelectromagnetics 15, 1994, 95) reporting behavioral effects of 2.45-GHz pulses at a SAR value of 0.6 W/kg on learning behavior of rats, additionally demonstrating that this influence can be reversed by a treatment with drugs. By a new statistical processing of data, Cobb and Adair could show that these conclusions are not justified.

Tests in humans

Several sections dealt with both low-frequency and high-frequency effects being examined in human test persons. In sections 2 and 4, 9 contributions dealt with the topic of cognitive effects caused by radiofrequency, though half of them did not refer to experiments conducted in test subjects and therefore will be treated elsewhere in this report. Section 6 included 6 contributions on in vivo studies in humans. Further, there were 11 posters on this topic area.

The lectures of sections 2 and 4 summarised available study results without offering new data. In her contribution, Mrs. Krause (2-1) summed up papers already published by her Finnish group concluding that at exposure to mobile radio fields, on the one hand, there was a speed-up of reaction times, and on the other side, a decrease of the time needed for resolving arithmetic tasks. She pointed to the difficulty to interpret these findings for the benefit of health protection.

Wood et al. (2-2) presented an overview of the topic: „Effects of Mobile Phone Fields on Human Perception Processes“. In this context, Wood pointed to a number of error sources having to be avoided by careful test design. According to him, it has to be guaranteed that participant numbers meet statistical requirements, that subjects represent average population (including children, older people, ill persons), that each subject is his own control, and, finally, that effects occurring after field exposure are measured, too. Also, he pointed to the fact that real mobile phones, in contrast to some experimental HF designs, emit low-frequency pulses, too (about 7.5 microtesla). Thus, it is important to examine whether HF fields emitted by the test device perhaps produce thermally caused noise in the foam shielding. This could lead to secondary effects, or would at least cancel the double-blind character of the test design. However, it seems strange that possible effects again and again are explained by the findings of Baldwin and Adey from 1976 on calcium excretion in brain tissue as a consequence of HF exposure, which never were reproduced and therefore since long have been abandoned by experts. Though wrong, they are handy and therefore long-lasting! (Adey himself, in his

contribution 4-1 did not even use this argument, though it would have fit there.)

On the basis of own studies and those of the group around DeLorge on behavioral effects on monkeys, as well as of experiments performed in other animals, D'Andrea (2-3), claimed possible effects on humans. The focus was on thermal effects. He as well explained the observed frequency dependence of effects on animal behavioral performance regarding resonance frequencies by thermal effects. From this perspective, he developed a phase diagram with ordinate = body temperature, and abscissa = time. Two lines time-exponentially decreasing towards an end value mark the area of insensitivity, the strain area, and finally the hazardous area in increasing order. The shorter the impact time, the higher the tolerance value of thermal impact.

Finally, Morrissey and Swicord presented a critical overview of the topic: „What is the Collective Message from Studies Looking at Human Brain Function and Mobile Phone Exposure.“ They concluded that, though there is a variety of measured reactions, they show a high degree of inconsistency. So, for example, replication of findings is lacking; measured effects are so small that they seem physiologically irrelevant; at times, test conditions are insufficiently controlled. One does not get the impression that one publication supports the other confirming and deepening found results. Thus, results do not suffice to draw any reliable conclusions on possible health damaging effects of mobile phone fields.

Section 6: „In Vivo Studies in Humans“, dealt with different topics. Alekseev et al. (6-1) presented theory and measuring of temperature distribution in the human skin after exposure to millimeter waves (75

GHz). They showed that thermal impact, mainly due to heat conduction of the tissue, penetrates deeper than radiation itself. The steady-state temperature of the skin at continuous irradiation depends on blood flow intensity.

Following the BEMS 2001 and their own publication (J. Comp. Physiol. A 186, 2000, 1007), Thoss et al. (6-2) presented further investigations of the influence of the geomagnetic field on differential light perception of humans. Both field strength as well as field direction affect the ability of a subject to distinguish a point of a light on a projection plane from that of the environment.

In his lecture (6-3), J.A. Elder dealt with the question: Are children really more at risk from mobile phone fields than adults? Generally, as an argument for suggesting higher sensitivity in children, possible disturbances during child brain development are pointed to. After conducting a literature study, the speaker concluded that this suggestion is not confirmed by experiments. Considering that the human brain already at birth is far more developed than, for example, that of a newborn rodent, these effects would have to show more distinct in these test animals than in humans. However, numerous long-term experiments using these animals could not prove any developmental defects.

Whereas the laboratory of Mrs. E.R. Adair (6-4) in the past focused on tests on thermoregulation response in participants after exposure to high frequencies (0.45 and 2.45 GHz) and with corresponding small penetration depth (Bioelectromagnetics 22,

2001, 246 and 429), the interest presently is on heat distribution in the body at an exposure of 100 MHz, that is, close to the resonance frequency of the body. As was expected, a different temperature distribution was shown which, obviously stimulated by deeper heat receptors, also activates the physiological heat regulation of the body and is neutralised by it.


J. Juutilainen (6-5) dealt with the question whether a low-frequency magnetic field may be able to change human light sensitivity related to the melatonin household. To this end, seamstresses in a garment factory were interviewed on their sleeping habits (light close to the bed, curtains, etc.); simultaneously, the urinary 6-hydroxy melatonin sulfate value was measured. The speaker was convinced that statistical evaluation confirmed his assumption of an existing association. The number of test subjects in the 4 groups created by the combination of categories „light at night“ and „magnetic field exposure“ on the one side, and increase of melatonin level: yes or no, on the other, was very small and very heterogenous varying between 4 and 32.

In the last contribution to this section (6-6), B.A. Chronik spoke about the problem of peripheral nerve stimulation by magnetic field gradients in NMR tomography. This effect prevents the desired increase of the gradient in commercial devices for image resolution and speeding up measurement time. But tests conducted in normal subjects (weight, body fat percentage, coronal profile, etc.) could find no correlation.

Summary

As always, the meeting offered a wide range of topics and material that can be properly sorted through and evaluated only in hindsight. Following are, in short, some of the issues and questions which emerged during and after the congress in the view of the rapporteur:

- Regrettably, we still haven't made any progress towards understanding the mechanisms underlying the effects of weak electromagnetic fields, neither in the NF range, nor for mobile radio frequencies. The conference did not provide any new ideas or theoretical approaches on this issue. Since secure experimental evidence for such effects ultimately is missing, too, the question would be if we perhaps search for a phenomenon that does not really exist.
- The current impression given by the area of medical applications of electromagnetic fields still is extremely heterogenous. In contrast to hugely successful, well-funded diagnostic methods, above all of NMI, as well as magnetic stimulation and partially also of hyperthermia as well-based therapeutical methods, there are other promising methods like bone growth stimulation by PEMF which after several decades still did not establish a scientific basis, or at least reach therapeutical relevance. We will politely keep silent about the unfortunately quite big number of charlatans participating in this meeting discrediting the principally promising area of therapeutical applications of electromagnetic fields.
- After a meeting has ended, we should not only ask: What happened there?, but also: What was amiss?

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- For example, where was the continuation of last year's discussion about the blood brain barrier to which then a whole section was devoted? The issue is as interesting today as it was then. Last year, at the 23rd congress in St. Paul, the Swedish group around L.G. Salford evaded discussion in spite of announcing a lecture; P.A. Mason promised to examine the results of this group and to report on them in the near future. Why was the topic of the blood brain barrier so marginal this time?
 - Where was M.H. Repacholi with the long-announced replications of his sensational study from 1997 which still today receives a lot of attention? Has it been impossible to replicate results? In this case, it would have been even more interesting to hear about it, especially since others already have made futile attempts to reproduce the study.
 - Recently, a series of papers on heat-shock protein expression at HF-field exposure have been published. Regrettably, this topic played a very minor role at the meeting.
 - Like last year, Japanese scientists strongly presented their studies on effects of static magnetic fields in the 10-T range and above. Apart from the issue of safe diagnostic NMR devices developed in Japan, the biotechnological aspect of these papers was plain to see. It is highly amazing that this topic is neglected by scientist groups from other countries.

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