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Session 1-1

WHO'S INTERNATIONAL EMF PROJECT AND RESULTS SO FAR

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Abstract

With growing concern being expressed that exposure to electromagnetic fields (EMF) may cause various health effects and that everyone in the world, both in developed and developing countries, is now subjected to EMF from manmade sources, WHO established the International EMF Project in 1996 to determine if there were adverse health effects that could result that needed to be addressed. Thus the Project was set up in a logical sequence of steps that would address this issue in a valid scientific manner over a reasonable time period.

Briefly the International EMF Project provides: a co-ordinated international response to the concerns about possible health effects of exposure to EMF; assesses the scientific literature and make status reports on health effects; identifies gaps in knowledge needing further research to make better health risk assessments; encourages a high quality, focused research programme to fill important gaps in knowledge; incorporates research results into WHO Environmental Health Criteria monographs, in which formal health risk assessments of exposure to EMF will be made; provides information on risk perception, risk communication and risk management as they apply to EMF; provides advice and publications to national authorities on EMF issues; and facilitates the development of internationally acceptable standards for EMF exposure. This presentation provides an update of activities and results of the EMF Project to date.

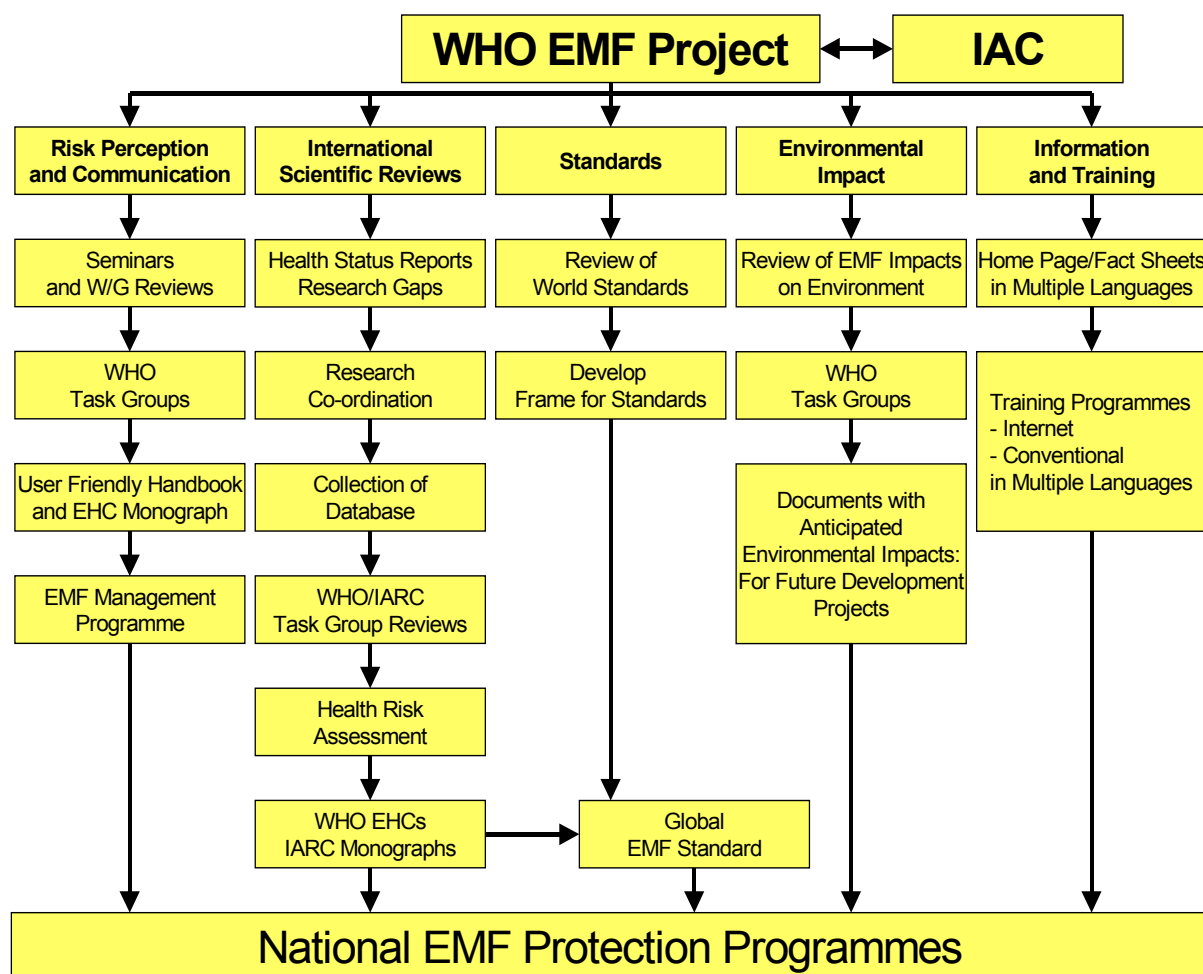
Introduction

The World Health Organization (WHO) takes seriously the concerns raised by reports about possible health effects from exposure to electromagnetic fields (EMF). Cancer, changes in behaviour, memory loss, Parkinson and Alzheimer's diseases, and many other diseases have been suggested as resulting from exposure to EMF. Everyone in the world is now exposed to a complex mix of EMF frequencies in the range 0-300 GHz. EMF has become one of the most pervasive environmental influences and exposure levels at many frequencies are increasing significantly as the technological revolution continues unabated and new applications using different parts of the spectrum are found. Major sources of EMF exposure include: electric power generation, distribution and use; transportation systems; telecommunications facilities and associated devices such as mobile telephones; medical, commercial and industrial equipment; radars; and radio and television broadcast antennas.

International EMF Project

WHO established the International EMF Project to assess health and environmental effects of exposure to static and time varying electric and magnetic fields in the frequency range 0 - 300 GHz. The Project commenced at WHO in 1996 and is scheduled for completion in about 2006. It has been designed to follow a logical progression of activities and produce a series of outputs to allow improved health risk assessments to be made and to identify any environmental impacts of EMF exposure. The ultimate objectives of the Project are to provide sound advice to national authorities on how best to manage the EMF issues, and to complete health risk assessments that will lead to the development of an international consensus on exposure guidelines. Details on the EMF Project are available on the home page at: <http://www.who.int/emf/>. An overview of the complete EMF Project is shown in figure 1.

Figure 1: A schematic outline of the activities and outputs of the International EMF Project.



The International EMF Project has recently conducted in-depth international reviews of the scientific literature on the biological and health effects of exposure to radiofrequency (RF: 10 MHz to 300 GHz), intermediate frequencies (IF: 300 Hz to 10 MHz) and static (0 Hz) and extremely low frequency (ELF: >0 to 300 Hz) fields. These reviews were conducted with the purpose of identifying;

1. health effects that can be substantiated from the literature, and
2. biological effects that are suggestive of possible health effects, but require further research to determine if exposure to EMF at the low levels of exposure normally encountered in the living and working environment has any impact on health.

Conclusions from the RF and static and ELF field reviews have been published (Repacholi, 1998; Repacholi & Greenebaum, 1999). The final scientific review of possible biological and health effects from exposure to EMF in the frequency range intermediate to the static and ELF and radiofrequency ranges, i.e. the range 300 Hz to 10 MHz, was held in Maastricht, The Netherlands, 7-8 June 1999. The summary report of the meeting has been published (Litvak et al, 2002). The proceedings of all papers have been published jointly by WHO and ICNIRP, and are available from ICNIRP.

Research agenda

Having completed the initial international scientific reviews, WHO is now urging EMF funding agencies world wide to give priority to this research, if it is their intention to obtain results that will assist both WHO and the International Agency for Research on Cancer (IARC) to make better health risk assessments. WHO's EMF research agenda is reviewed and updated during annual meetings of the Research Coordination Committee. A major review of the research needs will take place following the

International Advisory Committee meeting in Geneva from 10-12 June 2003. Following this meeting a revised WHO EMF Research Agenda will be issued.

Health risk assessment

Both WHO and IARC have already established a timetable for assessing health effects of EMF fields. In June 2001 IARC held a meeting to formally identify and evaluate the evidence for carcinogenesis from exposure to static and extremely low frequency (ELF) fields. This resulted in ELF magnetic fields being classified as a "possible human carcinogen". This result has been explained in a WHO fact sheet # 263.

IARC publish the results of this meeting in the IARC Monograph Series in 2002. The International EMF Project will incorporate the IARC conclusions on carcinogenesis into the results of a WHO evaluation of non-cancer health risk assessment of exposure to static and ELF fields in 2002-3. The results and conclusions will be published in the Environmental Health Criteria series. It is anticipated that sufficient results will be available for IARC to conduct a similar evaluation of evidence for carcinogenicity of RF fields in 2004. WHO would then complete an overall health risk assessment of exposure to RF fields in 2005-6.

Thermal workshop

A workshop, held in Geneva 2002, entitled "Adverse Temperature Levels in the Human Body" brought together scientists with expertise in biological effects of hyperthermia to review the data and determine the evidence that could be used to evaluate potential adverse effects from human exposures to radiofrequency (RF) electromagnetic radiation in the range of 10 to 2000 MHz. Standards for RF exposure in this frequency range are based currently on thermal effects. Information was reviewed on the ability of hyperthermia, either to the whole body or to part of the body to affect physiology, particularly the heart and circulatory system, to induce other thermoregulatory responses such as sweating, to affect the performance of simple and complex mental tasks, to induce various heat related disorders such as heat stroke, and to damage body tissue, particularly the central nervous system and gut. In addition, thresholds for effects on developing embryos and fetuses and possible carcinogenic effects were also examined. These findings were integrated and discussed in the context of known cellular and biochemical responses of cells and tissues to hyperthermia. The experts judged the relevance of each study for informing policy makers on the scientific basis for establishing safe exposure levels. The results of this workshop will be published as a special volume of the International Journal of Hyperthermia within the next few months.

EMF risk perception, communication and management

International seminars were held in Vienna (October 1997) and Ottawa (September 1998) to discuss application of the principles of risk perception and risk management to EMF fields. The seminars were followed by working group meetings to progress draft report on this topic. The proceedings of the Vienna seminar have already been published by ICNIRP (1998) and the Ottawa meeting proceedings were published by WHO in 1999.

A handbook called "Establishing a dialogue on risks from electromagnetic fields" was published in 2002. Its information will be useful to individuals and capable of helping them better understand the process of scientifically-based risk assessment, the approaches and assumptions involved, and their reliability. The handbook is a user-friendly, how-to publication with a format that is easily read and practical for EMF programme managers who need basic information on EMF risk perception, communication and management.

Application of the Precautionary Principle

A special workshop has been organized to address the application of the precautionary principle to EMF. Given the widespread exposure of the general public and of workers to ELF and RF fields, this workshop will focus on these regions of the non-ionizing frequency spectrum as candidates for application of the Precautionary Principle. The two key questions are:

- Should the Precautionary Principle be invoked for ELF and RF fields?
- If so, how do we decide what actions should be taken?

A working group report will be published in a scientific journal and the proceedings of the open session will be published by WHO, the EC and NIEHS.

Environmental Impacts

As technology has progressed, levels of EMF in our environment have increased steadily over the past 50-100 years. At specific frequencies, EMF emissions from man-made sources now exceed those from natural fields by many orders of magnitude and are detectable everywhere in the world. Significant increases in environmental EMF levels have resulted from major development projects such as high voltage transmission lines, undersea power cables, radars, telecommunication and broadcast transmitters, and transportation systems. Research has been focused to determine if EMF exposure of humans has any deleterious health consequence. By comparison, influences of these fields on plants, animals, birds and other living organisms have been less rigorously examined. Assessments of environmental impacts of EMF fields is important to:

Ensure the preservation of balances in natural terrestrial and marine ecosystems, since these directly impact on human life.

Preserve food supplies by ensuring there are no adverse impacts to fisheries, agricultural animals and plants.

An international seminar, organized by WHO and ICNIRP, and supported by the German Federal Office of Radiation Protection, was held in Ismaning, Germany 4-5 October 1999. It provided a summary of scientific knowledge about any consequences to the environment from man-made sources of EMF in the frequency range 0-300 GHz. Overviews of current knowledge in key areas were presented by a selected panel of recognized specialists. On the day following the seminar, working groups met (6 October 1999) to prepare conclusions and recommendations. The results of the working group meetings has been used to prepare a scientific paper for publication in a scientific journal. This has now been completed and awaits publication. The proceedings of all presentations have been published and are available from ICNIRP.

It is not anticipated that further meetings will be organized on this topic. The main purpose of this activity under the EMF Project is to provide information that specifically addresses environmental impacts of EMF fields. A comprehensive summary report on this topic will have at least two benefits. It will:

- be useful for both governmental and non-governmental institutions when conducting environmental impact assessments, and
- address any public concerns that EMF could be adversely affecting our environment.

Harmonization of EMF Standards

This WHO initiative to harmonize EMF standards is a response to the fact that many countries are considering new EMF standards. Globalization of trade and the rapid introduction of mobile telecommunications worldwide have focused attention on the large differences existing in standards. Differences in the EMF limit values in standards in some Eastern European and Western countries are, in some cases, over 100 times. This has raised concerns about their safety and has led to public anxiety about increasing EMF exposures from the introduction of new technologies.

The purpose of this activity is to work towards, and hopefully achieve, international agreement on a framework for developing guidelines on protection of the public and workers from exposure to EMF.

Development of the framework has been carried out by working groups formed to address the key components. Working group meetings have been held, generally in conjunction with scientific meetings in key geographical regions that will allow the input of scientists and government officials in those regions. One goal of setting up the working groups is to enhance the quality of communication among scientists and government officials, in examining the scientific basis for the standards and the assumptions that underlie them.

Scientific conferences organized to include working group meetings in key regions.

1. 2nd International EMF Seminar in China: Electromagnetic Fields and Biological Effects: Xi'an, China 23-26 October 2000.
2. WHO EMF Standards Harmonization Meeting: Brooks Airforce Base, San Antonio, Texas 13-14 November 2000
3. WHO/Peru Government regional seminar: Bioeffects and EMF Standards Harmonization, Lima, Peru 7-9 March 2001
4. WHO EMF Standards Harmonization regional meeting, Bulgaria 28 April - 3 May 2001
5. WHO EMF Biological Effects and Standards Harmonization regional meeting, South Korea 22-25 October 2001

6. WHO EMF Biological Effects and Standards Harmonization regional meeting, Cape Town, South Africa 5-7 December 2001
7. WHO EMF Biological Effects and Standards Harmonization, Moscow and St Petersburg 17-25 September 2002
8. WHO EMF Biological Effects and Standards Harmonization regional meeting, Guilin, Guangxi, China 13-17 October 2003 (Incorporates a working group meeting to finalize the framework prior to submitting to the international congress)

The overall plan is to comply with the World Trade Organization (WTO) recommendation that any standards that affect trade should be developed in conjunction with both developed and developing countries. Meetings have been established to cover all geographical regions to allow scientists to have input to a process that is envisaged to lead to a common international standard.

Further Reading

Non-ionizing radiation, Part 1: Static and extremely low-frequency (ELF) electric and magnetic fields, IARC Monographs 80, IARC Press: Lyon, (2002), pp 429.

Repacholi, MH (1998): Low-level exposure to radiofrequency electromagnetic fields: Health effects and research needs. *Bioelectromagnetics* 19: 1-19, 1998.

Repacholi MH & Greenebaum B (1999): Interaction of static and extremely low frequency electric and magnetic fields with living systems: Health effects and research needs. *Bioelectromagnetics* 20: 133-160.

E Litvak, KR Foster and MH Repacholi (2002) Health and safety implications of exposure to electromagnetic fields in the frequency range 300 Hz to 10 MHz., *Bioelectromagnetics* 23(1) 68-82.

Fact Sheets

The following WHO Fact Sheets concerning EMF have been published or are being drafted:

- Electromagnetic Fields and Public Health: The International EMF Project. WHO Fact Sheet #181 Oct. 1997, reviewed May 1998.
- Electromagnetic Fields and Public Health: Physical Properties and Effects on Biological Systems. WHO Fact Sheet #182 Oct. 1997, reviewed May 1998.
- Electromagnetic Fields and Public Health: Health Effects of Radiofrequency Fields. WHO Fact Sheet #183 Oct. 1997, reviewed May 1998.
- Electromagnetic Fields and Public Health: Public Perception of EMF Risks. WHO Fact Sheet #184 Oct. 1997, reviewed May 1998
- Electromagnetic Fields and Public Health: Mobile Telephones and their Base Stations. WHO Fact Sheet #193 (Revised June 2000).
- Video Display Units (VDUs) and Human Health. WHO Fact Sheet #201 July 1998
- Electromagnetic Fields and Public Health: Extremely Low Frequency (ELF). WHO Fact Sheet #205 November 1998.
- Electromagnetic Fields and Public Health: Radars and Human Health. WHO Fact Sheet #226 June 1999.
- Electromagnetic Fields and Public Health: WHO Backgrounder on Cautionary Policies. March 2000
- Electromagnetic Fields and Public Health: Extremely Low Frequency Fields and Cancer. WHO Fact Sheet #263 October 2001

APPLICATION OF PRECAUTIONARY PRINCIPLE TO EMF

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Introduction

The Precautionary Principle

“We live in a society exquisitely dependent on science and technology, in which hardly anyone knows anything about science and technology.”

This observation by Carl Sagan helps explain why scientific and technical innovations can be both welcomed and feared, often by the same people; and why the pace of technological change, like a roller-coaster ride, can generate excitement and fear in equal measure. Indeed there have been few technical developments so benign as not to be accompanied by some risk. By passing laws and promoting cautionary advice society tries to minimize these risks, while still enjoying the benefits. In making this risk-benefit trade-off society is guided by its culture, its traditions, its experience and its scientists. This arrangement works well when there has been time for experience to accumulate and scientists are trusted. When, however, the risk is a new one, where its impact cannot be gauged, and where trust in science has declined, we enter the province of the Precautionary Principle.

The Precautionary Principle is intended to prevent or limit the possible harm caused by agents or activities before it has been established that the activity or exposure constitutes a harm to health. As threats to human health and the environment become more complex, uncertain, and global in their nature and while recognising that injudicious measures could lead to disruptions to trade and other unanticipated costs, the value of adopting the Precautionary Principle as a risk management tool in providing guidance in this environment is under active debate[1].

Possible health effects arising from exposure to extremely low frequency (ELF) electromagnetic fields (EMF) have been the subject of research for many years, but without definitive scientific resolution. At radio frequencies (RF), the rapid growth of new technologies such as mobile wireless telecommunications has raised concerns that exposure to fields from mobile phones and base stations could have long-term health consequences.

Given the widespread exposure of the general public and of workers to ELF and RF fields, these regions of the non-ionizing frequency spectrum as candidates for application of the Precautionary Principle. The two key questions are:

- Should the Precautionary Principle be applied to ELF and/or RF fields?
- If so, how do we decide what actions should be taken?

WHO/EC/NIEHS organized a workshop that brought together scientists, engineers, lawyers, health professionals and concerned citizens with knowledge of the Precautionary Principle to contribute perspectives from health, government, academia, environmental advocacy groups and industry. The European Commission text, published in 2000, was been used as one of the key starting points for this Working Group report on the application of the Precautionary Principle [2].

Objectives of the Precautionary Principle

Protecting public health

When developing policies and actions to protect public health it is important that the definition of health is clearly stated. WHO defines **health** as a *state of complete physical, mental and social well being and not merely the absence of disease or infirmity*. Public health policies have always had measures

aimed at disease prevention. These measures can be extended to include potential risk factors that have not yet been established as the cause of the effect or where much uncertainty remains. In this way the Precautionary Principle can be naturally integrated within public health policy and actions.

*The Precautionary Principle is
a risk management concept that provides a flexible approach to identifying and
managing possible adverse consequences to human health even when it has not been
established that the activity or exposure constitutes harm to health.*

Objectives of the Precautionary Principle in health policies

There are three important reasons to invoke the Precautionary Principle within a public health policy:

- to be more anticipatory in terms of health and dealing with unknowns,
- to address public concern, which may be more directed at ensuring a potential problem is not ignored, in contrast to scientists who are often reluctant to give credibility to unproven possibilities. The Precautionary Principle can provide a framework within which these different positions can be reconciled.
- to provide an alternative to exclusively technology-based environmental management, in order to bring ethics into the discussion and give environmental rights a voice. The Precautionary Principle may also challenge the singularity of strictly financial cost-benefit analysis as a decision-making tool.

While appropriate action should be taken even when there is lack of scientific certainty, this does not necessarily mean that precautionary measures are required or justifiable when there is no particular evidence, scientific or otherwise, of the presence of possible harm.

The Precautionary Principle represents an anticipatory approach by nature, and precautionary measures have to be viewed as provisional (or temporary) rather than permanent, i.e. it should be subject to review in the light of new scientific findings.

Balance between scientific and social considerations

The Precautionary Principle is a risk management tool that is complex in its application. This complexity depends on the degree of scientific uncertainty, the potential severity of harm and the interplay between science and social factors. Risk is a complex social construct and its many facets can lead to different responses by individuals and to diverse reactions by the various stakeholders to the proposed risk-management options. The general public and scientists differ in their willingness to make a mistake about the existence of risk. Scientists usually require considerable certainty before accepting that a risk is real. This attitude is embodied in hypothesis testing used to evaluate statistically whether a risk is real or not. Conceptually, scientists will normally support a positive association (i.e. the risk is real) if the probability that the risk has arisen by chance is below 5%. Scientists are also often willing to 'miss' a real association (i.e. conclude the risk does not exist, when it actually does) with a probability of 20%. The public, however, is more concerned that any potential hazard or risk is not overlooked, irrespective of statistics. The Precautionary Principle needs to recognise these issues, and whilst remaining based on scientific evidence, must recognise the validity of social concerns as well.

Relation between Exposure Standards and the Precautionary Principle

All international and nearly all national guidelines limiting human exposure to EMF are based on health effects established by research results that are consistent, reproducible and confirmed by different laboratories. In addition, the exposure limits and guidelines incorporate safety factors to allow for some of the uncertainty in the thresholds for these established effects.

Thus, broadly speaking, Exposure Standards apply where there is scientific certainty, whereas the Precautionary Principle applies where there is uncertainty. The two should not be in conflict. The Precautionary Principle can provide a helpful framework to allow possibilities to be considered which

would be excluded from the approach employed to develop traditional exposure limits. Nonetheless, where international guidelines exist, it is important that the application of the Precautionary Principle does not undermine the scientific basis of the limits.

Different ways of deciding on precautionary actions

It is worth repeating that the objective of applying the Precautionary Principle is to deliver appropriate protective measures against uncertain hazards. Just as is the case with established hazards, the protective actions must be appropriate and proportionate. Not all established hazards are important enough to justify regulation. Even in dealing with established hazards, there has to be a weighing-up of the benefits and the costs of regulation. These costs will usually include ones that cannot be quantified easily in money terms (e.g. the value of a life). These factors apply equally when considering the precautionary actions to be taken in relation to uncertain hazards.

Central to the application of the precautionary principle presented here is a balancing of the consequences and benefits. This is conventionally referred to as cost-benefit analysis. Later sections discuss how “cost” is used in a wider sense than just financial. Nor does a cost-benefit analysis imply that the approach taken is purely utilitarian. Issues of social justice between individuals and communities, and ethical factors such as whether exposure is voluntary or involuntary, are also included. What is advanced here is an approach that allows all these different facets of health protection to be accommodated in a framework that nonetheless allows objective and defensible decisions to be made.

Precautionary approaches to EMF have already been advocated and adopted in various countries. These have rarely involved an adequate balancing of consequences and benefits. Instead, most existing approaches have tended either to specify the costs to be incurred, without balancing these costs against the benefits, or to set out the intended benefits without regard to their cost.

Examples of approaches that specify costs without placing a value on the benefits include:

- Requiring a certain percentage levy on the cost of a project to be spent on EMF mitigation measures, as has happened with some new transmission line projects
- Requiring a fixed sum to be spent on EMF mitigation in a defined situation, such as providing money to schools to be used to reduce exposures
- Advocating a variety of low-cost measures to reduce emissions or public exposures to EMF

Examples of approaches that, on the other hand, provide defined benefits without regard to costs include:

- Setting precautionary exposure limits (e.g. 1 μ T or 0.5 μ T)
- Advocating measures to reduce exposures (e.g. time limits on use of mobile phones or restrictions on children’s use of phones)
- Requiring exposures to be reduced by a stated amount or percentage compared to what they would have been previously
- Requiring exposures to be no higher than those already existing in an area
- Requiring use of best-available technology to reduce or minimize exposures

These examples of ways employed to reduce public exposure to EMF can be described as measures which reflect the policy of “prudent avoidance”. “Prudent avoidance” is an umbrella term for approaches that favour taking whatever field-reduction measures may be possible subject to the cost being financially “modest”. Prudent avoidance therefore fits in the category of setting (modest) costs without valuing or quantifying the benefits.

These approaches can not be completely satisfactory, as none properly weigh up or balances costs and benefits. With some of these schemes, costs and benefits are weighed implicitly rather than to a specific individual situation. For example, a decision to recommend 4% as an appropriate fraction of project cost to be applied to EMF reduction, could in principle be the result of a balancing of costs and benefits. However, this balancing, if done at all, could only have been done in a general way, averaged over many projects. There would be particular projects where 4% of the project cost could yield huge reductions in exposures and others where little reduction, if any, is possible. Thus, whilst each of these approaches may at times be able to generate the appropriate precautionary actions, there would also be situations where each generates inappropriate actions, and are therefore unsatisfactory.

Once a correct and full application of the Precautionary Principle has been achieved it is recognized that there may be value in expressing conclusions in a form that makes them readily applicable to practical situations. Such simplified “action rules” could look similar to some of the existing schemes listed above, but would differ in that (a) they would apply only to the limited and specified range of circumstances for which they are valid, and (b) they would follow from the full application of the Precautionary Principle, rather than reflect some arbitrary position.

As an example of “action rules”, a new proposed Charter between city halls and mobile phone operators has been developed by the French government [3] for improved management of new mobile phone mast installations. A number of administrative actions are initiated, based on criteria designed to evaluate the impact of a new base station, which include technical details concerning location (e.g. distance to urban areas, proximity to school) and social impact (e.g. aesthetics and public reaction).

When to apply the Precautionary Principle

Risks are present in all aspects of our lives, and there will always be some uncertainty associated with those risks. As individuals and as a society we regularly make decisions under uncertainty, without a full knowledge of the extent of the risk. While the possibility of risk does not in itself require action, uncertainty in itself does not justify inaction. The question then is: “When to act?” What **strength of evidence** is required to trigger action or invoke the Precautionary Principle? (e.g. a possible cause, no conclusive scientific proof, or sufficient evidence).

Risk Analysis

The analysis of risk encompasses three main elements, namely risk assessment, risk management and risk perception. Within this framework, the Precautionary Principle is relevant when considering the range of **risk management** options available. To be effective it must take into account both measured and perceived risk.

The following factors, important to the application of the PP, developed in a German report [4], are expanded and adapted here to the EMF issue:

- **Extent of damage:** Adverse effects can be quantified in different ways, depending on the end-point considered (e.g. in terms of number of lives lost to cancer, or production losses from electrically hypersensitive (EHS) people who cannot work due to their condition).
- **Probability of occurrence:** The existence of a potential adverse effect from an environmental exposure could trigger the Precautionary Principle. Knowledge of the probability of the adverse effect as a function of the level of exposure greatly enhances decisions; these probabilities are one of the most uncertain aspects of risk assessment, especially for EMF.
- **Uncertainty:** Uncertainties exist at every level of evaluation, from uncertainty about the presence of a hazard to uncertainty in the levels of exposure a person receives. The relevant metric is the most important uncertainty for the application of the Precautionary Principle to EMF.
- **Ubiquity:** Most common EMF exposures come from the use of cell phones and appliances as well as from electrical wiring in and outside of homes and proximity to mobile phone masts in urban areas. Ubiquity of this exposure is an important driver for the Precautionary Principle.
- **Pattern of Exposure:** In general, pattern of exposure including length, intensity, and fractionation can play a key role in their influence on disease incidence. This could be due to the existence of a threshold, complex dose-response pattern and adaptive response. Potential differences in effects due to low long term exposures from power lines and base stations vs. more intermittent but much higher exposure from appliances and cell phones have been suggested but not adequately examined.
- **Delayed effect:** Latency is the time between the initial exposure and evidence of disease. One of the main diseases of interest is cancer, which has latency from several years to decades. Thus, consideration of latency is important, particularly in the case of cell phones, where ubiquitous exposure is recent and where potential development-of brain cancer might be years away, thus calling for an anticipatory consideration of the Precautionary Principle.
- **Inequity and injustice** associated with the distribution of risks and benefits over time, space and social status (e.g. routing of power lines or erection of base stations in low-income areas)
- **Psychological stress and discomfort** associated with the risk or the sources of risk (e.g. people particularly sensitive to EMF). This has clearly been a driver for the application of the Precautionary

Principle to EMF

- **Potential for social conflict and mobilization:** Degree of interest and pressure from advocacy groups and associations. Again, this has occurred with the EMF issue, especially when new facilities such as base stations or power lines are proposed or built.
- **Voluntary vs. involuntary exposure:** People feel differently about risk when the choice is theirs. For EMF, higher exposures from cell phones and appliances have been of less concern to the public than lower but involuntary exposures from base stations and power lines.

Scientific Uncertainty

While the Precautionary Principle applies by definition to situations characterized by scientific uncertainty, its application to the EMF issue is especially problematic, because there is uncertainty not only as to whether exposure is associated with increased risk or not, but also:

- **Uncertainty about the magnitude and specificity of the risk.** The risk from exposure to EMF, if real, could be small but affect a large number of people. Alternatively, the risk could be large but affect only a small number of susceptible individuals. Other possibilities might include simultaneous exposure to another factor. Different possible relationships between risk and exposure may require different precautionary measures to reduce risk, making application of the Precautionary Principle particularly difficult.
- **Uncertainty as to which aspect of exposure might be harmful.** Certain actions, while reducing some aspects of exposure, might inadvertently increase risk by increasing some other, as yet unknown, aspect that might turn out to be the true cause. The concept of precautionary action is often rooted in the assumptions that less exposure is better and that reducing one aspect of exposure will also reduce other aspects that might be harmful. Neither of these assumptions, in the context of electric and magnetic fields, is necessarily valid. In fact, some laboratory research has suggested that biological effects due to EMF can vary within windows of field frequency and intensity. While such a complex and unusual pattern is unlikely and would defy most accepted tenets of toxicology and epidemiology, the possibility that it may be real must be considered when applying the Precautionary Principle to EMF.

The absence of a clearly elucidated, robust, and reproducible mechanism of interaction of EMF with biological systems and the plethora of field characteristics that could be relevant, make avoidance strategies that fall short of eliminating EMF exposure entirely both difficult to analyze and potentially counterproductive. Complete elimination of exposure could only be accomplished if no one were to use electricity or modern communications technology.

Triggers for the application of the Precautionary Principle to EMF

The Precautionary Principle should be invoked when:

- there is good reason, based on empirical evidence or a plausible causal hypothesis, to believe that harmful effects to people might occur, even if the likelihood of harm is remote; and
- a scientific evaluation of the consequences and probabilities reveals such uncertainty that it is **not yet possible** to assess the risk with sufficient confidence to inform decision-making.

adapted from the UK Interdepartmental Liaison Group on Risk Assessment [5]

There are three factors that might, in general, trigger the application of the precautionary principle:

- Recognition that there is objective scientific evidence that amounted to the possibility of a health risk. This is the situation where (as is the case with ELF magnetic fields) the International Agency for Research on Cancer (IARC) or a body with equivalent status classifies an agent as “possibly carcinogenic” or “possibly” a cause of other forms of ill health. Where there is no such classification, applying this criterion is less objective and less satisfactory.
- A recognition that there may be a very low cost intervention available, in which case an action may be justified even when the scientific evidence is weak, specifically when it is too weak even to be classified as “possible”. This is the case for the use of hands-free devices for mobile phones and limiting the amount of time children spend on these phones. This criterion needs to be applied with care to ensure that an apparently “low cost” option really is low cost. In principle, no matter how low

the apparent cost of an intervention, at least a rudimentary cost-benefit analysis should be undertaken.

- Public pressure. This would often result in consideration of precautionary actions even in circumstances where the evidence is weak and subjective, but nonetheless must be recognized as a practical consideration.

Note that these are triggers, not for *taking* precautionary action, but for *applying* the Precautionary Principle, that is, for making a detailed assessment of the benefits and consequences of action that may or may not be taken. The Precautionary Principle, when applied properly, should not result in unjustifiable or disproportionate actions. Therefore, in principle, it can be applied no matter how weak the evidence. The reasons for requiring a trigger are pragmatic; applying the Precautionary Principle properly entails much work. There is always the possibility of a superficial application resulting in inappropriate actions. It is therefore sensible not to invoke the Precautionary Principle without adequate justification.

Legal context of the precautionary principle

In some societies or sections of society, there is a reticence to adopt precautionary measures in case this is seen as an admission that the health risk is real. In part, this concern relates to public perception of the issue. This concern can be ameliorated, though not necessarily completely removed, by sensitive communication. In part, however, the concern is legal: that adopting precautionary measures could be construed as an admission of liability; that it might be taken to imply responsibility for similar exposures prior to taking precautionary action; and that it may put the person or company taking such actions in the position of having to justify, in a legal arena, why they took the actions they did and did not go further.

Such concerns about liability and admissions are detrimental to optimum operation of the Precautionary Principle and hence to optimum protection of public health. As far as possible the Precautionary Principle should be implemented in a way that is free from such legal connotations. How this is achieved will depend on the legal and regulatory frameworks of the countries concerned.

WHO is currently developing its guidance on application of the PP and this will be available later this year.

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Session 2-1

EMF EPIDEMIOLOGICAL STUDIES: RESULTS AND CURRENT CONCLUSIONS

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Epidemiology has been a driving force in the research on power frequency electro-magnetic fields and health effects partly because later studies and independent research groups often have replicated epidemiological results. The best example is the studies on leukaemia in children where IARC evaluators based on the consistent epidemiology have classified power frequency electro-magnetic fields as a possible carcinogen (2B). This classification was reached despite rather limited support from animal studies or other experimental research. Epidemiology has also been quite successful in rejecting hypotheses regarding other health effects. The starting point has often been one or several studies suggesting an effect that has later been followed by a sufficient number of negative studies to persuasively refute the hypothesis in question. In most instances the biophysical support has been negligible but there are also instances where there has been at least some amount of mechanistic support. A good example is cardiovascular disease. This may seem contradictory from a strict *Popperistic* view point according to which one can never prove the negative. Whether or not this is true, there is no doubt that the credibility in a hypothesis gradually decreases, and should do so, with an increasing number of negative studies. Thus, for power frequency fields epidemiology has been instrumental both to sharpen hypotheses about some health effects and to disprove some others.

The situation is still very different with radio-frequency fields where the literature currently looks my like the power frequency epidemiology did more than a decade ago. Although several studies, almost exclusively on brain or intracranial tumors, have been published, the results are overwhelmingly inconclusive. Because almost all of the studies have rather clear null results some reviewers use these studies as a basis to exclude the possibility of an effect, but given the obvious limitations of these studies this is hardly justified. On the other hand, since almost all the results in these studies are negative and because of all methodological problems there is very little, if any, support for a carcinogenic effect in them either. Thus, the RF epidemiology has so far been far from as informative and conclusive as the power frequency epidemiology. The methodological problems in the radio-frequency epidemiology are rather similar to the ones encountered in the power frequency epidemiology although the specific technical solutions may look different. Hopefully, however, the situation will quickly improve such that epidemiology will be able to make substantial contributions also for these frequencies.

Session 2-2

EPIDEMIOLOGICAL STUDIES OF EMF HEALTH EFFECTS IN CHINA: A REVIEW OF RECENT STUDIES

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The development and application of modern science and technology had improved the living standard of the public. Health effects of various sources of electromagnetic fields (EMF) induced from electric appliances and equipment as communication, broadcasting and high voltage power lines in different frequencies were being concerned by more and more people. Possible adverse health effects of long-term, low level exposure to EMF in various frequencies were reported by many researchers from in board and abroad. Extremely low frequency (ELF) electric and magnetic field were classified as possibly

carcinogenic to humans by International Agency for Research on Cancer (IARC) in 2001. A lot of lab research and epidemiological investigations had been performed in China on the biological effects and adverse health effects of ELF and RF. In this paper we summarized in some of the domestic epidemiological analysis published in the last 10 years on the public health of exposure to EMF in various frequencies.

Health effects of extremely low frequency electric and magnetic fields (ELF)

It had been reported by epidemiological surveys that ELF might cause adverse health effects to immune system and central nervous system.

Main effects of ELF upon the immune system were as follows, influence on the number of white blood cells and lymphocytes, influence on the activities of immunoglobulin, and influence on the activities and receptor expression of interleukin (IL). Zhu S. et al. investigated immune functions of 192 electric railway workers exposed to ELF (50Hz, 0.9-2.73kV/m.h, 0.33-0.45mT.h) chronically and reported that long-term exposure to 27.5 kV ELF significantly decreased the total number of white blood cells, the number of lymphocytes and the levels of IgG and IgA in serum ($P<0.05$ or $P<0.01$)^[1]. Also Zhu S. et al. reported 33 electric railway workers exposed to 50 Hz ELF (1.69-3.25kV/m.h, 0.245-0.938mT.h) and found that the extent of DNA damage in peripheral lymphocytes was associated with the exposure levels ($P<0.01$)^[2]. Zhao R. et al. investigated the contents of IgG, IgA, IgM, C₃, C₄, CRP and CIC in serum of 104 workers exposed to 500 kV ELF more than 3 three years, and found that the level of IgA, IgM and IgG were significantly lower compared to the unexposed^[3]. Xu M. et al. investigated 25 workers long-term exposed to ultra high voltage ELF (300kV, 20-58kV/m, 0.8-2.3mT) in IL-2 activity, expression of IL-2 receptor, ADCC, IL-15 activity, immunoglobulin level of IgG, IgM and IgA, and the results indicated that the activity of IL-2 and the level of IgG were significantly increased ($P<0.05$)^[4].

As is reported in many epidemiological surveys that exposed to ELF induced neurasthenia. Pan L. et al. performed a cross-sectional epidemiological study to show ELF effects on CNS and found that railway workers (n=1559) exposed to ELF (50 Hz, 2.3kV/m, 0.6mT) significantly increased the incidence rates of the following complaints, neurasthenia, alopecia, hyperhidross, and sexual hypoesthesia than control (n=788) ($P<0.05$)^[5]. Li D. et al surveyed 39 agents and 36 residents nearby 220 kV high voltage power line and 39 institute teachers, and found that exposed to ELF for 1-2 years can significantly increased the prevalence rate of neurasthenia, however, exposed to ELF for 3-4 years or more than 5 years did not show increased prevalence rate of neurasthenia, further analysis by logistic regression showed that there was no significant association ($P>0.1$) between ELF and neurasthenia, the level of 17-KS and VMA in urine did not change significantly.^[6]

Du T. et al. investigated chromosome aberration of 26 operators exposed to power station high voltage, 22 transformer operators and 24 controls, and found that the rates of chromosome aberration and SCE were significantly increased ($P<0.05$)^[7]

Health effects of radio frequency electric and magnetic fields

Quite a few published papers reported that RF field influenced neurobehavioral function, increased prevalence rate of neurasthenia, and resulted in adverse health effects on CNS.

RF effects upon CNS were centered by many epidemiologists. Neurobehavioral Core Test Battery (NCTB) recommended by WHO is the common measurement for neurobehavioral function in recent years. Zhu Q. et al. initiated WHO-NCTB among 38 communication operators exposed to low intensity microwaves ($1.5-7.5 \mu \text{W}/\text{cm}^2$) and 38 postal workers non-exposed to microwaves, and found that the exposure significantly decreased the response times in Simple Reaction Time Test, decreased the scores of Digit Span Test, Digit Symbol Test, Pursuit Aiming Test II and anger scores of mood state ($P<0.05$ or $P<0.01$)^[8]. Long Y. et al. measured neurobehavioral function of 50 microwave workers and 50 controls with WHO-NCTB, and found low intensity microwaves (2450 MHz, $35 \mu \text{W}/\text{cm}^2$) exposure significantly affected mood state and decreased the scores of Digit Span Test and Simple Reaction Time Test ($P<0.05$)^[9]. Li Z. et al. investigated 81 radar operators and 61 administrators of the same factory with WHO-NCTB and found that long term exposure to low intensity micromaves ($17.91 \pm 13.16 \mu \text{W}/\text{cm}^2$) did not influence on the scores of neurobehavioral function except for the scores in Santa Ana Manual Dexterity Test ($P<0.05$)^[10]. Duan L. et al. surveyed 57 workers exposed to high-frequency fields (200-300 kHz, 20-603 V/m) and 57 non-RF exposure workers with WHO-NCTB, found that the exposure resulted in significant decreases in most of scores of mood state, esp. for the type of T and A ($P<0.01$), whereas,

scores of Digit Span Test, Digit Symbol Test and Pursuit Aiming Test were associated with the prevalence rate of neurasthenia and decreased significantly ($P<0.01$), these scores were used to evaluate short term memory and attention^[11].

There were some indications in epidemiological studies that microwaves increased the prevalence rate of neurasthenia significantly, the most common complaint symptoms were dizziness, headache, dyssomnia, fatigue, hypomnesia, palpitation and some complaints of alopecia. A considerable body of reports declared that microwaves in communicating bands caused neurasthenia^[12]. Qiu Y. et al. studied the nervous system function of 108 radio radiation operators and the results showed increases in the complaints as headache, dizziness, fatigue, insomnia, hypomnesia, irritability, hyperhidrosis, xerostomia and palpitation ($P<0.05$ or $P<0.01$), and found abnormal Rheoencephalography ($P<0.05$)^[13]. Pan D. et al investigated 33 operators exposed to microwave (3783.5-3899.5 MHz, $75-175 \mu\text{W}/\text{cm}^2$) more than 2 years and 41 non-microwave exposure staff, found that the exposure significantly increased the complaints of neurasthenia as dizziness, headache, dyssomnia, fatigue and hypomnesia^[14]. Cao Z. et al. investigated 115 staff with handsets of cellular telephone and 101 staff without handsets of cellular telephone and found that there was some association between use of handset and the complaints of chest distress ($P<0.05$), nausea ($P<0.01$) and anorexia ($P<0.05$)^[15]. 88 of the 115 staff and 77 of the control were used to study the effects upon quality of users' sleeping and depression, and found that the exposure to cellular telephone microwave increased the prevalence rates of insomnia ($P<0.01$) and dreaminess ($P<0.05$)^[15]. Li H. et al investigated 157 male microwave operators exposed more than 3 months and 104 male non-microwave administrators, the results showed that there were 115 microwave devices (3981-4194 MHz) and the radiation intensity of 109 devices were $10-450\text{mW}/\text{m}^2$, the other 6 devices power density were $520-3000\text{mW}/\text{m}^2$, and found that exposure to communicating microwave increased the prevalence rates of neurasthenia and abnormal ECG (sinus bradycardia, sinus arrhythmia and abnormal EEG (abnormal undulate form, dissymmetric wave amplitude of two sides)^[16].

Radio frequency fields had some effects upon cardiovascular function, esp. influences on the electrophysiological activities. Tang G. et al initiated a 8-year cohort epidemiological study to dynamically analyze medium high frequency fields' effect upon cardiovascular function, they checked blood pressure and ECG every 2 years of 108 RF operators and 82 non-RF staff and found the exposure (0.999-30.000 MHz) resulted in abnormal ECG (sinus arrhythmia, sinus bradycardia, abnormal pacemaking, right bundle branch block, and chronic fatigue syndrome) of the examination in 1994, 1996 and 1998, no significant changes were found in the examined ECG of 1992 and 1994^[17]. Chen C. et al. checked ECG for 138 operators exposed to high frequency RF (134 kHz-510 MHz, 1-7.6 V/m, 0-1.2A/m; 2-150 V/m, 1-5.5A/m) more than 3 months and 72 non-RF operators and found that the exposure significantly increased the prevalence rate of abnormal ECG, esp. for sinus arrhythmia ($P<0.01$)^[18]. Ding C. et al. examined 212 radar (3000 MHz, $72-100 \mu\text{W}/\text{cm}^2$) soldiers and 309 non-microwave soldiers, among them 39 microwave operators and 35 non-microwave operators were required to examine flick fusion frequency (FFF), visual acuity, Rheoencephalography and ECG, and found that the exposure (3000 MHz , $72-100 \mu\text{W}/\text{cm}^2$) significantly decreased FFF and visual acuity ($P<0.01$), analysis of 75 Rheoencephalography showed significantly decreased speed of the cerebral blood flow ($P<0.05$); as to 178 microwave operators and 56 non-microwave operators, the exposure resulted in significant increase in the following complaints as headache, hypomnesia, palpitation, irritability, dyssomnia and dizziness in the morning ($P<0.01$)^{[19][20]}. Chen N. et al. explored a study of 62 radar operators and 57 non-microwave soldiers and found that the exposure ($18.7-85.2 \mu\text{W}/\text{cm}^2$) decreased the number of white blood cell, platelet, increased the number of acidophil and changed with professional exposure period.^[21] Zhang H. et al. checked ECG of 398 operators exposed to microwave more than 3 months and 172 non-microwave workers, and found that the exposure ($3.2-4.2\text{GHz}$, $<10 \mu\text{W}/\text{cm}^2$) significantly influenced ECG^[22].

As is reported that RF field mainly influenced the level of immunoglobins on immune system. Zhang H. et al examined the immune function of 310 microwave ($3.4-4.2\text{kHz}$, $<10 \mu\text{W}/\text{cm}^2$) workers and 109 non-microwave workers, the results showed that both immunoglobulin level of the exposed and control were within the normal limits, however, the IgG, IgM and IgD of the exposed were significantly lower than control ($P<0.05$), C_3 and IgA decreased as the time increase of microwave exposure^[23,24]. Yu S. et al. examined 42 microwave ($2-7 \text{ GHz}$, $1-15 \mu\text{W}/\text{cm}^2$) workers and 31 non-microwave workers, and found that the exposure decreased the level of IgG, IgA and IgM ($P<0.05$)^[25]. Jiang X. et al examined 62 workers exposed to high frequency ($200-300\text{kHz}$, $20-150 \text{ V/m}$, $3.0-13.0\text{A/m}$ for quenching; $0.2-125.0\text{V/m}$,

0.3-9.9A/m for welding; 70.0-600.0V/m, 0.0-7.0A/m for plastic heat sealing) and 56 non-high frequency workers, the results showed that the immunoglobulin level of quenching and welding workers increased ($P<0.01$), but only IgM for the plastic healing workers ($P<0.05$), and found significant differences in the prevalence rate of phacoscotasmus and in the level of LPO, GSH-Px, cAMP and cGMP ($P<0.05$)^[26]. The results were replicated by Jiang X. et al. in 1997^[27].

Phacoscotasmus is an adverse effect of RF fields. Dai S. et al. performed a 6-year cohort epidemiological study to evaluate the RF effect on eyes from 1984 to 1990, they examined 142 radar workers and 82 non-microwave workers, found that exposure to radar ($20-800 \mu\text{W}/\text{cm}^2$) increased the prevalence rate of phacoscotasmus ($P<0.01$) and the ratio of severe cases^[28]. Zhu H. et al. examined 61 workers exposed to high frequency field (200-500 kHz, 78-330V/m, 19.5-82.5A/m) and 56 non-RF workers, and found that the exposure significantly increased the prevalence rate of phacoscotasmus ($P<0.01$)^[29].

RF effects upon reproductive function were highly concerned. Wang G. et al. examined 212 female workers exposed to RF field (3-78MHz, 80V/m; 400-9400MHz, $20-98 \mu\text{W}/\text{cm}^2$) more than 1 year and 194 non-RF female workers, and found the exposure significantly increased the prevalence rates of menstruation, premonitory symptom, menoxenia, spontaneous abortion and complication of pregnancy ($P<0.05$, $P<0.01$)^[30]. Ding X. et al. examined 89 male workers exposed to high frequency field (6 MHz, 10-300W/m, 0-1.5A/m) more than 1 year and 95 non-RF workers, the results showed significant increase in the prevalence rates of fatigue, impotence, and sexual hypoesthesia, but no changes for sperm parameters and endocrine hormone were found^[31].

Health effects of Video Display Terminals (VDT)

VDT operators are influenced by not only intensive stress in mind, but also various hazards of physics and chemicals, the most common health effects of VDT showed by epidemiological studies were adverse health effects on vision, neurobehavioral function and muscles. Wang H. et al. studied 78 VDT ($8 \mu\text{W}/\text{cm}^2$) operators from telecommunication bureau and found that there were no significant differences in the scores of 5 items of passive mood state (tension, depression, anger, fatigue, bewilderment), the exposure significantly decreased the scores of vigor of positive mood state, Benton Visual Retention Test ($P<0.05$), Pursuit Aiming Test 2 and increased the scores of Simple Reaction Time Test ($P<0.05$)^[32]. Xu K. et al. examined 65 VDT (5-35V/m, 0-0.4A/m, $0-7 \mu\text{W}/\text{cm}^2$) operators from a financial institution and a college and 33 non-VDT staff, found that the exposure increased the incidence rates of the following complaints as fatigue, neck ache, omalgia, backache, dizziness, headache, arm pain and palpitation ($P<0.05$, $P<0.01$), increased the prevalence rate of phacoscotasmus, increased IgA level and the total number of peripheral blood lymphocytes, and showed that there were significant changes in the scores of tension-anxiety, fatigue, Simple Reaction Time Test, and Santa Ana Manual Dexterity Test ($P<0.05$, $P<0.01$)^[33].

Due to the big proportion of female operators, the effect of VDT on female reproductive function were concerned. Liu J. et al. studied 361 female operators from the city of Wulumuqi exposed to VDT for more than 2 hours continuously per day and 484 female workers from the same section, and found that the exposure significantly increased the prevalence rates of menoxenia (prolonged menstrual cycle, menstrual disorder, hypermenorrhoea, dysmenorrhoea, premenstrual tension), spontaneous abortion and gestation anaemia ($P<0.05$, $P<0.01$)^[34]. Ren D. et al. explored menstruation of 976 VDT operators from Shanghai and Nanjing and 1012 non-VDT staff from the same section, and found that exposure to VDT significantly influenced on the menstrual cycle and intermenstrual period ($P<0.05$, $P<0.01$)^[35].

As above mentioned, electromagnetic fields exerted various effects on human in epidemiological studies, however, most of the studies were cross-sectional epidemiological analysis with many confounding factors, the evaluation of EMF effects needs further scientific study from lab and spot investigations.

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Session 3-1

DISCOVERY SCIENCE AND MOBILE PHONE SAFETY: A NEED FOR THE NEW RESEARCH APPROACH

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Elucidation of the biological or health effects of the electromagnetic fields (EMF) has been done for decades but the reliable answers are still missing. It appears as if the bioelectromagnetics research has been caught in the “vicious cycle” of replicating and re-replicating of the few positive findings. This, although important, is often done without sufficient input of new ideas or modern techniques. At the same time, the negative results are often accepted as such. This attitude significantly slows down the clarification of the health hazard issue. At the same time pressure for the definitive answers from the politicians, industry and the general public is increasing. Most worryingly, the “gaps” in the knowledge are often filled-up by pseudoscientific speculations.

Extensive epidemiological studies are commonly expected to give the answers. However, finding and scientific validation of any potential health hazard (whether it is cancer or non-cancer effect) might not be possible using epidemiological approach alone because of the “low sensitivity” of this method. Recently, it has been suggested that high-throughput screening techniques (HTST) will be crucial in providing important information for thorough determination of all possible bio-effects of the EMF (Leszczynski, *Lancet* 358, 2001, 1733).

The “discovery science” term has been coined-in to define the new HTST-approach towards revealing new biological mechanisms, which are often unpredictable (Aebersold et al., Nature Biotechnology 18, 2000, 359). It postulates use of combination of data obtained by transcriptomics (global gene expression) and proteomics (global protein expression) to enumerate the behavior of biological system. The discovery science approach seems to be particularly suited for elucidation EMF health hazard issue. Because of the possibility of simultaneous analysis of thousands of genes/proteins and the interplay between them the discovery science approach will reveal a variety of unpredictable bio-effects. Also, it might provide valuable information about the potential long term chronic exposure effects that are largely unknown and unpredictable.

There are only a handful of published studies and conference abstracts where HTST were used to elucidate biological responses to EMF. In our own research (Bio-NIR group at STUK), we have used HTST to examine global gene and protein changes that occur in human endothelial cell lines during the 1-hour exposure to 900 MHz GSM signal at an average SAR of ~2.4 W/kg and at temperature of $37\pm 0.3^{\circ}\text{C}$. We found that few tens of genes (out of 3600 examined) alter their expression level. This was accompanied by changes in the activity of few hundreds of proteins (based on the protein phosphorylation status) and in the expression level of several tens of proteins (out of ~1300 examined). Combination of the HTST data on gene and protein expression and protein activity has revealed several signal transduction pathways that might be affected by RF-EMF exposure. This information will be a basis for further animal and human volunteer studies that will assess the impact of these EMF-affected pathways on the normal physiology.

In conclusion, although the use of discovery science approach employing HTST will not provide direct evidence of health hazard or its absence, it will be essential in unraveling of all biological effects exerted by EMF exposure. Further elucidation of the physiological significance of these biological effects for the health and well-being, in short- and long-term exposure conditions, will allow determination whether any health hazard might be associated with the use of EMF emitting devices at the present safety levels.

Session 3-2

***IN VITRO* EMF BIOEFFECT RESEARCH IN CHINA: DATA AND ITS IMPLICATIONS**

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China puts the bioeffect study of electromagnetic fields (EMFs) as one of its research priorities. In recent years, National Natural Science Foundation of China (NSFC) sponsored a series of grants to bioelectromagnetic research field, especially set two key projects in a row, which ensure the society to make a significant progress in understanding the biological effects of EMFs.

The focus of Chinese research is on non-thermal effects of EMFs, i.e to explore EMF biological consequence and its mechanism of action under no temperature change of exposed biological system. The data will guide us to get benefits from EMF good part and prevent EMF adverse health effects.

Chinese scientists believe that EMF's non-thermal effects have non-linear characteristics with obvious “frequency window” and “power density window” for the biological effects. Thus, we need to think about whether it is appropriate to employ linear analysis methods to judge the available data.

This review covered the main work done in China and published in domestic journals. Author apologizes to those whose work could not be cited due to space and my personal knowledge limitations.

Part I. The bioeffects of low-frequency electromagnetic fields

1. The effects of low-frequency electromagnetic fields on cell proliferation

Shu-de Chen et al. reported that only certain frequency ELF MF, which could fulfil the condition of K^+ cyclotron resonance, at intensity of 0.25×10^{-4} T inhibited growth of NIH 3T3 cells by using automated

cinematographic recording system (Chen S et al., 1993). They also observed there was difference between the changes induced by MFs and by lowering temperature, implying the intrinsic mechanisms are different. Both factors affected the dispersion of cell cycle distribution, but only the temperature change shifted the peak position of cycle distribution pattern (Chen S et al., 1994). Using MTT colorimetric assay, Chun-ming Huang et al. explored the effects of different frequency or flux density of ELF MFs on tumor cell SH-SY5Y and chromaffinoma PC-12 (Huang C et al., 1999a). Data showed that same MFs had different impacts on different cells, and same cells reacted diversely to distinct MF parameters (Table 1). Cui-lan Ding et al. reported that the inhibiting effects of 50 Hz sinusoidal MFs on human leukemia K562 cells and hybridomas WZDs were affected by the intensity of MFs (5-15 mT) and the exposure duration and times, suggesting there might have energy or bioeffect accumulation in the cells (Ding C et al., 1996).

Table 1 The effects of different parameters of ELF MFs on tumor cells

f (Hz) \ B (μ T)	0		25		50		75		100		300		500	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B
150		0	0	0	-	-	0	0		0				
300		0	0	+	-	0	-	0	-	0		-		0

A: SH-SY5Y cells. B: PC-12 cells.

0 means no reaction. - indicates inhibition and + represents promotion.

2. The effects of low-frequency EMFs on cellular signal transduction pathway

By employing a digital fluorescence image microscopy system, Chun-ming Huang et al. demonstrated that a 50 Hz, 100 μ T sinusoidal ELF magnetic fields significantly increased intracellular $[Ca^{2+}]_i$, whereas a static fields or a 2000 Hz one did not produce such an impact (Huang C et al., 2000). Based on nonlinear dynamic model for hormone-induced cytosolic calcium oscillations, he proposed this phenomenon would only happen when the frequency of MFs is close to the characteristic frequency of cytosolic calcium oscillations and the response of different cells to the same MFs might be different due to their distinct dynamic parameters (Huang et al., 1999b).

Prof. Huai Chiang at Bioelectromagnetics Laboratory of Zhejiang University chose certain intensities, which is lower than occupational exposure limit (0.5 mT) of ICNIRP for ELF MFs, to investigate the interaction between ELF MFs and cell signaling system and elucidate systematically its effects on intercellular communication and signal molecules in cellular membrane, cytosol, and nucleus.

i. Clarifying inhibition of the gap junctional intercellular communication (GJIC) function by ELF MFs and its mechanism of action (Li C et al., 1996, 1998, 1999; Hu G et al., 2001; Fu Y et al. 2002; Zeng Q et al. 2002a, b; Shen Y et al. 2002; Chiang H et al., 2002). 0.2mT MF enhances the GJIC suppression induced by TPA, while the inhibition threshold of ELF MFs alone is 0.4mT. The mechanism of GJIC inhibition by MFs is hyperphosphorylation and internalization of connexin protein, which could be elucidated by TEM analysis.

ii. Determining new interaction sites of ELF MFs with cell membrane (Zhou J et al., 2002; Shen W et al., unpublished data). ELF MFs can not only induce the clustering of EGF and TNF receptors on cell membrane, but also enhance the gene transcription of TNF receptor p75 and IL-6 receptor α .

iii. Demonstrating that ELF MFs activates several signal transduction pathways in cultured cells (Shen W et al., 1999, 2002a, b). ELF MFs induces the cellular protein tyrosine phosphorylation in a time-dependent manner, and activates the stress-activated protein kinase (SAPK) and p38 mitogen-activated protein kinase (p38 MAPK).

iv. Identifying two cellular transcription factors which can be activated by ELF MFs (Zhou J et al., 2002b, and unpublished data). ELF MFs enhances the binding activity of CREB (cAMP responsive element binding protein) and NF- κ B with specific DNA sequence.

v. Confirming that the noise magnetic field is one of the flexible methods to interfere the biological

effects of ELF MFs (Zeng Q et al., 2002a; Shen W et al., 2002c, and unpublished data). By using established biomarkers in the laboratory, they are able to confirm that noise MFs can interfere the GJIC suppression, SAPK activation, EGF and TNF receptor clustering induced by ELF MFs.

3. The effects of low-frequency EMFs on gene and/or DNA

Rui-ying Wu from Bioelectromagnetics Laboratory, Zhejiang University, reported that 0.4 and 0.8 mT MFs acted synergistically with carcinogen TPA to enhance *c-fos* transcription (Wu R et al., 1999a). MFs at 0.3 mT strengthened DNA damage induced by another carcinogen MNNG, and 1 mT alone broke DNA structure (Wu R et al., 1998). Lately, they identified 7 differentially expressed genes in Daudi cells exposed to 0.8 mT MFs by employing mRNA differential display technique (Wu R et al., 1999b), and cloned two of them (Wu R et al., 2000a, 2000b). Recently, Zhong T et al. identified another gene as Cytochrome Oxidase subunit 1, and revealed its responding universality in several MF-sensitive cell lines (Zhong T et al., 2002). Fan C et al. reported that 1.5 mT, 50 Hz MFs inhibited rDNA transcriptional activity of human T lymphocytes, suggesting its immune function was impaired (Fan C et al., 2000). However, Ding G et al. found that 5 mT MFs didn't change the mRNA level of p53 in MCF-7 cells by RT-PCR analysis (Ding G et al., 2002).

Based on reported scientific evidence, we concluded that the exposure limit for ELF MFs should be lower than 0.1 mT in order to prevent its possible health hazards.

Part II. The bioeffects of radio frequency electromagnetic fields

Wei-guo Liu et al. explored the effects of 900 MHz mobile phone signal at power densities of 0.025, 0.050 and 0.100 mW/cm² on cultured cerebral cortex neurons of newborn rat (Liu W et al., 2001). Data revealed that 12 h exposure of 0.050 mW/cm² or 8 h exposure of 0.100 mW/cm² caused outflow of lactate dehydrogenase (LDH) and cell death in a dose- and time-dependent manner, but not in the 0.025 mW/cm² exposure group. They concluded that long-term continual mobile phone radiation could damage rat cortical neurons *in vitro*. Prof. Baoyi Wang from Sichuan University investigated the *in vitro* effects of 915 MHz EMFs on membrane characteristics of rabbit red blood cells in a self-designed wideband transverse electromagnetic wave cell (BTEM CELL). Data showed that electromagnetic radiation with power density of 1, 3, 5, or 7 mW/cm² enhanced erythrocytes agglutination, suggesting an affinity increase of PHA receptor on membrane surface. Among them, 1 mW/cm² had the most significant impact. The authors reasoned that radiation induced a suitable conformation change of PHA receptor, which promote the interaction with its ligand PHA. Meanwhile, electromagnetic radiation blocked membrane's permeability, which is totally different from higher permeability induced by temperature increasing. Yang Chen et al reported that 17.8 MHz high frequency electromagnetic wave with power of 0.5, 0.8, and 1 W increased the ratio of sister chromatid exchange (SCE) in lymphocytes in a dose- and time-dependent manner.

Part III. The effect of electromagnetic pulse on cell function

Chen group at East China Normal University reported a two-phase response of fibroblasts to ELF pulsed electric fields ($f=50$ Hz, $t=20$ μ S, $E_{pp}=1$ V/m) (Zhang H et al., 1998). When the exposure time was less than 10 min, pulse fields stimulated dermal fibroblast cell proliferation with increasing membrane fluidity, which might be recovered after radiation. However, if the exposing time is more than 10 min, the cell proliferation was inhibited in accompany with decreased membrane fluidity. The data suggested that cell membrane fluidity is somehow related with cell proliferation status. Zhou F et al. revealed that 100 kHz transient electromagnetic pulses (EMP) stimulated the proliferation of lymphocytes, and 200 kHz one inhibited the cell proliferation instead (Zhou F et al., 2000).

Prof. Wang's lab studied the non-thermal bioeffects of weak transient EMP starting from mid-1990s (Wang B et al, 1996b; Liu Z et al., 1998, 1999; Zhang H et al., 1999, 2000). The employed EMP's electric field intensity is 10-20 V/cm, with a pulse width of 2.4 nS – 100 nS. Data showed that this kind of EMP caused severe damage of lymphocyte nuclei with multiple micronuclei and nuclear brokenness, and decreased the binding abilities of receptor protein on T cell membrane with sheep erythrocytes, which implied the damage of immune functions. By using scanning electron microscope, they found EMP radiation resulted in micropores on the membrane, and then formed electroporations, which was much bigger than the pore diameter produced by traditional strong electric fields.

Prof. Yao Guo's lab explored the bioeffects of electromagnetic pulse on human derived cells, and data showed that EMP reduced the cell survival ability, but the survival rate increased with time passing after irradiation, which is obviously different from the progressive decrease induced by ionizing radiation (Reng D et al. 2000). A group at Institute of Radiation Medicine, Academy of Military Medical Sciences,

investigated the effects of EMP on cell apoptosis (Cao X et al., 2002a, b; Zhao M et al., 2001a, 2002). The EMP used in experiments has electric field intensity of $6 \times 10^4 \text{V/m}$ with 20 nS rising time and 30 pulse width. The results indicated that EMP radiation not only inhibited cell proliferation of NIH 3T3 cells, and human lung carcinoma cell line A549 and GLC-82, but also induced cell apoptosis. Down-regulated protein level of bcl-2 and up-regulation of p53 expression were observed in irradiated cells, suggesting these two proteins involve in cell apoptotic process. As to rat hippocampal neurons, short EMP exposure (2min) damaged cell membrane with phenomenon of decreased membrane order and increased fluidity, and longer radiation caused cell apoptosis(Zhao Mei-lan, 2001b).

Part IV. Clinical application of EMF

The clinical application of electromagnetic fields is a hot-spot of EMF bioeffect research in China. Generally, EMF may relieve pain, accelerate wound and bone healing, treat cardiovascular disease and tumor, etc. To elucidate the mechanisms of action of various EMFs in medical practice, Chinese scientists have done huge number of in vitro experiments. I'll give few examples to go through this field.

1. The *in vitro* studies of EMF on bone healing

Qing-lin Kang et al found that the optimal parameters of low-frequency EMF to stimulate human embryonic tenocytes are at frequency of 1.7Hz, flux density of $5\text{-}6 \times 10^{-4} \text{T}$ (Kang Q et al., 1997). Further they proposed that ELF EMF might activate cAMP-PKA pathway, and then increase DNA synthesis and stimulate collagen secretion (Kang Q et al., 1998).Tang Q et al. reported that 1.15 mT, 50 Hz magnetic fields increased the percentage of S phase of osteoblasts, stimulated cell proliferation, and inhibited apoptosis, indicating one mechanism of EMF-enhancing fracture healing is to affect the growth of osteoblasts (Tang T et al., 1999).

2. The effects of EMF on cardiovascular system

The abnormal increase of blood viscosity is related with disease development. Either 50 mT rotating MFs or 200 mT static MFs improved deformability of erythrocytes, which might be used to low blood viscosity (Ke W et al., 1996; Wang Y et al., 2000). Meanwhile, MFs were demonstrated to increase electrophoresis speed of erythrocytes and platelet, suggesting MFs could be used clinically to treat thrombosis (Xie Z et al., 1997; Zhang Z et al., 1999). Jun Wen of the Fourth Military Medical University explored the possibility of improving hemorheological performance by using different $\Delta B/\Delta t$ 和 $\Delta E/\Delta t$ of pulsed electric or magnetic fields produced by EMG-1 type ELF EMF generator developed by themselves (Wen J et al., 2001, 2002). Data showed that EMP at $\Delta B/\Delta t = 2.5 \times 10^3 \text{T}\cdot\text{s}^{-1}$ or $\Delta E/\Delta t = 1.5 \times 10^9 \text{V}\cdot\text{m}^{-1}\cdot\text{s}^{-1}$ could decrease the blood apparent viscosity, the coagulation time, and the clotting strength, and increase erythrocyte electrophoretic mobility (EPM), which suggested this kind of EMPs might be used to treat blood hyperviscosity and hypercoagulation. Results also revealed that pulsed MF performed better than electric fields.

Percutaneous transluminal coronary angioplasty (PTCA) and in-stent is a main approach to treat coronary heart disease. However, coronary restenosis (RS) afterwards happened frequently, which is caused by blood vessel re-organization related with endothelial cells and hyperplasia of inner-vessel, mainly due to migration and proliferation of smooth muscle cells. A bunch of data demonstrated that constant and low frequency magnetic fields could inhibit the growth of smooth muscle cells and promote endothelial cell proliferation through enhancing the expression of nitric oxide synthase (NOS), indicating that these two kind of magnetic fields might be used to prevent or cure coronary RS (Lu A et al., 2000a, b; Feng X et al., 2001,2002; Hu T et al., 2001a, b, 2002).

In addition, Kou X et al. found that treating collected blood with 40 mT static magnetic fields improved the vitality of erythrocytes, thus prolonged storage time of blood at 4°C (Kou X et al., 1999).

3. The role of EMF in tumor therapy

Based on the evidence that certain types of EMFs might inhibit proliferation of tumor cells and induce its apoptosis, or might cause electroporation on cell membrane, thus facilitate the uptake of drug, it is generally accepted that EMFs may benefit tumor therapy.

Xiao-qiu Liu from Institute of Radiation Medicine, Chinese Academy of Medical Sciences, revealed that 250 Hz, 10 mT pulse magnetic field(PMF) induced HL-60 apoptosis by affecting its cell cycle, and enhanced significantly the cytotoxicity of ionizing radiation or anti-tumor drug 5Fu (Liu X et al., 1998a, b). By using much stronger PMFs, the data of Chang Xiao suggested that it could selectively inhibit the proliferation rate of human leukemia cells, but have no affection on normal lymphocytes (Xiao C et al., 1995). Ultra-wide EMPs with peak power density of 100W/cm^2 also damaged cultured lymphocytes (Wang Yong, 1998). Meanwhile, Static magnetic fields at 70-350 mT were reported to inhibit growth of a

variety of tumor cells, and increase cytotoxicity of anti-tumor drugs (He F et al., 1995; Han Z et al., 1997; Dong Q et al., 1997; Xia K et al., 1998; Xu Z et al., 1998; Yang Y et al., 1998).

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Session 3-3

RISK EVALUATION OF POTENTIAL ENVIRONMENTAL HAZARDS FROM LOW ENERGY ELECTROMAGNETIC FIELD EXPOSURE USING SENSITIVE IN VITRO METHODS (REFLEX)

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REFLEX, a project funded by the EU Commission, is the acronym for Risk Evaluation of Potential Environmental Hazards from Low Energy Electromagnetic Field (EMF) Exposure Using Sensitive in vitro Methods. The research is aimed at the investigation of cellular, sub-cellular and molecular responses of living cells exposed to EMF. Using the most powerful molecular biological tools currently available, the REFLEX project is to contribute to a better understanding of the biological effects of EMF. Since in many years of research epidemiology and animal experimentation were unable to answer the fundamental question whether or not EMFs may promote the development of chronic diseases such as cancer or neurodegenerative disorders, the main goal of the REFLEX project is to search for the fundamental mechanisms at the cellular and molecular level in the early stage of such diseases. (?) Most, if not all chronic diseases, including cancer and neurodegenerative disorders, are of extremely diverse and heterogeneous origin. This variability is to a great extent generated by a relatively small number of critical events. These are gene mutations, cell proliferation and apoptosis which are caused by or result in an altered gene and protein expression profile. The convergence of these critical events is required for the development of all chronic diseases. The REFLEX project is, therefore, designed to answer the question as to whether or not any of these disease-causing events might occur after EMF exposure in various cell systems..

The REFLEX data allow the conclusion that ELF- and RF-EMF produce genotoxic effects in vitro in various, but not all cell systems. Single and double DNA strand breaks are rapidly, but not error-free repaired as shown by various forms of chromosomal aberrations which follow the exposure. Furthermore, ELF- and RF-EMF affect the expression of various genes and proteins. This finding has already been

described by several other authors outside the REFLEX project. Since genotoxicity and gene expression may affect cell proliferation and apoptosis, which are - if not well balanced - the driving forces for the development of cancer and many chronic diseases, it will be most decisive to show whether or not such a relationship between these vital cellular processes and EMF exposure really exists. No convincing evidence was obtained in the REFLEX project to date that justifies such an assumption. The further elucidation of these biological effects should help to determine whether or not any health hazards may be associated with the use of EMF emitting devices at the presently allowed safety standards. Regrettably, the scientific database of these standards is rather poor. Therefore, one cannot exclude at present that it might be necessary one day to adjust them to a new reality. Our findings might show the way how science-based safety standards could be created.

The REFLEX findings do not provide an answer to the many open questions with respect to the significance of EMF exposure for human health, but they help to clarify where future *in vitro* EMF research should be directed to. New strategies and innovative concepts are urgently needed to make real progress in EMF research. Genomics and proteomics in the broadest sense may be the most powerful tools that can be applied in the search for and the understanding of EMF-induced mechanisms. They should allow to enable the unravelling of biological effects of EMF that might interfere with the functioning of cells and organs. Adequate research combined with adequate funding presupposed, the probability is rather high that the many still existing scientific uncertainties will find an answer in a not too far future.

Session 3-4

CELLULAR AND MOLECULAR EFFECTS OF ELECTROMAGNETIC FIELDS

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Summary: We designed and manufactured several equipments for exposure of cells to high-density (5 to 400 mT) ELF electromagnetic fields. This paper reviews our studies on genetic effects of ELF electromagnetic fields. There may be genotoxic activity due to exposure to high-density ELF electromagnetic field, such as 400 mT at 50 Hz. We observed significant increase in mutation at the HPRT gene and in expression of some genes in cultured cells after exposure to the 400 mT ELF electromagnetic field. Exposure of cells to the high-density 400 mT ELF electromagnetic field may affect the signal transduction in the cells, resulting in the enhanced gene expression.

Introduction: The increased use of electrical energy in modern society has subjected the general and working population to unprecedented levels of exposure to ELF electromagnetic fields. There has been speculation that ELF electromagnetic fields can act as promoters or co-promoters of cancer. Some epidemiological studies have revealed a positive association between exposure to ELF electromagnetic fields and the incidence of several types of cancer, particularly leukemia and brain tumors. However, other studies have failed to discern any association between ELF electromagnetic fields and the incidence of cancer.

In *in vitro* studies, the existence of the effects of the electromagnetic fields at low flux densities has been contradictory among reports. We designed and manufactured several equipments for exposure of cells to high-density (5 to 400 mT) ELF electromagnetic fields [1~3]. This paper reviews our studies on genetic effects of ELF electromagnetic fields.

Exposure units for ELF electromagnetic fields and X-rays: Details of the exposure units for 400 mT, 50 mT and 5 mT ELF electromagnetic fields were described elsewhere [1~3]. In brief, 5 mT (60 Hz \pm 0.1 Hz) ELF electromagnetic field exposure unit consists of a CO₂ incubator with a built-in magnet generator using two Helmholtz coils. For 50 mT (60 Hz \pm 0.1 Hz) ELF electromagnetic field exposure, the unit

consists of a magnet generator using two Helmholtz coils with a built-in CO₂ incubator. For 400 mT exposure, the magnetic field oriented vertically is generated by a pair of magnetic cores. An acrylic CO₂ incubator is installed between the cores. The power source is AC 200 V, 50 Hz (± 0.1 Hz), three phase, and 35 kVA. The waveform of these ELF electromagnetic fields was sine-wave. The temperature in the exposure space in these units was kept at 37 ± 0.2 °C. The mean induced current intensity in the outer ring of the 15 cm ϕ annular culture plate was estimated to be 115, 1150 and 7660 mA/m² at 5, 50 and 400 mT, respectively. For the control experiments, a conventional incubator in a separate room was used. The measured ELF electromagnetic fields in the conventional incubator was $< 0.5 \mu$ T. X-irradiation was performed using a Hitachi MBR-1520 at 150 kVp, 20 mA with 0.5 mm Al and 0.1 mm Cu filters with a dose-rate of 0.98-1.02 Gy min⁻¹ [4].

Gene expression: For the gene expression, the effect of 5 mT ELF electromagnetic field on *c-myc* mRNA expression was examined in Chinese hamster ovary (CHO) cells. No significant difference in the *c-myc* expression of CHO cells was observed with the ELF-field exposure, sham exposure and incubation in a conventional incubator [3]. Exposure of PC12-VG cells to 400 mT electromagnetic field enhanced the β -galactosidase gene expression stimulated by treatment of the cells with forskolin [5, 6]. The enhancing effect of the ELF electromagnetic field was inhibited by treatment of the cells with a specific inhibitor of PKC, calphostin C, as well as with the Ca²⁺ entry blockers nifedipin and dantrolen.

Enhanced expression of neuron derived orphan receptor (NOR-1) gene was also observed by exposure of CHO-K1 cells to 400 mT ELF electromagnetic field, but not to the 5 mT field [7]. The enhanced expression, reaching the maximum at 6 h, was transient and reduced to the control level after exposure to 400 mT ELF electromagnetic field for 24 h. The NOR-1 expression induced by treatment with forskolin and TPA was further enhanced by the simultaneous treatment with 400 mT ELF electromagnetic field, in which the maximum response was at 3 h.

Mutation: For the mutation induction, exposure to ELF electromagnetic field at 400 mT induced mutations in the hypoxanthine-guanine phosphoribosyl transferase (HPRT) gene of human melanoma MeWo cells [8 ~10]. The mutant frequency was enhanced both by increasing the exposure period and the induced current intensity. Mutations induced by X-rays were enhanced by the ELF electromagnetic field exposure. No significant increase in mutant frequency occurred when DNA replication was inhibited during ELF electromagnetic field exposure. Mutation induced by the ELF electromagnetic field increased during the DNA-synthesis phase in synchronously growing phase.

DNA replication error is suspected of causing the mutations produced by ELF electromagnetic field exposure.

Whether exposure to ELF electromagnetic fields at low flux densities induces mutations is debatable. We investigated the effect of long-term exposure to 5 mT ELF electromagnetic field at 60 Hz on mutant frequency. CHO-K1 cells were exposed or sham-exposed to the 5 mT ELF electromagnetic field for up to 6 weeks with or without X-irradiation (3 Gy), and the mutant frequency of the HPRT gene was analyzed [11]. Long-term exposure to 5 mT ELF electromagnetic field did not increase mutations, suggesting a threshold for mutation induction greater than a magnetic density of 5 mT. However, enhancement of the X ray-induced mutation rate was observed after treatment with X-irradiation followed by long term exposure to 5 mT ELF electromagnetic field.

These results suggest that exposure to more than 5 mT ELF electromagnetic field may promote X-ray-induced mutations.

Conclusion: Most of the published experimental results suggest that very low-density ELF electromagnetic fields do not have a clearly demonstrated potential to cause genotoxic effects. However, there may be genotoxic activity due to exposure to high-density ELF electromagnetic field, such as 400 mT at 50 Hz. We observed significant increase in mutation at the HPRT gene and in expression of some genes in cultured cells after exposure to the 400 mT ELF electromagnetic field. Exposure of cells to the high-density 400 mT ELF electromagnetic field may affect the signal transduction in the cells, resulting in the enhanced gene expression. These positive effects of the ELF electromagnetic field were not observed at lower density ELF electromagnetic field, such as 5 mT. There may be a threshold for mutation induction and gene expression, at least over the magnetic density of 5 mT.

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Session 3-5

GENE EXPRESSION PROFILING EXERTED BY MAGNETIC FIELDS (MF) OF 50 Hz AT 1.2 μ T AND 100 μ T IN AN MF-SENSITIVE MCF-7 CELL

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Background: Wertheimer and Leeper (1) reported a nearly threefold increase of breast cancer risk among women younger than 55 who lived near power lines, suggesting that MF exposure had accelerated development and growth of breast cancer. Stevens (2) hypothesized that MF can affect pineal gland melatonin secretion *in vivo*, which, in turn, can influence mammary (breast) carcinogenesis. Since then, a number of experimental studies have been conducted in order to test this hypothesis.

In *in vitro* studies, Blask and colleagues (3) demonstrated that melatonin at physiological levels inhibits MCF-7 human breast cancer cell growth. Using MCF-7 cells obtained from Blask, Liburdy (4) reported that MF inhibited the antiproliferative effects of the hormone, allowing the cancer cells to grow in the presence of melatonin. We previously also used MF-sensitive MCF-7 cells provided by Dr. Liburdy in order to reveal the molecular mechanism of the biological effects of MF and found that MF exposure causes the uncoupling of the melatonin signal transduction pathway (5). Thus, MF certainly exerts its effects on protein levels.

In this study, we examined whether MF would alter the levels of gene expression.

Methods:

Cell culture and MF exposure. MCF-7 cells were kindly provided by Dr. Liburdy (UCLA, Berkley) and grown in Dulbecco's modified Eagle's Medium (Invitrogen, Carlsbad, CA) supplemented with 10% FBS

(Gibco BRL), penicillin (100 U/ml), and streptomycin (100 µg/ml) in a humidified atmosphere of 95% air: 5% CO₂ at 37°C. The cells were subcultured (1:4) 1 to 2 times per week. In order to expose the cells to magnetic fields, a 50 Hz sinusoidal MF was generated in a mu-metal chamber with four Merritt-coil devices. The mu-metal chamber was a cube that was constructed of nickel (80%) and trace metals. The chamber had four ventilation holes (2.54 cm in diameter) on the top and bottom. A temperature probe was placed inside the chamber to monitor temperature continuously. The anti-parallel mode of operation generated opposing magnetic fields that cancelled and resulted in a true sham exposure. When a current was applied to the parallel configuration, a magnetic field was established. Two identical exposure systems were employed in this study. Each coil system was driven by identical signal generators obtained from NF Electronic Instruments Corp. (Yokohama, Japan). Cell viability was determined by means of the crystal violet staining method.

DNA array analyses. Total cellular RNA was isolated from control and MF-treated cells (1.2 µT or 100 µT; one week) by single-step guanidinium thiocyanate-phenol- chloroform extraction. The first strand DNA was synthesized using Moloney murine leukemia virus reverse transcriptase (Invitrogen) with random heximers as primers. The quality and quantity of RNA was measured by spectrophotometry and electrophoresis on denaturing agarose gel. Fluorescent-labeled cDNA probes were synthesized from 10 µg total RNA in the presence of dATP, dCTP, dTTP, dGTP, aminoallyl-dUTP, Cy3 mono-reactive dye (Amersham Pharmacia Biotech, NJ), Cy5 mono-reactive dye (Amersham Pharmacia Biotech), and PowerScript reverse transcriptase (Clontech). The labeled cDNA was purified using Atlas NucleoSpin Extraction Spin Columns (Clontech). Atlas glass Human 1.0 Microarray (Clontech) were prehybridized in GlassHyb hybridization buffer, containing the sheared salmon testes DNA for 30 min at 50 °C in a hybridization chamber (Clontech). The heat-denatured probe was hybridized overnight at 50 °C. The arrays were washed with 2 x SSC (1 x SSC = 150 mM NaCl/ 15 mM sodium citrate, pH 7.0) twice at room temperature for 5 min, twice with 2 x SSC plus 1% SDS at room temperature for 30 min, and twice with 0.1 SSC plus 0.5% SDS at room temperature for 30 min. The arrays were then scanned. Image acquisition and quantification were performed using an AtlasImage (Clontech).

Results: There were 1,081 genes on Atlas glass Human 1.0 Microarray. The gene expression levels were calculated as the ratio of the control cells. The levels of gene expression of 95% genes were unchanged. There were 39 genes in which the expression level was increased more than 2-fold, whereas the expression levels of 12 genes were decreased less than 2-fold by MF exposure (1.2 µT for 1 week). The similar patterns of gene expression were obtained by exposure of 100 µT MF for 1 week. The extents of the expression were also similar. The highest was about 6-fold.

Conclusion: We previously demonstrated that MF exerted its effects on the protein levels in an MF-sensitive cultured cell, seen as a disruption of protein-protein interactions in a melatonin-signaling pathway. It is still unknown what molecule would escape the inhibitory pathway of the hormone, in turn leading to carcinogenesis. In the present study, we examined the effects of MF on gene expression levels in MF-sensitive MCF-7 cells using DNA microarray. The gene expression of some oncogenes was increased and that of others was decreased by MF exposure. The patterns were similar in MF exposure of both 1.2 µT and 100 µT. The pathological roles of these alterations remain to be determined.

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Session 4-1

WORLD-WIDE EXPERIMENTAL RESEARCH OF ON EMF BIOEFFECTS RELATED TO HEALTH-RISK ASSESSMENT

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In the last two decades experimental research on biological effects of electromagnetic fields has increased greatly because of the rapid development of the electromagnetic environment in particular in the ELF and RF ranges. Data obtained in the laboratory on humans, animals and cells are used for risk analysis when they are of sufficient quality by experts groups such as ICNIRP.

The most recent development of the research world-wide will be described in terms of scientific findings, improvements in exposure systems, harmonization of protocols, and funding.

Major research programmes have been launched and some of them are in progress. An overview of these research efforts will be given along with the means implemented to determine the gaps in knowledge and foster the relevant research.

New techniques have recently been available in biology that may help get new answers. Their relevance in terms of risk analysis will be discussed.

There are currently disagreements on the interpretation of laboratory data in terms of human health assessment and risk analysis. The scientific journals, reports, Web and media are giving contradictory opinions that need clarification. Some thoughts will be shared about the current scientific and social situation and the consequences thereof for standardization of exposure limits and development of technology.

Session 4-2

BIOLOGICAL EFFECTS OF RADIOFREQUENCY ELECTROMAGNETIC RADIATION

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A review on recent research on biological effects of radiofrequency radiation (RFR) will be presented. There is no question that RFR affects functions in cells and living organisms. One important determinant of the effects is the amount of energy deposited in or absorbed by the exposed object. In addition, there are some indications that biological effects may also depend on how the energy is deposited. Different propagation characteristics such as 'modulation,' or different waveforms and shapes may have different effects on a living system. Different biological effects may result depending on the intensity, waveform, and duration of the exposure.

Biological effects can occur after exposure to high intensity of RFR that cause general or local heating. However, effects have also been reported in cells and animals after exposures to very low-intensity RFR that apparently cannot cause a significant increase in temperature. Actually, some of these reported effects occurred at surprisingly low intensities or SARs. It is apparent that low-intensity RFR is not biologically inert.

The majority of the biological studies on RFR have been conducted with short-term exposures, i.e. a few minutes to several hours. Little is known about the effects of long-term exposure. What are the effects of long-term exposure? Does long-term exposure produce different effects from short-term exposure? Do effects accumulate over time?

For decades, there have been questions about whether an effect of RFR is thermal (i.e., a significant

change in temperature) or non-thermal (i.e., no significant change in temperature). However, we actually don't need to know whether RFR effects are thermal or non-thermal to set exposure guidelines for RFR exposure. Most of the studies on biological effects of RFR carried out since the 1980's were under 'non-thermal' conditions. In studies using isolated cells, the ambient temperature during exposure was generally well controlled. In most animal studies, the RFR intensity used usually did not cause a significant increase in body temperature of the animals exposed. There are experimental arguments supporting the existence of 'non-thermal' effects.

Session 4-3

EFFECTS OF ELECTROMAGNETIC RADIATION ON ANIMALS (REVIEW OF CHINESE PAPERS)

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The literatures published in Chinese journals about the effects of electromagnetic radiation on animals were reviewed. Various exposure parameters were involved, including extremely low frequency magnetic field (ELMF), microwaves, millimeter waves, high peak pulse microwaves, both pulsed and continuous, both acute and chronic, etc. The animals used in the experiments consisted of mice, rats, rabbits, dogs and monkeys. The investigated effects involved the morphological, functional, biochemical, genetic, physiological, behavioral and cognitive aspects. Series of studies trying to confirm the cancer initiating or promoting capability of electromagnetic radiation were also involved.

For ELMF, the effects on cardiovascular, nervous, immunity, reproductive, endocrine systems, and skin were studied. The effects of ELMF on brain function under weightlessness condition were also studied. The results showed well correlations with the power density, and "cumulative effect" and "window effect" in some experiments, e.g. rabbits and mice were whole bodily exposed to 0.1 Hz 25~100 mT alternate or constant magnetic field intermittently for 7 or 14 days or to 3 mT alternate magnetic field continuously for 5 or 10 days. The results showed that magnetic field has the effects of dilating micro-vessel and improving microcirculation, and these effects will increase gradually with the increased field intensity. The synthesis and secretion of neuropeptides would be inhibited in the low intensity and promoted in the high intensity magnetic field, and the activation of marrow cells will be promoted prominently in 75 mT field intensity. For cancer studies, it was proved that the spontaneous incidence of cancer were not changed by ELMF, but enhanced by known carcinogens, whereas the growth of implanted tumors was alternated.

For microwave radiation, a lot of papers were published about the effects on reproductive system; the effects on cardiovascular, nervous, immunity system and eye were also studied. For morphological, functional, physiological and behavioral studies, the effects were closely correlated with temperature increase induced by microwave irradiation, but not for biochemical effect, e.g. the effects of 1, 2, 5 and 10mW/cm² microwave irradiation on Ca²⁺, Mg²⁺-ATPase activity of cerebral cortex, hippocampus, and thalamus of mice showed that different densities of microwave irradiation resulted in different reactions. In rats underwent 1mW/cm² exposure, the activity of Ca²⁺, Mg²⁺-ATPase of cerebral cortex, hippocampus, as well as thalamus increased significantly (P<0.05) compared with controls. For the rats underwent 5mW/cm² exposure, Ca²⁺, Mg²⁺-ATPase of in the preceding brain areas were not changed obviously, while it was in significantly decreased in cerebral cortex and hippocampus after exposed to 10mW/cm², and that in thalamus was not changed significantly.

For effects of millimeter wave on animals, the frequency of 33.3, 36.06, 36.11, 37.4, 42.2, 53.0, 60 GHz and power density of 0.1, 0.5, 1, 2, 3, 4, 6, 8, 10mW/cm² were used. Nearly all of the systems of the animals were studied in the experiments. The characteristics of effects of millimeter wave implied the existence of cumulative effects which was induced by nonthermal mechanisms. The threshold was

4-6mW/cm² for most selected measures. Damages resulted from millimeter wave increased with the increasing power density. In one experiment, BALB/c mice of 2 month old were separately exposed to millimeter wave at 53 GHz frequency with power densities of 1, 3, 5, 8mW/cm² for 2h daily from the 6th to 15th day of gestation. The test of learning capacity and memory of adult offspring was undertaken on Y-shaped maze. The content of cholinergic M receptor (M-R) and its affinity to ligand, the levels of monoamine transmitter and AVP in the brain of the fetus at full term and adult offspring were measured by using RBA, HPLC-ECD and RIA respectively. The results showed that millimeter wave at power densities of 3, 5, 8 mW/cm² depressed learning capacity and memory of adult offspring, and it also significantly increased the content of M-R in hippocampus of adult offspring and reduced the content of DA in brain of adult offspring and fetus at full term. Exposure at power density no less than 5mW/cm² significantly reduced the content of AVP in hypothalamus of adult offspring. There was a significant correlation among the parameters and power densities. This experiment suggested that the threshold of fetus injury induced by millimeter wave irradiation to pregnant mice at frequency of 53GHz is 1~3mW/cm². The decrease in learning capacity and memory of the adult offspring may be related to the decrease of the contents of AVP, DA in the brain, as well as reduced function of cholinergic nerves in the hippocampus. Another characteristic of the bio-effects of millimeter wave is "distant effect".

The pulsed microwaves with very high peak amplitude and extremely fast rise time with a wide bandwidth of frequency but low average power showed some different biological effects from other kinds of exposures. From the published data, the bio-effects induced by pulsed microwaves were nonthermal effect, which correlated with the rise time, power density and repetition rate. The central nervous system, reproductive system, cardiovascular system, as well as the kidney, retina, iris and corneal endothelium were reported to be susceptible to pulsed field. More research is needed to elaborate its mechanisms.

The data selected from different lab. Further research is needed to determine the significance of the effects on animals. Repetition and extension are needed in future investigations.

Session 4-4

ACUTE EFFECTS OF LOCAL EXPOSURE TO RADIO-FREQUENCY ELECTRO-MAGNETIC FIELDS WITH A LOOP ANTENNA ON THE CEREBRAL MICROCIRCULATION IN RATS

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Background: Biological effects of radio-frequency electromagnetic fields (EMF) on the blood-brain barrier (BBB) function has been extensively studied in experimental animals. Most of these studies, however, have been performed by the histological or morphological investigations due to postmortem examination. Besides these, little information are available about the exposure effects of EMF on cerebral microcirculation. A closed cranial window (CW) method have been widely used among many researchers as a beneficial method to investigate the cerebral microcirculation including BBB function [1]. We partially modified this method for evaluating the exposure effect to EMF on the cerebral microcirculation. Our previous results from acute exposure effects of EMF using a monopole antenna showed that no noticeable changes have been recognized due to EMF exposure [2]. The present study aims to investigate the acute exposure effect of EMF on the cerebral microcirculation in rats using the loop antenna that enabled more local exposure to the brain than the monopole antenna does.

Methods: Nineteen male Sprague-Dawley rats (B.W. 426±19 g) were used in the study. Both CW implantation and the intravital-microscopic observation were performed under anesthesia with a cocktail (100mg/kg i.m.) of Ketamine hydrochloride and Xylazine hydrochloride (10:1, w/w). EMF exposure system consisted of a small anechoic chamber and a loop antenna. The head of rat was positioned 2mm

under the loop antenna and was locally exposed to 1,439MHz electromagnetic near-field TDMA (time division multiple access) signal for PDC (Personal Digital Cellular, Japanese cellular telephone standard) system. The intensity of EMF exposure was controlled by average specific absorption rate (SAR) of the brain at 0.53-0.88, 5.3-8.8, and 20-33W/kg. The EMF exposure duration was 10 minutes. After exposure to EMF, the animal's head was immediately positioned in a stereotactic frame for microscopic observations. The exposure for 10 min and the observation for 20 min were performed sequentially from the smallest SAR value. The pial microcirculation within a CW was investigated by a fluorescent microscope equipped with an SIT camera and a confocal scanning laser microscope. In order to measure hemodynamic changes, plasma velocities, leukocyte behavior and BBB-function, two-types of fluorescent dye and fluorescent microparticles were administered via the tail vein. Results are given as means±s.e. mean. The statistical analysis was performed by Student's t-test or ANOVA.

Results: In order to investigate the detail of hemodynamic changes and leukocyte behavior in the pial venule, each parameter was separately measured at postcapillary venule (8-30µm) and collecting venule (31-50µm).

1. The values of vessel diameters did not significantly change between pre- and post-exposure at any SAR values.
2. The maximal plasma velocity in the collecting venule was significantly decreased ($p<0.01$) due to EMF exposure at 2.0W/kg SAR, however, there were no significant changes in postcapillary venule due to EMF exposure at any SAR values.
3. In order to evaluate the permeability of BBB due to exposure, sodium-fluorescein was administered after each exposure. Extravasation of sodium-fluorescein from the pial venule was measured with the confocal scanning laser microscopy. In all measurement points, the fluorescent intensity profile did not change at any SAR values. FITC-Dx was administered before EMF exposure in order to detect the extravasation of dye during exposure. The fluorescence in the brain surface within pial microcirculation was measured with the fluorescent microscopy until the end of experiment. However, there was no significant difference between sham group and exposure group in the fluorescent intensity at any SAR values.
4. The numbers of sticking and rolling leukocyte to the pial venular endothelia were measured. The number of sticking leukocyte did not significantly different between pre- and post-exposures. The number of rolling leukocyte tended to decrease corresponding to increasing SAR values. The number in the collecting venule at 5.3-8.8W/kg SAR was significantly decreased ($p<0.05$) compared with those of pre-exposure.

Conclusion: In the present experiment, we used a loop antenna for more local EMF emission to the rat brain. The average whole body SAR was less than 1/20 of the average brain SAR. The average whole body SAR used in the present study keeps below the level that may cause thermal effect due to EMF exposure.

No extravasations of both sodium-fluorescein and FITC-Dx from the pial venul were observed following EMF exposure at any SARs. This indicates that no disruption of the BBB function have been recognized due to EMF exposure emitted from the loop antenna which agrees with our previous results using the monopole antenna [2]. An increase of sticking leukocytes to the pial venular endothelia is closely related to induce to the disruption of BBB [3]. In the present experiment, the number of rolling cell decreased due to EMF exposure at 0.53-0.88W/kg SAR, however, it was also found that there were no changes in the number of the sticking leukocyte after exposure of EMF at any SARs. This finding may support a hypothesis that EMF exposure does not disturb BBB function.

The plasma velocity of the collecting venule significantly decreased at 5.3-8.8W/kg SAR. However, the venular diameter, which is associated with the change of a blood flow, was not affected at any SARs. Thus, further studies on this dissociation are needed.

Whereas the number of sticking leukocyte did not change after EMF exposure, the number of rolling leukocyte tended to decrease corresponding to the increase in brain SAR. However, no significant differences were recognized between the values of pre- and post-exposures, except for the values obtained from collecting venule at 0.53-0.88W/kg SAR. In this study, we may need to consider a temporal effect of anesthesia, for one experimental sequence was 110 min from the beginning to the end. The changes in rolling counts and plasma velocity may be affected with the depth of anesthesia.

In conclusion, the results suggested that no noticeable changes in the BBB function, the venular diameter, and the number of sticking leukocyte under the present EMF exposure conditions. However, a temporal effect may relate with the changes of plasma velocity and rolling leukocyte counts. Further investigations are required.

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Session 4-5

ALBUMIN LEAKAGE AND NERVE CELL DAMAGE IN RAT BRAIN AFTER WHOLE BODY EXPOSURE IN TEM CELLS TO MICROWAVES FROM GSM MOBILE PHONES

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Background: Since 1988, we have studied in a rat model the effects of microwaves at 915 MHz upon the blood-brain barrier (BBB) of the brain capillaries. In series of more than 1600 animals, we have studied the effect from both pulse-modulated and continuous RF fields— including those from real GSM mobile phones. We have shown that microwave exposure at sub thermal levels gives rise to a significant leakage of albumin through the BBB of exposed rats. The albumin diffuses out into the brain tissue and accumulates in the neurons and glial cells surrounding the capillaries [1-3]. Similar results have been found in other laboratories [4,5] while others have not been able to record the albumin leakage. In the present study including 142 rats we have investigated the long term albumin leakage over the BBB and whether it might cause damage to the neurons.

Method: In the present study 32 young rats were exposed during two hours to 900 MHz microwaves emitted by a GSM mobile phone. Three groups of each 8 rats were exposed in TEM cells to average whole-body specific absorption rates (SAR) of 2 mW/kg, 20 mW/kg and 200 mW/kg, respectively. Eight rats were simultaneously kept for 2 hours in non-activated TEM-cells. By the end of the period they were anaesthetized and sacrificed by perfusion-fixation with 4% formaldehyde. Brain slices were stained for RNA/DNA with cresyl-violet to show damaged (dark) neurons and with albumin antibodies (Dakopatts) to reveal albumin as brownish spotty or more diffuse discolorations.

Results: When the rats were sacrificed at 50 days after exposure we found that exposed animals usually showed several albumin positive foci around the finer blood vessels in white and grey matter. The albumin had spread in the brain tissue between the cell bodies, and surrounded neurons, which were either free of albumin or in some foci containing albumin. We found highly significant ($p < 0.002$) evidence for neuronal damage (dark) neurons in cortex, hippocampus and the basal ganglia in the brains of the exposed rats. The occurrence of dark neurons under the different exposure conditions shows a significant positive relation between EMF dosage (SAR: 2-200 mW/kg) and number of dark neurons.

Conclusion: We have found evidence for neuronal damage caused by non-thermal microwave exposure from a GSM mobile telephone. Damaged neurons are recorded in the cortex as well as the hippocampus and the basal ganglia in the brains of exposed rats. Although the present study comprises few animals, the

combined results are highly significant and exhibit a clear dose-response relation. The neuronal albumin uptake and other changes described would seem to indicate a serious neuronal damage, which may be mediated through organelle damage with release of not only hydrolytic lysosomal enzymes but also e.g. sequestered harmful material, such as heavy metals, stored away in cytoplasmatic organelles (lysosomes).

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Session 4-6

MICROWAVES EMITTED BY MOBILE PHONES DAMAGE NEURONS IN THE RAT BRAIN

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Background: We have earlier described the effects of continuous wave (CW) and pulsed modulated microwaves at 915 MHz upon the blood-brain barrier (BBB) in rats exposed in TEM-cells, and have shown that they give rise to a significant leakage of albumin through the BBB of exposed rats as compared to non-exposed animals, and with an uptake of albumin in neurons and glial cells^(1,2). These results are duplicated recently in another laboratory⁽³⁾. We have now examined whether a pathological leakage over the BBB might be combined with permanent damage to the neurons and have recently published such results for the first time⁽⁴⁾

Methods: Thirty-two male and female Fischer 344 rats, aged 12 - 26 weeks, were divided into 4 groups of each 8 rats. The peak output power from the GSM mobile telephone fed into two TEM-cells simultaneously for 2 hours were 10 mW, 100 mW and 1000mW per cell, respectively. This exposure resulted in average whole-body specific absorption rates (SAR) of 2 mW/kg, 20 mW/kg and 200 mW/kg, respectively during the exposure in the TEM-cells of the awake rats. The fourth group of rats was simultaneously kept for 2 hours in non-activated TEM-cells. The animals in each group were allowed to survive for about 50 days after exposure. Then they were anaesthetized and sacrificed by perfusion-fixation with 4% formaldehyde. The brains were removed and sectioned coronally in 1-2 mm thick slices, which all were embedded in paraffin and cut at 5 micrometer, stained for RNA/DNA with cresyl violet to show dark neurons. The microscopical analysis was performed blind to the test situation. The occurrence of "dark neurons" was judged semi-quantitatively by the neuropathologist as 0 (no or occasional dark neurons), 1 (moderate occurrence of dark neurons) or 2 (abundant occurrence). The Kruskal Wallis one-way analysis of variance by ranks was used for a simultaneous statistical test of the score distributions for the 4 exposure conditions. When the null hypothesis could be rejected, comparisons between controls and each of the exposure conditions was made with the Mann-Whitney non-parametric

test for independent samples.

Results: In one control animal a moderate amount of dark neurons were observed, while in all the other controls no such change was present. In the exposed animals scattered and grouped dark neurons were seen in all locations, but especially the cortex, hippocampus and basal ganglia, mixed in among normal neurons. In animals exposed to 2 mW/kg, 4 had no dark neurons, 2 had moderate occurrence and 2 had abundant occurrence, for 20 mW/kg the corresponding numbers were 0, 4 and 4, and for the 200 mW/kg they were 1, 2 and 5 respectively. A significant positive relation between EMF dosage (SAR) and number of dark neurons was shown for 20 mW/kg: $p=0.01$ and for 200 mW/kg: $p=0.03$. A combined non-parametric test for the 4 exposure situations simultaneously revealed, that the distributions of scores differed significantly between the groups ($p<0.002$).

Conclusion: The reason for our choice of 12 to 26 weeks old rats is that they are comparable to human mobile phone addicted teen-agers with respect to age. The intense use of mobile phones by youngsters is a serious memento. A neuronal damage of the kind, here described, may not have immediately demonstrable consequences, even if repeated. It may, however, in the long run, result in reduced brain reserve capacity that might be unveiled by other later neuronal disease or even the wear and tear of ageing.

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Session 4-7

CRITICAL EVALUATION OF IN VITRO AND RELATED IN VIVO REPORTS OF RADIO FREQUENCY EXPOSURES

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Objective 1: The first objective is to make the distinction between a biological effect reported to be due to a radio frequency exposure, and the suggestion of an adverse human health effect.

Conclusion 1: A positive indication reported for in vitro systems, even when substantiated, does not prove that the effect leads to subsequent biological events. It is these biological events which can have a physiological effect in vivo. A physiological effect must be established before any statement can be made about a human health effect. The human health effect could be beneficial as well as adverse.

Objective 2: The second objective is to present a list of experimental details that are important to consider in designing experiments. Information about these details is essential to include in a publication.

Conclusion 2: The absence of these details from the publication at best would lead to the paper being of no or marginal assistance for establishing the presence or absence of an RF effect. At worst, the absence of detail would lead to speculation that the study was not performed properly.

Objective 3: The third objective is to discuss scientific information about radio frequency exposures of

different kinds and durations and cell toxicity.

Conclusion 3: A wide range of short term and chronic low level exposures in vitro and in vivo do not result in cell death; i.e., RF is a non-toxic agent.

Objective 4: The fourth objective is to critically examine a number of published positive reports that RF exposures cause genetic damage.

Conclusion 4: The weight of evidence available today supports the conclusion that radio frequency exposures of different types are not genotoxic. The types of evidence to be discussed include the induction of DNA strand breaks, chromosome aberrations, micronuclei formation, DNA repair synthesis, sister chromatid exchange, and phenotypic mutation. In some instances, the interaction of RF with chemical agents will be discussed. The conflicts between biological events that would arise if some reported RF effects occurred will also be discussed.

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Session 5-1

STATE-OF-THE-ART OF MEASUREMENT AND SIMULATION TECHNIQUES OF DOSIMETRY AND LOCALIZED TEMPERATURE HOTSPOTS

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The need for accurate experimental and numerical dosimetry has become more pronounced during the last decade. Requests have been made by bodies setting standards for compliance testing as well as by WHO, identifying an urgent need for improved dosimetry in bioexperiments. Significant progress has been achieved in all areas of dosimetry.

Experimental Dosimetry and Compliance Testing

The scientific basis, technology and measurement guidelines [IEC62209, IEEE 2003, ARIB] for compliance testing of mobile phones operating next to the ear has been developed during the 1990' s. This encompasses greatly improved probes integrated into scanning systems, appropriate phantoms and advanced procedures enabling the provision of conservative exposure assessment for handheld mobile phones [IEEE 2003, Schmid et al. 1996, Kuster and Balzano 1996, Kuster et al. 1997, Kuster 1998]. The accuracy of calibration procedures for tissue simulating liquids has been enhanced by several factors [Meier et al. 1996, Pokovic 1999]. Precision of better than 20% is currently state-of-the-art for compliance testing. Most recently, the technique has been extended to 6 GHz, the probes for which require a diameter of smaller than 3mm. For body-worn applications, improved scientific data are needed before scientifically sound and conservative compliance procedures can be established.

Spatial resolution for specialized dosimetric probes has been pushed to below 1mm³, even with diode-loaded probes [Pokovic et al. 2000b]. These probes show low boundary effects and enable measurements closer than 0.5mm from material boundary interfaces. Typical applications are reference measurements and assessment of SAR distributions inside tiny structures, such as rodent tissues or Petri dishes, etc. Novel probes enable assessment of the polarization [Pokovic et al. 2000a] as well as measurements in the time or frequency domain based on electro-optical or active sensors [e.g.,

Heinzelmann et al. 2000, Mann and Petermann 2002].

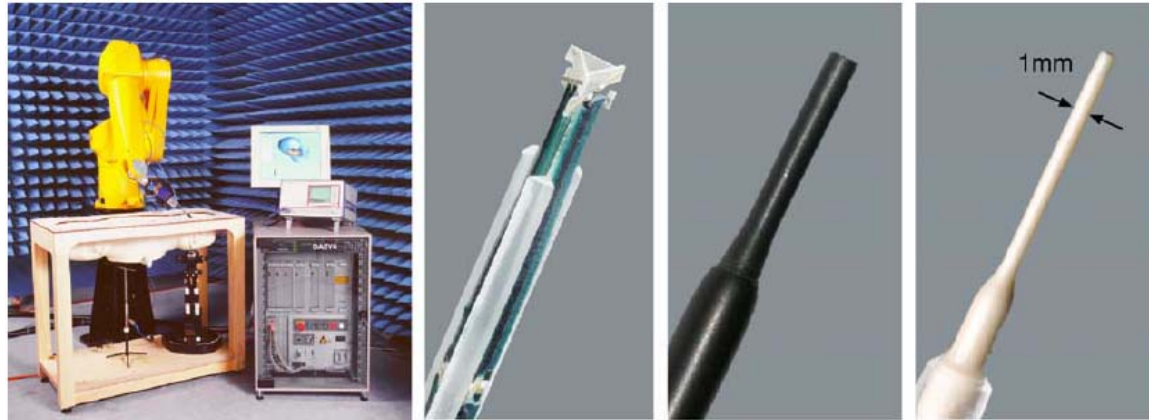


Figure 1: State-of-the-art scanning system for compliance testing and specialized dosimetric assessment as well as for general near-field evaluations, such as base stations, etc. (left). Advanced high sensitivity probe with interleaved dipoles (2nd from left), isotropic probe suitable for standard evaluation of up to 6 GHz with a tip diameter of only 2.5mm (2rd from right) and probe with a spatial resolution of better than 1mm³ for highly specialized dosimetric evaluation (right).

Numerical Dosimetry

Significant progress has also been achieved in computational electromagnetics, offering more stable algorithms and greatly enhanced computational power. Spatial resolutions of better than 0.1mm have become state-of-the-art [Chavannes and Kuster 2003]. Today, various numerical animal and human models are available with resolutions of much better than 1mm. Knowledge about the interaction of transmitters in the vicinity of the body has also greatly increased [Burkhardt and Kuster 1999]. There is a clear need for TCAD tools providing resolutions of better than 0.01mm in order to enable direct PCB layouts into electromagnetic models. New solvers such as ADI-FDTD have recently been introduced, promising great potential for dosimetric applications [Staker and Holloway 2003].

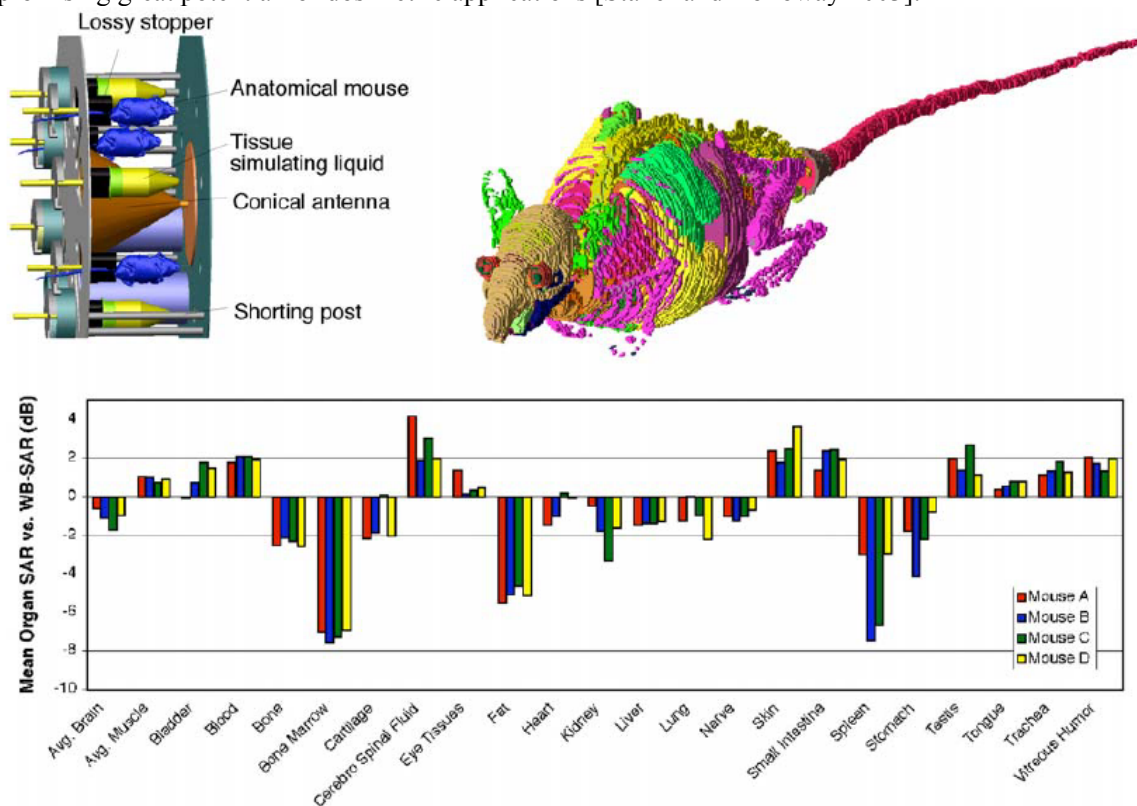


Figure 2: Numerical model of an exposure apparatus for *in vivo* studies (top left). Advanced numerical phantoms of animals with a spatial resolution of better than 0.1mm³ (top right). An example for dosimetric organ-specific evaluations (bottom).

Localized Temperature Hotspots

Localized temperature hotspots are a major source of artifacts for *in vitro* and *in vivo* experiments and require special attention. Highly sensitive probes with spatial resolutions of smaller than 0.01mm³ have been developed, enabling the detection of very localized hotspots. The sensitive area of the currently smallest probe is based on a highly resistive 0.05 x 0.1mm layer of amorphous germanium processed on a glass tip. The temperature resolution of the probe is 4mK. The small dimensions allow measurements with a distance as close as 0.15mm from solid boundaries and provide a short response time in the order of 10ms. Its performance thus also allows dosimetric measurements in strong absorption gradients [Schuderer et al. 2004]. Thermal and coupled electromagnetic-thermal solvers have also become available and are suitable for the assessment of thermal loads and localized hotspots in bioexperiments [Van Leeuwen et al. 1999, Samaras et al. 2000].

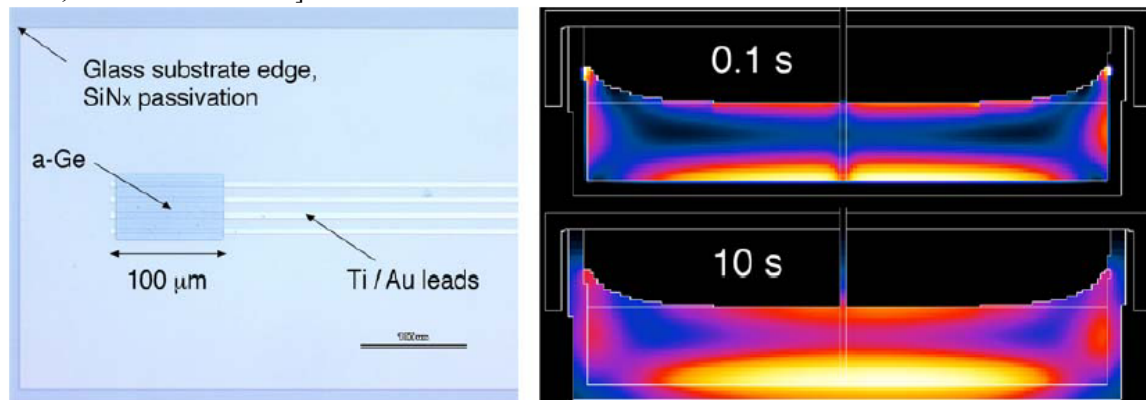


Figure 3: Sensor head based on an amorphous germanium layer, processed on a Pyrex glass substrate and connected via titanium gold conduction paths (left). Temperature distribution dependent upon exposure duration, normalized to the corresponding maximum values of the shown slices (right).

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Session 5-2

PHYSICAL ASPECTS OF EMF NEEDED FOR BIOLOGICAL STUDIES

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Introduction: Considerations of physical aspects are crucially important when we investigate biological effects of electromagnetic fields (EMF). Observation of difference in the responses of biological specimen with and without exposure is not sufficient to provide the basis for health risk assessment. Careful consideration of physical aspects must follow the observation to confirm the biological significance of the observation.

Physical aspects are important in the description of the initial event of interaction. Electric and magnetic fields exert forces on charges. The forces on charges should be the initial interaction of electric and magnetic fields with matter including biological body. In some cases the force might directly affect some biological process. In other cases, however, it just causes changes in physical environment of the specimen, which affects biological function indirectly.

Another physical aspect of importance is "electromagnetic dosimetry". Charges and polarized molecules in matter are forced to move when the material is exposed to electric and/or magnetic fields. Thus the electric and magnetic fields in tissue *in situ* are different from the incident fields. Electromagnetic dosimetry is the analysis and experiments to identify the resultant electric and magnetic fields *in situ*. The development of dosimetry has contributed to improved accuracy of exposure condition and reproducibility in biological experiments.

In this paper we discuss these physical aspects of EMF which are needed for biological studies.

Static fields: It is not known whether static electric and magnetic fields might cause adverse health effect. However, interactions of these fields with matter have been well investigated. Nuclear magnetic resonance and electronic spin resonance, for example, have been applied in material characterization and medical imaging, and so on. It is not known, however, whether these interactions could affect biological functions.

Effects of static magnetic fields on chemical reactions have also been well investigated¹. It is not known whether the effect also exists in biochemical reactions *in vivo*. Health consequence of these effects, if any, is not known.

Recently very strong magnetic fields of more than 10 T have become much easier to achieve owing to the progress in superconducting magnet. Very strong magnetic fields can affect the gas flow. Equilibrium state of gas and liquid is also affected. Strong magnetic field can affect dissolved oxygen concentration. This change results in an apparent change in catalytic activity of catalase², though magnetic field does not directly affect the enzymatic activity. It is not known, however, that this mechanism should have any significance in biological function *in vivo*.

Spatial gradient of magnetic field exerts translational force on magnetic moments. The magnitude of the force is proportional to the product of magnitudes of the gradient and the magnetic flux density. Thus the force is proportional to the square of the magnetic flux density if the spatial distribution is the same. Magnetic field with very high gradient can affect even non-magnetic material by the magnetic force. "Moses effect" is a well-known phenomenon, for example³. Water surface is not flat in a high gradient magnetic field due to the magnetic force. This phenomenon can result in loss of medium in the center of

the dish for in vitro experiments.

It is important that we should scrutinize the physical effect of the field when we observe any change in an experiment on EMF exposure effects. Some observation may be explained by physical mechanism, which might be rather trivial in the sense of biological significance.

Extremely low frequency (ELF) magnetic fields:

Effect of ELF magnetic field is a combination of effects of a quasi-static magnetic field and effects of electric fields (or currents) induced by time derivative of the magnetic field.

Electromagnetic dosimetry has been developed to estimate induced electric field and current in tissue. Recent progress in computer technology enables us to deal with anatomically based numerical models of human body. This technique provides realistic estimation of induced field and current in tissue. A numerical whole-body human model with 2 mm resolution consists of about 10^7 voxels. This scale of computation is possible in many laboratories.

However, a finer model is hardly used because of the limitation of memory size and computation time. On the other hand it is known that many organs are covered by thin membranes. Cells, which constitute organs and tissues, also have very thin membrane in microscopic level. These thin structures are not considered in a voxel models. We need another approach to consider the role of membrane structure in the induced current in tissue. "Microscopic" dosimetry is also needed in physical consideration of EMF effects.

Radio frequency (RF) fields and microwaves (MW):

It has been established that heating of tissue due to absorbed energy of RF and MW fields can cause adverse health effects. Thus quantitative analysis of power absorption is important in the exposure assessment of RF and MW. Specific absorption rate is defined by absorbed power in a unit mass of tissue. Electromagnetic dosimetry has been developed to determine SAR in a body exposed to RF & MW fields. Numerous studies have been done by both numerical and experimental approaches.

Non-thermal effects have also been a matter of a great concern though numerous studies have failed to prove the existence since 1960's. Microwave auditory effect is only one phenomenon of non-thermal origin that is established both experimentally and theoretically⁴). This phenomenon is attributed to the sensation of weak elastic waves in the head produced by the thermal expansion of tissue caused by rapid absorption of energy from pulsed microwaves. Physical consideration played a crucial role in establishing this phenomenon.

Physical considerations also play an important role in the characterization of exposure conditions of experimental setups to search for possible non-thermal effects. SAR is no more a good parameter to describe the exposure condition but electric field and magnetic field *in situ* in the specimen must be determined, as SAR reflects only the internal electric field. Thermal analysis in the exposure setups are required in order to exclude the effects of thermal origin. Physical considerations are also important for this purpose.

Concluding remarks:

Physical approaches are very important in the studies on EMF biological effects. An interactive approach between physical and biological ones will help us better understand the effects of EMF. Tight cooperation is indispensable between physicists and biologists. Physicists design good exposure setups and well characterize the exposure condition. Biologists design biological endpoints to be observed and make a good laboratory practice. Modification of exposure condition will reveal physical nature of the observed effect. Then biological consideration will reveal purely biological nature of the phenomenon. Interactive study in this way will contribute to the development of our knowledge in the possible EMF effects that have not been established yet.

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RADIO FREQUENCY RADIATION DOSIMETRY IN WHOLE-BODY AND PARTIAL-BODY HUMAN COMPUTER MODELS

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Accurate dosimetry is a critical part of any scientific effort to assess the effects of electromagnetic fields (EMF) on biological systems. In addition, conducting high quality dosimetry and reporting detailed descriptions of the dosimetry are essential to permit precise replications of experiments by independent laboratories. Dosimetry includes the prediction and/or measurement of the incident and internal fields. These fields can be quite different, depending upon the characteristics of the object, including: size and shape, electrical properties, orientation with respect to the incident field, and the frequency of the incident field. The development of mathematical dosimetry modeling techniques and relatively powerful computer hardware has resulted in computer modeling as a principal tool in assessing the biological dose resulting from EMF exposure. Only with the use of realistic anatomical models and methods such as the finite difference time domain (FDTD) has the ability to estimate both whole body and localized specific absorption rate (SAR) values become possible. Laboratory research is aided by the FDTD analysis by indicating where localized SAR measurements should be made. The FDTD analyses show that whole body SAR values exhibit frequency-dependent resonances; as do individual organs and body sections (e.g., limbs, head).

The man dosimetry model developed by the U.S. Air Force and Navy was used in the present study to determine resonance frequencies as a function of: 1) object orientation with respect to the incident field and 2) use of whole body or partial body (e.g., head only) models. Consistent with the Radio Frequency Radiation Dosimetry Handbook (Durney *et al.*, 1986), the resonance frequency for the whole body standing man is approximately 70 MHz when exposed in the EHK orientation. When this incident field is propagated in the ventral-to-dorsal direction, the resonance frequency for the brain, oral cavity, and testicles is approximately 800 MHz. When the incident field is propagated in the dorsal-to-ventral direction, the resonance frequency for the cerebellum and brain stem is approximately 240 MHz.

Comparison between whole-body model and the partial-body model produced substantial differences in localized SAR values. These differences are important to note since partial body simulations may be used to limit the computing resources required. Different results with whole- versus partial-body simulations would tend to limit the value of partial-body models and suggest that partial-body models must be employed with care.

Since validation of human dosimetry models is difficult or impossible with living human subjects, we have also developed animal dosimetry models that we compare to empirical animal data. Good agreement between the theoretical and empirical animal data provide support for the validity of the SAR values predicted in the man model. Validation of the computer models with empirical results and the subsequent refining of the models are essential in order to earn the confidence and credibility needed to use these models to establish or revise exposure standards.

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**DEVELOPMENT AND VERIFICATION OF
REVERBERATION-CHAMBER-TYPE EXPOSURE SYSTEM FOR *IN VIVO* STUDY AT A CELLULAR-PHONE FREQUENCY**

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Background: A reverberation chamber must have a suitable dimension at lowest useable frequency (LUF) to satisfy the requirements for the minimum number of mode that is necessary for proper field uniformity. We developed a reverberation-chamber-type exposure system for animal study at cellular-phone frequency (848.5 MHz) and its performance was verified by numerical analysis and measurement.

Methods: 1. The dimension of the chamber is 2293 mm x 2296 mm x 1700 mm, and it has a mode stirrer for field uniformity. It also provides a proper ventilation and illumination. The chamber was designed to expose 24 cages that will be put on the table with the height of 180 cm. Each cage allows 6 mice, and thus 144 mice can be exposed at the same time. 2. To design the chamber, the field distribution inside the reverberation chamber was simulated using SEMCAD. The field distribution was measured at 24 points on the table by taking average of the fields for 72 angles of the mode stirrer, and the results were compared with the computed ones. 3. The field uniformity in the exposure region was confirmed by measuring the 10 minutes' average of rms field strengths at 18 points inside and on the surface of a cage in a typical exposure location. 4. The SAR distribution in a mouse was evaluated using the well-known FDTD method. We assumed the field strengths from each direction and for each polarization are uniform and uncorrelated. The size of the mouse is 8.2 cm in length (X), 1.7 cm in height (Y), and 2 cm in width (Z), and modeled with 25 tissues, utilizing the model of U.S Air Force Research Laboratory. The cell size for simulation is 0.072 cm (X) x 0.078 (Y) cm x 0.039 cm (Z). 5. The linearity of the SAR values with respect to the input power was also tested by measuring the 5 minutes' average of rms field strengths at the center of the exposure region, and then by computing the corresponding SAR values from the simulation results.

Results: 1. The measurement results for field distribution are compared with the simulated results in figure 1, which shows a fairly good agreement. 2. Figure 2 shows the measurement results for field uniformity. It can be seen that the field uniformity is quite good 3. The calculated SAR values in terms of input power are shown in table 1, which are obtained from the measured RMS field strengths and the FDTD simulation. The linearity with respect to input power is excellent.

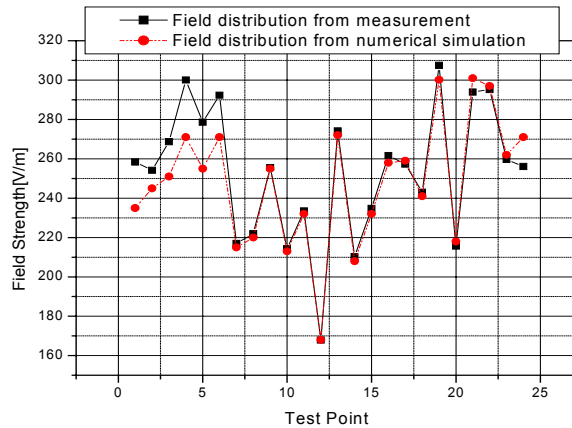


Figure 1. Comparison of the field distribution in the reverberation chamber.

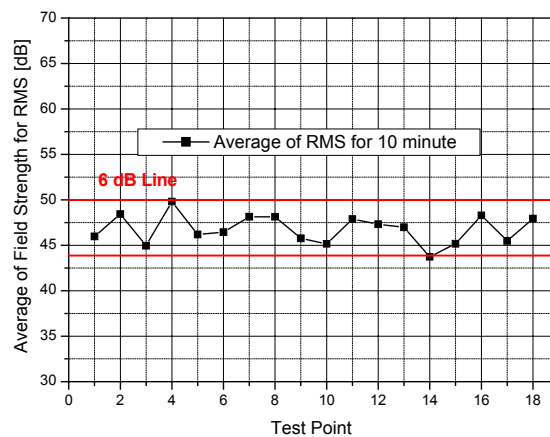


Figure 2. Field uniformity

Table 1. RMS field strengths and SAR values for different input power level

Input Power [W]	Field Strength [V/m]	Whole-Body Averaged SAR [W/kg]	Local Peak SAR [W/kg]
30	133.76	1.18	7.30
40	151.13	1.51	9.32
50	168.26	1.87	11.55
60	189.95	2.38	14.73

Conclusion: 1. We have developed a whole-body exposure system using a reverberation chamber. The measurement results show that the field uniformity in the exposure region is good. 2. The maximum whole-body averaged SAR obtainable in the exposure system is about 2.4 W/kg and the maximum local peak SAR is about 15 W/kg. The system is currently in use for long-term animal experiments in Seoul National University.

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DESIGN OF 20 kHz MAGNETIC FIELD SOURCE IN THE INCUBATOR FOR IN-VITRO EXPERIMENTS

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Background: A three-stage Helmholtz coil was designed for in-vitro study of the triangular waveform magnetic field at 20 kHz. Since the coil is operated in the metallic cavity of an incubator and the coil dimension is comparable to the cavity size, it is necessary to shield the magnetic flux from the coil to minimize the eddy currents on cavity walls which would again distort the magnetic field pattern in the coil geometry.

Methods: Incubators in which temperature and humidity can be controlled are usually used for in-vitro study. The inner dimension of the incubator for the experiments is 490 mm x 505 mm x 690 mm (W/D/H)[1].

In order to isolate the magnetic source from the conductive incubator cavity walls, the magnetic shielding structure in the cavity was designed with 19 mm thick ferrite grids used for RF absorption in the compact EMF anechoic chamber[2]. The grid structure as a shielding wall was chosen to permit free flow of air and light. The inner dimension of the shielding structure was 302 mm(W) x 242 mm(D) x 442 mm(H).

The coil sustaining structure of 270 mm(W) x 200 mm(D) x 422 mm(H) was made by bakelite. The numbers of coil windings derived from the numerical analysis are 40 turns (top and bottom) and 34 turns (middle) turns, which will give the least magnetic field variation along the coil axis. The three top, middle and bottom winding were connected in series, and the serial inductance was 2.94 mH at 10 kHz test frequency.

Results: For the triangular waveform magnetic field, the square wave voltage was driven to the serial coils. The measured inside field intensity was between 5.2 and 67.5 μ T rms as the square wave input voltage was varied from 10 Vrms to 130 Vrms.

The Helmholtz coil was installed in the shielding ferrite grid structure and magnetic fields were measured on the outside surfaces of the six ferrite walls. The shielding effectiveness of the ferrite walls ranges from 13.0 dB to 14.5 dB depending on places.

Conclusion: A 20 kHz triangular waveform magnetic field source inside of the ferrite grid shielding structure was designed. The shielding effectiveness is satisfactorily good enough for the biological experiments in the conductive incubator cavity.

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Session 5-6

SAR CALCULATION USING FDTD TECHNIQUE WITH PERFECT MATCHED LAYER BOUNDARY

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While the measurement of SAR very complexity and time taken, our object is to find a simple way to replace.

In this paper, three-dimensional finite-difference time-domain (FDTD) method and perfect matched layer (PML) boundary condition are applied to the computation of specific absorption rate (SAR). The antenna used are dipole and monopole on a metal box. The head is approximated by small cubes. These are formed into discrete approximation to a sphere. The results include near field distribution, SAR, relationship between radiation efficiency and distance from lossy dielectric.

In conclusion, the SAR value can be derived from the radiation efficiency.

Index words: FDTD, PML, radiation efficiency , SAR

Session 5-7 I

DOSIMETRY OF MMW POWER DENSITY AND POWER ABSORPTION DENSITY FOR CELLS IN CULTURE DISHES PART I: 6mm MMW IRRADIATION

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Introduction: More attention has been given to the exploration of millimeter-wave (MMW) biological effects in recent years as bioelectromagnetic research sails into the uncharted territory [1]. Here we just concentrate into the dosimetry in experiments of MMW biological effects in the cellular and sub-cellular level where culture dishes serve as containers holding the cell monolayer or the cell solution. The culture dishes are necessary devices in these experiments and based on the previous study [2], it is quite certain that the MMW power density (PD) irradiated into the cells and the power absorption density (PAD) of the cells are influenced significantly by many factors. So the evaluation of the PD and PAD for cells should be carefully administrated. The study here as part I and part II intends to provide a relatively accurate and precise description of the PD and PAD for a certain culture dish in specified conditions so as to present a general understanding of MMW dosimetry in related experiments.

Methods: The typical culture dish used in experiments searching for MMW biological effects are similar to other culture dishes with the only exception that its diameter are usually smaller. Most experiments are carried out with a culture dish containing a cell monolayer growing on the upper surface of the dish bottom with a cover of culture solution. With a high conductivity, the culture solution absorbs the MMW energy so efficiently that perhaps no MMW could directly reach the cell monolayer if it was introduced from the

above of the culture dish. The upward irradiation direction is selected deliberately to avoid the embarrassing situation. This is also acceptable in other experiments where the cell solution takes the place of the cell monolayer.

The finite-difference time-domain (FDTD) numerical technique [3] is employed for obtaining the PD and PAD of the cells in the culture dish. 6mm wavelength (50GHz) sinusoidal uniform plane MMW with an incident PD of $1.0\text{mW}/\text{cm}^2$ is taken into account. The second order approximation of the absorbing boundary conditions (ABCs) [4] is used to compute the electric field on six sides of the computational domain.

It should be noted that during the analysis, the cells, either a cell monolayer or cells dispersed in the solution, are considered as part of the culture solution because of their similar electromagnetic properties. So the PD and PAD somewhere in the culture solution are those of the cells if they exist right there.

Results: Resultant data are exhibited as graphic illustrations in Figs. 1 to 6, where the units are mW/cm^2 for the PD data and $\times 10^{-2}\text{mW}/\text{cm}^3$ for the PAD data.

Conclusion: The results illustrated in Figs. 1 to 6 provide an understanding of the MMW PD and PAD distribution in the culture solution. It is obvious that the PD and PAD are not uniform and their values change greatly with the change of position. For example, in Fig. 2a, which shows the PD distribution on the bottom of the culture solution, the PD in the darker area is only half of the PD in its adjacent brighter area, thus indicating a 8-time difference of PD on the solution bottom where the cell monolayer exists if it is the biological sample in experiments.

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Session 5-7 II

DOSIMETRY OF MMW POWER DENSITY AND POWER ABSORPTION DENSITY FOR CELLS IN CULTURE DISHES PART II:INFLUENCE OF DISH CONFIGURATION

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Introduction: The study presented in part I revealed the millimeter-wave (MMW) power density (PD) irradiated into cells in the culture solution and the power absorption density (PAD) of the cells in specified conditions. It is obvious that the PD and PAD are influenced by many essential elements, including the electromagnetic properties of media, i.e., permittivity and conductivity of the culture dish and culture solution, the dish configuration, the MMW wavelength, etc. Consequently, MMW dosimetry should be

conducted cautiously for each individual experiment to provide a rigorous dose evaluation serving as a strong technical background thus improving the quality of researches in the cellular and sub-cellular level on MMW biological effects [1].

The study reported in this part is a supplementary to that of part I, displaying and comparing the PD and PAD for culture dishes of different configurations with another MMW wavelength of 8mm .

Methods: Three culture dishes different in their configurations are considered. One is the circular culture dish that has already been introduced in part I, another culture dish is square-shaped and the other is a small-caliber culture dish since its inner diameter is rather small and absolutely comparable to the MMW wavelength.

The PD and PAD in the culture solution are computed by the finite-difference time-domain (FDTD) numerical technique [2]. The involved MMW is an 8mm wavelength (37.5GHz) sinusoidal uniform plane wave whose incident PD is 1.0 mW/cm^2 . The second order approximation of the absorbing boundary conditions (ABCs) [3] is used to compute the electric field on the truncated boundaries of the computational domain.

As is considered in part I, the resultant PD and PAD of the culture solution are those of the cells since the cells, either a cell monolayer or cells dispersed in the solution, can be regarded as part of the culture solution.

Results: Resultant data are exhibited as graphic illustrations in Figs. 1 to 6, where the units are mW/cm^2 for the PD data and $\times 10^{-2} \text{ mW/cm}^3$ for the PAD data.

Conclusion: The PD and PAD distribution patterns are evidently related to the culture dish configuration. This fact leads to the extrapolation that the nonuniformity of the PD and PAD distributions results mostly from the side shape of the culture dish whose dimensions are comparable to the MMW wavelength. So the nonuniformity is possibly avoidable in the central area of a culture dish with a diameter much larger than the MMW wavelength. If this is true, large-diameter culture dishes should be recommended for these experiments. This conclusion has been reached by the previous study [4].

The preliminary study introduced here as part I and part II for the seminar has again proved that experimental dosimetry is very complicated but highly important for researches on MMW biological effects to be carried out in the days to come. And the cooperation between dosimetry study and experimental study are to be encouraged if we look forward to fresh findings in this new territory of biological science.

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**DOSIMETRY OF MMW POWER DENSITY AND POWER
ABSORPTION DENSITY FOR CELLS IN CULTURE DISHES
PART III:IMPROVEMENT ON DOSE DISTRIBUTION UNIFORMITY**

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Introduction: With detailed illustrations, part I and part II of the study have provided a clear view of the influence of the culture dish configuration upon the millimeter-wave (MMW) power density (PD) and power absorption density (PAD) distributions. It is found that the PD and PAD distributions are not uniform. Actually, the PD and PAD values in different positions inside the same culture dish may double several times. It is certain that the MMW irradiation doses highly different in the PD and PAD values may quite possibly result in different biological effects in cells dispersed in different places within the same culture dish. If this should happen, statistical results derived from these experiments are not as accurate as expected.

Methods are tested in the third part of the study for improving the PD and PAD distribution uniformity since it is a key factor in upgrading these experiments. Based on the conclusion from the second part, the first method is to enlarge the diameter of the culture dish because the nonuniformity of the PD and PAD distributions results partially from the side shape of the culture dish.

While the other factor responsible for the PD and PAD distribution nonuniformity has not been mentioned up to now. As a figurative comprehension of the irregular PD and PAD distributions, we may think of the culture dish as an open-ended waveguide facing directly to the incident MMW. The incident MMW excites many modes at the aperture of the open-ended waveguide that is actually the bottom of the culture dish. The superposition of these modes forms a plane MMW at the aperture with a uniform irradiation pattern. However, these modes have to propagate through the waveguide while dissipate differently along the route. Most of them, especially the higher modes, tend to diminish to zero after traveling a very short distance. When these modes reach the culture solution, they are unable to form a uniform MMW a second time since different attenuations have worked upon them. As a result, the PD and PAD take on an irregular pattern.

The second method to be tested is aimed at limiting the influence of the factor mentioned above. The point is to decrease the attenuation of different modes. In order to do this, we have to reduce the thickness of the culture dish bottom to a very small value. If the above comprehension is correct, this method is expected to be more effective than the first one.

Methods: 6mm wavelength (50GHz) sinusoidal uniform plane MMW with an incident PD of $1.0\text{mW}/\text{cm}^2$ is considered. The PD and PAD on the bottom of the culture solution where the cell monolayer exists are calculated for three culture dishes with the finite-difference time-domain (FDTD) numerical technique [1] and the second order approximation of the absorbing boundary conditions (ABCs) [2]. The first culture dish has a diameter of 25mm and a bottom thickness of 2mm . The second culture dish is enlarged to 50mm in diameter while the bottom thickness keeps unchanged. The third culture dish is the same in diameter as the second one but its bottom thickness is reduced to 0.4mm .

Results: Resultant data are exhibited as graphic illustrations in Figs. 1 to 6, where the units are mW/cm^2 for the PD data and $\times 10^{-2}\text{mW}/\text{cm}^3$ for the PAD data.

Conclusion: The area of the cell monolayer is indicated as a dotted circle in Figs. 1 to 6. The standard deviation (SD) and the relative standard deviation (RSD) of the PD and PAD inside the area of the cell monolayer for different culture dishes are calculated and compared in Table 1. Both methods have been proved to be effective in improving the uniformity of the PD and PAD distributions.

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TABLE 1 Uniformity of PD and PAD distributions in culture dishes

Culture dish	PD		PAD	
	SD(mW/cm ²)	RSD (%)	SD(mW/cm ³)	RSD (%)
1	0.0294	20.4	2.914	20.73
2	0.0150	10.1	1.530	10.55
3	0.0120	3.33	1.193	3.329

Session 5-8

A NUMERICAL MODEL FOR EVALUATING THE INTRACORPOREAL THRESHOLDS OF ELECTRICAL AND MAGNETIC PHOSPHENES REGARDING ELF ELECTROMAGNETIC FIELDS

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Research background: According to the literature the eye is the most sensitive organ regarding non-adequate stimulation by low-frequency electrical or magnetic fields which leads to a perception of light flickering, a so-called phosphene [1,3]. This is the result of rough estimations of the current densities inside the organ, assuming a widely homogenous conductivity distribution, which nevertheless is the cornerstone of official limit values for extremely low-frequency fields.

Objectives: The central aim is to determine the current density threshold of phosphene excitation, separately for electrical and magnetic phosphenes. Therefore, the intracorporeal current density distribution has to be calculated. On account of comparisons of different pathological organs, we concluded that a magnetic fields induces a current inside the head that eventually serves the same mechanism as electrical phosphenes and that the excitation of phosphenes takes place in the synaptic layer of the eye.

Methods: To calculate the current distribution inside the human body, two numerical models were created using specifically measured conductivities in the LF range: The *head model* takes into consideration the six most important tissues as well as their conductivities. This model allowed to calculate the eddy currents which are induced in the head by the external magnetic field. The setup and the coil configuration were aligned to typical investigations with volunteers.

Since the eye and its periphery contains a wealth of small structure parts like tiny blood vessels, a highly detailed geometrical model of the orbita in original submillimeter resolution was constructed using data from a number of sources, data of imaging methods like MRT as well as tables [4]. This *orbita model* was used to calculate the current density excitation threshold.

The threshold of magnetic phosphenes were calculated in two steps: first, the overall current density distribution of the head model was calculated, and then this result was used as the input for the orbita model. To calculate the current density excitation threshold of electrical phosphenes, the currents known from experimental investigations were used as the input variable of the orbita model.

Results: We found that the current distribution — and with it the excitation threshold of the phosphenes — depends to a considerable degree on the small-scale structure of the *Bulbus oculi* and the surrounding orbita which were not taken into account by previous models [5]. This may explain the dependence of numerical results on the resolution of the used medical imaging method [2] as well as the differences found in inter-laboratory comparisons [6].

The derived current density threshold values of electrical phosphenes were 1800 mA m^{-2} at 60 Hz and 300 mA m^{-2} at 25 Hz, based on the experimental current threshold values of 0.2 mA and 0.04 mA respectively [1]. These values are comparable with values of other excitable tissues. As a result for the magnetic phosphenes, a minimum threshold of at least 80 mA m^{-2} for 50 Hz can be indicated, resulting from the experimental flux density threshold of 5 mT where the field passed along the body axis. With a refinement, the threshold of the magnetic phosphenes converge to the threshold of the electrical phosphenes.

These values has to be compared with the ICNIRP recommendation of 2 mA m^{-2} for general public exposure, which is two orders of magnitude lower than the lowest plausible threshold.

Conclusion: Rough estimations of the current densities which can trigger an electrical or magnetic phosphene made in earlier viewings lead to extremely low thresholds, thus the eye was regarded as the most sensitive organ regarding the non-adequate stimulation by electromagnetical fields. According to our results, the eye has the same order of magnitude of sensitivity as other excitable organs.

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ICNIRP - BASIS FOR EMF EXPOSURE GUIDELINES

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Introduction

ICNIRP guidelines for limiting exposure of people to electromagnetic fields (EMF) and for other non-ionising radiations are intended to provide a framework for a system of protection by recommending

- limits on exposure, termed basic restrictions, to avoid the adverse health consequences of exposure
- Other measures for reducing the risk of adverse effects

In addition, ICNIRP provides reference levels. These are expressed as field and electric current quantities in order to enable the investigation of compliance with the basic restrictions in specific practical exposure situations. ICNIRP's advice has not been prescriptive with regard to setting field limits. This allows the health and safety professional to use the most up-to-date measurement and computational techniques in assessing compliance with ICNIRP's recommended basic restrictions. This system has proved effective in practice and has been adopted by a number of national advisory bodies. The principles and the methodology by which ICNIRP develops its advice on limiting exposure to EMF has been published (ICNIRP 2002a).

This paper summarises:

- the role of science in the development of exposure guidelines. Specifically, the role of different medical and scientific disciplines, including epidemiology, biology and computational dosimetry and
- the basis for ICNIRP's EMF basic restrictions.

The Process

ICNIRP's exposure guidelines derive from extensive reviews of the science, including consideration of uncertainties in the scientific data, carried out in partnership with the World Health Organization. ICNIRP's advice on exposure restrictions requires judgements to be made by experts covering the different scientific disciplines involved in such reviews as to the relative importance and practical significance of the results of different studies. Much of this work is carried out by ICNIRP's four Scientific Standing Committees and in consultation with other experts, often through scientific seminars and workshops.

In practical terms this ultimately requires judgements to delineate between those adverse health effects that can be considered as having been demonstrated to be caused by exposure to EMFs and where supporting scientific data are sufficient to be able to quantify appropriate basic restrictions on exposure and those adverse effects that can be considered as having been demonstrated as being associated with EMF exposure but where the scientific data are insufficient to make a judgement on causality nor to quantify appropriate basic restrictions on exposure.

Science and Exposure Guidelines

In common with other expert bodies, ICNIRP has concluded that there are scientific data that indicate appropriate quantitative restrictions on exposure. These data derive from experimental studies related to effects of EMF on the central nervous system and effects of heating on the body. The nature of such effects and the mechanisms underlying them are well understood and the quantitative limits on exposure (basic restrictions) advised by ICNIRP are derived from data on these effects.

Knowledge of effects associated with EMF exposure, but where the scientific data are insufficient to make a judgement on causality nor to quantify appropriate exposure restrictions, derive principally from epidemiological studies and from some experimental studies. The main, but not sole, subject of such studies has been cancer. The results of such studies have been reviewed extensively by international and national expert groups. ICNIRP has concluded that currently the results of these studies on EMF and health, taken individually or collectively are insufficient to derive quantitative basic restrictions on exposure to EMFs (ICNIRP 2001). They do however provide a pointer to the need to consider further aspects of precaution with regard to EMF exposure.

ICNIRP recognises that all scientific investigations are subject to uncertainties, as is the interpretation of the results with respect to judgements on likely adverse effects on the health of people. An example of

the latter is the inter-species differences that exist and the resultant uncertainties in extrapolating from the results of studies of the effects on animals (for example, rodents) to possible effects in people. Even the results from well designed and conducted epidemiological studies give rise to uncertainties that can be statistically quantified, but sometimes cannot be explained. Thus, the risk assessment process should address these uncertainties in life science data and dosimetry.

In respect of providing a basis for developing EMF exposure guidelines, the health risk assessment can also include recommendations, based in part on these scientific uncertainties, to ensure that the recommended guidelines on limiting exposure provide general community protection. Thus, an intrinsic part of the EMF risk assessment process is the exercise of caution (that is leaning towards the side of “safety”) based on knowledge and understanding of the sources of uncertainty in the scientific data. In ICNIRP’s basic restrictions, the scientific uncertainties are considered and addressed using reduction factors. The degree to which caution is applied in the interpretation of the scientific evidence is a matter of professional judgement of the scientific experts involved. Such an approach includes the need to consider additional aspects of precaution where exposure is of the general public in areas with unrestricted access..

In principle, the results of studies most closely related to the actual exposure of people to electromagnetic fields and the physiological and/or adverse health effects that might result from or correlate with such exposures are of greatest importance to the development of exposure guidelines. That is, well controlled human laboratory and epidemiological studies.

Epidemiology

Epidemiology is generally observational rather than experimental in nature. In contrast to controlled studies in which subjects are randomised to receive, say, a treatment or a placebo, epidemiologists cannot influence who does or does not receive an exposure. Consequently, epidemiological studies may be affected by bias (i.e. systematic errors in the design or conduct of the study) or confounding (i.e. spurious findings due to the effect of a variable that is correlated with both the exposure and disease under study).

Biology

Biological studies include laboratory experiments with volunteers, as well as those with various animal species including rats and mice, and with cultured cells. Exposure may last from a few minutes in the case of volunteer studies, to several years in the case of animal longevity studies. The main objective of these studies is to determine the sorts of biological responses that occur as a result of exposure to electromagnetic fields, and to evaluate any uncertainties concerning the rigour with which these responses can be defined. With respect to their use in developing exposure guidelines, studies can be further evaluated for their consistency with other experimental results, their biological plausibility and their coherence, or lack of conflict, with current scientific understanding.

Dosimetry

Computational dosimetry provides both knowledge of the nature of the physical interactions of electromagnetic fields with living matter (people, animals and *in vitro* preparations) and links the strengths of external fields to which people may be exposed with those of fields induced in their bodies as a result of such exposures. Experimental dosimetry also plays an important complementary role with computational dosimetry in standards development but more with regard to the measurement of people’s exposures and testing compliance with exposure guidelines than with the development of exposure guidelines *per se*.

Basis for ICNIRP’s EMF basic restrictions

Static and extremely slowly time-varying electric and magnetic fields (0-1 Hz)

In this frequency range electric and magnetic fields must be treated separately.

Static and extremely slowly time-varying electric fields interact with people in two important ways:

- They act on the outer surface of the body. This may be accompanied by hair movement and other sensory stimulation. Electric field strengths greater than about 10 kV m⁻¹ can be detected on the surface of the body.
- They induce surface charges on conducting objects. Currents may pass through grounded persons in contact with such objects (see special considerations below).

For static and extremely slowly time-varying magnetic fields there are several established physical mechanisms through which the fields interact with people. The most important is magnetic induction, which is relevant to both static and time-varying magnetic fields and is produced by:

- electrodynamic interactions with moving electrolytes and moving conductive tissues, giving rise to induced electric fields and currents;
- induced electric fields and currents in living tissue from time-varying magnetic fields.

Basic restrictions

The basic restrictions for static magnetic fields are expressed in terms of the magnetic flux density in the unit tesla (T). For time-varying electric and magnetic fields the basic quantity is the induced current density, expressed in the unit ampere per square metre ($A\ m^{-2}$).

Biological data for static magnetic field exposure indicate that there are no adverse health effects on people at levels below about 2 T. This value is considered suitable as a basic restriction for whole body exposure with a relaxation of up to 5 T for exposure of the limbs alone. However, as there is a lack of long term exposure data it is considered advisable to limit the average exposure for the whole body during the whole working day to 200 mT (40 mT for the public). However, a ceiling level of 2 T applies under such circumstances (ICNIRP 1994).

Special considerations

In addition to the basic limits, the following precautionary measures should be noted.

- Strong electric fields induce electrical charges in conducting objects, that may then pass through grounded persons in contact with the objects. Field strengths greater than approximately $5\text{--}7\ kV\ m^{-1}$ can produce a wide variety of hazards such as startle reactions associated with spark discharges and contact currents from ungrounded conductors within the field. Care should be taken either to eliminate ungrounded objects, to ground such objects, or to use insulated gloves when ungrounded objects must be handled. Reference levels for contact current are provided in ICNIRP (1998).
- Safety hazards associated with combustion, ignition of flammable materials and electroexplosive devices may exist in the presence of a high intensity electric field.
- The magnetic field exposure of persons with conductive implants, especially when made of ferromagnetic materials, may constitute an additional hazard.
- Workers with cardiac pacemakers and electrically active implants may also be at increased risk from exposure to particularly high field strengths.
- Because of existing electromagnetic compatibility problems, or field influence on magnetic data storage devices, additional restrictions may be necessary.

Time-varying electric and magnetic fields (1 Hz-100 kHz)

The basic restrictions in this frequency range will prevent harmful effects on the function of the nervous system, electrical stimulation of tissues and shocks and burns due to transient discharges or contact currents. Some reported effects such as interactions at the cellular and sub-cellular levels have also been observed, however their relevance to human health is not clear. In establishing its exposure guidelines, ICNIRP reviewed the scientific literature on observed short-term as well as long-term biological effects including those relevant to cancer.

Associations between cancer incidence and exposure to power-frequency magnetic fields have been reported in epidemiological studies (ICNIRP 2001). However, the data do not establish a causal relationship nor do they provide a basis for quantitative exposure restrictions.

Basic interaction mechanisms are:

- *Direct coupling between electric and magnetic fields and living organisms*

Electric fields induce a surface charge on an exposed body. This results in a current distribution inside the body, depending on exposure conditions, size, shape and position of the exposed body in the field. Effects can be:

- vibration of body hair,
- stimulation of sensory receptors,
- cellular interactions.

Magnetic fields induce electric fields and currents in the body depending on exposure conditions and body dimension.

- *Indirect coupling mechanisms*

Electric and magnetic fields coupling to conducting objects may cause electric currents to pass through the human body in contact with the object. The magnitude and spatial distribution of such currents depend on a number of factors including frequency and impedance path. Transient discharges (sparks) can occur when people and conducting objects exposed to strong fields come into close proximity. The performance of cardiac pacemakers and other medical implants may be adversely affected by exposure to electromagnetic fields (ICNIRP 2002b).

Basic restrictions

For time-varying electric and magnetic fields the basic restriction quantity is the induced current density, unit ampere per square metre ($A\ m^{-2}$). The frequency dependence of the basic restriction follows the frequency dependence of the excitation thresholds of peripheral nerves and the cardiac muscle (UNEP/WHO/IRPA 1993), including reduction factors by considering the scientific uncertainties about adverse CNS effects below the stimulation thresholds (say affecting synaptic processes). The basic restriction of $10\ mA\ m^{-2}$ for occupational exposure between several Hz and 1 kHz excludes known synaptic processes (e.g., electric and magnetic phosphenes) For the general public, an additional factor of 5 is applied.

To avoid hazards due to contact currents advice is provided as a reference level for current with the unit ampere (A).

The scientific basis for the basic restrictions and the frequency dependent values are described in ICNIRP (1998).

Special considerations

Special consideration should be given to the protection of workers having implanted medical devices.

The sensitivity of a person to shocks from transient discharges depends on the sensitivity of the involved part of the body and the age and gender of the person. For occupational exposure, protective measures such as wearing protective shoes or gloves can prevent excessive contact currents.

Radiofrequency fields (100 kHz-300 GHz)

There are well documented biological effects linked to excessive temperature elevation in this frequency range. Such effects have been observed from exposure to radiofrequency (RF) radiation resulting from whole body or local heating. Compliance with the basic restrictions will prevent harmful effects due to heating, electric shocks and radiofrequency RF burns. In establishing its exposure guidelines, ICNIRP reviewed the scientific literature on observed short-term as well as long-term biological effects including those relevant to cancer.

Basic restrictions

In the frequency range 100 kHz to 10 GHz, the basic restrictions on exposure are specified in terms of limiting whole body or partial body specific energy absorption rate (SAR). The basic restriction of the whole-body SAR of $0.4\ W\ kg^{-1}$ provides adequate protection for occupational exposure. An additional reduction factor of 5 is applied for the general public. Localised SAR restrictions of $10\ W\ kg^{-1}$ and $2\ W\ kg^{-1}$ for occupational and public exposure, respectively have been chosen, to be averaged over any 6 minute interval and any 10 g of contiguous tissue of head and trunk. However, it should be noted that in the frequency range 100 kHz to 10 MHz restrictions on both SAR and induced current density apply (ICNIRP 1998).

For the frequency range 10 to 300 GHz, the basic restrictions are set out in terms of power density in the unit watt per square metre to prevent excessive heating in tissue at or near the body surface.

Special considerations

Special consideration should be given to the protection of people having an implanted medical device.

The sensitivity of a person to burns and shocks associated with radiofrequency radiation depends on the sensitivity of the involved part of the body and personal characteristics including the age and sex of the person. For occupational exposure, protective measures such as wearing protective shoes or gloves can prevent excessive contact currents.

For special exposure conditions, for example working with RF dielectric heaters and sealers, limits of exposure for limb currents are provided in (ICNIRP/WHO/ILO 1998).

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PROGRESS OF IEEE C95.1 –1991 RF SAFETY STANDARD REVISION

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The *IEEE C95.1 Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz* was published in 1991 and modified in 1999 with essentially no changes in the exposure limits and without updating and reevaluating the supporting scientific literature. A complete revision of the standard now in progress will be based on the literature published up to the end of 2002 that is listed in a database containing 1829 references. Relevant research papers (more than 1000) are evaluated by two randomly selected members of the Engineering Evaluation Working Group and by two members of the appropriate biological evaluation working group (in vitro, in vivo, and epidemiology). In addition, white papers have been prepared on cancer, reproduction, calcium efflux, behavior, thermoregulation, nervous system, ocular and auditory effects, homeostasis and metabolism, longevity, epidemiology, and in vitro studies. The white papers have been submitted for publication in *Bioelectromagnetics*. Summaries of working group evaluations are forwarded to the Risk Assessment Working Group (RAWG) to evaluate the levels of possible risk to humans and define the lowest threshold SAR above which potentially deleterious effects are likely to occur. A Mechanisms Working Group works in parallel with the RAWG to evaluate possible mechanisms of interaction between electromagnetic fields and biological entities and to address the scientific basis for effects reported at SAR levels well below the threshold established for thermal mechanisms. The current draft revised standard retains the same whole-body-average SAR basis and MPE limits as before. Peak spatial-average SAR limits have been harmonized with those of ICNIRP, although the parts of the body that these limits apply to are not identical. A final draft of the revision will be discussed by subcommittee 4 (SC4) in June 2003.

IEEE safety standards are developed through a fully documented and open process in which broad scientific consensus and involvement of all interest groups are essential. The 121 members of SC4 are from 19 countries where they work in government, academia, industry, and consultancies. Approval of the draft by SC4 and subsequently by its parent committee require consent by at least 75% of the voting members of each group after circulation and resolution of concerns raised on negative ballots. This process serves the goal of developing scientifically based exposure limits that protect against known adverse effects with an adequate safety margin.

Session 6-3

HARMONIZATION OPTIONS FOR EMF STANDARDS: PROPOSALS OF RUSSIAN NATIONAL COMMITTEE ON NON-IONIZING RADIATION PROTECTION (RNCNIRP).

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Russian National Committee on Non-Ionizing Radiation Protection (RNCNIRP) supports the development of WHO framework document on harmonization of the electromagnetic field standards, which document would contain basic concepts, proposals and recommendations to determine EMF maximum permissible levels for population of different countries.

For the international scientific community discussion RNCNIRP proposes the following issues seem to be included into the above mentioned document:

1. Electromagnetic fields are the biologically effective factor which should be obligatory standardized.
2. The human exposure to low intensive EMF is able to induce both physiological reactions and the tension of systems of adaptation and compensation and stress reactions as well.
3. Non-thermal mechanisms of low intensive EMF health effects are manifested both in case of acute and chronic exposure and would determine endpoint health effects.

The definition of MPL concept is the important starting point to choose criteria of danger and MPL assessed values.

DISCUSSION ON THE RATIONALE FOR CHINA EMF EXPOSURE STANDARDS

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1. Rationale for current China RF EMF Exposure Standards

The current RF exposure standards were set up in 1988 and 1989, which based on a Chinese Tentative Standard (Chiang, 1981).

- (1) The basic consideration: Assessment of health hazard for setting standards should rely mainly on the health status of personnel exposed to RF EMFs. The results of experimental animals and theoretical calculation could be supplements to the human exposure data. We may evaluate whether the really exposure levels are hazardous according to the above data and set safe exposure limitation.
- (2) Some investigations on the health effects of occupational and environmental exposure to different frequency EMFs were performed in China. The results showed that chronic exposure to EMFs are associated with a variety of non – specific symptoms, including increased frequency of neuroses, liability of vegetation nervous system, and slight changes in peripheral blood, lens, and non – specific immune function. These effects seem to be similar to some animal experiments, and to other investigations conducted in some other countries. The threshold levels of health effects are 50-100 V/m at 0.1 – 30 MHz and 50-200 $\mu\text{W}/\text{cm}^2$ for > 30 MHz.
- (3) Animal experiments: Changes in ECG and immune function may occur at 0.2 – 1.0 mW/cm^2
- (4) Possibility to meet the standards at no cost or low cost.

2. Rationale for the current amending EMF exposure standards (draft) of China

The current RF EMF exposure standards in China have been performed for over 10 years. They have promoted many valid measures to reduce significantly the exposure levels in work places and in environment in China. However, because of the new and rapid development of telecommunication facilities, the economic globalization, and the need for standard harmonization, a draft of the amended EMF exposure standards was proposed by an United Working Group in China. The EMF standard draft covers the entire frequency ranges of time-varying EMF as ICNIRP guidelines. Also there are two classes, i.e. basic (preliminary) restrictions and reference levels (exposure limits), and the basic restrictions are current density (for electric field only), SAR, and power density. Two tier standards, i.e. occupational and general public, are also adopted.

The main differences (with ICNIRP) and its own rationale are as follows:

(1) ICNIRP guidelines are based on short-term, immediate health effects such as stimulation of peripheral nerves and muscles, and elevated tissue temperature resulting from absorption of energy during exposure to EMF (thermal effects). However, there is a body of literature, which reports that health effects can be shown at such a level of radiation that does not produce heating or stimulation.

For RF exposure, the SAR thresholds of behavior-disruption have been observed at the levels much lower than 4 W/kg. For example, D'Andrea et al (1986, a, b) reported that the threshold for behavior effects of chronic RF exposure in the rats occurs between 0.14 and 0.7W/kg. There are many other studies showing the lower threshold for behavior effects: DeWitt et al (1987): 0.14W/kg; Thomas et al (1975): 1.5-2.7 W/kg ; Schrot et al, (1980): 0.07 W/kg; Lai et al (1989): 0.6 W/kg. To elucidate the underlying neural mechanism in the last study, Lai et al revealed that both cholinergic and endogenous opioid neurotransmitter system in the brain are involved in the microwave-induced spatial memory deficit (Lai et al, 1989). Sanders et al (1985) reported a decrease in concentration of ATP and CP in the cerebral cortex following exposure of the rat to pulse microwave at SAR 0.1-0.5 W/kg, and concluded that the radiation decreased the activity of the mitochondrial electron transport system. A decrease in the mitochondrial marker enzymes, SDH and MAO, was also observed following exposure of mice to pulse microwave at SAR equal to or above 0.5 W/kg (Chiang et al, 1984).

Immune system is very important for health. A series of experiments on immune function of chronic exposure were reported in Russia. Using methods of complement binding reaction, degranulation of

basophils, and plaque-forming cell assay, chronic exposure of animals (rats, guinea pigs, and rabbits) to 2450 MHz microwave at $50 \mu\text{W}/\text{cm}^2$ or $500 \text{uW}/\text{cm}^2$ resulted in damage to brain protein structures and production of cytotoxic antibodies with subsequent development of the autoimmune process (Vinogradov and Dumanskij, 1975; Shandala et al, 1985). Vinogradov et al (1991) further demonstrated that the prolonged microwave exposure at $500 \mu\text{W}/\text{cm}^2$ induced autoimmune reactions by transferring the immunocompetent cells from the exposed animals to recipient rats. The development of autoimmune status in pregnant rats induced by $500 \mu\text{W}/\text{cm}^2$ microwave exposure was demonstrated, and a marked suppression of mitogen induced lymphocyte blast transformation was also observed (Shandala et al, 1982). Suppression of neutrophil phagocytosis occurred after chronic exposure of guinea pigs to microwave at $50 \mu\text{W}/\text{cm}^2$ (Vinogradov and Dumanskij, 1975). Though there were no SAR values provided in the above-mentioned experiments, the estimated SAR for about 2450 MHz microwave exposure must be far below $0.5 \text{ W}/\text{kg}$ at any polarization in these animals under reported irradiation conditions. That chronic exposure of mice to microwave at even lower power densities resulted in bi-phasic changes in immune system was reported. Exposure of mice to sinusoidal microwave at $1 \mu\text{W}/\text{cm}^2$ for 24 h increased the TNF production in peritoneal macrophages, and chronic exposure for 7 days induced the decreasing of TNF production (Fesenko et al, 1999). The effects of exposure of mice to pulsed microwave at $30 \mu\text{W}/\text{cm}^2$ rms ($0.01 \text{ W}/\text{kg}$), both with and without concurrent amplitude modulation (AM), were studied. In the absence of AM, no changes in immune functions (with plaque-forming cell assay) was observed. In contrast, under the combined-modulation condition the radiation resulted in significant augmentation or weakening of immune responses (Veyret et al, 1991). The bi-phasic changes in immune function of neutrophil phagocytosis were also observed in human exposed to environmental low-level RF radiation (Chiang et al, 1989).

In vitro studies, the evidence of RF non-thermal bioeffects is increasing (de Pomerai et al, 2000; Kwee et al, 2001), and the knowledge regarding the molecular mechanisms of low-level EMF potentially adverse health effects is growing (Goodman and Blank, 2002; Lin et al, 2001; Leszczynski et al, 2002). Increase in brain barrier permeability and induction of DNA strand breaks by low level microwave exposure were reported once again (Leszczynski et al, 2002; Phillips et al, 1998).

In summary, there are many reports of non-thermal potential health effects from microwave radiation using both *in vivo* and *in vitro*, and some of them are cited above. The SAR threshold for the adverse effects in the frequency range from 100 kHz to 10 GHz may be at 0.5 to $1.0 \text{ W}/\text{kg}$, rather than $4.0 \text{ W}/\text{kg}$. Thus, a whole body average SAR of $0.1 \text{ W}/\text{kg}$ is chosen as the restriction for occupational exposure, and $0.02 \text{ W}/\text{kg}$ for general public exposures in the draft of amending China exposure standard.

For power frequency (ELF) magnetic field (MF), the exposure limits in ICNIRP were derived from the assumption that magnetic fields act through its induced electric fields, and the current density of $10 \text{ mA}/\text{m}^2$ is adopted as the basic restriction to prevent stimulation of peripheral nerves and muscles for occupational exposure. However, there is growing evidence that the magnetic fields penetrate cells, tissues and cause bio-effects by themselves. For example, the suppression of gap junction intercellular communication (GJIC) is induced by MF itself rather than the induced electric field (Chiang et al, 2002). GJIC plays an important role in the maintenance of cell proliferation and differentiation, and is regarded as an index of inspection of possible cancer promoter. The threshold of GJIC suppression caused by 50 Hz MF exposure is about 0.4 mT , and 0.2 mT MFs enhanced TPA induced GJIC suppression (Hu et al, 2002; Li et al, 1999). The mechanisms of the GJIC inhibition induced by 50 Hz MF exposure, hyperphosphorylation of connexin43 and internalization of connexin43 from plasma membrane to cytoplasm, have been also discovered in our laboratory (Hu et al, 2001; Zeng et al, 2003). Goodman and Blank and their colleagues have reported rapid induction of heat shock proteins by 60 Hz MF exposure at only microtesla level with the related molecular mechanism. They found that the induction of HSP70 gene expression is at transcription level and mediated through C-myc protein binding at 3 sequence sites that are not required for common heat shock responsiveness. And the ELF MF may interact directly with moving electrons in DNA (Goodman and Blank, 2002; Lin et al, 2001; Blank and Soo, 2001). Chronic exposure decreases HSP70 level and lowers cytoprotection (Di Carlo et al, 2002).

There are many reports showing that 0.1 mT ELF MF exposure may affect cell functions. For example, 50 Hz MF at 0.1 mT specifically interacts with 5-HT_{1B} receptors, inducing structural changes of the protein that result in a functional desensitization of the receptors. Thus it may be involved in mood disorders complained by exposed workers (Massot et al, 2000). Induction of DNA strand breaks by intermittent exposure to 50 Hz was observed with a dose-response relationship at the threshold level of $0.07 - 0.1 \text{ mT}$ (Ivancsits et al, 2002).

Coincidentally, adverse health effects induced by 0.1 mT ELF MF exposure were also reported in *in vivo* studies. For example, 0.1 mT 50 Hz MF exposure significantly facilitates the development and growth of mammary tumors, particularly in cranial cervical part of the mammary gland, in the DMBA rat model of breast cancer (Thun-Battersby S et al, 1999; Loscher, 2001). Enhancing activity of ODC, a key enzyme in cell proliferation, after exposure of rats to 0.1 mT 50 Hz MF for two weeks was also observed. And it was found that the cranial cervical complexes being particular sensitive to ODC alterations in response to the MF (Mevisen et al, 1999). The cytotoxicity of NK cell in male mice was significantly affected following exposure to 0.1 mT 60 Hz for 49 and for 105 days (Marino et al, 2000).

Since IARC has concluded that the power-frequency MF are possible human carcinogens, and the increasing in the biological plausibility in mechanism and supportive data from animal experimental studies, the exposure limit for ELF MF exposure are suggested to be lower than ICNIRP's, i.e. for occupational exposure: < 0.08 mT, and for general public: < 0.03 mT in the draft.

It is noteworthy that in the research field of bioelectromagnetics, the published reports lacked consistency, and there are many negative results reported. Why the pattern of positive and negative reports occurs so commonly? Using different animal substrain or cell line, with different genotype composition, might be one of the main reasons. For example: The Hannover group (Fedrowitz et al, 2003) compared MF effects in the DMBA model with different substrains of SD rats. The results showed that the MF exposure increased mammary tumor development and growth in SD1 but not SD2 rats. The inhibition of melatonin antiproliferative effect of ELF MF on MCF-7 cells (from UCLA, Berkeley) were reported independently by some laboratories, but they have not been reproduced with the MCF-7 cells supplied by the American Type Culture Collection (Ishido et al, 2001). Using genomics and proteomics, the observed varying responses of cells with different genotype composition suggest that the response and possibly its severity might be influenced by the genotype (Leszczynski F et al, 2003). Secondly, Marino et al (2001) indicated that relationship between an applied EMF and its associated bioeffects was general nonlinear in nature. But it was assumed that any response of a subject to a field would be governed by a linear law, and that inter-subject measurement differences were due solely to stochastic processes. With nonlinear laws, they found statistically significant changes in lymphoid phenotype (ten immune parameters) after mice were exposed continuously to 0.1 mT 60 Hz MF for 175 days. However, no significant differences were observed in the above experiments with linear statistical analysis. Besides, the statistical chance to reproduce weak effects of EMF exposure is also a factor causing inconsistency of the study results. For instance, the chance of repeating the potential co-carcinogenic effect of ELF MF exposure, reported by Hannover group, with 100 rats per exposure group is only 75% (Anderson, 2000). Thus, some important effects, such as those just mentioned above, will be considered as not established effects and rejected as providing a basis for standard setting. Because of the inconsistency, the public health significance of EMF has been underestimated.

(2) Limitation and application of SAR

The SAR is a valid measure of energy absorption rate during RF exposure, but not a quantity indicator of biological effects. For example, the significantly different bioeffects between continuous and intermittent RF exposure, between modulated and unmodulated microwave exposure, under the same SAR questioned the issue of using SAR as a basic restriction. Since the mechanism of low level RF exposure is not well known, the SAR is now useful at extrapolations from animal experiments to human at specific frequencies, but has its limitations. In the draft of amending exposure standards of China, actually the named basic restriction is preliminary restriction. The exposure limits (reference levels) are not only derived from the SAR values, which are also based on exposure duration and considering the data of human epidemiological studies (including non-cancer).

The ICNIRP guidelines indicated that if measured values are higher than reference levels, it does not necessarily mean that the basic restrictions have been exceeded. However, in the draft, the exposure limits rather than the preliminary restriction SAR is used to determine if it is compliance with the standards.

(3) As to the localized SAR restrictions, ICNIRP sets up the partial body limits to prevent any possible temperature rise which may occur in the eye to 1°C or less. With the same reason as the whole-body exposure and the practical possibility, half of the ICNIRP's SAR limits were suggested in the draft. For example, the localized SAR (head and trunk) for public exposure is 1.0 W/kg in any 10 g of tissue, which is close to 1.6 W/kg in any 1 g tissue adopted by IEEE at present. However, since the exposure duration for mobile phone users are very short, usually less than one hour per day, and actually mobile phones are

consumer products related to individual behavior like smoking, it may be further loosen if it is needed.

3. The present knowledge in assessment of possible health effects related to exposure to EMF has not provide sufficient rationale for establishing satisfactory and general acceptable exposure limits yet, though there are growing evidences of highly potential health effects from EMF exposure. The draft of the amending exposure standard in China is still questionable and far from perfect, but it is reasonable and has scientific basis. As the scientific advances, including the rapid development of molecular biology with powerful techniques and adoption of novel concepts, researchers may settle many arguments about the health effects of EMFs. However, the exposure standards are aimed at protecting people, and the development of electricity and communication are of great benefit to people, a general acceptable and practical exposure standard should be produced after taking cost and benefit analyses with precautionary principle.

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Session 6-5

IMPLEMENTING GUIDELINES FOR RADIOFREQUENCY ELECTROMAGNETIC FIELDS IN THE UNITED STATES

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Background: Over the past twenty years the United States Federal Communications Commission (FCC) has developed a program and adopted regulations for implementing guidelines for human exposure to radiofrequency (RF) electromagnetic fields from telecommunications sources such as radio and television broadcast stations, wireless base stations, and mobile telephones. Exposure guidelines have been adopted based on recommendations of the National Council on Radiation Protection and Measurements (NCRP), the Institute of Electrical and Electronics Engineers (IEEE) and health and safety agencies of the U.S. Federal Government.

Program description: The FCC program includes a policy group and an office that is responsible for enforcement of the regulations. For fixed transmitters, the FCC requires compliance with limits for power density and electric and magnetic field strength. Manufacturers of devices such as mobile telephones must demonstrate compliance with exposure criteria in terms of Specific Absorption Rate (SAR). Violators may be subject to fines and other penalties. The FCC program also provides information and assistance to consumers, industry and other agencies with respect to the safety of telecommunications sources. An internet web site has been developed to further assist with this activity: www.fcc.gov/oet/rfsafety.

FCC exposure limit values: The FCC has adopted exposure limits for members of the general public and for workers. Two tiers of values for Maximum Permissible Exposure (MPE) were adopted based on NCRP and IEEE guidelines. MPE values are dependent on frequency, and time-averaging of exposure is allowed in certain situations. Partial body SAR values were adopted for public and occupational exposure. For members of the public the adopted exposure value for mobile telephones is 1.6 W/kg averaged over one gram of tissue.

Future activities: FCC staff members participate in groups and committees that monitor issues related to RF exposure and develop standards. These include a Federal Government Inter-agency Working Group and various IEEE committees. IEEE committees are currently developing standards and recommendations for evaluating mobile telephone exposure, for occupational RF safety programs, and for revising basic MPE and SAR values. The FCC may consider adopting or revising its own guidelines and procedures in the future based on these forthcoming recommendations.

Session 6-6

POSSIBILITIES FOR HARMONIZATION OF STANDARDS FOR RADIOFREQUENCY AND MICROWAVE RADIATION BETWEEN DIFFERENT SCHOOLS DEVELOPING EXPOSURE LIMITS

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Background: There are big differences between standards for radiofrequency/microwave radiation. Most of them are in terminology, exposure limits, etc. The main reason for these differences is the philosophy for developing standards, as well as the misunderstanding between the schools developing exposure limits. Many activities have to be done to settle these differences to get a harmonization of standards worldwide.

Methods: 1. Creating expert groups of specialists from different countries dealing with developing exposure limits. 2. Literature review of studies in Slavonic languages for developing standards. 3. Developing numerical methods for determining the relation between SAR and other dose parameters used in standards.

Results: 1. The exposure assessment of radiofrequency (RF) and microwave radiation using both whole body SAR values and “dose approach” is correct for the staff in radio and TV stations, physiotherapy and others. 2. There are many similarities between different schools for developing standards as some definitions, parameters, basic restrictions, fields of action of the standard, terminology, etc. They could be used for future developing of a framework for standard harmonization.

Conclusion: 1. It is possible to use both SAR and “dose approach” for exposure assessment of radiofrequency and microwave radiation. These parameters are adequate for exposure limits as well. 2. We need a methodological handbook for carrying out studies for developing standards. 3. We need also a harmonized glossary for standards. 4. The literature review is a method for developing standard but it should cover more studies from the East countries.

Session 6-7



THE “ROUND-TABLE-CONSENSUS -MODEL”(SO CALLED “SALZBURG MODEL”)AS A POSSIBLE REGULATORY FRAMEWORKFOR THE INSTALLATION OF MOBILE-PHONE-BASE STATIONS

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Keywords: mobile-phone-base-station-siting, round-table-consensus-model, precautionary principle

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ABSTRACT:

Protests of the neighbourhood population of planned or new mobile-phone-base stations are a world-wide problem for providers and authorities. This situation is expected to increase dramatically with the erection of the UMTS-infrastructure.

The actual world-wide procedure of mobile-phone-mast installation

- compromises democratic rights
- leads to health fears irrespective of the ICNIRP guidelines, which typically are met
- creates problems and/or significant costs for mobile phone system providers, for public administration and health-insurances.

As the EU-precautionary principle and the WHO-definition of health do not comply with the EU-ICNIRP-WHO-EMF-limit-value recommendations and due to the on-going protest of citizens, we need new strategies.

The “Round-Table-Consensus-Model”, between providers, the community and the citizens in the neighbourhood of planned sites, had been developed in 1998 on the occasion of the occupation of mast-sites in the city of Salzburg and could be

- a possible regulatory framework for the European Community,
- is technically feasible (ref. to measurements in Salzburg, Linz, Vienna and Germany)
- avoids compromising democratic and social standards, health and well-being.
- may be an innovative, technically achievable problem- and cost-reducing approach to mobile-phone base-station erection.

FROM A STATE- TO PRIVATE COMPANIES:

Historically seen, the first mobile phone companies developed from a state company when they became privatised. However, in most countries, these new companies and their competitors typically still benefit from privileges of a state company:

For base-station-siting there is in general no need for trade-regulations-procedures and/or environment-compatibility-procedures, or even to prove the economic necessity of a specific siting.

This is an absolutely new situation which raises the following issues:

1. What regulations are necessary to protect citizens for not becoming the victims of private mobile-phone-companies who are commercial-competitors to each other?
A normal citizen may be a victim in more than one sense: possible health-risks, property-devaluation, commercial losses e.g. rental-incomes, hotel-returns, etc.
2. In most of the countries, protection of health is guaranteed by the constitution.

Therefore it appears problematic, that private mobile-phone companies with specific commercial interests can impose possible health risks on citizens without having the necessary financial backing and/or compulsory insurance (e.g. car owners) to cover possible health-risks and taking the liability.

COMPROMISE OF DEMOCRATIC RIGHTS

Neo-liberalism which allows the mobile-phone companies “everything”, while people have to accept everything, has to be considered as anti-democratic and a not-acceptable privilege for only one sector of private economy.

According to our experience, the siting of base-stations, especially in residential areas but also near schools and kindergartens, is cause of considerable concern and distress. The complete absence of public consultation and planning process is a major cause of grievance, fears (for good or less good reasons) and frustration in people and more and more also in local authorities.

This way of acting and the resultant frustration also have negative effects on people’s health and well-being and therefore should be duly avoided. The important health-costs resulting from that also

should be taken into consideration.

HEALTH PROTECTION – A MATTER OF POINT OF VIEW

The health risk of EMF is hardly insurable.

Major insurance companies who evaluated the scientific literature refuse to cover the risk and possible personal injuries in the future from EMF exposure (e.g. Swiss Reinsurance-Company - Wiener Städtische Versicherung, Austria – Gerling, Austria – Lloyds, London).

Therefore private mobile-phone-companies are imposing possible health-risks without taking the responsibility/liability and/or without having the financial backing for compensations.

The current ICNIRP-guidelines as well as the EU-Council Recommendation of 12 July 1999 inform that they “don’t preclude interference with, or effects on, medical devices such as metallic prostheses, cardiac pacemakers and defibrillators, and cochlear implants. Interference with pacemakers may occur at levels below the recommended reference levels” as well as that “the guidelines are based on short-term, immediate health effects..... and elevated tissue temperatures resulting from absorption of energy during exposure to EMF.”

So, the anxiety that people feel when this uncertainty is ignored, can in themselves affect their well-being.

LACK OF REGULATION

ICNIRP guidelines and therefore also the EU-recommendation basically consider short-term-effects.

But people are exposed 24hours/24 - day for day.and the existing rental-contracts from providers are irrevocable for 20 years!

For base-stations-siting, there is no need for a full planning procedure, no need to keep the immission as low as possible, no independent audit after installation, no database available to the public.

“Blue collar”- workers (roof-maintenance, etc.) hardly have any information on the EMF-exposure when working close to antennas and may gain access to regions where even the thermal limits are exceeded.

The public is, as well as the local authorities, missing openly available information, especially about the operating characteristics of base-stations, like in a nation-wide register of base-stations and a national database set up by Government giving details of all base-stations and their emissions.

THE NEED OF STRATEGIES FOR CURRENT PROBLEMS AND QUESTIONS IN THE FUTURE:

Actually, the principle of EMF-exposure standard-setting is very different to standard-settings in other areas like pharmacology, chemicals or air pollution.

ICNIRP demands scientific proof, does not cover long-term effects and during every-day life-conditions the combination of more than one appliance may lead in case of mobile-phones to an exceeding of the ICNIRP-limit-value-recommendation.

In the mobile-phone-base-erection process, citizens find themselves in a “no say – no chance” situation:

A POSSIBLE ANSWER: THE SO CALLED “SALZBURG MODEL” AS A ROUND-TABLE-CONSENSUS-MODEL:

The so called “Salzburg model” was created in the city of Salzburg in 1998 after the building site for a mobile-phone-mast has been occupied by concerned citizens.

- showed a possible way in form of a round-table- and consensus-model for neighbours, communities and the mobile-phone providers to avoid the conflict even when some of the questions below remained without solution (e.g. liability),
- enabled one Austrian mobile phone provider in 1998 to install base-stations at sites that were lost after activists "conquered and occupied" the building-sites á la „rien ne va plus“
- with involvement of the neighbours in the planning phase
- with inspection of alternative locations for the siting
- with calculation of the expected RF immission and exposure before realisation of the siting

- with outdoor exposure as low as 1 mW/m² (furthermore for the sum total of all immissions from ELF pulse modulated HF exposure facilities according to the scientists vote at the Salzburg conference in June 2000)
- was awarded the Austrian Public Relations price in 1998
- was at the base of the siting-network from the 4th Austrian GSM-provider from 1999 to 2001 and for a number of sites for the other three Austrian GSM-providers until 2000.

From 1998 to 2001 this consensus-model was proving in every-day-practical experience that it is possible to build mobile-phone-base-stations with involvement of neighbours and respect of an outdoor-exposure of 1 mW/m² for the sum total of all immissions from ELF pulse modulated HF exposure facilities, according to the scientists vote at the Salzburg Conference in June 2000 and the Ischia-Resolution of October 2001.

THIS CONSENSUS-MODEL IS A PRACTICALLY EXPERIENCED MODEL IN RESPONSES TO THE FOLLOWING NEEDS AND STATEMENTS,

even when some requirements (e.g. liability/insurance) must already be included

• **WHO-Definition of Health:**

“Health is a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity.”

• **WHO- Press Release/45 – 28 June 2000 - revised recommendations:**

“...siting decisions should take into account aesthetics and public sensibilities.”

• **WHO-fact sheet 193 – Revised June 2000 – Electromagnetic Fields and Public Health:**

“.....Precautionary measures should be introduced as a separate policy that encourages, through voluntary means, the reduction of RF fields by equipment manufacturers and the public....

Simple protective measures: Fences or barriers or other protective measures are needed for some base-stations (principally, those located on building rooftops) to preclude unauthorised access to areas where exposure limits may be exceeded siting decisions should take into account aesthetics and public sensibilities.

Siting base-stations near kindergartens, schools and playgrounds may need special consideration. Open communication and discussion between the mobile phone operator, local council and the public during the planning stages for a new antenna can help create public understanding and greater acceptance of a new facility....

An effective system of health information and communications among scientists, governments, industry and the public is needed to raise the level of general understanding about mobile phone technology and reduce any mistrust and fears, both real and perceived....”

Statements of Dr. Michael Repacholi, WHO, at the ERA-conference, 2001:

Voluntary measures:...

“Encourage manufacturers to keep exposures to the minimum needed for the technology

Better risk communication (honest and accurate information),

Public involvement in decision making

Siting facilities to minimise public exposure and concerns.”

Independent Expert Group on Mobile Phones IEGMP (2000):

1.30 . “The siting of bases-stations in residential areas can cause considerable concern and distress. At all our open meetings and in written evidence we heard concerns about the location of base-stations in sensitive sites. These include schools, residential areas and hospitals. This concern relates, in part, to the fact that base stations up to 15 m (48 ft) in height can be installed in residential areas without the need for a full planning application. We consider this to be unacceptable.”

1.31. “We are concerned at the indirect adverse impact which current planning procedures are having on those who have been, or are, subjected to the often insensitive siting of base-stations. Adverse impacts on the local environment may adversely impact on the publics well-being as much as any direct health effects.”

1.35 . “Overall we consider that public concerns about the siting of base-stations demand changes in the planning process.

1.62. “We recommend that an Ombudsman be appointed to provide a focus for decisions on the siting of

base-stations when agreement cannot be reached locally, and on other relevant issues.”
6.38. “There is now scientific evidence, however, which suggests that there may be biological effects occurring at exposures below these guidelines.....”

German Radiation Protection Commission SSK:

In the publication of 13./14. September 2001 the German Radiation Protection Commission SSK suggests several changes to the current policies, to incur protective measures beyond the protection quality of the ICNIRP guidelines:

- Safety distance considerations should also include and account for background levels of all EMF immission
- the minimisation of EMF exposure should become a quality criterion
- all EMF-emitting appliances and installations should carry labels providing the product information
- standardised labels which give a measure for human exposure
- Immissions should be controlled regularly
- Increased information and citizen involvement before the fixed installation of EMF emitting appliances
- Increased involvement of the local communities in the planning phase

Furthermore the SSK requests a health impact evaluation before the market admission of new technologies and requests to make public all available data concerning health issues. It is clear that these requirements will not be met by the launch of the UMTS mobile phone system.

- German Federal board for Radiation Protection (BfS) considers the current regulations insufficient, when it recommends in a press-release of Feb 1st 2002 that
 1. unnecessary exposure should be avoided and
 2. unavoidable exposure should be minimised.

The possible risk may be small, but one has to consider that these presumably small risks concern several millions of people. There is a demand for action to meet the precautionary principle requirement. Exposure has to be kept at a minimum, the public has to be informed.

The German Federal board for Radiation Protection considers it a duty of the mobile phone system providers to minimise public exposure via the site selection of fixed EMF emitting appliances.

It recommends to make siting processes more transparent by involving citizens and involving the communities in the planning phase such as participation in the selection of sites is possible.

- The application of the Precautionary Principle: COM 2000 (1) final – 2. 2000
Summary 5. “...Decision-makers faced with an unacceptable risk, scientific uncertainty and public concerns have a duty to find answers.” (p.3)

1. “...the precautionary principle has been politically accepted as a risk management strategy in several fields.” (page 8)

“Although the precautionary principle is not explicitly mentioned in the Treaty except in the environmental field, its scope is far wider and covers those specific circumstances where scientific evidence is insufficient, inconclusive or uncertain and there are indications through preliminary objective scientific evaluation that there are reasonable grounds for concern that the potentially dangerous effects on the environment, human, animal or plant health may be inconsistent with the chosen level of protection.” (p.9)

6.2. “The absence of scientific proof of the existence of a cause-effect relationship, a quantifiable dose/response relationship or a quantitative evaluation of the probability of the emergence of adverse effects following exposure should not be used to justify inaction. Even if the scientific advice is supported only by a minority

fraction of the scientific community, due account should be taken of their views, provided the credibility and reputation of this fraction are recognised.” (p.16)

...to involve all interested parties at the earliest possible stage.” (p.16)

6.3.4. “The Commission affirms, in accordance with the case law of the Court that requirements linked to the protection of public health should undoubtedly be given greater weight than economic considerations.” (p.19)

6.4. “...Action taken under the head of the precautionary principle must in certain cases include a clause reversing the burden of proof and placing it on the producer, manufacturer or importer.....” (p.20/21)

- Jurisdiction of EU Court:

“Where there is uncertainty as to the existence or extent of risk to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent.” (Cases C-157/96 and C-180/96 of 5.May 1998, Grounds 63).

“Requirements linked to the protection of public health should undoubtedly be given greater weight than economic considerations” (Order of 30 June 1999, Case T-70/99).

- Resolutions of International Scientists:

Vienna EMF-Resolution 1998, Salzburg Resolution 2000, Ischia Resolution 2001, Catania-Resolution 2002

- Resolutions of the Austrian National medical consultant group:

18.11.2000:

“...the “siting” must be approved and examined by the authorities based on clear guidelines

“...with legal regulations, the providers should be brought to minimise the immissions due to EMF even below guideline levels.”

08.03.2002:

“...it should be aimed at guideline levels that are at least by a factor of 100 below limit values and the facilities should be examined under this view“

- Facts about electromagnetic fields”

“No authority concerned with exposure standards produced exposure guidelines with the aim to protect from long-term EMF-health-effects, like a possible cancer risk.”

“Facts about Electromagnetic Fields” – joint publication of the Austrian Government with WHO, published as information-paper for decision makers - Broschüre des Bundeskanzleramtes, Verkehrsministeriums und der WHO, für Kommunalbehörden, Seite 9)

CONCLUSION:

Statement of Christoph Schieble LL.M Chicago, University of Berlin and Bamberg “Precaution, Safety and Standardisation”¹⁹ at the ERA-conference 30.11.2001 in Luxembourg:

“Risk management follows risk assessment. When scientific risk assessment produces no clearcut results, risk management is faced with a dilemma. While adverse effects on human health cannot be proven beyond doubt, they cannot be ruled out either. This is the dilemma in the case of EMF, but it is not confined to this issue. On closer observation, one can identify similar problems in other fields such as environmental policy (ozone layer, climate change), food- (BSE) and toy-safety (PVC softeners).

The main legal instrument to deal with this dilemma is the so-called precautionary principle. The EC Treaty refers to it only in the context of environmental policy (Art. 174). But recent developments have proven that the precautionary principle also has a role to play in other fields of law such as product safety.The Commission has taken the lead on 2 February 2000 by issuing a Communication on the

precautionary principle. This Communication provides guidelines for decision-makers to cope with a situation in which risk assessment has not provided sufficient results.”

“The precautionary principle enables a decision-maker to act even if there is no scientific certainty. During the BSE-crisis for 1996, the Commission’s export ban on beef from the United Kingdom was upheld by the European Court of Justice (Judgements of 5 May 1998, Cases). The Court held:

“Where there is uncertainty as to the existence or extent of risks to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent.”

Therefore a mobile phone-base-station-erection-process with transparent participation and permission procedure with

- information ahead
- active involvement in the siting-process of the local public
- inspection of alternative locations for the siting
- considerations on conservation of land- and townscape
- computation and measurement of exposure
- considerations on existing sources of HF-EMF exposure
- inspection and monitoring after installation.
- National database on a governmental level giving details of all RF transmitters and open for public (e.g. map of Zürich in the internet)
- Exposure guidelines with respect of the Precautionary Principle, the international Scientists Resolutions and the WHO-definition of health

is, as the practice in the city of Salzburg demonstrated from 1998 to 2001, a very practicable, efficient, time- and expense-minimising solution for all involved parties: local authorities, local public and the providers,

- able to avoid conflicts and a state of “rien ne va plus”,
- with respect of democratic rights and public health,
- minimising expenses on all sides and building mutual trust.

As public pro- and contra-information-discussions in Austria show, the active involvement of the public and local authorities in the base-station-siting-process as well as the pre-information of the expected immissions are the base of an acceptance of the mobile-phone-base-station-infrastructure.

Therefore and according to our experience, the presented Consensus-Model can and should be a possible regulatory framework for the European Community, as it warrants the future development of mobile phone infrastructure with respect of democratic rights and public health. Existing base-stations should and must also be taken into consideration. The question of liability has to be solved.

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SESSION 6-8

"THE FIRST WEST-EUROPEAN APPROACH TO THE EMF-FRAMEWORK BASED ON THE PRECAUTIONARY PRINCIPLE: THE ITALIAN-SWISS-APPROACH."

Livio Giuliani

ISPESL Venezia, Italy - Charged of Italian government within the EMF-working-group of the EU-Council (1998/1999) for the Recommendation 1999/512.

On the end of '90 years, in Italy as well as in Switzerland, the risk assessment related to EMF exposure of workers and people was considered suitable to involve the Precautionary Principle (PP) in determining the risk management and stating the restrictions for the workers' and people's exposures.

For extremely low frequencies (ELF) the epidemiological results, starting from the Wertheimer and Leeper studies, through the Swedish Karolinska Institutet investigations, until the Theriault data concerning electric workers in Canada, as well as many other data (from Ohlsen in Denmark, Floderus in Sweden, etc.), suggested the assumption of the PP in EMF risk management.

Such an assumption was confirmed by in vitro and in vivo experimental results, particularly from Blackman and Blanchard, Liboff, Zhadin (the so called BLZ-effect), that suggested that weak variable magnetic fields could interact with the cell membrane inducing ion currents, able to overcome the brownian strengths within the cell and determining intensive transmembrane ion effluxes.

For very- and ultra- high frequencies (RF/MW) the similarity of the biological effects induced by ELF and by ELF-AM-RF or ELF-pulsed microwaves has been considered as well as data concerning possible adverse effects induced into the cell metabolism (calcium pump alteration, Blackman C.F. et al., 1980, 1985), into the tissues functionality (decreased NK functionality, Leyle D.B. et al, 1983), into living complex organisms (increased lymphoma expression in genetically modified mice, Repacholi M. et al., 1997).

Moreover the RF/MW risk management has forced to take in account that exposures caused by the mobile phone terminals were at the same order of greatness then the threshold for thermal health effects (4 W/kg, ANSI 1981, IRPA 1982, 1988, IEEE 1992, CENELEC 1994, ICNIRP 1998).

Such a consideration induced to keep as low as possible the whole body exposures caused by

broadcasting and mobile phone antennas.

To get such a task, both ELF and RF/MW risk matrixes were examined and the technological capabilities were stressed to contain the whole body exposures.

For ELF they discovered that the ceiling values suggested by the six Swedish Institutes for Safety (few microTesla, 1996) could be easily reached.

For RF/MW fixed antennas they appreciated that levels at the order of $0,1\text{W}/\text{m}^2$ could be not exceeded. Such a quality target was confirmed in Italy at the Conference between ISPESL (Health Ministry) and the Italian networks (RAI, MEDIASET, TMC, TIM; OMNITEL VODAPHONE, WIND), held in Naples on October 1 1998 and a consensus-document was subscribed on Dec. 22, 1998. So the application of the Precautionary Principle to EMF was taken in agreement with the Italian broadcast- and mobile-telephone-industry.

Such an approach lead to the Italian decree 381/1998 and to the Swiss Federal ordinance 840.710/1999 that stated the following limit-values for RF/MW whole body exposures (Tab. 1). The same Swiss Federal ordinance stated also the limit values for the exposures to 50 Hz magnetic fields, in Italy fixed by two different decrees, on 1992 and 2003 (Tab. 2). The Italian decree on 1992 provided also minimal distances to be observed between houses and high voltage power lines (Tab. 3). Another decree on 1991 already stated the minimal distances between houses and middle voltage lines in the range 1,000-60,000 V.

Such distances shielded people from high exposures to the 50 Hz magnetic field.

Tab. 1	Occasional exposures	Long exposures *
RF/MW Exposures Limits		
Italy, 1998	$9 \text{ W}/\text{m}^2$ if $0.1 \leq f < 3 \text{ MHz}$ $1 \text{ W}/\text{m}^2$ if $3 \leq f < 3000 \text{ MHz}$ $4 \text{ W}/\text{m}^2$ if $3 \leq f < 300 \text{ GHz}$	$0.1 \text{ W}/\text{m}^2$ if $0.1 \leq f < 300,000 \text{ MHz}$
Swiss, 1999	$2 \text{ W}/\text{m}^2$ if $10 \leq f \leq 400 \text{ MHz}$ $0.005 * f$ if $0.4 \leq f \leq 2 \text{ GHz}$ $10 \text{ W}/\text{m}^2$ if $2 \leq f \leq 300 \text{ GHz}$	$0.024 \text{ W}/\text{m}^2$ if $0.3 < f < 900 \text{ MHz}$ $0.042 \text{ W}/\text{m}^2$ if $0.9 < f < 1 \text{ GHz}$ $0.096 \text{ W}/\text{m}^2$ if $1.8 < f < 2.4 \text{ GHz}$

Where f is the frequency.

* More than 4 hours a day, in Italy. For each antenna, in Swiss.

Tab. 2	Exposures to old plants*	Exposures to new plants **
50 Hz Exposures Limits	Italy, 1992; Swiss, 1999	Italy 2003; Swiss, 1999
Italy, 1992	0.1 mT if $f = 50 \text{ Hz}$	0.003 mT if $f = 50 \text{ Hz}$
Swiss, 1999	0.1 mT if $f = 50 \text{ Hz}$	$0,001 \text{ mT}$ if $f = 50 \text{ Hz}$

Where f is the frequency.

* More than 4 hours a day, in Italy.

** For each antenna, in Swiss.

Tab. 3	132 kV / 375 A max	220kV/1000A max	380 kV / 1500 A max
Distance Restrictions			

Italy, 1992	10 m	18 m	28 m
Italy, 1991	(300 + T) cm where T is the voltage in kV		

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Session 6-9

EMF STANDARDS AND RESEARCH ACTIVITIES IN KOREA

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INTRODUCTION

Public concerns associated with power lines, mobile phones and base stations have been increasing. However, this phenomenon has arisen mainly from the press reports which have not been based on the exact knowledge of the health effects from the electromagnetic field (EMF) exposures in many cases. This has caused to prevail that EMF facilities would be hazardous.

Attitudes to EMF effects on human in papers and broadcasts in Korea have not been friendly. In fact, 56 % of the EMF news were negative and only 29 % of the news were neutral in the press between April 2000 and May 2002[1]. According to the survey conducted in 2002, 89 % of people believed that EMF exposures could cause adverse health effects regardless of its level and 85 % of them answered that the information was from TV[1]. However, only 17 % of them knew that there was no scientific evidence for adverse health effects of a long-term weak EMF exposure in the survey.

In this paper, details of EMF standards and policies in Korea will be discussed. In addition, EMF researches including dosimetry and EMF measurement, in vivo and in vitro studies for EMF exposures, epidemiological study and volunteer study in Korea will be introduced in the following sections. It is expected that scientific results from the EMF researches in Korea would contribute to the world EMF project.

EMF STANDARDS AND POLICIES

In December 1999, the article 47-2 of "The Radio Wave Act" was revised in the National Assembly in order to enact a provision for protection from the EMF exposures and then it was proclaimed in January 2000. Furthermore, in December 2000, the Ministry of Information and Communication (MIC) of Korea announced officially four separate ordinances for exposure limits: measurement methods for EMF intensities and specific absorption rate (SAR) values, and installations and devices to which the exposure limits apply. They have been enforced from 1 January 2002.

The exposure limits of the electric and magnetic fields in the frequency ranges up to 300 GHz are

regulated in the ordinance (see Tables 1 & 2). The SAR values for mobile phones are also regulated in the frequency ranges between 100 kHz and 10 GHz. The exposure limits for EMF intensities follow the ICNIRP guideline and the SAR limits are based on the IEEE/ANSI guideline. The ordinances, except the SAR limit for mobile phones, are not mandatory but recommendatory. Precautionary policies have not been adopted yet in Korea.

Regarding the mobile phones, the SAR values for each mobile phone available on the market have been published in the internet homepage of mobile phone manufacturers from 1 September 2003. The government has also adopted a mandatory rule to restrict the use of mobile phones in moving vehicles. Hands-free devices should be used while driving. The law has been enforced on 1 July 2001.

For the public, a booklet of “EMF in Everyday Life and Human Protection” has been published by the MIC in cooperation with the EMF expert group in Korea. In addition, a new EMF internet web site for the two-way communication (www.emf.or.kr) was opened on December 2002. The main contents of the web site are as follows: EMF news, FAQs, bulletin board for two-way communications, a general introduction to EMF, research trends, established facts on the EMF biological effects, laws and policies, other relevant information. Main communication topics in the bulletin board were as follows: actual exposure levels, health effects of EMF from mobile phones, transformer stations, power lines, broadcasting stations, base stations, and electric appliances.

Table 1 - EMF exposure limits for the public^[2,3]

Freq Range	E-field strength (V/m)	B-field strength (A/m)	B flux density (μ T)	Power density (W/m^2)	
< 1Hz	–	320,000	40,000		
1Hz – 8Hz	10,000	$320,000/f^2$	$40,000/f^2$		
8Hz – 25Hz	10,000	$4000/f$	$5000/f$		
25Hz – 800Hz	$250/f$	$4/f$	$5/f$		
0.8kHz – 3kHz	$250/f$	5	6.25		
3kHz – 150kHz	87	5	6.25		
150kHz – 1MHz	$87/\sqrt{f}$	$0.73/f$	$0.92/f$		
1MHz – 10MHz	$87/\sqrt{f}$	$0.73/f$	$0.92/f$		
10MHz – 400MHz	28	0.073	0.092		2
400MHz – 2GHz	$1.375\sqrt{f}$	$0.0037\sqrt{f}$	$0.0046\sqrt{f}$		$f/200$
2GHz – 300GHz	61	0.16	0.20	10	

Table 2 - EMF exposure limits for workers^[2,3]

Freq Range	E-field strength (V/m)	B-field strength (A/m)	B flux density (μ T)	Power density (W/m^2)
< 1Hz	–	1.63×10^5	2×10^5	
1Hz – 8Hz	20,000	$1.63 \times 10^5/f^2$	$2 \times 10^5/f^2$	
8Hz – 25Hz	20,000	$20,000/f$	$25,000/f$	
25Hz – 820Hz	$500/f$	$20/f$	$25/f$	
0.82kHz – 65kHz	610	24.4	30.7	
65kHz – 1MHz	610	$1.6/f$	$2.0/f$	
1MHz – 10MHz	$610/f$	$1.6/f$	$2.0/f$	
10MHz – 400MHz	61	0.16	0.2	10
400MHz – 2GHz	$3\sqrt{f}$	$0.008\sqrt{f}$	$0.01\sqrt{f}$	$f/40$
2GHz – 300GHz	137	0.36	0.45	50

EMF RESEARCH ACTIVITIES

In 2000, a five-year EMF research project funded mainly by the government (MIC) has been started. The total amount of the budget will be reached about \$8.5m for the duration of the project. Main research topics are as follows: dosimetry, in vivo and in vitro studies for intermediate frequency (IF) and radio frequency (RF) exposures, epidemiological studies. Several other research projects such as health effects for the extremely low frequency (ELF) exposures have been investigated. It has been supported by other

government ministries such as Ministry of Environment and Ministry of Commerce, Industry and Energy.

For ELF, MF and RF studies, researches have been carried out in Electronics and Telecommunications Research Institute (ETRI), Korea Electromagnetic Engineering Society (KEES) and Radio Research Laboratory. On the other hand, the ELF studies have been investigated by other research organizations such as Korea Electric Power Company, Korea Electricity Research Institute and Korea Electric Power Research Institute.

Research projects for recent years are summarized in the following sections.

Dosimetry and EMF Measurement

Researches on numerical and experimental assessment of SAR for wireless devices have been performed. Research topics are as follows: SAR reduction technique of a mobile phone; ERP test method of a small transmitter; evaluation technique of exposure level near a base station for mobile communication; numerical techniques for computational dosimetry; measurements for dielectric properties of cancerous tissues.

Methods for the SAR reduction have been developed. A new folder-type mobile phone with the dual antennas was designed to reduce SAR on the human head[4]. In order to achieve the optimal performance in the phone, it was designed that PIFA was operated only if the folder was opened while calling.

SARs for mobile devices such as PDA, IMT-2000 phone and hand-held PC have been studied using a numerical analysis method. A whole body model of the numerical phantom using a volunteer has been developed[5]. In addition, a high resolution head model for children has been under constructed. Exposure levels near a base station for mobile communication have been evaluated and SARs for whole body exposure from base station antennas have been analyzed.

The dielectric properties of various cancers such as brain tumour, breast cancer, gastric carcinoma and colon cancer were measured in the frequency range of 500 MHz to 5 GHz[6]. Cancers were cultivated applying the xenograft model of growing human cancerous tissues using the specific pathogen free homo inbred mouse (or a nude mouse). The results showed that measured values of complex permittivity for all four cancerous tissues were similar with little variations over the frequency range used.

Recently, a calibration system of the electric and magnetic field probe has been studied to measure SAR exactly and near field strength from electronic devices or wireless communication systems in Korea[7~14]. The technology to generate the standard electric and magnetic fields that are almost the same level of International Council for Non-Ionizing Radiation Protection (ICNIRP) has been studying in electromagnetic susceptibility (EMS) testing. The effective and total radiation power of mobile phones and radiated electromagnetic fields from printed circuit boards (PCB) have been also studying[15~20].

In Vivo and In Vitro Study

Several in vivo studies for IF and RF exposures have been carried out. Rats have been exposed to saw tooth magnetic fields of 20 kHz in order to elucidate the effects of the MF exposures on subacute toxicity, malformation upon gestational age and carcinogenic effects combined with environmental carcinogens^[21-23]. There were no significant differences comparing to the control. Teratological effects were also studied by exposing pregnant ICR mice. Mortality, growth retardation, changes in head size and other morphological abnormalities were examined and no significant effect was found.

In vivo studies for IF exposure will be carried out until 2003. The studies will be focused on the effect of 20 kHz magnetic field on mammary tumorigenesis and 2-year long-term bioassay in Sprague-Dawley rats. An in vitro study for IF exposure is also ongoing to investigate the effect of micronucleus formation and induction of apoptosis in human peripheral blood lymphocytes exposed to 20 kHz magnetic field.

Human fibroblast cells and T-lymphocyte cells have been exposed to fields of 848.5 MHz and 1.8 GHz which have been used in mobile telecommunications^[24]. Cell proliferation and destruction, cell transformations, chromatic aberrations, alterations in gene expression and stress responses have been investigated^[25,26]. The results showed that EMF exposures from mobile phones do not cause any direct short-term effects on chromosome. However, stress response and reversible suppression of cell growth could be caused. Further studies are under way to investigate long-term effects and changes in mRNA expression by the DNA chip technique.

Epidemiological Study

Epidemiological studies of carcinomas (leukemia, malignant lymphoma, brain tumor, breast cancer)

for the residents near AM radio stations were performed^[27]. The purpose was to investigate an association between residing near radio broadcast towers and carcinogenic appearance based on a geographical correlation design. Among ten exposed areas, two areas were showed significantly high incidence for leukemia and brain tumor compared to control areas. For malignant lymphoma and breast cancer, however, there were no significantly increased areas. Results suggested the necessity of further analytical epidemiological studies with more precise exposure measurement and information of confounding factors.

For the RF exposures from mobile phones, a cross-sectional symptom survey was carried out^[28]. The preliminary result showed that there would be a correlation between the number of phone uses and thyroid carcinoma. However, there was no correlation for brain tumor and breast cancer. Symptoms such as dizziness, nausea, heat perception in cheek, fatigue in eyeball and pain in ears were reported. Positive dose-response relations were observed. Further analytical study with more information of confounding factors will be investigated until 2004.

Volunteer Study

A volunteer study for a mobile phone exposure is under way and has been studied from 2001 to 2004. Young and healthy volunteers were organized into three groups (long-term-using group, short-term-using group, and non-using group) and EEG tests were performed^[29]. No significant difference was found. Further investigations are ongoing to find the possible relationship between immune system activity/brain function and mobile phone use. Another volunteer study for the mobile phone exposure was started in 2002 and will be finished in 2004. More comprehensive investigations will be performed for the possible EMF effects of mobile phones on brain functions and immune systems.

CONCLUSIONS

EMF standards and policies in Korea were introduced. EMF researches including dosimetry and EMF measurements, in vivo and in vitro studies for the EMF exposures, epidemiological studies and volunteer studies were also discussed. It is expected that scientific results from the EMF researches in Korea would contribute to the world EMF project.

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Discussion

CONSIDERING FACTORS IN CHINESE EMF STANDARD

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ABSTRACT: Chinese environmental quality standard “EMF Protection Standard” GB8702-88 has been applied for more than ten years. It should be updated according to the program of standard establishment. In order to draft a more reasonable and uniform restriction for EF or MF or EMF exposure, the amendment should consider the current EMF exposure standards in china and in other countries. Several seminars have been held for dealing with the problem, and there are two different opinions in china. Industries suggest adopting ICNIRP Guidelines, but EPA and the Ministry of Health consider that the Guidelines are inadequate to protect people and ecological environment. This paper focus on the considering factors in Chinese EMF standard amending.

Purpose of the standard:

1. To manage and supervise all the facilities which emits EF, MF, or EMF, and thus to satisfy requirements of society and economy development and protect public health and ecological environment. The final purpose is to fulfil sustaining development of society and economy and environment.
2. To protect people from the EMF adverse effects .

Foundation of Law:

2.1 <Environmental Protection Law of P.R.China>:

No.1 “Protecting and improving living environment and ecological environment, preventing pollution and other social effects of pollution, protecting public health, accelerating development of socialistic modernization. ”

No.24 “Preventing the waste gas, waste water, waste solid, radioactive matter and EMF,....., which are made from production”

No.9 “Department of national environmental protection make up the environmental quality standards”
<Preventing Occupational Diseases Law of P.R.China>

No.1 “Preventing, controlling, eliminating occupational risk, preventing and curing occupational diseases, protecting public health, and relevant rights and interests, improving development economy.”

No.11 “National healthy standards of preventing and cruing occupational disease should be established by the ministry of health. ”

The Purpose, Scope, and EMF exposure restrictions in the standard should be in compliance with these laws.

Definition of Health

“Health is a state of complete physical, mental and social well-being, and not merely the absence of disease and infirmity”(WHO). Namely, people are in good status of physical, mental and social well-being.

Health effects:

Different levels of health effects can be induced by EF, MF, and EMF exposure.

1. Exposure to EMF results in no any potential adverse effects on public health and ecological environment.
2. Exposure to EMF may result in slight changes in a few physiologic indexes , but can be reversed soon after stopping the exposure.
3. Exposure to EMF can result in physiologic functional disorders and leading to highly potential

adverse effects, but may be recovered gradually by stopping the exposure.

4. Exposure to EMF can lead to human or organism irreversible pathological changes or disease.

ESTABLISHMENT OF EMF EXPOSURE LIMITS FOR THE STANDARD:

The principle of determining the exposure limits are based on the thresholds of potential adverse effects and the practice experience accumulated in the past 10 years. We have determined that the potential adverse effects which should be protected are the health effects induced by EMF between 2nd and 3rd level mentioned above. Based on this conclusion, the EMF exposure threshold are established and n listed in table 1.

Table 1 The Thresholds of Potential Adverse Effect for 50Hz, 100kHz-300GHz EMF Exposure

Frequency Range	Quantities	Thresholds
50Hz	B	100uT
100kHz-10GHz	SAR	1W/kg
10GHz-300GHz	S	4mW / cm ²

The Standards would not prevent the developing of related industries.

The EMF Protection Standard GB8702-88 has been performed for 17 years, and plays an key role in preventing pollution of EMF radiation, protecting environment, and protecting public health. The standard helped to accelerate the development of EMF related industries under legal practice. R&T system, telecom system and electric power system in china have been developed rapidly in the past 10 years. Most of them are in compliance with the EMF Protection Standard GB8702-88 in which the exposure limits lower than those in the amending exposure standards.

1. EMF from R&T emission station in cities.

table 2, R&T emission station

City	Height of tower (m)	Total power (kW)	Ground value		Roof value		
			Distance from tower (m)	power density $\mu\text{W}/\text{cm}^2$	Distance from tower (m)	Floor No	power density $\mu\text{W}/\text{cm}^2$
Beijing	410	240	250	2.84	400	FL.6th	3.28
Shanghai	468	210	250	0.87	173	FL.22nd	2.50
Tianjin	415.2	107	600	1.82	400	FL.24th	0.53

The data in table 2 showed that the power densities which may affect people are in the range of 0.53-3.28 $\mu\text{W}/\text{cm}^2$, which are much lower than exposure limit($40\mu\text{W}/\text{cm}^2$).

2. The exposure levels of short wave emitted from radio broadcast station in some locations were higher than standard (28-87V/m), however, the problem has been resolved after antennae adjusting and resident migration. For example, the electric field strength is much lower than the limit (28V/m) at a distance of 40m or more from a 100kW antenna.

3. Mobile phone base station

Mobile phone is growing so rapidly and there are over 200 million users in china at the end of 2002. In some big cities, such as Beijing, shanghai, Guangzhou, the distance of basic stations between each other is about 300 meter. There are less than 1% basic stations with an exposure level over $8 \mu\text{W}/\text{cm}^2$. And there are only a few stations over $40 \mu\text{W}/\text{cm}^2$, however, most of them have been resolved by heightening antenna, changing orientation of radiation and adjusting the location of antenna equipment.

4. Telecommunication satellite stations are usually set up at the countryside around large cities. The satellite antennas have a diameter of 13m with the highest emission power of 3kW. The microwave exposure levels measured in Beijing, in the worst case(slp angle 10°) were in the range of $10-33 \mu\text{W}/\text{cm}^2$ less than the limit at the distance of 20-100m from the above-mentioned antenna.

5. Electric field (EF) from high voltage power line

The EF strength levels directly beneath the line with the voltage of 110 kV or 220 kV are usually less than 4kV/mm. For 500kV power line, the exposure limit may be met at 5m away from its corridor.

In summary, the current EMF exposure standards for general public do not block the development of related industries in china and economic prosperity.

Session 7-1

STUDY ON MEMBRANE ELECTROPORATION OF SEVERAL NEURONS AND CELLS INDUCED BY EMP AND HPM

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Background: Electromagnetic radiation (EMR) can be divided into ionizing radiation (γ -ray, X-ray) and non-ionizing radiation (laser, microwave, radiation frequency), in which high power microwave (HPM) and electromagnetic pulse (EMP) belong to non-ionizing radiation. HPM and EMP occurred not only in peace time (radar, cell phone, TV-pad, et al), but also in war time, e.g. nuclear explosion, HPM weapon, EMP weapon, bomb explosion, et al. The experimental study and epidemiological survey have confirmed that HPM and EMP could induce human injury and health risks, even fatal effects.

Experimental animal investigation indicated that main target organs included brain—particular hippocampus (nerve-behavior abnormality), endocrine glands, heart —particularly transmission fiber (heart dysfunction, blocking), gonad — test, ovary (dysgenesis, testosterone descent), eye— (lens opacity), lymphatic tissue (immune function descent), hemopoietic tissue (hemopoietic function descent), in which brain was one of the most sensitive.

The injury effects of EMP and HPM were divided into 4 phases: immediate, early phase (within 1 week), middle phase (2-4 weeks), late phase (>4 weeks, e.g., lens opacity, encephalatrophy, tumor, dysgenesis, hereditation). After high intensity EMP and HPM irradiation, fatal effects also occurred. The main lethal causes were infection, hemorrhage, and emaciation— dyscrasia. We found the sensitivity of injury and lethal effect have phylogenic difference: monkey was the most, below in proper order were dog, rabbit, rat (mouse).

The mechanisms of injury in HPM and EMP include thermal effect and Non-thermal effect. In the former, temperature of tissue rises about 5-11°C, e.g., after mice were irradiated by 2450MHz microwave, the temperature of skin, thoracic cavity and brain rises about 5-10°C, 5-9°C, 6-11°C, respectively, and result in the degeneration, apoptosis, necrosis of cells; In the latter, the damage region involved mainly cell and molecular structure, including biophysical reaction, biochemical reaction, gene mutation, cellular factor and signal transmission abnormalities, finally result in the injury of tissue, organ, and organism.

In order to study the mechanisms of non-thermal effects, this article observed the electroporation effect of EMP and HPM on cultured neurons of hippocampus and hypothalamus, cells of hypophysis and myocardium; investigated the alternation of several ions in cells and culture-liquid; and reveal the significance of electroporation on cell membrane.

Methods: Neurons of hippocampus and hypothalamus, cells of hypophysis, myocardium and testis (Leydig's cells) of Wistar rat were separately cultured in six 6-hole boards, one board was control sample. In every cell, the all five boards were irradiated by high field strength 5 EMP within 2 minutes (electric field intensity 60 KV/m, rise time 20nsec, pulse width 30 μ sec), in which myocardial cells were separately irradiated by HPM (power density 950mw/cm², pulse width 0.35 μ sec, irradiated time 60 sec.)

and ^{60}Co γ -ray (dose 8 Gy).

The changes of structure on surface of cell membrane of all neurons and cells were observed using Atomic Forces Microscopy (SPM-9500J3, Japan) after irradiation. The concentration of Ca^{2+} , K^+ , Na^+ , Mg^{2+} , Cl^- , LDH, AST, CHE in culture medium were measured at 0h,1h,6h,12h,24h and 48h by reagent boxes (Beijing Zhongsheng high-tech bioengineering Company). The concentration of $i[\text{Ca}^{2+}]$ in cells and neurons were measured using Laser Confocal Scanning Microscopy (Radiance2000,Bio-rad). Moreover, the growth activity (MTT) and apoptosis, necrosis (FCM) of various cells and neurons were examined at 0h, 6h, 2h, 24h, 48h after irradiation.

All dates were analyzed by statistical software SPSS 8.0.

Results: 1. In EMP and HPM groups, the electroporation of cell membrane occurred in all cells (neurons of hippocampus and hypothalamus, cells of hypophysis and myocardium). The number, shape, size and depth were different in various cells, in which the number of hole were more, and bigger, wider, deeper in HPM group than that in EMP group. In all irradiated cells the cell membranes were penetrated (the depth was generally 13-130nm). In γ -ray group, the electroporation of membranes did not occur.(Fig 1-5).

2. The concentration of $i[\text{Ca}^{2+}]$ in all irradiated cells and neurons was apparently decreased ($P<0.01$) than that in control group (Fig6).

3. The concentration of Ca^{2+} , Mg^{2+} , Na^+ , K^+ , Cl^- and LDH, AST, CHE in culture-liquid of various cells and neurons were obviously increased ($P<0.01$) than that in control group(Fig7-12).

4. The percentage of apoptosis and necrosis in various irradiated neurons and cells were obviously increased ($P<0.01$) than that in control group (Fig13-14, Table1).

5. The growth activity in all irradiated cells was obviously descent ($P<0.01$ or < 0.05), particularly, at 12h (Table 2).

6. Kinetic servation shows that membrane electroporation of leydig's cell of testis could be recoverable at 30th minits after EMP irradiation.

Conclusion: 1. EMP and HPM could injure and electroporate the membranes of neurons of hippocampus and hypothalamus, cells of hypophysis and myocardium. Above mentioned electroporation did not occur after γ -ray irradiation.

2. The membrane electroporation induced outflow of multi-ions from cells and occurrence of apoptosis and necrosis of cells.

3. The damage degree of electroporation effect in HPM group was more severe than that in EMP group.

4. Membrane electroporation of leydig's cell of testis could be recoverable after EMP irradiation.

Key Words: HPM, EMP, membrane electroporation, neurons, multi-ions

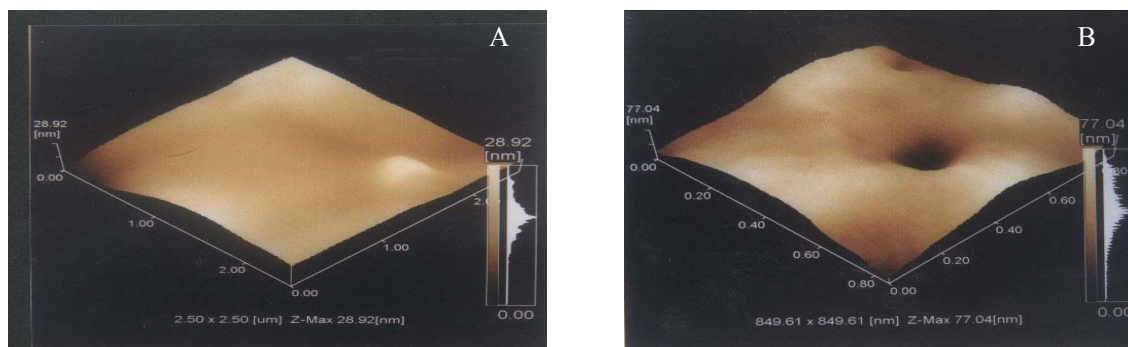


Fig1. electroporation of hippocampus neuron
A: control. B: irradiated by EMP 60 KV/m.

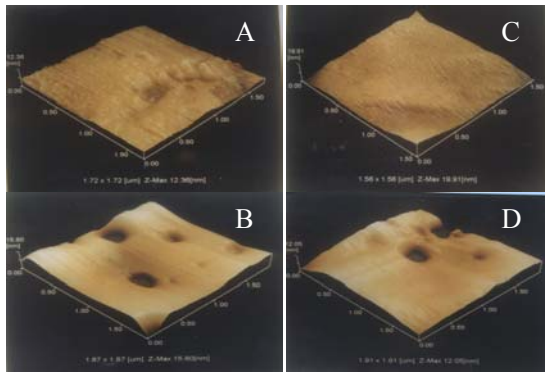


Fig2. electroporation of endocrine gland
Left: hypothalamus; right: hypophysis
A,C: control; B,D: irradiated by EMP

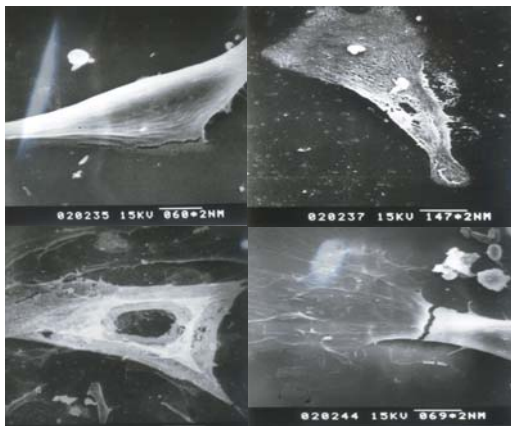


Fig4. electroporation of myocardium in SEM

Table 1. Rate of apoptosis and necrosis of myocardial cells (HPM)

Death	Control	6h	24h
Apoptosis	2.36 ± 0.87	26.76 ± 5.12**	26.44 ± 2.67**
Necrosis	1.05 ± 0.96	24.78 ± 6.52**	21.35 ± 5.43**

Table 2. The growth activity of myocardial cells after HPM

	0h	6h	12h	24h	48h	72h
EMP	0.40 ± 0.07*	0.36 ± 0.05**	0.18 ± 0.08**	0.31 ± 0.07**	0.49 ± 0.05	0.54 ± 0.10
Control	0.59 ± 0.09	0.53 ± 0.12	0.57 ± 0.06	0.62 ± 0.13	0.56 ± 0.02	0.58 ± 0.09

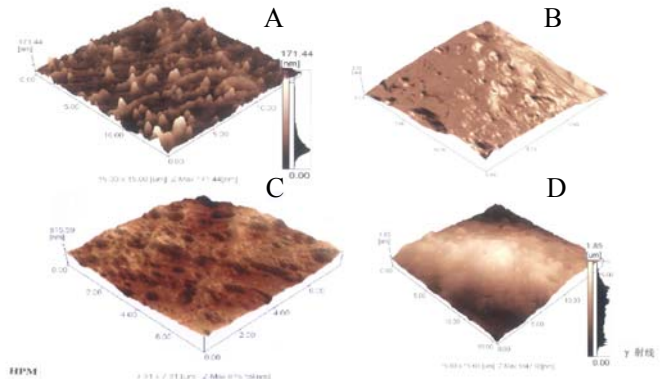


Fig5. electroporation of myocardium
A: control; B: irradiated by EMP;
C: irradiated by HPM; D: irradiated by γ -ray

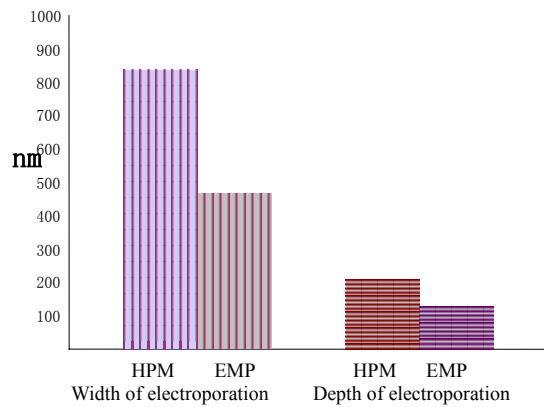


Fig5.comparison of electroporation between HPM and EMP group

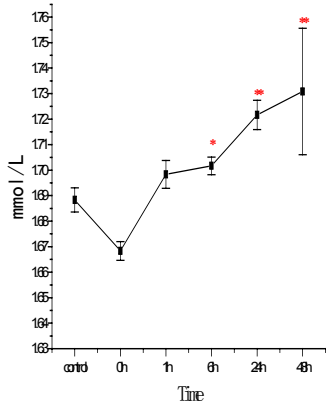


Fig7. concentration of Ca^{2+} in culture-liquid after HPM

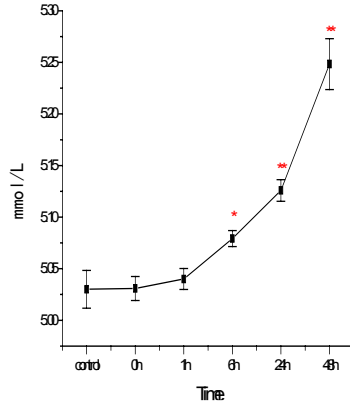


Fig8. concentration of K^{+} in culture-liquid after HPM

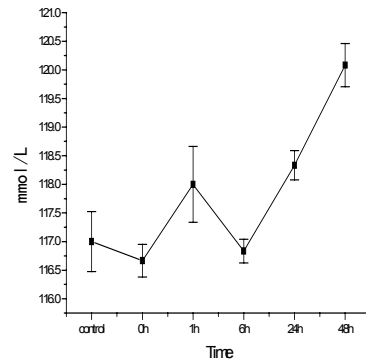


Fig9. concentration of Cl^{-} in culture-liquid after HPM

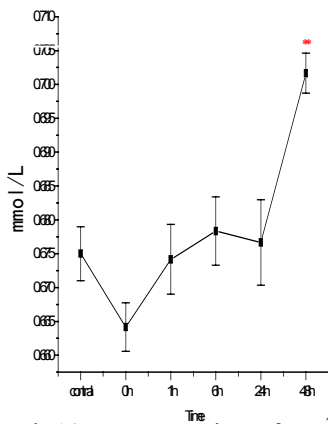


Fig10. concentration of Mg^{2+} in culture-liquid after HPM

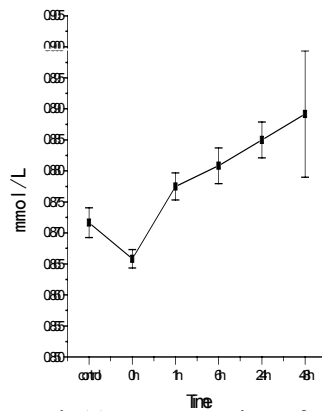


Fig11. concentration of P^{3+} in culture-liquid after HPM

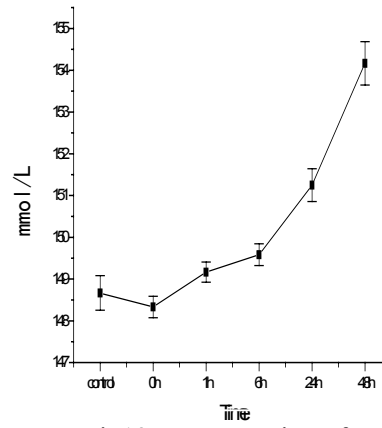


Fig12. concentration of Na^{+} in culture-liquid after HPM

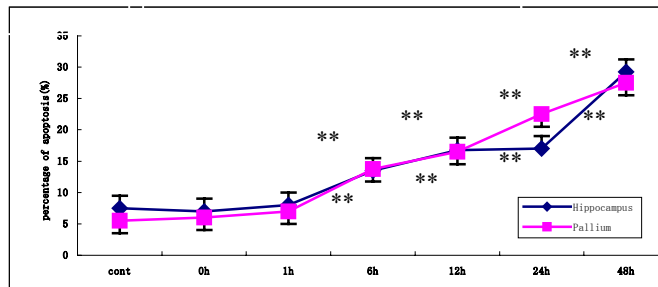


Fig13. results of tunnel (percentage of apoptosis after EMP)

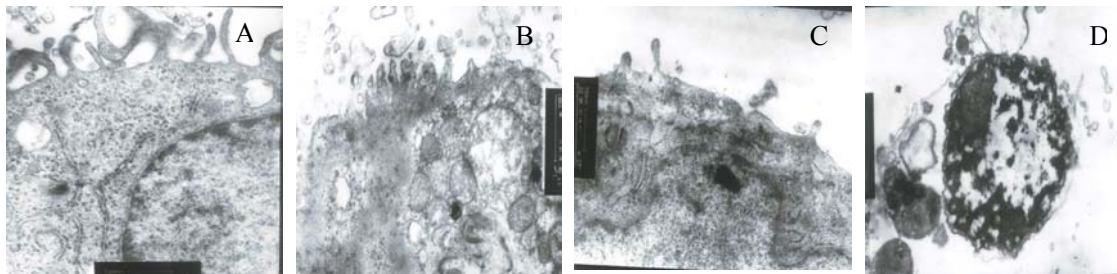


Fig14. Apoptosis and necrosis of myocardial cells in TEM.
A: control; B, C, D: irradiated

IN VITRO MODEL RESEARCH INTO BIOEFFECTS OF EXTREMELY HIGH POWER MICROWAVE PULSES

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Recent advances in pulsed power technologies have resulted in increased availability and wider use of microwave transmitters that can emit nano- and microsecond pulses at peak powers of hundreds of megawatts and even gigawatts. High-peak, low-average power radiation from such transmitters may cause biological reactions that are qualitatively different from known microwave effects, thereby representing a new, unknown, and potentially hazardous environmental factor. However, current knowledge of bioeffects of extremely high power microwave pulses (EHPP) remains very limited. The few studies that have explored peak specific absorption rate (SAR) levels of 0.1-20 kW/g have produced isolated and generally inconclusive data (see [1, 2] for review). EHPP bioeffects at still higher peak SAR (> 100 kW/g) remain mostly "uncharted territory" for biologists and safety specialists.

However, EHPP studies in animals are very costly, because they require gigawatt-output transmitters and custom-made exposure facilities, such as specialized anechoic chambers. Alternatively, many key aspects of EHPP biological action can be studied *in vitro* in cell and tissue models. Concentrating radiated energy in a small sample (e.g., 0.1-1 ml) can produce very high peak SAR (up to 1 MW/g) at relatively low transmitter output power (e.g., 250 kW). Other advantages of the *in vitro* approach are the possibilities for precise control of temperature and SAR in the exposed sample, greater flexibility of pulsing regimens, and safety of the exposure system for personnel and laboratory equipment.

In 1998, a one-of-a-kind EHPP exposure system designed specifically for *in vitro* biological research was assembled and put in operation at Brooks AFB Tri-Service Directed Energy Bioeffects Facility in San Antonio, TX, USA. In its current configuration (after several upgrades), this system is based on a model 337X magnetron transmitter (Applied Systems Engineering, Inc.) with the peak output of 230-260 kW at carrier frequencies from 9 to 10.5 GHz. The pulse duration can be varied between 0.5 and 2 μ s, at any pulse repetition rate less than 300 Hz. The peak E-field in the waveguide (WR90, 22.86 x 10.16 mm) reaches 1.57 MV/m. For comparison of biological effects, the system can also be energized from a "regular" microwave source (HP 8690A sweep oscillator and Hughes 8020H amplifier) in CW or pulsed regimens, at the same carrier frequency and time-average power as the EHPP transmitter.

The chamber for exposure of biological specimens is made atop a vertical end section of the waveguide. The waveguide is sealed with a sapphire matching plate flush with the flange, and the chamber is filled with an appropriate electrolyte solution (e.g., a culture medium or a Ringer solution). Local SAR in solution above the matching plate was calculated theoretically (by an analytical technique and by a finite difference time domain modeling), and was measured using a novel method of precision high-resolution dosimetry [3]. The latter technique was particularly useful, including such tasks as SAR mapping within the exposed volume and local SAR measurements inside biological samples. It was established that our EHPP system is capable of producing peak SAR of up to 1 MW/g, which is about 20 times higher than ever reported by other investigators.

So far, EHPP effects have been explored in several biological models using various endpoints, including changes in the pacemaker rate in isolated, spontaneously beating frog heart slices [4]; the growth rate of gel-suspended yeast cells [5]; function of voltage-gated calcium channels in the membrane of cultured mammalian cells [6]; synaptic transmission and long-term potentiation in isolated rat hippocampal slices [7]. Exposure duration varied from less than a second to several hours, at pulse repetition rates from 0.1 Hz (practically no heating) up to 10-50 Hz (up to 20 °C temperature rise). Details of these studies, specific research techniques, objectives, and findings will be reviewed during the presentation. Overall,

EHPP exposures produced no biological effect if the temperature rise during exposure was negligible. On the contrary, when the temperature rise exceeded some 0.2-0.5 °C (depending on test sensitivity), EHPP produced same effects as CW irradiation at equal SAR or conventional heating of the same intensity. Within studied limits, no EHPP-specific bioeffects could be observed. One can speculate that all the tested biological objects just happened to be insensitive to EHPP; however, there is no guidance or indications that any other objects or processes might be more vulnerable. As of the up-to-date knowledge, EHPP appear to be a no more dangerous modality than CW emissions, and the safety standards based on general microwave heating of tissues should be just as applicable to EHPP as to “regular” microwave radiations. To test this implication, future studies should explore effects of still shorter pulses and at different carrier frequencies; also, special attention should be given to the possibility of delayed biological effects of EHPP exposure.

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Session 7-3

9.37GHz microwave irradiation alter NMDA mRNA expression in the hippocampus of rats

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The nervous system is very sensitive to electromagnetic irradiation and hence is one of the major targets of microwave bioeffects. Disturbance to nervous system leads to behavioral changes. Dysfunction of learned behaviors is the prominent effect of microwave irradiation in experimental animals. However, the exact mechanisms of microwave irradiation induced behavioral disorders remain to be elucidated. In the past several years, we have been focused on exploring the possible role of NMDA receptors in functional changes of learned behaviors following exposure to 9.37GHz microwave.

Expressions of different NMDA receptor (NR1, NR2A, NR2B, NR2C, NR2D) subunit mRNA and formation of NMDA-dependent long term potential (LTP) were determined by RT-PCR, Western blotting and patch clamp technique in Wistar rats with 9.37 GHz microwave irradiation. It was found that: ①

exposure to 9.37 GHz microwave impaired induction of LTP in hippocampus slices, which was correlated with the memory deficits of the rats; ② expression of NR1 subunit mRNA was significantly down-regulated, reflecting the decrease in NMDA receptors in hippocampus after exposure ; ③ disturbances of NR2A, NR2B, NR2C, NR2D subunit expressions functionally altered NMDA receptors and these changes were in accordance with the suppression of LTP formation in the primarily cultured hippocampal neurons; ④ CAMPK II protein phosphorylation was markedly inhibited following exposure to microwave irradiation. This indicated that the signal transduction pathway of NMDA-dependent LTP induction was inhibited by microwave irradiation.

These results could be of importance in understanding the molecular mechanisms for microwave induced behavioral disorders, specifically the learning and memory deficits.

Session 7-4

EFFECTS OF PULSED MAGNETIC FIELDS AND ROTATING MAGNETIC FIELDS ON INTRACELLULAR FREE CALCIUM IN HEPG2 CELLS

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Background: Epidemiologically, it was reported the associations between the environmental magnetic fields and the occurrence of cancers. Therefore, many researchers are devoted to defining possible mechanisms. Calcium biochemistry has been a central focus of many of the studies because calcium is a ubiquitous second messenger to regulate molecular events. Unfortunately, there is an apparent lack of consistency among research groups on the effects of electromagnetic fields on cellular calcium mobilization throughout the field of research into the biologic effects of electromagnetic fields. As a result, researchers in our laboratory measured the changes of intracellular free calcium concentration in HepG2 cells after magnetic fields treatment to confirm the exact effect of electromagnetic fields on intracellular calcium.

Methods:

1. Cell culture: HepG2 cell was grown in MEM containing 10%FBS, 100IU/ml penicillin, 100 μ g/ml streptomycin, 15mM HEPES and 26mM sodium bicarbonate in a humidified incubator with 5% CO₂ at 37°C.

2. Preparation of Fura-2 loaded cells: The cells collected were adjusted to a cell density of 1.0 \times 10⁶/ml and incubated for 60 min in culture medium containing 2 μ M Fura-2 (1mM stock in DMSO): cells exposed to the pulsed magnetic field were incubated in a humidified incubator with 5% CO₂ at 37°C, while cells treated with rotating magnetic field were incubated at 23°C in a water bath. Then the cells were spun down and resuspended in the culture medium without Fura-2 to the initial density for another 30 min incubation. Afterwards, the cells were washed two times with calcium free HEPES buffer (5.4mM KCl, 30mM NaCl, 1.0mM NaH₂PO₄·2H₂O, 5.5mM Glucose, 50mM HEPES, pH 7.4).

3. Magnetic fields exposure: (1) A cylindrical solenoid placed in the incubator, could generate square waves and the current in the coils was adjusted to generate an alternating flux density of 16Hz, 1.55mT (average value). Cells were disposed in the middle of the solenoid during incubation in the incubator for 60 min. (2) HepG2 cells were also exposed for 5 min after being washed with calcium free HEPES buffer to a 300mT-16Hz rotating magnetic fields exposure system, whose field strength of the magnetic fields and frequency could be adjusted from 1mT to 300mT, 0Hz to 10Hz.

4. Calcium measurements: The measurement was carried out on a HITACHI F-4500 fluorescence

spectrophotometer. The fluorescence of Fura-2 was measured continually with filters for excitation at 340nm and 380nm and for emission at 510nm. A 1.5ml cell suspension was transferred into quartz cuvette, gently stirred and measured the fluorescence of the sample for 600sec. The steady-state fluorescence was recorded in the first 400 sec. 1%(w/v) Triton-X 100 and 1mM CaCl₂ (stock solution 20% Triton-X 100 and 20mM CaCl₂) was added at 400sec to achieve the maximal ratio value (R_{max}). 10mM EGTA (stock solution 200mM EGTA, pH9.0) was added at 500sec to generate the minimal ratio value (R_{min}) for the last 100sec. The values of calcium concentration were obtained using the equation: $[Ca^{2+}]_i = K_d(F_0/F_s)(R - R_{min}) / (R_{max} - R)$, where R is the fluorescence ratio of samples at 340nm and 380nm (F₃₄₀/F₃₈₀), F₀ and F_s represent the fluorescence strength of Fura-2 at 380nm at zero and saturated Ca²⁺, and K_d of Fura-2 was determined to be equal to 224nM at 37°C, 120nM at 23°C.

Data analysis. All comparisons for significance were made using Student's *t*-test, and all hypothesis tests used a criterion level of $\alpha=0.05$.

Results:

1. Effect of pulsed magnetic fields: According to the $[Ca^{2+}]_i$ calculation equation, there was a positive relation between intracellular ca²⁺ concentration and R value. The intracellular calcium of HepG2 cells, which were exposed to the pulsed magnetic field at 1.55mT in 16 Hz for 1 hour, had slightly increased according to the change of R values (control:2.4519±0.2378; exposure:2.5266±0.2915), but there were no significant differences being observed between the exposure and the control ($P>0.05$, n=23) (Fig. 1).

2. Effect of rotating magnetic fields: HepG2 cells were exposed to the rotating magnetic field at 300mT in 2Hz for 5min just before calcium measurement. The intracellular free calcium concentration of HepG2 cells remained unchanged according to the change of R values (control:1.3650±0.0626; exposure:1.3602±0.0771), and no significant difference was detected by Student's *t*-test (Fig. 2).

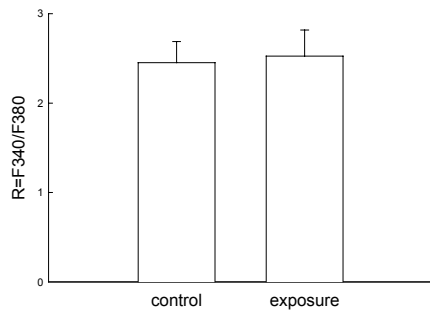


Fig. 1 the effect of pulsed electromagnetic fields on intracellular free calcium concentration
Mean±sem, n=23

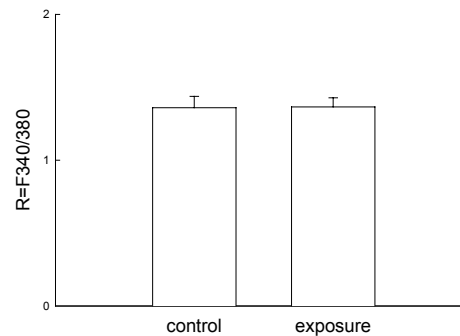


Fig. 2 the effect of rotating permanent magnetic fields on intracellular free calcium concentration.
Mean±sem, n=9

Conclusion: The effects of the pulsed magnetic fields at 1.55mT in 16Hz and the rotating magnetic fields at 300mT in 2Hz on the intracellular free calcium concentration were not detected under the experimental condition we examined and the assay methods we applied. Since the possible changes of the intracellular calcium concentration caused by stimulation will restore to the basal concentration in a short time, we plan to design one kind of device as the accessory of the fluorescence spectrophotometer to examine the real-time change of the intracellular calcium concentration.

Session 7-5

EFFECTS OF THE MAGNETIC FIELD ON THE BONE MINERAL DENSITY, INTENSITY AND METABOLITE OF OVX MICE

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Experiment 1

Materials and Methods: 60 pure SD rats were divided into 6 groups: the sham-operation control group (control group, 7 case), ovariectomized group (OVX group, 10 case), Ovariectomized and supplement of Ca²⁺ (OVX+Ca²⁺ group, 8 case), Ovariectomized, supplement of Ca²⁺ and exposure to magnetic field 30min/d (OVX+Ca²⁺+EM30', 10 case), Ovariectomized and exposure to magnetic field 30min/d (OVX+EM30', 10 case), Ovariectomized and exposure to magnetic field 60min/d (OVX+EM60', 7 case). The groups of exposure to magnetic field were exposed to the strong magnetism therapeutic apparatus with permanent-magnets rotating at low frequency (HMF-6000) designed by Shenzhen University (The patent number in China is: zL93118017.1 and the patent number in America is 5667.469). The exposure time last one month. The bone mineral density, intensity, the contents of alkaline phosphatase (ALP), phosphorus and calcium in the serum were measured

Results:

1. The levels of bone mineral density (BMD), phosphorus and calcium in the serum of OVX group were lower evidently than those of the other groups.
2. The BMD was highest in the group of just exposure to magnetic field 60 min/d (OVX+EM60'), but the other indexes, such as energy absorption, elastic energy absorption, maximum load, elastic flexibility and bone mineral contents (BMC), were highest in the group of OVX+Ca²⁺+EM30'.
3. There weren't effect on the weight of uterus of rats of supplement of Ca²⁺ and exposure to magnetic field.

Experiment 2

Materials and Methods: 60 pure SD rats were divided into 6 groups. Three were controls and three were experiment groups. All experiment groups were exposed to the magnetic field for 90min/d. The exposure time lasted one month and the control group I and experiment group I were sacrificed after the exposure end. The control group 2 and experiment group 2 were sacrificed after they were breed normally another one month and the groups 3 were breed the third month. BMD, estradiol and BGP contents were measured.

Results:

1. It's possible too longer to exposure the magnetic field for 90min/d because BMD in the experiment group 1 was lower that in the control group, but the increase degree of BMD in the experiment group was higher than that in the control group after the exposure to the magnetic field end 1-2 month.
2. There weren't evidently different about estradiol and BGP content between the control and experiment groups

Experiment 3

Materials and Methods: BMD of 10 voluntary osteoporosis patients (age about 60) were measured using the DEXA BMD before exposure to the magnetic field. Then they were exposed to the magnetic field for 90min each day for 15 days. BMD was measured after exposure to he magnetic field end one month.

Results:

1. BMD increased at different extent for 10 volunteers and the ache and clonus were alleviated obviously.
2. Extent of increased BMD of the position exposed to the magnetic field was higher obviously than that of the position which wasn't exposed. For example, if BMD of vertebra increased more, BMD of thighbone

increased less. Vice versa. It is because if the range of exposure is vertebra, thighbone couldn't be exposed. It suggested that increase of BMD was related to direct exposure to the magnetic field. It didn't due to affect other factors, such as estradiol and BGP for the magnetic field to increased BMD.

Conclusions:

1. Exposure to the magnetic field improved BMD. It didn't due to affect other factors, such as estradiol and BGP for the magnetic field to increased BMD. Hosokawa et al's experiment results showed that ELF magnetic fields facilitated collagen synthesis and suppressed strongly Ca^{2+} releasing from intracellular stores, but inhibited partially Ca^{2+} influxing through membrane.
2. There were 'window' and 'lag' effects of treatment of the magnetic field.

Session 7-6

THE BASIC THEORY OF ELECTROMAGNETIC WAVE ON CELL MEMBRANE AND TISSUE*

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Background: The representative fact in athermal effects of electromagnetic wave on biology is influence upon the transmembrane movement of ions, such as Ca^{2+} , thus cause change in ion concentration in cell. In this paper, it was discussed that the basic theory for the athermal effects related to change in the ion concentration is caused by electromagnetic wave (EMW), in order to provide theory foundation studying the mechanism of the athermal effects of EMW on cells.

Method: This theory is based on two aspects: the one, cell membrane and biological tissue are regarded as a general electromagnetic medium, that is, based on physics viewpoint; The two, the cell membrane are regarded as a special living material, that is, based on biology viewpoint.

Results: In order to have quantity conception in the results of this paper, it is supposed that the frequency $f=10^{11}$ Hz and the power flux density $P=10mW/cm^2$ respectively of EMW, and the EMW is normal incidence to the surface of a biology body. If based on physics viewpoint, when cell membrane and biological tissue interact with EMW, change in intrasurface and extrasurface charge density of cell membrane are taken place, which is about 1‰ of the inherent quantity on surface of a normal cell; If based on biology viewpoint, when biological tissue and cell membrane interact with EMW, the variation in concentration of intracellular and extracellular ion are taken place, the amount of change in the ratio between concentration of intracellular and extracellular ion is about 10^{-4} .

Conclusion: The amount of change is similar to the inherent ratio between concentration of intracellular and extracellular Ca^{2+} of a normal cell, and the change corresponds to about 10^6 two-valence ions through the cell membrane in 1 second, which much greater than the requirement amount caused change in cells physiological and biochemistry states, i.e. is about 10^3 which was confirmed by chemotaxis experiment from Grimes et al. The physiological and biochemistry states of cells will be changed by the changes in ion concentration in cell and by informations carried by charges and ions of the transmembrane movement.

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THE EFFECT OF PULSED ELECTRIC FIELD ON THE LEVEL OF TYROSINE PHOSPHORYLATION AND GENE EXPRESSION LEVEL OF HUMAN HEPATOCYTES MEDIATED BY INSULIN

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INTRODUCTION

In 1997, Kirka Reinbold [1997] found that constituents within serum mediated the effects of EM fields on cells, which may provide a resolution pathway to the dilemma imposed by theoretical arguments regarding the possibility of biology effects of electromagnetic fields. Our previous studies showed that the structure of the insulin be changed by the electromagnetic (EM) field. The exposed insulin solution caused decrease in the proliferation of the L02 cells. The binding capacity of the exposed insulin molecule with the insulin receptor may be responsible for the decrease. In this paper, we decided to prove the exposure information could be transmitted through the cell membrane and discuss the mechanism of the effect inside the cell membrane. The level of tyrosine phosphorylation is critical to the activity of the insulin receptor and the signal pathway of insulin. The tyrosine phosphorylation level should be investigated. The gene expression level was also tested using gene chip analysis to show the effect on the gene expression.

MATERIALS AND METHODS

Insulin was exposed to the pulsed electric field (PEF) for 0 min or 20 min before being added into the culture medium of L02 human hepatocytes. Thirty minutes later, the tyrosine phosphorylation level of the cells of each group was monitored by a flow cytometry. After we cultured the cells in the medium with the exposed insulin or the normal insulin for 68 hours, the gene expression levels were measured by using gene expression chip using the Human Genome U95Av2 Array (Affymetrix). This single array represents about 12,000 sequences previously characterized in terms of function or disease association.

RESULTS

Field influence on tyrosine phosphorylation level mediated by insulin

Thirty minutes after the normal insulin solution was added into the culture medium, the cells of control group showed an increase of about 44.14% in the tyrosine phosphorylation level compared with the blank group. The test group also showed an increase of about 29.26% compared with the blank group. Parallel the test group with the control group, the phosphorylation level caused by the exposed insulin decreased 10.33%.

Field Influence on the gene expression mediated by insulin

The change of fifty-five out of 12,000 gene sequences of the test group was obvious compared to the control one. Many genes are signal proteins of the insulin signal pathway such as the human tyrosine phosphatase mRNA (increased), the human tyrosine kinase (TXK) mRNA (increased) and the small GTP-binding protein (increased). Some are growth factor and proliferation genes, for example, the human sapiens mRNA for connective tissue growth factor, the H.sapiens CYR61 mRNA and the homo sapiens endothelin-1 (EDN1) gene.

CONCLUSION

Protein-tyrosine phosphatases (PTPases) play an essential role in the regulation of reversible tyrosine phosphorylation of cellular proteins that mediate insulin action. In the gene expression experiment, we found that an increase in tyrosine phosphatase expression level of 2.4-fold. Li PM concluded that overexpression of the protein-tyrosine phosphatase LAR in hepatoma cells suppressed the insulin receptor activation. Kulas DT discovered that overexpression of the transmembrane protein-tyrosine phosphatase (PTPase) CD45 in nonhematopoietic cell results in decreased signaling through growth factor receptor tyrosine kinases. The increased PTPases level might be responsible for the cell proliferation inhibition caused by the exposed insulin. But the tyrosine kinase expression level also increased 2.8 fold, which added to the complexity of the possible cell proliferation reason. Hirsch's experiments indicated that the inhibitors of tyrosine kinases and tyrosine phosphatases could be the promoter mitogenic activation. The long-term treatment of exposed insulin might downregulate some unknown inhibitors that promoted proliferation, thus both the tyrosine kinase and phosphatase was raised. Another possible reason was that

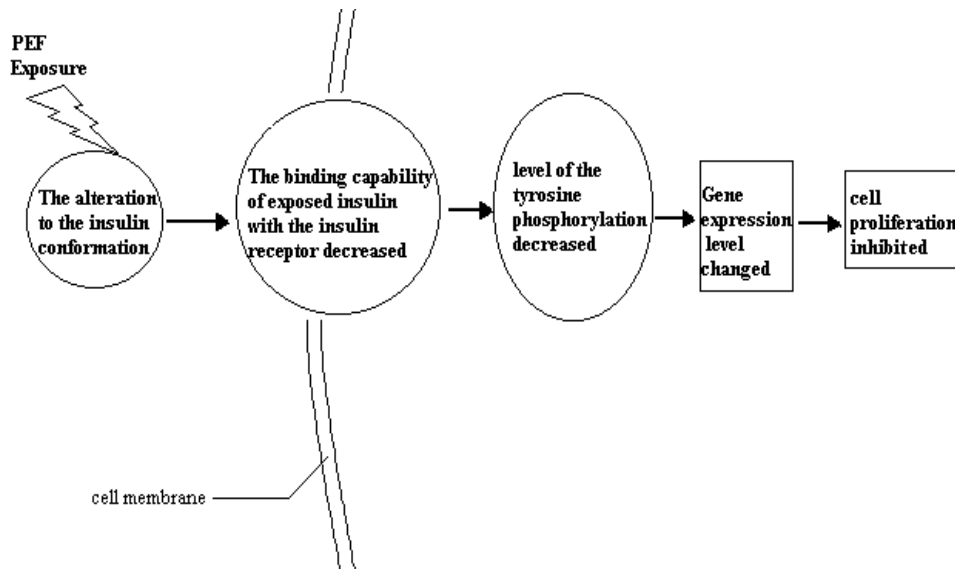


Fig.1 The PEF exposure pathway into the cells via insulin.

the expression level of the tyrosine kinase, tyrosine phosphatase and the small GTP-bind protein were raised in order to make up for the partially incompetence of the exposed insulin molecule to activate the cell growth.

The signal pathway could be affected by the exposed insulin, which means that the exposure signal could be transferred into the cells and influence their metabolism and proliferation indirectly. Our studies shed light on the fact that the EM field changed the structure of the insulin molecule. The molecule carried the exposure signal into the cell, affected the level of tyrosine phosphorylation and the gene expression level by the decrease of binding capability with the insulin receptor and consequently inhibited cell proliferation. (see Fig 1). These studies proposed that: the intercellular signal molecule such as insulin can be the target of the electromagnetic field and acts as a signal carrying the information of PEF, which consequently causes biological effects.

DISCUSS THE INFLUENCE OF EMF ON KINASES BASED ON BIOINFORMATICS

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Background:

Cell signal transduction system can receive, magnify and assemble external signal, and respond to external stimulus. External signal transfer intercellularly and endocellularly by signal transduction molecules, then influence cell gene expression, replication and differentiation. Here, kinase participate directly in the process of cell signal transduction^{1, 2}. The activation of kinase can beget the start-up of signal transduction. Therefore, kinase play a key role in the pathway of cell signal transduction.

The essential premise to study the mechanism of bio-effect of electromagnetic field is to disclose the principle and related process of interaction between electromagnetic field and tissue, cell and molecule. The current research productions show that electromagnetic field in a certain intensity and frequency can affect the activation of kinase in a certain extent. For the basic in-depth research, besides analyzing frequency of electromagnetic field, it is very important for us to study the related effect targets of kinases, which are sensitive to electromagnetic field.

Model and method of calculation

We adopt mutiple sequence alignment program ClustalX1.8 to analyze protein sequence, and then build up Hidden Markov model (HMM)^{3, 4} shown in figure 1. We input the output files from ClustalX1.8 program into the HMM. HMM introduces two reciprocally correlative random process to describe the statistical characteristics. One process is a hidden (can't be observed) Markov chains which have definite states, the other is a random process of observation result, which is associated with each state of Markov chains. The traits of hidden Markov chains can be disclosed by observable signal. The arithmetic of HMM can pick up the sequence traits of homologous sequence in protein family, such as common conservative sites. Thereby, we can search other protein sequences and databases according to the traits of sequence family, and then find the interesting related protein sequence.

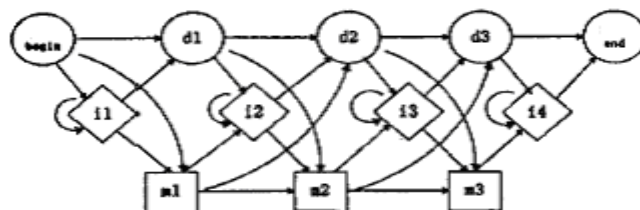


Fig 1 HMM

Result:

We enter National Center of Biotechnology Information in USA by internet with <http://www.ncbi.nlm.nih.gov> and inquire the protein sequences of protein kinase A, protein kinase C and tyrosine kinase, whose names is listed in figure 2.

At first, we make the mutiple sequence alignment of the searched 12 kinases by ClustalX program and the alignment result is shown in figure 2 (part of alignment sequences). According to figure 2, we can come to the conclusion that the sequence segment has good conservation.

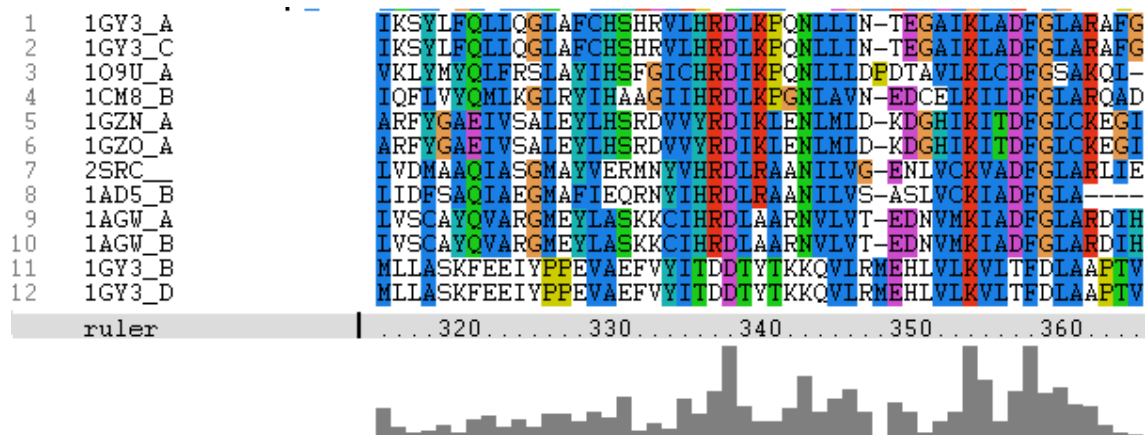


Fig 2 Result of mutiple sequence alignment (histogram show the conservative degree)

Afterward, the HMM can be trained based on these alignment results. We do some searching in PFAM protein database after calibrating the HMM. The parameters used in the process of sequence search are E-value and Bit-score, whose threshold are 10 similarly. In this case, we search some homologous sequences such as 1CM8_A,1GZ8_A,1AD5_A which belong to stress-activated protein kinase, protein kinase A, protein kinase C respectively. These protein kinases pertain to the sequences which are sensitive to electromagnetic field. Therefore, the HMM and related arithmetic can classify the homologous sequences well. The mutiple sequence relative relationship can be deep understood by analyzing the phylogenetic tree which is shown in figure 3.

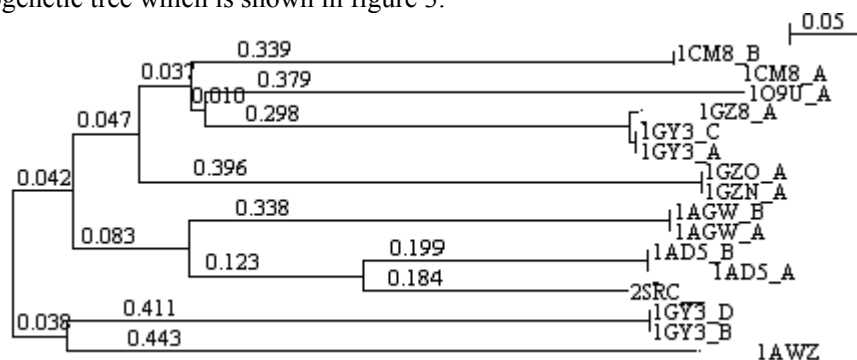


Fig 3 Phylogenetic tree of kinases

According to Fig 2, the sequence (IKSYLFQLLQGLAFCHSHRVLHRDLKQPQNLINT EGAIKLADFGLA) can be analysed ulteriorly by hydrophobicity figure 4.

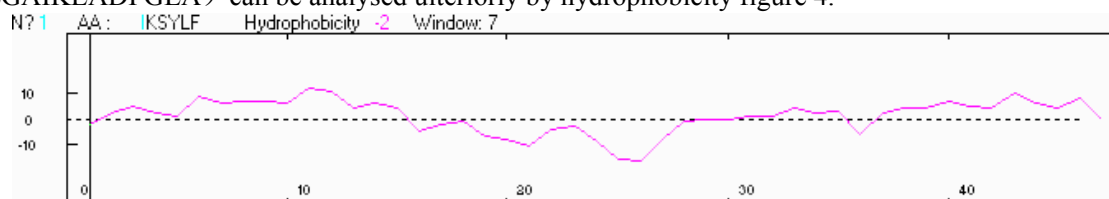


Fig 4 Hydrophobicity analysis of conservative sequence

We can speculate the polarity of the conservation sequence based on Fig 4. Polarity distribution can be helpful to explain the molecularly orientation of effect targets of EMF bio-effect.

Conclusion:

Based on known materials about influence of EMF on protein kinases' activation, it is very attractile to probe into EMF bio-effect of homologous unkown protein by use of HMM and related arithmetic. Namely, by analyzing current bio-molecular experimental data which reflect sensitivity to EMF, we can mine interesting data and sum up rules, then build up corresponding model, look for the characteristic sequences sensitive to EMF. EMF can produce bio-effect by affecting these characteristic sequences. So, it is helpful to predict if bio-molecules are sensitive to EMF and instruct related experiments. For instance, if the protome and genome databases sensitive to a certain frequence and intensity EMF can be built completely, it is

available to search and predict if SARS has the related proteins and genes which are sensitive to a certain frequency and intensity EMF. Therefore, it is very helpful to develop the great project to therapy SARS by using EMF.

The method to search protein sequences is very accurate, fast, convenient and fit for high flux disposal of and analysis on a mass of protein data. The method provides the available schemes to mine and identify potential sequences which are sensitive to EMF from large-scale protein data. Therefore, we can study deep the molecular mechanism of EMF bio-effect by adopting the method and combining related experimental data.

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Session 8-1

DISCUSS ON MECHANISM OF ELECTROMAGNETIC BIOEFFECTS

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We always hold that, thermal, nonthermal or resonant effects are the mechanism of electromagnetic bioeffects. But I think these are the goal or target points, not the bioeffect itself. The difference between living and nonliving material is that, the organism can maintain its own internal environment – homeostasis, according to regulation among its own organs, nervous system, endocrine system, immuno-system, circulatory system ect. with each other. The thermal, nonthermal, resonant are only the switch points of bioeffects. The changes after switch on are more important. Certainly the changes thenafter are complicated and difficult to research, But we can't evade the crucial question with a simple explanation.

CHANGES IN PATTERN OF GENE EXPRESSION IN RAT BRAIN CELLS INDUCED BY IN VIVO GSM MICROWAVE EXPOSURE.

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Background: The health-related effects of microwaves such as induction of DNA double-strand breaks (DSBs) and leakage in brain blood barrier have previously been reported [^{1, 2}]. Biological effects of microwaves depend on several physical parameters including frequency, modulation, polarization and intensity [^{3, 4}]. This makes it very important to test specific types of modulation (e.g. GSM), which are used in mobile phones. Here, we investigated whether GSM microwaves induce DNA breaks, changes in chromatin conformation and in gene expression.

Methods: An installation employing GSM signal, all standard modulations included, was used. This installation was based on a GSM900 test-mobile phone. The output of the phone was connected by coaxial cable to a transverse electromagnetic cell (TEM-cell). The test-mobile phone was programmed to use the mobile phone channel where the transmission frequency is 915 MHz. The test phone had a programmed regulation of output power in the range of 0.02 - 2 W (13-33 dBm). We used maximum power level, 2 W, which corresponds to SAR being 400 mW/kg. Rats, 4 animals in each group, were exposed or sham-exposed in parallel, in couples, to microwaves during 2 h. After exposure, rats were sacrificed and brains were dissected into gray matter and white matter. Cell suspensions were prepared from these samples, as well as from spleen and thymus. Small brains were frozen in RNAlater for extraction of RNA and analysis of gene expression patterns. The changes in chromatin conformation, which are indicative of stress response, were measured with the method of anomalous viscosity time dependencies (AVTD). DNA DSBs were analyzed by pulsed-field gel electrophoresis (PFGE). The level of mRNA expression was studied by gene microarrays using Affymetrix U34 GeneChips representing 8800 genes. The data were analyzed with the t-test and the Affymetrix Microarray Suite (MAS) 5.0 software.

Results: 1: No effects of GSM exposure was observed on conformation of chromatin as studied by the AVTD method. 2: No microwave-induced DNA double strand breaks were detected using PFGE in all four types of cells. The employed PFGE technique was sensitive to detect the DNA fragmentation immediately after irradiation of lymphocytes with 0.5 Gy of γ -rays. 3: Six samples from exposed and sham exposed groups, 3 versus 3, were selected for microarray analysis based on RNA quality control. Eleven genes were up regulated in all exposed animals and one gene was down regulated. These changes did not exceed 2-fold but were statistically significant in all 9 comparisons.

Conclusions: The data showed that GSM microwaves did not induce DNA breaks and changes in chromatin conformation, but affected expression of genes in rat brain cells under specific conditions of exposure.

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Session 8-3

CYTOGENETIC STUDIES IN HUMAN BLOOD LYMPHOCYTES EXPOSED *IN VITRO* TO RADIOFREQUENCY RADIATION USED AT TWO CELLULAR TELEPHONE FREQUENCIES (835.62 MHZ & 847.74 MHZ)

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Background: The widespread use of cellular telephones and other types of handheld transceivers have led to rising concerns about the potential human health hazards of increased and chronic exposure to radiofrequency radiation (RFR). The data on the cytogenetic response of human blood lymphocytes exposed *in vitro* to RFR at two frequencies used for cell phone communications (835.62 MHz and 847.74 MHz) are reported here.

Method: Separate experiments were conducted using freshly collected peripheral blood samples from four healthy non-smoking human volunteers. The samples were diluted with tissue culture medium and exposed *in vitro* for 24 hours to continuous wave RFR: (1) 835.62 MHz (FDMA, forward power 68 W, power density 860 mW/m² and average specific absorption rate 4.4 or 5.0 W/kg), and (2) 847.74 MHz (CDMA, forward power of 75 W, power density 950 W/m² and average specific absorption rate 4.9 or 5.5 W/kg). Aliquots of blood samples which were sham-exposed or exposed *in vitro* to an acute dose of 150 cGy of gamma radiation were included as controls. The temperatures of the medium during RFR- and sham-exposures in the radial transmission line facility were controlled at 37±0.3°C. Immediately after the exposures, lymphocytes were stimulated with phytohemagglutinin and cultured at 37±1°C for a total period of 48 or 72 hours. The extent of genetic damage was assessed from the incidence of chromosomal aberrations and micronuclei. The kinetics of cell proliferation was determined from the mitotic indices in 48 hour cultures, and from the incidence of binucleate cells in 72 hour cultures.

Results: The data indicated no significant differences between RFR- and sham-exposed lymphocytes with respect to mitotic indices, frequencies of exchange aberrations, excess fragments, binucleate cells and micronuclei. The response of gamma-irradiated lymphocytes was significantly different from both RFR- and sham-exposed cells for all of these indices.

Conclusion: There was no evidence for induction of chromosomal aberrations and micronuclei in human blood lymphocytes exposed *in vitro* for 24 hours to RFR at 835.62 MHz and 847.74 MHz, at specific absorption rates of 4.4 - 5.5 W/kg.

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EFFECTS OF ELF MAGNETIC FIELD ON PROTEIN EXPRESSION OF HUMAN BREAST CANCER CELL (MCF7)

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INTRODUCTION: The biological effects and action of mechanism of extremely-low frequency magnetic field are not fully elucidated. Previous studies have showed that ELF MF may induce changes in gene and protein expression. but those contradictory reports still remain in the literature. Traditionally, scientists prefer to explore the response of single protein after EMF exposure. Proteome analysis is a direct and high-throughput method to investigate whole-scale proteins level / modification simultaneously between two different states of cells or organisms.

OBJECTIVE: In this project, we are using proteomics analysis to determine whether ELF MF exposure changes in proteins expression.

METHODS: 1. The exposure system consists of three groups of Helmholtz coils, two power regulators and a set of CO₂ incubator. The 50Hz sinusoidal MFs were generated from line current, and the magnetic flux densities could be regulated from 0 to 0.8mT. Magnetic flux density was determined using a power frequency field meter (WG EFA-2, Germany). The AC background field was 1~2 μ T, and static magnetic field was 18.5 μ T, with a 14.1 μ T horizontal and 12.0 μ T vertical component. The temperature in the exposure area was monitored by an electronic thermometer and kept at 37 \pm 0.2 °C throughout the experiment. The dishes containing MCF7 cells were placed coaxially with the centerline in the central area of the coils. Two groups were conducted: a) sham exposure, b) 0.4mT MF exposure. And the exposure time was 24hr.

2. MCF7 cells were grown in Dulbecco's modified Eagle's medium supplemented with 10% FBS in 5% humidified CO₂ at 37°C. The whole proteins were extracted and 200 μ g protein was subjected to 2-dimentional electrophoresis. The pH gradient of the first-dimension electrophoresis was pH3-10 and the IPG strips were 17cm. The silver stained images of the gel were analyzed with PDQuest analysis software (protein expression). The results were analyzed on the overlay of three repetition experiments.

RESULTS: There are approximately six hundred proteins detected using 2-D PAGE. fifty-two proteins among all of the detectable protein spots showed significant changes (at least 2-fold increase or decrease) after exposure to 0.4mT MF for 24hr. Thirty-five proteins disappeared in exposure group, comparing with control group. Based on Mr and pI of all detected change spots, We searched the SWISS-PROT database and found that all of them fall in five categories:(i) cytosolic transport proteins; (ii) regulators of some protein phosphorylase; (iii) ion channel (especially Ca²⁺ and K⁺) proteins located on cell membrane and nuclear membrane; (iv) proteins associated with cancer genesis(p52K, and Zn—alpha 2—glycoprotein); (v) some transcriptional coactivator.

CONCLUSION: Our preliminary finding shows that 50Hz 0.4mT MF may alter expression of various proteins. These detected changes in protein expression will be determined by MS/MS mass spectrometry.

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ESTIMATION OF MUTAGENICITY AND PERTURBATIVE EFFECTS BY EXPOSURE TO STRONG MAGNETIC FIELDS

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Background: Various guidelines to limit exposure to extremely low frequency (ELF) magnetic fields (MFs) were published by international agency such as International Commission on Non-Ionizing Radiation Protection (ICNIRP) ^[1,2] and national organizations such as Japan Society for Occupational Health (JSOH) ^[3], American Conference on Governmental Industrial Health (ACGIH) ^[4], National Radiation Protection Board (NRPB) ^[5] and other organizations. However, these guidelines did not state genetic and carcinogenic effects because of lack of clear scientific evidences that indicate the effect of ELF MFs. On the other hand, several epidemiological studies suggest an association between weak ELF-MF exposure and several types of cancer. Recently, the scientific working group of the Monographs Program of the International Agency for Research on Cancer (IARC) (<http://www.iarc.fr>) stated that environmental exposure to ELF MFs is categorized as possibly carcinogenic to humans (Group 2B) while static MF is categorized as could not be classified as carcinogenic to humans (Group 3) because of limited evidence. In such situations, investigation of the biological effects of exposure to various MFs has a high priority to establish the convincing scientific evidences.

In our study, we decided to investigate biological effects of high density MFs since that is a common strategy for safety evaluation of chemical substances and ionizing radiation although the final goal of our study is to estimate the effect, especially carcinogenicity of weak MFs that we are actually exposed to. In this study, we examine the mutagenicity and perturbative effects of strong static and 50 Hz MFs using budding yeast and discuss the estimation of risk by exposure to MFs in our living environment.

Methods: Budding yeast *Saccharomyces cerevisiae* 4228 (IAM4206, diploid, wild type) and XD83 (*MATa/MATa*, *lys1-1/lys1-1*, *arg4-4/+*, *+/arg4-17*) were used in this study. Two kinds of superconducting magnets (JS-500, Toshiba Co., Japan and SCM type 14/70/1 Oxford Instruments, U.K.) were used for exposure to static MFs and a Helmholtz coil (ISM-12K12-2, IDX Co., Japan) was used for exposure to 50Hz MFs. These magnets were located in constant temperature rooms and exposure space was maintained at 30±0.5°C.

In mutagenicity assay, precultured cells were harvested and washed with 0.1 M phosphate buffer (pH 7.4) and re-suspended in same volume of phosphate buffer. 0.1 ml of cell suspension was mixed with molten soft agar (0.6% Bacto-agar, 0.5% NaCl) and poured on to SD plate containing a trace of lysine for detecting point mutation frequency on *lys 1-1*. 0.1 ml of 1/100 diluted cell suspension was mixed with molten soft agar and poured on to SD plate with amino acids containing a trace of arginine for detecting gene conversion of recombination frequency on *ARG4* allele (between *arg 4-4* and *arg 4-17*). At least 6 plates were made both conditions respectively and then randomly divided two groups. One group was exposed to a MF for 5 days at 30±0.5°C and the other group was incubated in conventional incubator as control. Number of colony on each plate was scored as revertant and calculated the mutation frequency.

In a experiment of perturbative effects, DNA microarray technique was used to determine the cellular response. Yeast Chip which includes 5,876 cDNA out of 6,400 ORFs of *S. cerevisiae* (DNA chip research Inc., Japan,) was used. RNA isolation, cDNA preparation and hybridization were performed by the protocols which provided by the manufacturer with slight modification. The data obtained from each spot were normalized and ratios of gene expression in exposed cells compared to that of control cells were calculated. Clustering analysis was performed with selected genes related to several cellular processes (TCA cycle, DNA damage response, oxidative stress response, protein synthesis and other stress response which was annotated by the *Saccharomyces* genome database (<http://genome-www.stanford.edu/Saccharomyces/>)) using Cluster and TreeView software (Stanford Univ., USA). At least two

independent experiments were performed under every experimental condition.

Results and Discussion:

When yeast cells (strain XD83) cells were exposed to a 5T static MF, reverse mutation frequency in *ARG4* locus slightly increased while reverse mutation in *lys1-1* was not altered. This mutagenic effect disappeared on exposure to a 2T static MF and was lower than the control on exposure to a 1T static MF. When cells were exposed to 0.5T static MF, there was no difference in the frequency of reverse mutation in both *ARG4* and *lys1*. These results suggest that the threshold of the mutagenic effect of static MF was above 2T in this DNA repair proficient strain. Moreover, it is inferred that static EMF exposure caused chromosomal recombination or gene conversion but not point mutation. These results are consistent with the results of our previous study that suggested that exposure to a 5T static MF cause an increase in chromosomal recombination in fruit fly *Drosophila melanogaster*^[6]. On the other hand, exposure to a 50Hz, up to 40mT MF did not affect the frequency of reverse mutation either in *ARG4* or *lys1-1*. This suggests that 50Hz MFs weaker than 40mT do not cause point mutation or gene conversion.

In transcriptome analysis, expression of approximately 90% of the whole ORFs of yeast genome was examined using DNA microarray. When cells were exposed to a 14T static MF, weak inductions of several genes including respiratory processes were repeatedly observed. On the other hand, no significant difference was observed by exposure to a 5T static and a 40mT, 50Hz MFs. To compare the change in gene expression profiles by various stresses, we investigated the global gene expression profile in DNA damaged cells by chemical mutagen and oxidative stressed cells by microaerobic grown to aerobic cultivation. DNA repair genes and oxidative stress response genes were strongly induced by exposure to chemical mutagen, N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG, 30µg/ml). Oxidative stress response genes as catalase, cytochrome-c oxidase and respiration related genes were strongly induced by transferring cells to aerobic cultivation from microaerobic environment for 3h. On the other hand, exposure to MFs did not cause clear induction of specific gene cascades or operons even in a 14T strong static MF. It is inferred that the exposure to static MFs up to 14T or 50Hz MFs up to 40mT does not cause major changes in gene expression profiles in *S. cerevisiae* under the experimental conditions used in this study.

These experimental results suggest that exposure to a 5T static MF has a small effect in increasing chromosomal recombination, while up to 14T static MFs did not cause reproducible alteration of any specific gene cascade in genome-wide expression analysis using DNA microarray in this study. Although the mutagenic effect of MFs was detected in static MF, weak UV irradiation, which estimated to be approximately 1/5 to 1/10 that of average sunlight in Japan, caused drastically increase of both *ARG4* and *lys1* reverse mutations. In a comparison of the results of exposure to MFs and the UV irradiation in this study, the extent of mutagenicity of MFs was estimated to be extremely small since weak UV exposure (18 J/m²) is approximately 20 times more effective than MFs which are at least 10,000 times stronger than those in the environment. In addition, a 50Hz, 40mT MF did not affect either mutation frequency or gene expression profile under experimental condition. These results suggest that the mutagenic and perturbative effects of static and 50Hz MFs in environment would be negligibly small.

Conclusion: Mutagenic and perturbative effects of MFs in budding yeast was able to detect in high density, however, the extent of the effect was small. It suggests that effects of ELF-MFs on cellular function which belongs to single cell itself, not tissue or organ, would be small. Moreover, it also suggests that the effects on basic cellular function of environmental density of ELF-MFs would be negligibly small. In further study, the effects of high density MFs on the specific function or index of tissue and organ will be investigated to establish the clear scientific evidences of biological effect by exposure to MFs.

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Session 8-6

THE CLUSTERING OF GROWTH FACTOR AND CYTOKINE FACTOR RECEPTORS WAS INDUCED BY 50 HZ MAGNETIC FIELD AND BLOCKED BY NOISE MAGNETIC FIELD

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Abstract To study the possible effects of 50Hz magnetic field (MF) exposure on clustering of cell surface receptors, explore the mechanism of signal transduction of ELF-MF and confirm whether or not the noise magnetic fields (MF) interfere these effects induced by 50 Hz MF. Chinese Hamster Lung (CHL) cells were respectively exposed to 50Hz MF, noise MF with 0.4 mT, and combined MF which was superposition of 50 Hz MF with noise MF for different exposure durations (5, 15 and 30 min). Cells treated with 100ng/ml epidermal growth factor (EGF) or 10ng/ml tumor necrosis factor (TNF) for 15 min served as positive control. The clustering of EGF and TNF receptor was analyzed with confocal microscope. The results showed that, like the EGF and TNF, 50 Hz MF at 0.4 mT could obviously induce the clustering of cell surface receptors after exposure for 5 min, while the noise MF alone with the same intensity did not induce receptor clustering. When superposed of noise MF with the same intensity, the receptor clustering induced by 50Hz MF was inhibited. It suggested that the membrane receptors would be the target sites where MF interacts with cell, and the noise MF could interfere these effects.

Keywords: 50 Hz magnetic fields; receptor; clustering; noise magnetic field; interference

That the electricity was widely used in our society made the extremely low frequency electromagnetic fields (ELF-EMF) in environment more and more high. Evidence is accumulating that exposure to ELF-EMF may produce a lot of biological effects. Especially, some reports showed that ELF-EMF such as those from electric power transmission and distribution lines have been associated with increased risk childhood leukemia, cancer of the nervous system, lymphomas and breast cancer^[1-6]. However, the mechanism of ELF-EMF biological effects is still unclear. Our previous study showed that 50 Hz magnetic field (MF) with 0.4 mT could phosphorylate and activate the stress-activated protein kinase (SAPK) and P38 mitogen-activated protein (MAP) kinase (P38 MAPK)^[7, 8]. Kie et al.^[9] also showed that ELF-EMF induced the mitogen-activated protein (MAP) kinase (Erk1/2) activity. These are evidences that ELF-MF exposure may activate signal transduction pathways. Yet, where and how the EMF signal transfers into biological signal in cells is unknown. Since many low-energy electromagnetic fields have little energy to directly traverse the membrane, it is possible that they may modify the existing signal transduction procession in cell membrane, thus producing both transduction and biochemical amplification of the effects of the field itself^[10]. In the present study, we explored if exposure cells to 50Hz MF can induce clustering of cell surface receptors like their ligands, and also investigate whether noise MF can interfere the receptor clustering caused by 50 Hz MF, as we found that the noise MF block the SAPK activation^[11].

Materials and methods

(i) Exposure system. The single 50 Hz MF exposure system consists of three groups of Helmholtz coils with 36cm width, 8cm height, two power regulators and a set of CO₂ incubator (Model 3164, Forma). Three square coils which the upper, middle, and lower coils are 168, 60, 168 turns separately were in series

connection, and were set up in an iron-shielded box. The iron box (containing three square coils) was put into CO₂ incubator, and three coils contacted with two power regulators outside the CO₂ incubator in series connection. A very uniform 50Hz sinusoidal MF was generated in the center of the coils (10×10×10cm³ of three dimensional space) when the coils are energized. The combined exposure system of 50 Hz sinusoidal and noise MF has the same components as the single MF system, but Helmholtz coils are circled with crewel brass wire, which connect with different MF signal, one for 50 Hz sinusoidal MF and the other for noise signal. The noise signal was supplied by Litovitz Lab (USA). The MF signal was monitored with oscillograph. Magnetic flux density in the central area of exposure system was measured by a power frequency field meter. Cell dishes were placed in the central area of the coils and the MF was perpendicular to the dishes. The AC background field was 1~2 μT, and static magnetic field was 18 μT with a 14.1 μT horizontal and 12.0 μT vertical component.

(ii) Antibody and Chemicals. EGF and TNF- α (Calbiochem), Anti-EGFR and Anti-TNF-R1 (Santa Cruz), NP40 (Fluka), Propidium iodide (SIGMA), RPMI medium 1640 (Gibco BRL), Goat anti-rabbit IgG-FITC (Sino-American Biotech. Co.).

(iii) Cell Culture, Group and Treatment. Chinese hamster lung line (CHL) cells were cultured on glass cover slips in RPMI medium 1640 containing 15%FCS 100U/ml of penicillin, 100 μg/ml streptomycin, 100 μg/ml kanamycin, at 37±0.5°C with 95% air and 5% CO₂. Three days (72h) late, all cells were deprived of serum and cultured in serum-free medium for 12 hours. Then CHL cells were treated. The cells in the experiment were divided into five groups: a) positive control (with ligands), b) sham exposure, c) 0.4mT 50 Hz MF exposure, d) 0.4mT noise MF exposure, and e) 0.4 mT 50 Hz MF combined with 0.4 mT noise MF exposure. The positive control was treated with 100ng/ml EGF or 10ng/ml TNF for 15 min. Exposure cells were cultured in exposure system for various times (5, 15, and 30min) with the same condition, and the MF was perpendicular to the dishes. Following different treatment, cells were rinsed with phosphate saline buffer, fixed with paraformaldehyde, treated with NP-40, sealed with goat serum, incubated with antibodies of receptors, goat anti rabbit IgG-FITC and propidium iodide. Finally, the clustering of EGF or TNF receptors was analyzed with confocal microscope (Leica, TCS-SP). Experiments were repeated more than three times.

Results

The results showed that the EGF and TNF could cluster their receptors. Like EGF and TNF, 50 Hz MF at 0.4 mT also obviously induced the clustering of EGF and TNF receptors after exposure for 5 min. However, the noise MF with the same intensity didn't induce receptor clustering. When superposed of noise MF, the receptor clustering induced by 50Hz MF was inhibited (fig. 1 and 2).

Discussion

The receptor on the cell surface is one of important action sites for the extracellular signals, such as hormones, cytokines, et al., and the specific binding between extracellular signals and receptors is usually the beginning for signal transduction. Normally, some ligands (such as EGF) binding to corresponding receptors could induce the receptor clustering, and then activate the cellular signal transduction pathway. So the receptor clustering is usually the initial process of cell signal transduction, and it becomes the index that shows whether extracellular factors interact with receptors. Some studies showed ELF-MF could activate the signal transduction pathways^[7-9]. But the initial site for ELF-MF interacting with cell is also unclear. Devary^[12] found Ultraviolet (UV) light maybe activated the SAPK pathway through cellular membrane, and Rosette^[13] confirmed the growth factor and cytokine receptor is the site from which the UV light activates the SAPK cascade. ELF-MF is similar with UV in essence. So we supposed the receptor maybe one of the targets for ELF-MF. The results of the present study showed exposure to 0.4mT 50 Hz MF could induce the clustering of EGF and TNF receptors. It indicates that 50 Hz MF may interact with signal pathways normally used by growth factors and cytokines. The cellular membrane may be the initial sites where EMF acts with cell and transfer its signal into biological signal. But exactly how the 50 Hz MF lead to multimerization of cell surface receptor is not clear. Physical perturbation of the plasma membrane or a conformational change caused by 50 Hz MF may be the mechanism. The significance of clustering of cell receptors induced by MF is being studied. Litovitz^[14] first found that the superposition of incoherent MF could block the enhancement of ODC activity by a coherent MF in L929 cells if the incoherent field is equal to or greater than that of the coherent field, and thought that the superposition of an incoherent field on a coherent would lead to a total field that is incoherent, and the degree of the incoherent was dependent on the relative amplitudes of the noise and coherent components. The experiment was repeated in

developing chick embryos^[15]. The noise MF with the same intensity didn't induce the receptor clustering, and inhibited the sinusoidal MF effects while combined with sinusoidal MF. Based on the present study, we concluded that the receptors on cell surface are the possible target sites that EMF acts on organism. We also confirmed the noise MF could interfere the effects of ELF-MF

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ELF MAGNETIC FIELDS PROMOTE H₂O₂-INDUCED APOPTOSIS AND NECROSIS AND ITS MOLECULAR MECHANISM

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Background: The possible harmful effects of extremely low frequency (ELF) magnetic fields generated by power lines and household electric appliances on human health has recently led to a growing interest. A possible association between ELF magnetic field exposure and cancer has been suggested, but not unequivocally demonstrated (1, 2). It is well established that apoptosis and necrosis are two distinct modes of cell death. Under damaged conditions, severely hit cells die passively by necrosis, whereas those that have been mildly damaged cells die through apoptosis. Apoptosis plays an important role in maintenance of cellular homeostasis. Several labs have studied the effects of exposure to ELF magnetic field on apoptosis in mammalian cells, but the results are contradictory (3, 4).

Objective: H₂O₂ is an important intracellular compound. As a reactive oxygen species, H₂O₂ can cause cell death through both apoptosis and necrosis. The aim of this study was to determine the effects of 60 Hz 5 mT magnetic fields on H₂O₂-induced apoptotic and necrotic cell death as well as its molecular mechanism in HL-60 cells.

Methods: Human HL-60 (leukemia) cells were cultured in RPMI 1640 medium supplemented with 10 % inactivated fetal calf serum. Exponentially growing cells were seeded in Ø 10 cm dishes at a concentration of 1 × 10⁵ cells/ml, and were then treated with H₂O₂ for 0.5 h-24 h in combination with or without exposure to a 5 mT magnetic field. Two different H₂O₂ concentrations (85 and 100 µM) were used. H₂O₂ was freshly diluted and added to the medium immediately before exposure to ELF magnetic field. Viable cells, apoptotic and necrotic cells were determined by Annexin V flow cytometry assay. The levels of apoptosis-related proteins (Caspase-3, Caspase-7, Bcl-2 and Bax) and poly (ADP-ribose) polymerase (PARP) were detected using western blotting. Statistical analyses were performed using the Student *t*-test. P-values ≤ 0.05 were considered to be statistically significant.

Results: Following treatment with 5 mT magnetic field for 24 h, the number of viable cells did not exhibit any obvious changes in comparison with sham-exposed cells. Simultaneous treatment with 85 or 100 µM H₂O₂ and exposure to the magnetic field for 24 h increased the number of apoptotic and necrotic cells significantly and decreased the number of viable cells significantly compared with H₂O₂ treatment alone. The protein levels of Bax and Bcl-2 showed no differences between H₂O₂-treated cells and those treated with both H₂O₂ and ELF magnetic field. Exposure to the magnetic field also had no effect on H₂O₂-induced Caspase-3 activation. However, the protein levels of active caspase-7 in cells simultaneously exposed to ELF magnetic field and H₂O₂ for 2 h and 8 h was higher than that of H₂O₂ treatment alone. In addition, simultaneous exposure to ELF magnetic field and H₂O₂ caused PARP cleavage and induced early inactivation at 2 h while H₂O₂ treatment alone did not produce this effect until 4 h.

Conclusions: These data suggest that although magnetic field itself cannot induce apoptosis and necrosis,

it exerts a promoting effect on H₂O₂-induced cell death, and demonstrates that caspase-7 as well as PARP may be involved in this process.

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Session 8-8

HEALTH ASSESSMENT OF EXPOSURE TO MF AND RF ON KOREANS

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A pilot study on health assessment of exposure to MF and RF was performed to examine melatonin levels in urine for MF exposure, whereas heart rate, ST segment in ventricular, and ventricular premature beat for cardiac function were evaluated RF exposure from cellularphones of the selected forty subjects during June 2001 to April 2002. Each of 20 subjects in occupational group with cellularphone user and non-occupational group with non-user was measured personal 24-h continual exposure, using EMDEX II (for 40-800Hz, Enertech Consultant, Inc.).

An urine samples for analysis of melatonin excretion level were collected one times a day(immediately after wake-up) for five days from each subjects and analyzed by radioimmunoassay, HRV-test for relationship between heart rate and MF exposure was performed heart rate beat using Holter for subjects, whereas a double EEG-test was performed in 10 long-term users of the cellularphones when using and not using them, and a single EEG-test in 10 short-term users of the cellularphones. Each EEG-recording took 40 min consisting of 30 min filed exposure and 10 min measurement. And it was also estimated the economic value of the potential damage of electromagnetic radiation from cellular phone, and the willingness to pay of people for the study of the radiation damage led by the government, by applying contingent variation method. The results of this study are as follows;

1. The mean personal exposure levels of occupational group with cellularphone user were 0.21 μ T, whereas non-occupational group with non-user were 0.12 μ T. Occupational group were exposed more highly while at work.
2. There seemed not to be significant difference for the subjective average melatonin levels between occupational and non-occupational groups exposed to electromagnetic fields.
3. There seemed not to be difference in the awake EEGs in terms of spectral power density measures between long-term users and short-term users of cellular phones.
4. This study suggested that the economic value of the potential damage by the radiation for a typical cellular phone user is about 20,000 won per year, it means that he would be willing to pay about 1,800 won per year for the study. When the estimates are extended over all cellular phone users in Korea, the

economic value of the potential damage by the radiation is estimated about 600 billion won per year. Also it is estimated that people would be willing to pay about 54 billion won per year for the study.

Finally, this study would provide significant data for further study of risk assessment of magnetic fields. A large scale study concerning more detailed exposure assessment should provide important information on health risk assessment of MF and RF. Further study should provide information on the contribution of various sources and the relationship between human health effect and exposure of magnetic fields.

Session 9-1

EFFECTS OF ALTERNATING MAGNETIC FIELDS ON MALARIA PARASITES

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According to a 1996 World Health Organization report, it is estimated that there are about 500 million clinical malaria infections with 1.5-2.7 million deaths each year worldwide. The development of drug-resistant malaria parasites, beginning about 40 years ago, has drastically eroded the therapeutic efficacy of chloroquine, once the most used anti-malarial. The need for new targets or novel approaches for malaria treatment is enormous. We have been investigating such a novel approach for the treatment of malaria using an alternating magnetic field.

Malaria parasites feed on hemoglobin in erythrocytes of the host. The globin portion of the hemoglobin molecule is broken down in the food vacuole of the parasite by proteases to amino acids that are used by the parasite for protein synthesis and, in some instances, for energy. The heme portion, ferriprotoporphyrin IX, is left intact, since the parasite lacks the enzyme heme oxygenase, which normally carries out further degradation of heme molecules. Free heme is highly toxic to the malaria parasite, because it can cause a chain reaction of oxidation of unsaturated fatty acids and macromolecules involving free radicals, leading to cellular damages.

To eliminate the toxic effects of free heme, heme molecules in the food vacuoles of the parasite are packed into a quasi-crystalline array called malarial pigment or hemozoin by the enzyme heme polymerase, thus rendering the heme molecules less toxic. In hemozoin, the heme polymer is formed by covalent bonding of the iron of one heme molecule with the oxygen of the carboxylate group in one of the side chains of another heme molecule. This molecular arrangement makes hemozoin super-paramagnetic and it behaves like a small bar magnet in a magnetic field. We hypothesized that exposure of the parasites to an alternating magnetic field would shake hemozoin molecules inside the parasite. If the energy exerted on the molecules by the magnetic field is large enough, the rate of formation of hemozoin by heme polymerase would be decreased. Accumulation of free heme in the parasite would then produce toxic effects. Another possibility is that oscillation of hemozoin could lead to mechanical damage to the organelles of the parasite. Significant osmotic and/or colligative imbalance caused by the damage could result in death.

In this paper, we report the effects of an alternating magnetic field on growth of malaria parasites cultured in erythrocytes. Our experiments indicate that the number of parasites (parasitemia) and synthesis of macromolecules (³H]-hypoxanthine incorporation into DNA and RNA) are both decreased in malaria parasite samples exposed to a magnetic field (5-Hz with a duty cycle of 1 second on, 1.5 seconds off, and a peak-to-peak intensity of 1.5 millitesla), in comparison to sham-exposed controls.

WIDEBAND ANTENNA FOR MEDICAL MICROWAVE RADIOMETRY

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Background: Microwave radiometry, as a non-invasive technique which don't pierce inside human and can measure the temperature, is to diagnose early the disease or abnormality by measuring the temperature inside human. It is accompanied with the increase or decrease of temperature in tissue arisen from a disease or abnormality, and as temperature changes, radiated microwaves also change^[1-4].

Because this antenna is contacted to human body, it has very high efficiency and smaller size than the general communication antenna. Numerical approach of design theory is different from that of the general antenna. Because antenna with the wideband characteristic can measure the various frequency ranges, it is possible to search more exactly the position and size of region having the disease.

Methods: Fig. 1 shows the dipole-type antenna contacted to the breast tissue. The designed antenna that has the structure of loop-type dipole antenna is deformed from general dipole antenna. We analyzed an antenna by using the MWS program based on FIM (Finite Integration Method) algorithm. And we measured an antenna to compare with simulated results.

Results: The comparison of the simulated and measured return losses of an antenna is shown in Fig.2. The simulated bandwidth based on 10 dB is about 125% (0.65 GHz-2.82 GHz) and the measured one is about 130% (0.8 GHz 3.8 GHz).

Fig. 3 represents the power distribution of a near field along the X-axis. The power distribution along the X-axis is symmetrical about the Z-axis without regard to the parameter "z" which represents the inner direction of the breast tissue. This power distribution shows the smaller lateral spreading and deeper penetration at 2.0 GHz. This is the desirable effect as a radiometry antenna for tumor detection^[1].

Radiation pattern of the vertical plane (XY plane) is shown in Fig. 4. We can see the suppressed farfield at a direction of a breast tissue. This is because a breast tissue absorbs the power radiated from an antenna.

Conclusion: In this paper, we suggested a dipole-type antenna for measuring human radiometric signals having a small size and ultra wideband characteristic. To have a small size and wideband characteristic, we designed a circular loop-type dipole antenna.

The designed antenna that gets the wideband bandwidth as a result of measurement is suitable for measuring human radiometric signals.

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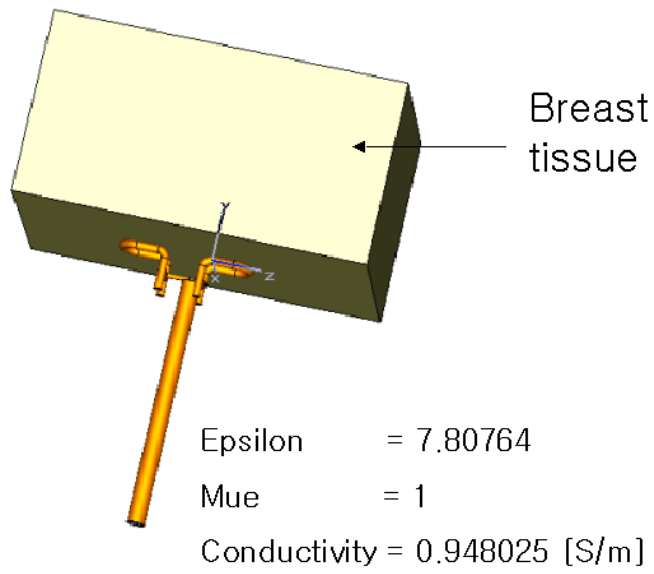


Fig. 1. Dipole-type antenna structure contacting breast tissue.

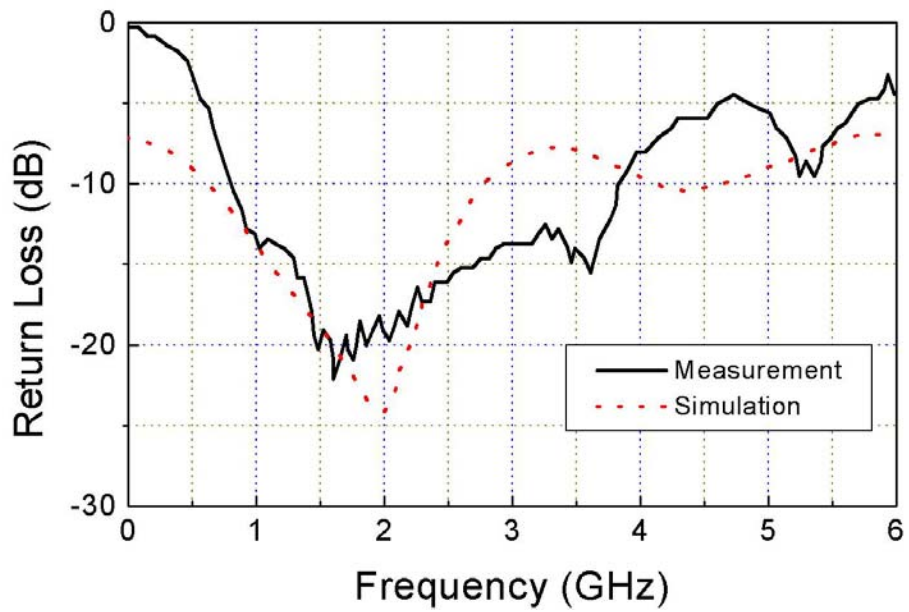


Fig. 2. Comparison of simulated and measured results.

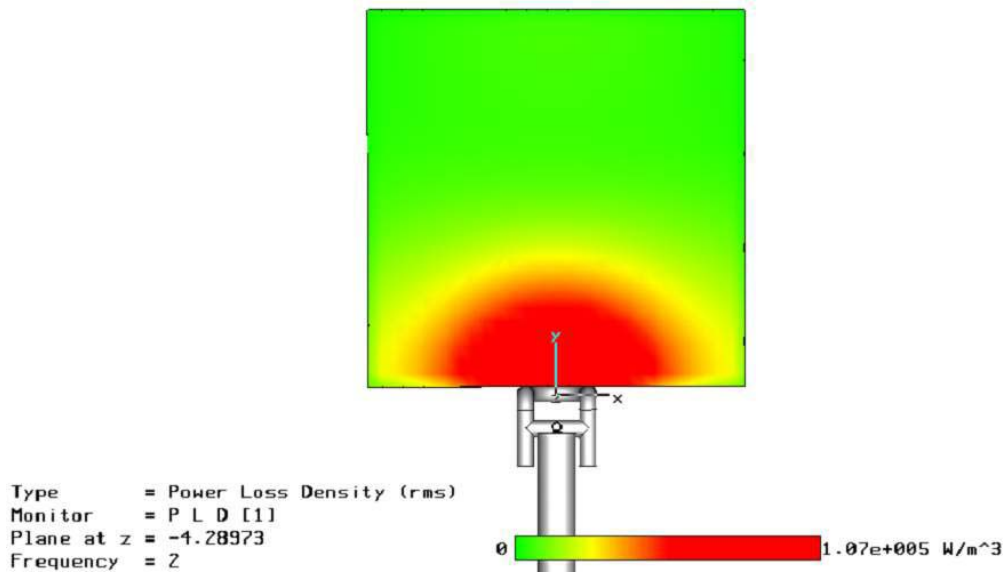


Fig. 3. Power distribution of the near field.

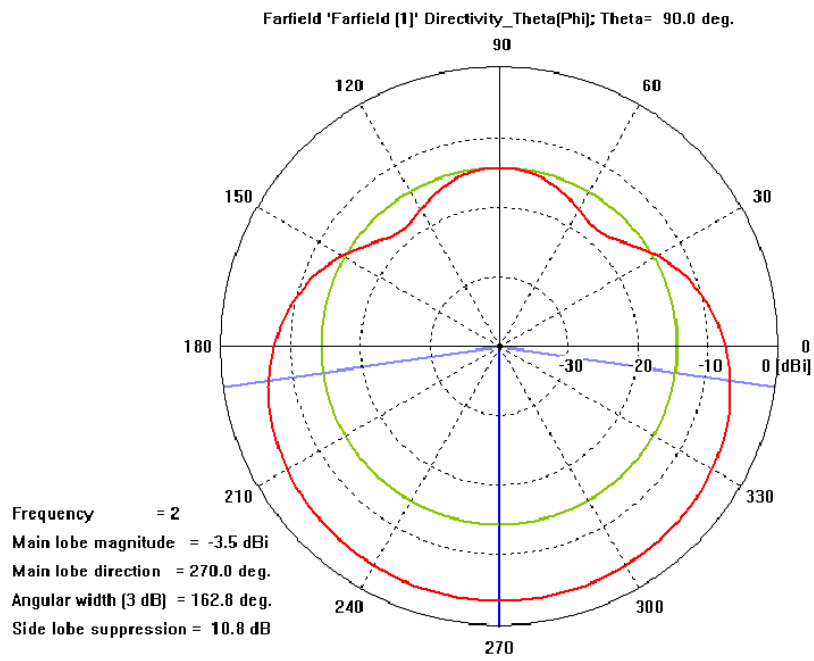


Fig. 4. Radiation pattern of the vertical plane (XY plane).

Session 9-3 I

MECHANISM AND PROPERTIES OF THERMALLY BIOLOGICAL EFFECTS OF THE MILLIMETER WAVES

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Thermally biological effect of millimeter wave is a very important and interesting problem. We think that the thermally biological effects of millimeter waves are caused by the thermal motions of water molecules in the living systems, according to experimental fact that the millimeter waves can heat water, and the skin effect on the surface of the biological tissues arising from the millimeter waves. For clarifying this idea we studied the states and features of the liquid water and calculated the rotational energy-spectra of water molecules in the living systems by quantum mechanics. As known, the energy of rotation for

water molecule is $E = \frac{1}{2} I \omega^2 = \frac{P^2}{2I}$, where ω , P and $I = \sum_i m_i r_i^2$ are its frequency of rotation, moment

of momentum and moment of inertia, respectively, m_i is the mass of the atom, r_i is orthogonal distance of the atom relatively to the rotational axis. Accordance to quantum mechanics, it can denoted as

$E = \frac{h^2}{8\pi^2 I} J(J+1)$, where h is Planck constant, J is quantum number of the moment of momentum.

Thus the wavelength of the light resulting from the transitions in these rotation energy-levels for water molecules is

$$\frac{1}{\lambda} = k = \frac{E' - E}{hc} = \frac{h}{8\pi^2 Ic} [J'(J'+1) - J(J+1)] = 2BJ' \quad (1)$$

where $B = \frac{h^2}{8\pi^2 I}$, $J'=1,2,3,\dots$, k is wave number, its unit is cm^{-1}

From Eq.(1) we can find out that free water molecule can absorb the millimeter waves with wavelength $\lambda = 0.73\text{mm}$. However, the water molecules are polarized with certain dipole moment in the living systems, They are always related with neighboring molecules via the hydrogen bonds. Thus the hydrogen bonded systems containing 3, 4, 5, 6 and more molecules. Rough estimates give 200- 240 molecules in the clusters at room temperature, 150 at 37°C , 120 at 45°C ^[4]. Therefore practical water molecules in the living systems can absorb the millimeter waves with longer wavelengths from 1 to 8mm. Then we can use the frequency spectra of millimeter waves to observe the rotational features of these water molecules. These water molecules will be rotated or twisted, when it absorbs the energy of the millimeter waves. The rotational energy of these water molecules can only transform as their kinetic energy of thermal motion to result in increase of temperature of the liquid water due to the fact that there are not the mechanism to transport the rotational energy from one to places other in these free water molecules and small hydrogen-bonded chains. This is just the mechanism of thermal effect of the millimeter waves in the living systems. This mechanism is verified by our experiments. In our experiment the temperatures of four samples of amino acid molecules, Gly., Glu., Ser and Arg., containing water exposed in the millimeter waves with wavelength 8mm or frequency 37.5GHz and the density of power $60\text{mW}/\text{cm}^2$. increase all 0.5°C relatively to that of the four same samples without exposing samples. Very naturally, the heating water can result in a lot of changes of biological phenomena, for example, (1) facilitating and enhancing the bio-chemical reactions in living systems; (2) enhancing breeding and fecundity of cell; (3) enhancing variations of conformations and states of hydrophilic and hydrophobic protein molecules and DNA and their biological functions. (4) enhancing transport of ions including Na^+ , K^+ , Ca^{++} and Mg^{++} and Cl^- on the membrane and the rate of molecules across cell membrane. (5) facilitating the circulation or microcirculation of blood and for the flow of lymph.

Another mechanism of thermally biological effect of the millimeter waves is caused by the skin effect of millimeter waves in surfaces of biological tissues. According to electromagnetic theory we can find that

the millimeter waves can propagate in the surfaces of human beings and animal and biological tissues with thickness $L = 1/\left|\frac{\vec{\tau}}{\tau}\right|$, $k \cong \tau = \sqrt{2\pi\mu\sigma\omega}/c$, The Joule-Lenz heat energy, arising from the penetration or

skin effect of the millimeter wave, can be denoted by $E_{heat} = 0.24\sigma E_o^2 t$, here t is the time propagating. Obviously, the large for the σ , then the large for the heat energy. For the surface skin of human beings and animal, the $\sigma = 17\text{S/m}$, $\epsilon = 12$, therefore, the Joule-Lenz heat energy cannot be ignored. Owing to this thermal effect occurs only on the surface skin of human beings and animal and the membranes of cell, thus its biological effect is only to facilitate increase of the blood circulation in them.

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Session 9-3 II

MECHANISM OF NON-THERMALLY BIOLOGICAL EFFECT OF MILLIMETER WAVES OF ITS PROPERTIES

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As known, we now come in the electromagnetic and electronic times. A variety of electronic and electric instruments, equipments, materials and components as well as television station and radiobroadcast stations, and so on, have been extensively used in mills and countryside and city. Therefore the electromagnetic waves or fields accompany always with us from morning to night. In such a case it is very necessary to know whether the electromagnetic waves including microwaves can influence the hearth of human beings. First step solving these problems are to have an insight and reveal the electromagnetic features of biological organizations and components. According to molecular physics and microwave theory we attend mainly the electromagnet features of biomacromolecules, for example, protein, DNA and lipid molecules, when we study the non-thermally biological effect of the millimeter waves.

As known, these biomacromolecules consist of small molecules through covalent bond, ionic bond, hydrogen bond, van der Weels bond, two sulphur bond and salt bond, etc.. These bonds are formed by electromagnetic interactions. In such a case these amino acid residues in the protein and bases in DNA are polarized, they have certain charge or the dipole moment, for instance, the dipole moment of the amino acid residue is about 0.29 – 0.31 Debyes, the A-T base pair is about 5-7.55-6.44 Debyes and the G-C base pair is 6.004- 6.483 Debyes, and so on. Therefore we may say that the biomacromolecules are a kind of electromagnetic interaction systems. They can interact with the millimeter waves.

According to molecular physics the rotational motions of molecules is related to the millimeter waves. Thus we calculate the rotational energy-spectra of these biomacromolecules by quantum mechanical

method. The kinetic energy of rotation for the biomacromolecules is $E = \frac{1}{2}I\omega^2 = \frac{P^2}{2I}$, where ω , P and $I = \sum_i m_i r_i^2$ are its frequency of rotation, moment of momentum and moment of inertia, respectively, m_i is the mass of the atom, r_i is orthogonal distance of the atom relatively to the rotational axis. According to quantum mechanics, the quantum energy of rotation is $E = \frac{h^2}{8\pi^2 I} J(J+1)$, where J is quantum number of angle momentum of rotation. Thus the wavelength of the lights produced from these transitions between the rotation energy levels for these molecules is

$$\frac{1}{\lambda} = k = \frac{E' - E}{hc} = \frac{h}{8\pi^2 Ic} [J'(J'+1) - J(J+1)] = 2BJ' \quad (1)$$

where $B = \frac{h^2}{8\pi^2 I}$, $J'=1,2,3,\dots$, k is wave number, its unit is cm^{-1} . From Eq.(1) we can find out the rotational spectra and corresponding wavelength λ of absorption, arising from the rotations of these molecules of the biomacromolecules, for example, α -helix protein molecule, DNA and lipid molecule. They are about 2-9mm. This shows that the proteins, DNA and lipid molecules can absorb the millimeter waves by means of the resonant mechanism. In such a case these biomacromolecules occur to rotate or twist, when it absorbs the energy of the millimeter waves, Thus the conformations and structures of these biomacromolecules changes, i.e., the electromagnetic energy of the millimeter waves transforms as the mechanical energy of change of conformation of these biomacromolecules. Obviously, this is a nonthermally biological process. Therefore it is just the mechanism of nonthermally biological effect of the millimeter waves. This mechanism is verified by our experiments. In our experiment the crystalline amino acid molecules are separated into two sets which have same mass and put in two dishes in same environment. However, one set is exposed in the millimeter waves with wavelength 8mm or frequency 36.36GHz and the density of power $3.3\text{mW}/\text{cm}^2$, but other is not exposed. We found no changes of temperature for the two set of samples, but the conformation of these amino acid molecules exposed in the millimeter waves change obviously relatively to without exposed samples. Thus we can conclude that the millimeter waves can change the conformations of amino acid molecules or protein molecules, but its temperatures change not. This shows that the millimeter waves absorbing by the protein molecules can result in changes of its conformations, but no increase of its temperature. These changes will result in stretchings and deformations of the hydrogen bonds, chemical bonds, van der waals bonds, two sulphur bond and salt bonds in these molecules. When the strength of the millimeter waves is small, these changes are also small, but when its strength is larger, larger stretching and deformations of these bonds will result in destructions of them. Thus structures and conformations of these biomacromolecules are broken, then its biological functions change considerably. Some illness will occur in such a case. Therefore, the heart of human beings and animals are affected when exposed in the millimeter waves, the larger for the millimeter waves, then more larger for the disadvantageous influences of the heart. However, for some illness related to the changes of conformations or structures of the biomacromolecules if they absorb the appropriate millimeter waves, their conformations or structures can recover to normal states from the illness state through their rotations, then such millimeter waves could be used to cure some sickness. This is just the reasons and mechanism cured some sickness by using the millimeter-wave medical instruments and equipments in hospitals. Therefore, the millimeter waves have certain medical effects.

Next, the millimeter waves can influence the proton current in the proteins and ionic current in the cell membranes and electron transfer in the biomacromolecules, and affect also the biological functions of these molecules. This is another mechanism of the nonthermally biological effect of the millimeter waves.

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THE EFFECT OF MILLIMETER WAVE ON HACAT KERATINOCYTES

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BACKGROUND: Numerous publications have reported that over 50 diseases and conditions have been treated successfully with millimeter wave (MW) alone, or in combination with other treatment modalities in over 3 million patients in the former USSR. However, there are no clear mechanisms available to explain the biological effects elicited by MW exposure. Gap junctional intercellular communication (GJIC) plays an important role in the maintenance of cell proliferation and differentiation. We previously found that certain intensities of extremely low frequency magnetic fields (ELF MF) exposure could inhibit or enhance the inhibition of GJIC induced by TPA in CHL or NIH3T3 cells. However, there has been few report about the effect of MW on GJIC.

OBJECTIVE1: To test the effect of MW with/without TPA (5 ng/ml) on GJIC in HaCaT keratinocytes.

OBJECTIVE2: Genechip analysis, a high-through technology was employed to investigate gene expression pattern in response to MW exposure.

METHODS: The MW exposure setup consists of a tunable MW generator, waveguide, attenuator, frequency meter, a horn antenna and a chamber. The generator produced a continuous wave at a frequency of 30.16 GHz which was connected through the waveguide to a horn antenna. Cell cultures were placed for exposure resting on top of the antenna.

In the first study, Six groups were used: (1) control (0 mW/cm² MW and without TPA treatment), (2) 1.0 mW/cm² MW exposure for 1h, (3) 3.5 mW/cm² MW exposure for 1h, (4) 1.0 mW/cm² MW combined with TPA treatment for 1h, (5) 3.5 mW/cm² MW combined with TPA treatment for 1h, (6) TPA (5 ng/ml) treatment for 1h. The fluorescence recovery after photobleaching (FRAP) technique was employed to determine the function of GJIC with laser confocal scanning microscope. Analysis of the Variance (One Way ANOVA) is adopted to analyze the experiment result and the level of statistical significance was set at P<0.05.

In the second study, HaCaT Keratinocytes were attached on the bottom of the culture dish (60 mm diameter) and sham exposed or exposed to MW from bottom (30 min per day, for 4 days). The power density in exposure area was regulated to 3.5 mW/cm². RNA was extracted after exposure. Gene expression levels were quantified using an Affymetrix human genome U95 GeneChip and changes were determined by comparing data from MW-exposed cells to data from sham-exposed cells. Then gene expression level was validated by RT-PCR.

RESULTS: 1. The results showed that MW exposure at both intensities for 1h didn't affect GJIC in HaCaT keratinocytes. After treating the cell with TPA (5 ng/ml) for 1h, an apparent inhibition of GJIC was detected. When 1.0 mW/cm² MW exposure was combined with 5ng/ml TPA treatment for 1h, the fluorescence recovery index was significantly higher than that in the group treated with TPA alone, but lower than that in the control group. Meanwhile, 3.5 mW/cm² MW combined with TPA treatment increased the fluorescence recovery index approaching the control level (Tab.1 and Fig.1). **2.** The data showed that totally 18 genes were up-regulated more than 3 times in response to MW stimulation. Among them, Human proteinase-activated receptor-2 gene (PAR-2) was of particular interest and validated by RT-PCR (Fig.2). PAR-2 is widely distributed in the mammalian body, including the gastrointestinal tract and the circulatory, respiratory and nervous systems, modulating a variety of physiological functions. Thus, PAR-2 gene may be related to some biological effect elicited by MMW exposure.

CONCLUSIONS: 1. The results showed that TPA inhibited GJIC of HaCaT keratinocytes and MW could abolish GJIC suppression by TPA. **2.** The gene expression data suggests that MW could stimulate HaCaT keratinocytes by changing mRNA level of related genes. However, the biological consequence of gene expression change is needed to be further explored.

This work was sponsored by National Natural Science Foundation of China (grant number: 39970189).

TABLE 1. Effects of MW and/or TPA Exposure on GJIC in HaCaT keratinocytes

MW	Fluorescence recovery index (Mean±SD)	
	Without TPA (n)	With TPA (n)
0	55.32±16.76 (50)*	34.24±12.83 (74)
1.0 mW/cm ²	51.71±16.32 (40)	46.85±15.87 (45)**
3.5 mW/cm ²	50.14±16.68 (53)	49.90±15.79 (40)*

n number of tested cells

* P<0.001 Vs. TPA (5ng/ml) alone

** P<0.01 Vs. TPA alone, P<0.05 Vs. Control

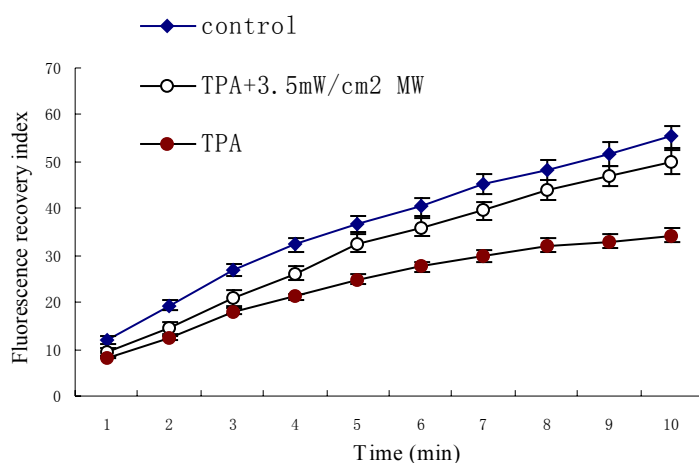


Fig.1 fluorescence recovery index after photobleaching in HaCaT keratinocytes treated with 3.5 mW/cm² MW/TPA. Data presented as the groups means±SEM.

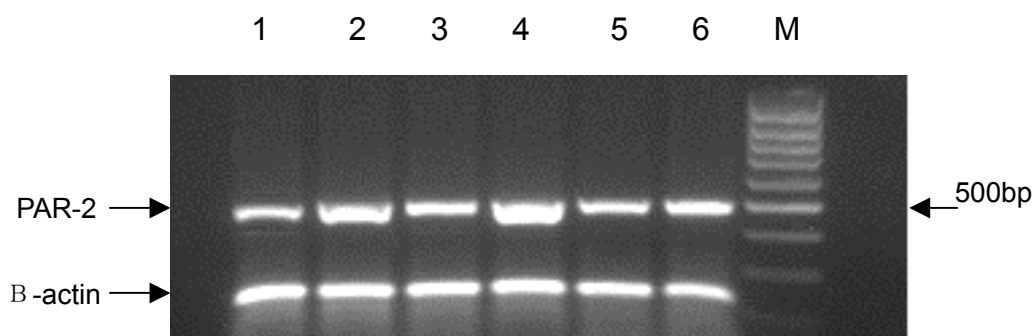


Fig.2. Semi-quantitative analysis of RNA expression by RT-PCR. The RT-PCR product obtained by using primers respectively specific to PAR-2 gene. Lane M, 100bp DNA Ladder; lane 1,3,5, PAR-2 in control cells; lane2, 4,6, PAR-2 in MW exposed cells.

Session 9-5

SPATIAL AND TEMPORAL COHERENCE AFFECTS THE RESPONSE OF BIOLOGICAL SYSTEMS TO ELECTROMAGNETIC FIELDS

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The last ten years studies on radiation similar to that emitted by Cell Phones have shown a majority of results showing biological effects. Out of the 154 studies 88 or 57% showed biological effects, such as cancer, genetic, molecular and cellular changes, electro physiology effects, behavior changes etc. Survey by Dr. Henry Lai, Washington University, Seattle 2003.

Even though it is still a question whether these biological changes indeed will cause health effects, the amount of evidence for biological effects and the characteristics of these are so alarming, that all efforts should be dedicated to find a way to minimize these effects.

The Noise Field theory is based upon research originated by the U.S. Army, Walter Reed Army Institute in 1986, initially performed by the Catholic University of America (CUA) in Washington D.C. by an interdisciplinary team of 15 physicists, biochemists, biologists and engineers, and replicated by six other Universities in three different continents from 1993 to 2002.

After six years of comprehensive studies the CUA published at August 15th 1991 a scientific paper, titled: " *Effect of Coherence time of the applied magnetic field on ODC activity*", in the scientific journal: "Biochemical and Biophysical Research Communication".

In this paper CUA introduced the preliminary result that an exposure of mouse cells (L929 murine) to a regular 60Hz electromagnetic field doubled the activity in the cells of the critical enzyme, Ornithine Decarboxylase (ODC), which is involved in DNA and cell reproduction, **i.e. the EMF field was shown to cause biological effects.**

The 60 Hz EMF field used in these studies is within the so called extremely low frequency field (ELF) range (0 – 1,000 Hertz), but further research done by CUA also showed that the whole spectrum up to visible light, i.e. ELF, Radio frequency (RF) (1,000 Hertz – 0,8 Ghertz) and ELF Microwave, 0,8 Ghertz – 1 Ghertz) cause the same effects and responds equally to the EMX Noise field technology.

More important still, the scientists at the CUA discovered during their studies that the increase in ODC activity did NOT occur if they made the exposing field vary randomly between 55Hz to 65Hz at intervals of less than one second.

In 1993 the CUA scientists published these results in three papers in the scientific journal: "Electricity and Magnetism in Biology and Medicine".

In one of these papers titled: " *Spatial and temporal coherence affects the response of biological systems to electromagnetic fields*", the scientists drew the further logical conclusion, that by superimposing a random EMF field on the constant, bioeffective field, the total of the two fields should be random and therefore not bioeffective.

This noise field theory was later repeated in eight different studies from 1993 to 2002:

In the same period these scientific findings by the CUA were replicated (in all experiments the bioeffects were neutralized) by six other leading Universities in USA, Europe and Asia, in the most comprehensive replication program ever undertaken in the field of bioelectromagnetism:

Columbia University, New York, USA Professor Reba Goodman. Department of Pathology, College of Physicians and Surgeons. Sponsored by the Office of Naval Research, US Department of Energy and NIEHS.

EMF-enhanced gene expression (oncogenes, stress genes, household genes in Human Leukemia cells, EMF-induced stress response in Human Breast Cancer Cells, EMF-induced suppression of neurotransmitter dopamine in PC-12 Cells.

University of Washington, USA, Dr. Henry Lai. Bioelectromagnetics Research Laboratory and Professor Baoming Wang. Department of Biomedical Engineering. Tianjin Medical University, China. Sponsored by EMX Corporation.

EMF induced memory loss in rats and DNA strand breaks in rat brain cells.

University of Western Ontario, Canada, Professor A.H. Martin. Department of Anatomy. Department of Biochemistry, Victoria Hospital. Sponsored by Health and Safety Agency, Ontario, Canada.

EMF induced changes in enzyme nucleotidase levels in chick embryo brain cells.

University of Aarhus, Denmark. Professor Sianette Kwee, Institute of Medical Biochemistry. Sponsored by Danfoss A/S Denmark.

EMF accelerated cell proliferation rate in human amnion cells.

University of Aalborg, Denmark. Professor P. Raskmark, Institute of Communication Technology. Sponsored by Danfoss A/S Denmark.

EMF accelerated cell proliferation rate in human amnion cells.

Zhejiang University, China. Professor H. Chiang et al., Bioelectromagnetics Laboratory.

EMF induced suppression of the gap-junctional intercellular communication in Hamster Lung Cells and enhancement in SAPK Phosphorylation activity in Mouse Fibroblast cells.

Conclusion: It is demonstrated in the majority of the 154 published scientific studies about radiation similar to that emitted by cell phones, that nonthermal EMF fields in the ELF, RF and microwave frequency area can cause biological effects, which can be, but not necessarily are, harmful to the exposed human or animal cellular system.

All 19 studies in the noise field research program referred to in this document have shown that by superimposing a random noise field on the regular electromagnetic field, the combined field became neutral to the exposed tissue and not biological effective.

Table 1

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TABLE 2. The effectiveness of the Noise Field Theory

Laboratory / Team testing	Biological System tested	Biological condition tested	Biological effect Induced by EMF	Effectiveness of EMX Technology
Catholic University Krause & Co.	Mouse cells	Activity of Ornithine Decarboxylase (ODC) – Enzyme related to growth and cancer	EMF cause a two-fold increase in enzyme activity relative to natural level – condition related to cancer	Natural condition restored: Enzyme activity brought back to normal
Catholic University Krause & Co.	Human lymphoma cells	Activity of ODC	Significant increase	Natural condition restored
Catholic University Doynov & Co.	Chicken embryos	Ratio of truncal abnormalities in embryo	EMF cause more than a doubling in abnormality ratio	Abnormality ratio brought back to natural level
Catholic University Farrell & Co.	Chicken embryos	Activity of ODC	Significant distortion from natural level	Natural condition restored
University of Western Ontario Martin & Co.	Chicken embryos	Activity of Nucleotidase – Enzyme related to	EMF suppress enzyme activity compared to	Natural condition restored: Enzyme activity brought

		DNA production	natural level	back to normal
University of Western Ontario Martin & Co.	Hatched chickens	Activity of Nucleotidase (cerebellum)	Enzyme activity suppressed compared to normal	Natural condition restored: Activity normalized
Columbia University, N.Y. Lin & Co.	Human leukemia cells	Transcription of c-myc proto-oncogene (cancer related gene)	Over-expression of c-myc proto-oncogene compared to normal level – increased cancer Risk	Natural condition restored: Proto-oncogene expression brought back to normal level
Columbia University, N.Y. Goodman & Co.	Human breast cancer cells	HSP90 stress protein	EMF cause the on-set of stress protein production	Cells released from stress condition
Columbia University, N.Y. Opler & Co.	PC-12 cells	Dopamine. Hormone related to Parkinson's Disease.	EMF cause a decrease in the level of dopamine compared to normal condition	Natural condition restored
Catholic University Litovitz & Co.	L929 Murine (mouse) cells	ODC activity	Cellular phone EMF signals Increase activity from normal level	Natural condition restored: Enzyme activity normalized
Aalborg and Aarhus Universities Denmark Raskmark and Kwee	Human epithelial amnion cells	Cell proliferation rate	EMF increase cell proliferation rate by 20% compared to natural level	Condition normalized: Cell proliferation rate brought back to natural level

Catholic University Di Carlo et Al	Chicken Embryos	Activation of HSP70 Heat shock protein and Cytoprotection level (Potential cancer promotor)	Long term exposure to EMF causes significant decline in HSP70 and Csytoprotection level	Normal condition restored. Brought back to normal
University of Washington Henry Lai, P. Singh	Rat Brain Cells	Level of DNA single and double strand breaks (Potential cancer promotor)	Significant Increase in the level of DNA single and double strand breaks	Normal condition restored brought back to normal
University of Washington	Rats	Spatial learning	Significant deficit in learning	Normal condition restored brought

Henry Lai, P. Singh				back to normal
Zhejiang University, China Zeng, Chiang Et Al	Mouse Fibroblast Cells	Cap-Junction intercellular communicator GJIC (Potential cancer promotor)	Significant Inhibition of GJIC	Normal condition restored brought back to normal
Zhejiang University, China Zeng, Chiang Et Al	Hamster Lung CHL cells	Level of Sapk Phosphorylation (SAPK)	Significant Increase in the SAPK Phosphorylation	Normal condition restored brought back to normal

Session 10-1

DISCUSSION

Session 10-2

DISCUSSION

Session 10-3

RF RESEARCH IN VITRO CRITERIA UPDATE.

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Cytotoxic & genotoxic research in vitro investigates “nonthermal” dose-effects of RF around ICNIRP guideline limits. Recent reports suggest small temperature changes (0.03 °C; below the sensitivity of temperature probes) in warm-sensitive C-fiber, unmyelinated, afferent neurons, can initiate physiological responses (R. Adair, 2001; E. Adair Cost 281, 19/11/02). Cerebrospinal fluid bathes the preoptic, brainstem and spinal cord nuclei that control thermoregulation. The rapid mobilization (< 60 sec) of appropriate thermoregulatory responses during RF human exposure (100-200 MHz) is proof of thermal input to the critical sensory neurons in the brain. Studies involving in vitro systems, TEM cells, etc. should be analyzed with care and precision before concluding that a bioeffect is non-thermal (i.e. HSP70, Leszczynski ‘02). Cell cycle details (W-U. Müller, G. Stephan, Vijayalaxami Löwenstein 25-27/11/02) and appropriate sample size are also essential in the analysis of genotoxic effects on micronuclei (2000), chromosome aberrations (1000) and sister chromatid exchange (100) (G. Stephan, , 25-27/11/02). Because cell cycle can be controlled in human blood lymphocyte cultures, they are used to test for RF-induced direct & indirect effects on chromosome damage (G. Stephan, Vijayalaxmi). During RF exposure of the culture medium both experimental and numerical dosimetry are required to monitor ongoing temperature and SAR variability throughout the culture medium (They can vary 10X; Korenstein URSI, Maastricht, 17-24/08/02).

Session 10-4

MOBILE MANUFACTURERS & THE INTERNATIONAL EMF RESEARCH AGENDA

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An overview and update on the mobile phone industry's approach to mobile phone health and safety issues particularly in terms of research in the field of health and safety of mobile communications equipment.

The MMF has responded to the research recommendations of the World Health Organization's Electromagnetic Fields Project, and has coordinated its global activities to correspond with these recommendations. The presentation will review the research objectives of the various projects being supported including the Perform A and B group of studies, the UK national research program, the mechanisms project as well as the other studies supported in Europe, the US and China. These projects have been established in a manner that assures maximum scientific independence for the researchers while ensuring appropriate project accountability to the funding bodies. It is expected that the outcomes of this research will form a key input to the plan by the WHO to conduct a formal health risk assessment of radio frequency

(RF) fields in the 2005 timeframe.

The presentation will conclude with an overview of how the MMF considers the numerous expert reviews of the related science and the role of these assessments in formulating policy approaches.

I -1

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KNOW ABOUT THE FEATURES OF ELECTROMAGNETIC RADIATION IN MOBILE BASE STATIONS AND PROTECT THE ELECTROMAGNETIC ENVIRONMENT TO REALIZE THE MOBILE SUSTAINABLE DEVELOPMENT

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Abstract: This essay introduces the survey about the developments of mobile at home and abroad and utilizes the wireless relay communication theory to conclude that the development of mobile phones must be based on the development of mobile base stations. Through the analysis of the electromagnetic radiation features of base stations, it puts forward that the goal of developing the mobile communicative net as well as protecting the electromagnetic environment in cities can be reached if we position the base stations reasonably.

Key Words: mobile base stations, features of electromagnetic radiation

1、 The development of mobile communication is the trend of world economy and the development of science and technology, and also the need of information era

Since 1980s, with the development of science and technology and the progress of the society, the mobile communication net has been developed dramatically all over the world. The mobile communication technology consists of mobile net, pager communication net, professional communication net etc. Among these, mobile communication is in people's good graces because of its flexibility and the ability of duplex communication among different regions and the ability of global roaming communication. At present, the global mobile users have reached 1 billion, or one phone owned per six persons. In the economically developed countries, the cell phone users have accounted for about 60-70% of the total population, and in Finland, the rate is 80%.

China has experienced the transfer from TACS to GSM, from the TDMA to CDMA since the formally running of mobile in Guangzhou, Beijing and Shanghai in 1987. Now the absolute amount of cell phone users of China has been in the first place in the world. The cell phone users increase in the amount of 5 millions per month in China and it is expected to exceed 200 millions at the end of 2002. The mobile phone users are from general presidents of giant corporations down to the peasants, so the mobile communication has a considerable prospect. The general situation of the development of mobile phone users in China is listed in Stable-1. The amount of mobile phone users of China Mobile Communication Corp. accounts for 70% of the total and that of China Unicom Corp. accounts for 30% of the total.

The construction and development of mobile phone net which give dramatic convenience to people's work and life have produced considerable social and economic profits. However, at the same time new problems of electromagnetic environment have emerged in the developing process . In some cities, the construction of mobile base stations has been so disputable that the conflicts between the companies and the local residents occurred occasionally.

Stabl-1 General situation of the development of mobile phone users in China

Year	Cell phone users	Remarks
1986	Formally running in Guangzhou, Beijing and Shanghai	
1990	18,000 nationwide	
1994	1,568,000 nationwide	
1997	13,233,000 nationwide	
1999	43,296,000 nationwide	
2000	84,533,000 nationwide	
2001	145,000,000 nationwide	Occupy 11.2% of the total population
July,2002	180,000,000 nationwide	Occupy 14% of the total population

2、 Know about the electromagnetic radiation features of Mobile Communication Base station

The construction and development of mobile base stations are the foundation of the development of the mobile users. The mobile base stations are made up of receivers and transmitters with antennas of different height, which can realize wireless to wireless communications and wireless to wired relay communications. A base station is consisted of three parts: receivers and transmitters, antennas and feeder lines. Each base station covers a wireless wave servicing area. The adjoining areas interact to make mobilizing cell phone users communicate without suspending. It's necessary to the environmental protection and mobile communication undertakings that know about the electromagnetic radiation features.

2.1 Mobile Base Stations are Cellulated Positioned

When mobile users converse, a frequency, a channel or a group of codes are occupied in the space. The limited frequency resources in the space make the mobile phone net adopt the technology of channelling(that is the repeated usage of one frequency in different areas), that forms the cellular features of mobile base stations and with the increase of users and the base stations should be divided further.

2.1.1 Because of the constant increase of the mobile base stations, some base stations have to located in the residential areas. The antennas are either erected on the top of the elevator rooms of high-rise buildings or on the antenna frames on the top of walkup buildings. The colorful, tasteless, invisible and untouchable features of electromagnetic waves make the natives of the buildings and of the surrounding buildings feel terrible and unsafe.

2.1.2 In order to avoid one frequency interfering due to the channelling in the further divisions of the base stations, the heights of base station antennas lower accordingly, which increase the chances of electromagnetic waves transmitted and reflected among buildings.

2.1.3 The further divisions cause the distance between base stations shortened, and the power of the transmitters lowered accordingly. Generally, the electromagnetic density at the distance of 30-50 meters in the main direction can reach the standard of China that is $40 \mu w/cm^2$. This is beneficial to the electromagnetic environmental protection within the residential area.

2.2 The Electromagnetic Horizontal Directive Map of the Antennas Like Clover

The base stations are equipped with three directional antennas(each covers an area of 120°) whose electromagnetic horizontal directive map is like a clover(each main lobe width is 65° and the electromagnetic density in the main transmitting direction(that refers the main lobe)is strong and that in the non-main transmitting direction(that refers the secondary lobe) is weak. In the planning layout of antennas, the main transmitting direction should not direct the surrounding buildings, which on the one hand can protect the buildings from the electromagnetic waves pollution, on the other hand, can be benefit to the propagation of the useful signals.

2.3 Features of the Electromagnetic Vertical Directive Map of the Antennas

The lobe width of the antennas in vertical direction is some degrees to some twenty degrees. The antennas should be erected with some certain heights in order to make the electromagnetic main transmitting directions higher than the surrounding buildings, which can ensure the uninterrupted propagation of the electromagnetic waves as well as the unpolluted environment around.

2.4 The transmitting power of base stations is much less than that of broadcast base station

Broadcast is the single-direction communication whose principle is that the receivers sensitivity doesn't need to be high (simple manufacture, low price and easy to be popularized) but the transmitting power must be high enough to guarantee the receiving quality within the serving areas. The power is ranged from tens of kilometers to hundreds of kilometers. On the contrast, the mobile is the duplex wireless communication, which require higher receiving sensitivities to both sides. Furthermore, the servicing area of each base station is smaller (usually hundreds of meters in urban) , therefore the transmitting power is lower. Generally, the nominal power is 30 Watts, but the usable power is only some Watts.

3. Protecting electromagnetic environment to realize the sustainable development of mobile communication

From the above analysis of the electromagnetic radiation features of mobile base stations we can conclude that electromagnetic radiation pollution is preventable if the base station positions are arranged scientifically. Specifically speaking, the goal of developing mobile communication as well as protecting electromagnetic environment can be achieved on conditions that the main lobes in three sectors both in vertical and horizontal directions avoid the front buildings or ensure no buildings within 30 meters. The power density limit of $40 \mu \text{w}/\text{cm}^2$ for the mobile frequency range in China is practical both in the developing mobile communications and in the protecting electromagnetic environment.

Reference:

“Research on Electromagnetic Radiation of Mobile Base stations and Analysis of the reason of higher density than the National Standard in Native areas” , 《China Environmental Monitor》 the 3rd issue, 2002.

I -5

CONTROL BIOLOGICAL ELECTROMAGNETIC ENVIRONMENT BY NEW CONCEPTION

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From many survey and experiments, we found that some of the domestic and external standards are not suitable reality of human being. Some of them decrease productivity, some of them degrade the quality of life.

There are two problems in existing IEEE Std C95.1, COVNCIL RECOMMEND ATION, WHO ICNIRP, GB and GJB One is using 377Ω and SAR by mistake, the other is lack of experiments for human being.

We invented the new technology to set limit salfty in 1999. The technology is more compatible and humane. Standard used for the public does not destroy body's intenal balance, standard used in the workplace is enduring and recoverable for people. This new salfty limit to control biological electromagnetic environment is more scientific than various existing standards nowadays.

THE ELECTROMAGNETIC PULSE TRANSFORMATION FROM ACTING ON HUMAN BODY TO EXPERIMENT MOUSE*

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Background: This paper aimed at the study of the absorption of SAR by human body exposed to EM pulse. And what EM wave experiment mouse should be exposed to is discussed. Fourier transform is employed to transform wave from time domain to frequency domain. Each frequency components act on human body should be found out and transformed to what act on experiment mouse, then return it to time domain.

Bioelectromagnetics Dosage consists two parts, experimental and theoretical. The former is to measure total power absorbed by target body (average SAR) or interior field distribution inside target body (local SAR). Measurement can be performed on biosystem simulation model or experiment animal. Practically, since simulation material is not perfect, experiment usually performed on experiment animal. But what we concerned at last is the human body expose to EM wave. So average SAR absorbed by experiment animal must be equal to that of human body in experiment, to simulate the effect of human. But the size of animal does not equivalence to that of human, and resonance frequency of animal is not equivalence to that of human either. To deal with this, the parameter of EM wave act on human body must be transform into that act on animal in stage of experiment design.

Method: A man of height 175 cm expose to plane wave, parallel to E direction. EM wave is period rectangular pulse with period T, $\tau = 10\mu s$, maximum electric field intensity of $86.83v/m$. The problem is how to simulate such an effect of human body by exposing a middle size little mouse of length 7cm.

Results: The given period rectangular pulse should be transformed into frequency domain. Figure out a series of amplitude power flux density P_n_human that correspond to frequency point f_n_human in spectrum. Then find out SAR_n_human at this frequency point. Figure out the frequency points f_n_mouse which corresponding to f_n_human by $f_mouse = \frac{f_human \times h_human}{h_mouse}$. Work out power flux density P_n_mouse corresponding to f_n_mouse on condition that absorbed SAR equal to SAR_human by $P_n_mouse = \frac{SAR_human \times 1mw/cm^2}{SAR_mouse_united}$. Then figure out E_n_mouse . This is the spectrum of EM wave the mouse should be exposed to. Then return it into time domain by inverse Fourier transformation.

Conclusion: Resonance frequency of the mouse is 25 times that of human body, so the resonance problem can be ignored. Amplitude of effective frequency component is decrease as frequency increase. So higher frequency component should be ignored in this problem.

* The Project Supported by National Natural Science Foundation of China

NUMERICAL SIMULATION OF HUMAN BODY ILLUMINATED BY NUCLEAR ELECTROMAGNETIC PULSE

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Abstract: A computation is performed of the human body illuminated with nuclear electromagnetic pulses (NEMPs) by frequency-dependent finite-difference time-domain ((FD)²TD) technique. The simulated human model employed in this paper is a uniform infinite long ellipsoid cylinder of dielectric property characterized by a five-term Debye relation. The results show that NEMPs exhibit strong penetration through human body with a large current produced and a little electromagnetic energy absorbed. This will give insight into the effect of electromagnetic pulse on human body.

Key words: (FD)²TD, NEMP, Specific energy absorption

Introduction.

Electromagnetic pulse (EMP) is one of the most important electromagnetic environments. Though bio-effects caused by EMP have been noted for a long time, there is still very little published quantitative research. In view of its potential applications in such fields as medical treatment and military, it is essential to give much attention to EMP.

In this paper, an infinite long elliptoid cylinder human model composed of uniform muscle illuminated by NEMP is calculated with (FD)²TD technique. The dielectric properties of muscle at overall band are given by a five-term Debye relation which has been experimentally proved to be right. The results show that NEMP has a very strong penetration through human body. Though energy deposited in the body is very little, a large induced current occurred which may has potential hazard to nerve system.

Simulation model

Fig.1 illustrate the computational schematic. The incident NEMP is given by

$$E_{inc}(t) = \begin{cases} E_0(e^{-\alpha t} - e^{-\beta t}) & , t \geq 0 \\ 0 & , t < 0 \end{cases} \quad (1a) \quad H_{inc}(t) = \begin{cases} E_0 \sqrt{\frac{\epsilon_0}{\mu_0}}(e^{-\alpha t} - e^{-\beta t}) & , t \geq 0 \\ 0 & , t < 0 \end{cases} \quad (1b)$$

where $E_0=5 \times 10^5$ v/m. α , β have two group of values: $4 \times 10^7 s^{-1}, 6 \times 10^8 s^{-1}; 4 \times 10^6 s^{-1}, 4.76 \times 10^8 s^{-1}$. The propagation direction is vertical to the z axis, and the E component is parallel to z axis.

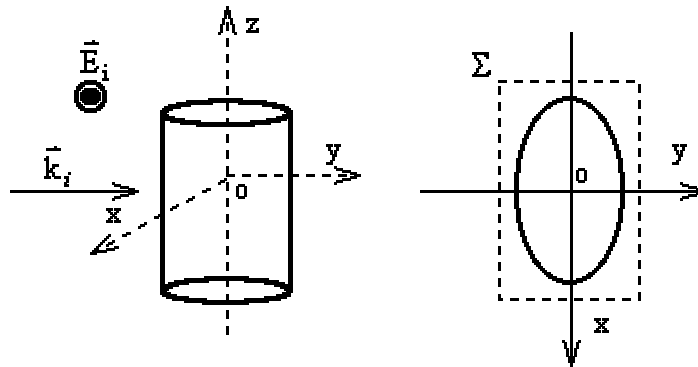


Fig.1 The computation schematic

Dielectric properties of the muscle tissue are given by

$$\epsilon_r(f) = 4.3 - i \frac{0.0762}{2\pi f \epsilon_0} + \frac{8 \times 10^5}{1 + i \frac{f}{69}} + \frac{8.19 \times 10^4}{1 + i \frac{f}{4.3 \times 10^4}} + \frac{1.19 \times 10^4}{1 + i \frac{f}{6.7 \times 10^5}} + \frac{32}{1 + i \frac{f}{2.3 \times 10^8}} + \frac{45.8}{1 + i \frac{f}{2 \times 10^{10}}} \quad (2)$$

Results

Fig. 2 illustrates the E field in the center of the model.

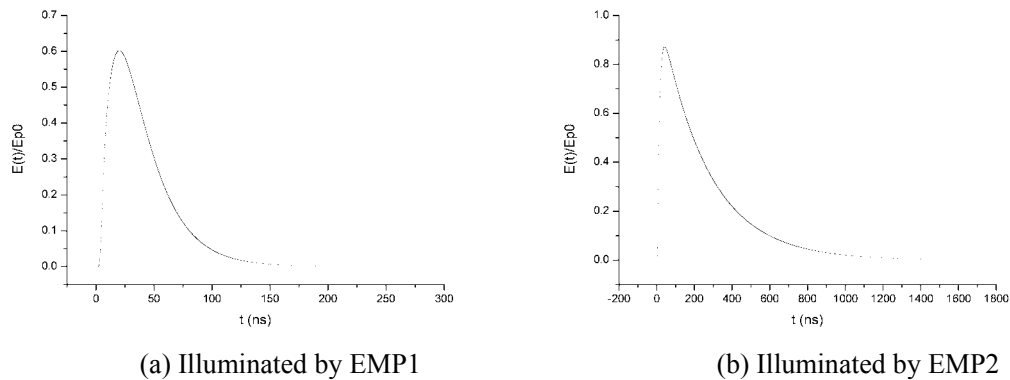


Fig. 2. E as a function of time in the center of the model

The waveforms of E field in the model haven't very much variation compared to the incident field. The shorter the rise-time, the more the waveform variation.

Fig. 3. shows the current density in the model center. eld in the center of the model.

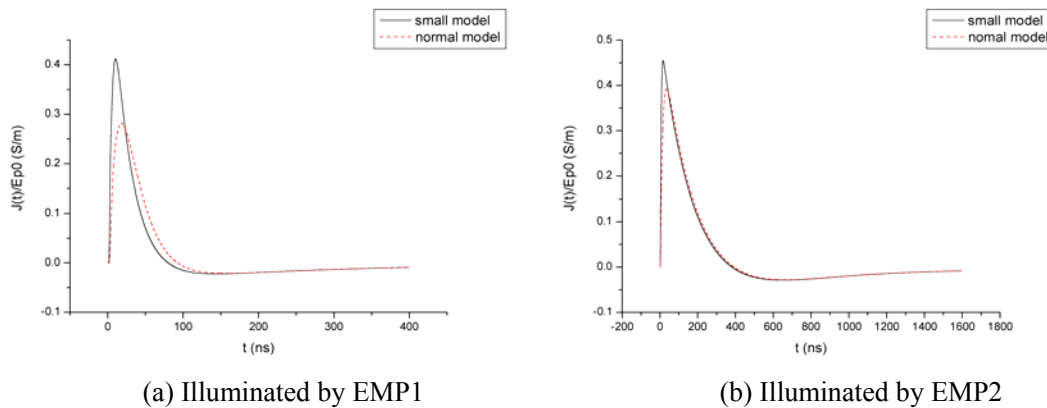


Fig. 4. The current density in the model center

From Fig. 4., we can see that very large induced current density is produced by the NEMP.

Conclusion.

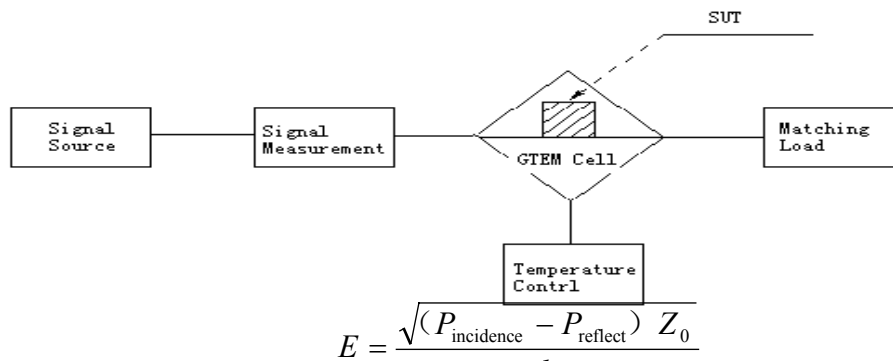
1. NEMP has a very strong penetration through human body.
2. Waveforms in the body haven't much alteration compared to the incident NEMP.
3. In one pulse, the deposited energy is small enough to make us neglect its thermal effect.
4. A very strong induced current is produced by the NEMP, its potential hazards remains unknown.

ELECTROMAGNETIC EXPOSURE SYSTEM IN STUDY OF BIOLOGY EFFECT*

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Background: In study the effect of electromagnetic wave on biology tissues, the results of the examination always can not be repeated and compared with each other, because of the difference in the dosimetry. A system using in studying the electromagnetic athermal effects is designed to solve this problem, which is advantageous to compare the examination results between different scholars and different examinations.

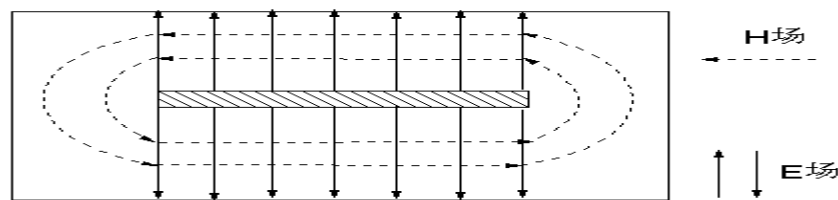
Method: The system consists of signal source, signal measurement system, GTEM cell, temperature control system and SUT (sample under test), based on electromagnetic theory and biology principle, as follows:



Here, Z_0 is the characteristic impedance of the GTEM cell, and h is the distance from core board to the top board. The operating power of the system is 0~10W, the operating frequency 0~750MHz.

Results: GTEM cell is a transmutative rectangle coaxial line with rectangle main part transited to 50Ω coaxial sockets. Because of the capacitive character when biology put into the cell, characteristic impedance of cell is set to 52Ω as compensate.

When a high frequency electromagnetic energy fed to the cell, a uniform TEM wave is set up in it. The electromagnetic distribution is as follows:



The electric field intensity between the core and top board is E_v (virtual value), which is

$$E_v = \frac{U}{h} \text{ (v/m)}$$

Here, U is the input voltage, and h the distance the top board apart the core one.

If known the input power, the electric field intensity is

$$E_v = \frac{\sqrt{P_n R_c}}{h} \text{ (v/m)}$$

P_n is the net power of input into the cell, R_c is the real part of complex characteristic impedance.

There are both electric field and magnetic field in the cell, which both are in the cross section with the electric field line normal to the core board and the magnetic field line circle the core board to a close line.

The power flow density is expressed as follows:

$$S = \frac{E^2}{\eta_0} \quad (\text{W/m}^2) \quad (\eta_0 = 377\Omega).$$

The transmission frequency of TEM wave is limited by the cell's dimension, because which is transfiguration of coaxial line. When the frequency exceeds the cut off frequency, higher mode wave will appearance. So the operating frequency of TEM cell should be lower than the cut off frequency of TE_{10} mode (f_c).

$$f_c = \frac{75}{a} \sqrt{1 + \frac{4ab}{\pi b^2 \ln[8a/(\pi g)]}}$$

The cut off frequency of this GTEM cell is 749.9670MHz.

The tests of TEM cell include standing wave coefficient of input port, impedance in time and frequency domain, insertion loss, all of which can be measures by network analyzer and impedance analyzer. The field distribution of the cell inner can be tested by electric doublet antenna or FM2000 wide band field intensity tester which produced by AR company.

Temperature controlled system: The heat will be produced in biology tissues during exposure to the electromagnetic fields, for the biology tissues are dissipative medium, which will cause the variation of temperature and submerge the athermal effect. So the environmental temperature should be controlled in accurate, and the temperature control system consists of temperature sensor, insulation can, temperature controlled section.

Conclusion: Special requirements of biology experiment are satisfied in the system which can reproduce the same electromagnetic environment parameter which can be controlled accurately, and avoid the interference from outside.

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PRERESEARCH ON SHEILD MATERIAL OF MAGNETIC-PREVENTING CLOTHING

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Background: When the electromagnetic mine sweeping utensil was running used on minesweeper, the environment of ship will be polluted ineluctability by magnetic field, which would influence health of the sailor^[1,2]. In order to reduce the pollution and protect the health of the occupational personnel, it was necessary to take effective personnel protective measure while taking certain engineering protective method. At present, the research on personnel protective material mainly focused on electromagnetic radio frequency session. The reports on extreme low frequency and stationary magnetic field were very few. The purpose of this study was to develop new appropriate material by sift material on the market.

Methods:

1. The basic principle and requirement: When the H-lines entered the ferromagnetic matter from the air. Because the permeability of ferromagnetic matter was several hundred or even several thousand times bigger than the air permeability. So the H-lines deviate from the normal lines very greatly, and the H-lines gather to the ferromagnetic matter strongly. The magnetic screen was made according to the principle. Inside the empty cavity of the ferromagnetic matter, almost no H-lines passed through. And the magnetic field intensity inside the empty cavity was very weak.

The aim of designing the protecting clothing was to cover the whole body of the personnel with shield material and placed them in the screened space. The screened space should conform to the body outline of personnel wearing protecting clothing, its screening mechanism was reflecting and absorbing energy^[3]. The material of the clothing was composed of some magnetic shield material and nonmetal fabric material. The magnetic shield material should possess the quality of preventing H-lines and other property fit for clothing basic requirement such as no physical and chemical irritation, natural free breath, softness, resisting wear and resisting aging, and etc.

2. The material classification: Metal cloth, metal membrane cloth, ooze metal cloth and absorbing material may be used as shield materials. But now riper technology and extensive application material is the ooze metal cloth. It were that one or many kinds of metal ions were oozed into the chemical fiber or the pure cloth by means of chemical processing (chemical plating, chemical modification, electroplating, vacuum evaporated plating, gluing the electric or magnetic conduction matter on the surface). The protecting material had higher screening efficiency. Using effective absorbing material to attenuate the space field energy was one kind of useful protection technique.

3. Instrument and source of field: ① Instrument : The LDJ-511P mould Gauss meter and CTS-27 mould tesla meter were used as measuring instrument; ② Source 1 (small magnet) : The cylinder small magnet (diameter, 6mm, length, 19mm) was used as field source, with the strongest magnetic induction density of 200mT. ③ Source 2 (BE-S-ELF magnetic source equipment) : The were a of magnetic section was 1050mm×525mm, gas gap was 200~700mm, it uses constant and alternating magnetic field and the alternating period can be controlled. The magnetic induction density on the center of the gas gap was 5~100mT^[4].

4. The evaluation method: ① When the source 1 was used, the position (with 6~8mm distance) of the small magnet and the probe of the measuring instrument should be fixed to measure the magnetic induction density without shield material (before shielding). Then the magnetic induction density with shield material (past shielding) was measured by putting the shield material behind in between the small magnet and probe of the measuring instrument. The percentage of difference between value of before shielding and past shielding to measure value of before shielding was used as shielding efficiency.②

When the source 1 was used, the probe of the measure instrument was fixed in a place of the gas gap of the magnetic source equipment, adjusting the magnetic induction density to needed value, recording the value (before shielding); use the shielding material of single or multi-layer to wrap the plastic round pipeline, and one of its mouth was open to the air. Put the pipeline around the probe of measure instrument, then measure the value of magnetic induction density (past shielding). The percentage of difference between value of before shielding and past shielding to measure value of before shielding was used as shielding efficiency.

Results:

1. The measurement of the electromagnetic shield material on the market: We had collected 9 kinds of materials from the market (which were used to shield the radio frequency electromagnetic field), and wrap them around the plastic pipeline of 200mm long and 32mm outer diameter. Use the field source 2 to observe its effect of shielding the mine sweeper from magnetic field. The results showed that few had the shielding effect (shielding efficiency was lower than 0.5%).

2. Measurement of membrane-smeared shield material: In order to select the material, according to the basic principle of the magnetic field shielding, we test 8 kinds of materials spread with iron, nickel and iron + nickel, use source 1 to observe its effect of shielding the mine sweeper from constant magnetic field. The results showed that nothing but 2 kinds of materials spread with pure iron had the shielding effect (shield efficiency was 6.5%).

3. Measurement of shielding effect of plate, net and wire material: On the basis of the basic principle of magnetic field shield, we made 3 kinds of ooze metal cloth by plating with ferromagnetic material such as iron, nickel and iron + nickel, selected several kinds of net and wire materials, and used source 1 to observe the shielding effect of the materials to constant magnetic field. The measurement showed that ooze metal cloth had no shielding effect to constant magnetic field, that the galvanized iron net and galvanized iron wire fabric had some shielding effect (shield efficiency was 16.7%~85.3%), and that stainless steel material had no shielding effect.

4. The shielding effect of different shielding bodies: To compare the shielding effect of different shielding bodies, we use the same metal fabric to make 2 kinds of shielding bodies. Shielding body1[#]: shielding materials were wrapped around plastic round pipelines (260mm long, outer diameter, 75mm) with one end open. Shielding body2[#]: it was made into clothing sample of short sleeve, which was equal to a shielding body of pipeline shape (900mm long, outer diameter, 360mm). We tested the two shielding bodies in source 2 to observe the shielding effect. The measurement showed that shielding body1[#] was superior to shielding body2[#], and the shielding effect of shielding body when fabric metal wire was perpendicular to pipe axis of the shielding body was superior to that when they were parallel. It was found in the same time that the shielding effect of the two shielding bodies decreased with the increase of the magnetic intensity.

Conclusion:

1. The shielding materials had a limited scope of application.
2. The continuity of the permeability affected the shielding effect.
3. The shielding effect was related to the composition of the shielding body.
4. It was difficult for materials of good magnetic permeability to become membrane or net materials.

The ferromagnetic fabric can be used as shield material in minesweeper magnetic-protective clothing, but many problems remain in making magnetic-preventing clothing with the material.

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No translation

I -11

THE RESEARCH FOR ELECTRICAL OSCILLATION ON CHAY NEURON BY SYNAPTIC INPUT

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Background: The research for nonlinear properties of neuronal oscillation can explain mechanism of neural oscillation and help to improve biological experiments. We aim to identify the great scale nonlinear patterns for collective neurons to study epilepsy, because widespread firing of neurons in seizure offers so many clear cases of population cells dynamics.

Nonlinear oscillation of population cells depends on synapses. Almost all communication between cells can be finished by the special structure. Chemical synapse is main structure in connecting neurons. There are many experiment results for the effect on cells population by excitory and inhibitory synapse. These results indicated that they can bring spontaneous epileptiform activity. The experiments and researches in recent years indicated that illness in nerve system such as seizure is relation to gap junction, and many electrophysiological experiments and clinical EEG data show that seizure is correlation with synchronous activities of neurons, it is meaningful work to study the relation between synchronous activity and gap junction by studies of abnormal rhythm. Our further research will focus on epileptic wave propagation and the effect of magnetic fields.

Methods: 1.Electrical oscillation of Chay model by excitory and inhibitory synapse input. We use the three-variable model made by T.R.Chay in 1995. The model studied the abnormal rhythm of neuron caused by Ca^{2+} -sensitive- K^+ channel, which affected the depolarization of excited neuron. We use the potential equation, other formulae and the meaning of variables see reference 1.

$$-C_m \frac{dV}{dt} = g_I m_\infty^3 h_\infty (V - V_I) + g_K n^4 (V - V_K) + g_{PP} (V - V_K) + g_L (V - V_L) \quad (1)$$

The electrical properties of excitory and inhibitory synapse derived from Alpha function. We give the current expressions which origin from reference 2, the meaning of variables see the reference.

$$I_{ext}(t) = g_{inhib,excit}(t)(V_{inhib,excit} - V) \quad (2)$$

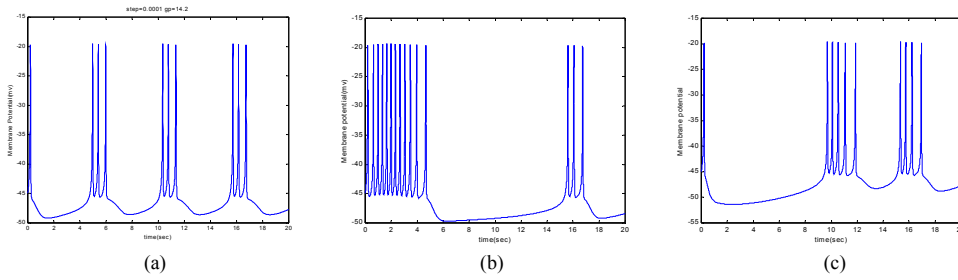
$$g_{inhib,excit} = \frac{g_{max}}{t_{max}} t \exp\left(1 - \frac{t}{t_{max}}\right) \quad (3)$$

2. Electrical oscillation of Chay model by gap junction input. In formula 1, arithmetic is added to the equation.

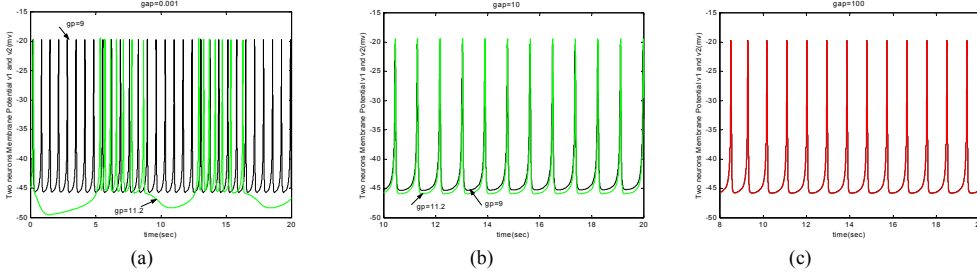
$$C_{m1} \frac{dV_1}{dt} = -\Sigma I_{jin}^1(V_1) - \Sigma I_{jout}^1(V_1) + (V_2 - V_1)Gap \quad (4)$$

$$C_{m2} \frac{dV_2}{dt} = -\Sigma I_{jin}^2(V_2) - \Sigma I_{jout}^2(V_2) + (V_1 - V_2)Gap \quad (5)$$

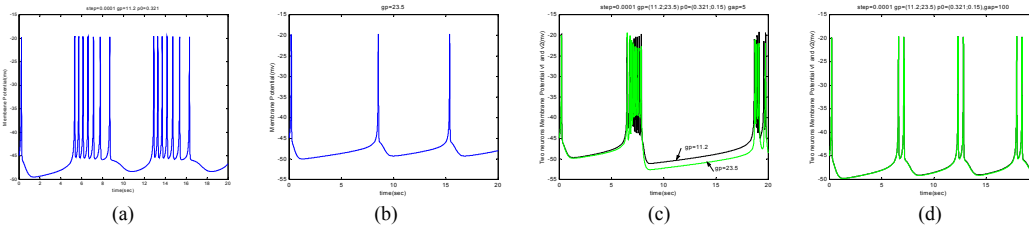
Results: 1. The figures show the dynamics of chaotic neuron by excitory and inhibitory synapse input. (a) is the membrane potential of chaotic neuron without synaptic input (reference Chay model). (b) is the membrane potential by excitory synapse input at $t=0s$. (c) is the membrane potential by inhibitory synapse input at $t=0s$.



2. The figures give numerical results with different gap junction strength, which one neuron is repetitive spike, and the other is burst chaotic. We observe the synchronous oscillation when couple strength is large enough.

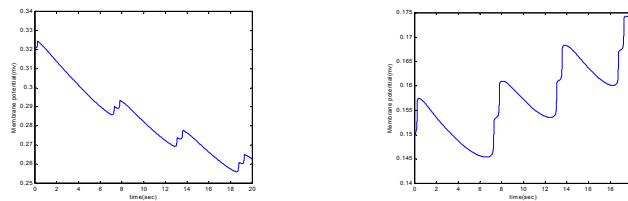


3. The figures give another results that two neurons are all abnormal, one neuron is burst chaotic in (a), another is single burst in (b). We also observe synchronous oscillation in part in (c), and synchronous oscillation in (d).



Conclusion: 1. It is apparent that couple strength is the main factor of synchronous oscillation, because synchronous activities occur only when the couple strength is large enough.

2. Ca^{2+} concentration is not synchronous. In the figures, we give Ca^{2+} concentration time sequence of two neurons in synchronous oscillation in above figure (d). We can conclude that synchronous oscillation is related to the membrane potential, not Ca^{2+} concentration.



3. spike frequency is larger and hyperpolarization is longer during excitory synapse input inphase opposition to the effect of excitory synapse input.

4. When two abnormal neurons are coupled by gap junction, abnormal activity is enhanced, behaving more spikes and shorter hyperpolaritation time.

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No translation

THE CONTROL AND OPTIMIZATION OF VIVO SYSTEM

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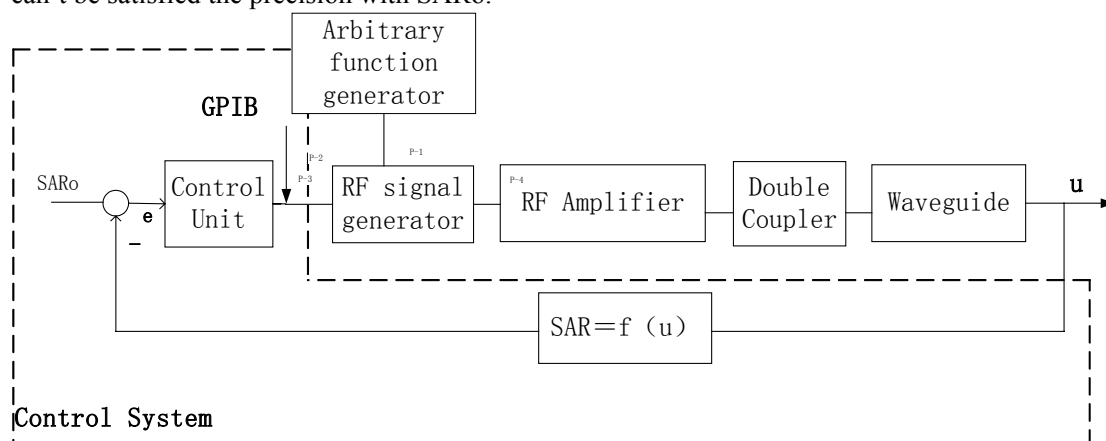
Key words: SAR, VIVO cell-exposure system, GPIB

Abstract: The graduation-design which is based on LF modulation microwave cell-exposure experiment will accomplish a set of control-monitor computer system. the autocontrol of exposure-intensity through computer control system, will achieve that the GSM 1.8G RF signal control the ration exposure of cell in waveguide . the aim of this experiment is to research the influence on organism-cell by different exposure ration.

The signal unit consists a RF signal-generator (HP-E4021B) that can be modulated by an arbitrary function generator to generate any modulation signal with a 16K points length and a frequency of less than 15MhHz. In order to simulate talk and environmental usage of GSM phones , a GSM fram generator has been developed enabling switches between the discontinuous transmission mode (DTX) and non-DTX. Firstly , Control system adjust the waveguide to resonance status. Then RF signal-generator product 1800M simulation-mobile signal modulated by arbitrary function generator include CW,217Hz,GSM basic ,GSM DTX only,GSM talk, GSM environment . RF-amplifier amplify the RF-signal 37db and control system select the Sham group and the experiment group .PC calculate the correspond SAR and complete the whole feedback control of VIVO cell-exposure system by collecting the diode-voltage and GPIB .

As the above , RF-signal generator can be used to change the RF signal frequency and power and GPIB can be used to control the whole system by PC .

P is the power of RF-signal generator , SARo is the initialization value and SAR is the vector of controlled . SAR can be calculated by the voltage collected by data-logger, and should be controlled if it can't be satisfied the precision with SARo.



From Radiofrequency Radiation theory , FDTD and simulation of SEMCAD

If σ, f^2, V_{medium} can be sured , the SAR of DMEM

$$SAR = a \times U_{HF}^2 + b \times U_{HF} + c$$

if the time of exposure is long enough , the temperation raising of DMEM

$$\Delta T \approx \tau_{on} \frac{SAR_{med}}{c_w}$$

H : the H-field amplitude of waveguide in A/m

U_{HF} : the voltage output at the HF-detector in V

$crest_factor$: the ratio between the peak power and average power of the signal whereas the period would be the reputation time of the pulse structure.

σ : the conductivity of the used cell medium in S/m;

f : resonance frequency of waveguide in Hz ;

V_{medium} : DMEM volume of the cell medium in ml ;

$SAR_{monolayer}$: the SAR upon the cell medium in W/kg;

SAR_{medium} : the medium average SAR in W/kg;

τ_{on} : the time-constant corresponding to V_{medium} ;

$$c_w = 4187 \frac{J}{kgK}$$

Control algorithm:

Initialize V_{medium} , $crest_factor$;

do

 initialize SAR_0

until ($\Delta T < 0.1$ °C)

do

 adjust signal generator with Golden Section algorithm;

until (waveguide resonance)

record f ;

do

 feedback control with 0.618 algorithm ;

until ($|SAR_0 - SAR| < \varepsilon$)

/* ε is the precision of initialization , ε must be less than 5% */

This algorithm is based on the V_{medium} is almost constant . But V_{medium} will be decreased if the time of exposure is long enough . But if the time of exposure is less than 4h , the change of V_{medium} can be ignored . In the future , we'll observe the change rule of V_{medium} -Time , then develop our algorithm to satisfied new request of exposure-experiment .

STUDY ON THE EFFECTS AND INJURY PROTECTION OF 2450MHZ MICROWAVE

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Background: The electromagnetic wave brings convenience to human and has work automation and life electrification. But at the same, it brings serious electromagnetic pollution to our environment, especially computer, mobile, broadcast, TV, other electric equipments; other equipments of health care and treat are used widespread, it awakes human to understand the endanger and safe of electromagnetic pollution, and the scientists take it seriously too.

Methods: To investigate the effects of electromagnetic wave, we choose BALB/c mice exposure 2450MHz microwave to study the effects and injury protection.

Results:

1、 After 2450MHz microwave exposure

- (1) The number of WBC and bone marrow nucleated cells (BMNC) first increase and then decrease as the exposure time extends;
- (2) Marrow cell GM-CFU forming and T lymphocyte cell proliferative ability increases; it can accelerate the G₁ cell into G₂ and S cell;
- (3) The rate of lymphocyte cell HPRT gene mutation rises as exposure intensity increased;
- (4) Sperm number decrease and deformity rate increased; morphology and structure of testis and sperm changed after exposure.

2、 LIBIDUO (Traditional Chinese medicine) can protect and cure the injury of and change of T cell ability after microwave exposure;

3、 J005A electricmagnetic wave shielded fabric can protect the damage of microwave exposure validly.

Conclusion:

1、 2450MHz microwave can change hemopoietic system, immune and reproductive function, the changes have relation with exposure time and intensity;

2、 LIBIDUO (Traditional Chinese medicine) and J005A shielded fabric can protect and cure the injury of 2450MHz microwave exposure. (2003.02.17)

EXPERIMENT STUDY OF CD31 REDISTRIBUTION, EXPRESSION AND PHOSPHORYLATION IN ENDOTHELIAL CELLS POST MICROWAVE IRRADIATION

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Background: We have found that normal tissues exposed to certainly dosage of microwave irradiation became hyperemia, hemorrhage, edema and infiltrated with leukocyte. These pathologic changes suggest that microwave radiation cause vascular injury and induce elevation of vascular permeability. This damager may be a major factor contributing to the pathogenesis of radiation injury and infiltrated leukocyte may be a secondary damage factor by releasing proinflammatory factors in addition to that direct

injury mediated by electromagnetic irradiation. Therefore it is important to elucidate the molecular mechanisms mediating leukocyte infiltration to tissue post electromagnetic irradiation. In this paper, we have studied CD31, an adhesion molecules contribute to the adhesion junction and the process of leukocyte infiltration, distribution, expression and phosphorylation in endothelial cells post microwave irradiation.

Methods: **1. In vitro study:** Confluent endothelial cells from rat pulmonary blood vessel were irradiated by microwave. At different times post irradiation, the following parameters were measured. (1) Distribution of CD31 and F-actin: Cells were grown on glass coverslips and exposed to microwave. 2h after irradiation, cells were fixed with 2% paraform and incubated with primary mAb to CD31, followed by appropriate FITC tagged second Ab. For F-actin stain, cells were permeabilized by incubating in 0.1% Triton X 100 for 1 minute, washed with PBS/1% BSA and incubated with fluorescein-labeled phalloidin. Coverslips were then mounted and observed in fluorescence confocal microscopy. (2) Analysis of CD31 expression by Western blot. 2, 4, 8, 24h post irradiation, cells were extracted and proteins were conducted 6% SDS-PAGE. After SDS-PAGE, gels were incubated with transfer buffer and transferred electrophoretically to PVDT membranes. After incubated with primary mAb and secondary Ab, filters were stained and detected. (3) RT-PCR analysis for CD31 mRNA expression. Total RNA was extracted from cells 2h, 4h, 8h, 24h post microwave radiation. After cDNA synthesis as usual, the cDNA was used for PCR. Forward primer 5'-CAA CGA GAA AAT GTC ATA-3', antisense primer 5'-GGA GCC TTC CGT TCT AGA GT-3'. The thermocycling sequence was as follows: 60 seconds at 94°C, 60 seconds at 56°C and 90 seconds at 72°C. (4) Phosphorylation analysis of CD31. Cells were incubated with ³²Pi (0.1~2mCi/ml) at 37°C for 2h. ³²Pi-labeled cells were exposed in microwave. 2h, 4h after exposure, cells were lysed. For immunoprecipitation, cell extracts were mixed with anti-CD31 mAb, followed by protein A-Sepharose. Immunoprecipitates were then resolved by electrophoresis on 6% SDS-PAGE and visualized by autoradiography. (5) Effect study of mAb CD31 on HL-60 cells transendothelial migration. The promyelocytic cell line HL-60 cells were terminally differentiated to a monocyte-like phenotype by 4 to 5 day culture in the presence of 5 μM retinoic acid. Endothelial cells grown to confluency on Transwell were exposed to microwave. 8h after exposure, endothelial cells were incubated with 1-5 × 10⁵ /ml differentiated HL-60 cells and CD31 mAb (5ug/ml) for 2h. For transendothelial migration, migrated leukocytes were recovered from the bottom of the well, centrifuged, stained with 0.2% trypan blue and counted microscopically. **2. In vivo experiments.** The influence of tyrosine kinase inhibitor Lavendustin A on permeability of blood vessel in mice. Lavendustin A was injected i.p at a dosage of 0.05 μg/g b.w in BALB/c mice 30min before microwave irradiation. 30min after exposure, leakage of FINa from pulmo, liver, kidney and testicle vessels were detected.

Results: (1) Redistribution of CD31 and F-actin after microwave exposure. We found that after exposure to microwave, CD31 disappeared from cell-cell contact to a more diffuse presence over the entire cell surface. These changes of CD31 were accompanied by F-actin disruption and redistribution from the cell periphery in resting endothelial cells to a tangled network of centrally located filaments. (2) Expression of CD31 protein and mRNA after microwave exposure. We found that 8h after irradiation, expression of CD31 increased 35% compared with control and enhanced more than 50% 24h post exposure. Expression of CD31 mRNA increased 30% compared with control 4h post microwave radiation and keep high lever 8h to 24h post exposure. (3) Phosphorylation of CD31 after microwave exposure. It was found that microwave irradiation increased the phosphorylation of CD31 and phosphorylation level reached peak value 2h after exposure, it was 3.9 times of control. Phosphorylation lever declined 4h after exposure, but there were 2 times raise than control. (4) Antibody to CD31 significantly inhibited the transmigration of monocyte like HL-60 through a monolayer of irradiated endothelial cells. The migrated cell number decreased 50.6% compared with no treatment group. (5) In vivo administration of Lavendustin A, an inhibitor of tyrosine kinases, protected endothelial cells from irradiation-dependent vascular leakage in different tissues of mice. FINa contents in pulmo, liver, kidney and testicle blood vessels were decreased respectively 46.2%, 43.3%, 51.7% and 35.5% compared with no treatment group.

Conclusion: These findings suggest: (1) Microwave irradiation causes phosphorylation of CD31 that may have effect of signal transduction and induce changes in biological behavior of proteins related to vascular barrier. Inhibition phosphorylation of CD31 has some effect to protect blood vessel permeability from damage caused by microwave. (2) Redistribution of CD31 caused by radiation influences the cell shape and

cell adhesion junction, it becomes the structural basis of leukocyte infiltration and permeability dysfunction. (3) Upregulation expression of CD31 mRNA and protein induced by irradiation provide a precondition for leukocyte to interact with endothelial cells and directly influence the transendothelial migration of leukocyte. Antibody against to CD31 could inhibit transmigration of monocyte like HL-60 on endothelial cells induced by microwave significantly.

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II-3

No Translation

II-4

ADVANCES IN THE EFFECT OF MICROWAVE ON CENTRAL NERVOUS SYSTEM

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Microwave is a kind of electromagnetic wave whose frequency range from 300MHz to 300GHz. It has been widespread used in agriculture, transportation, communication, medicine and military. In recent years, more and more concerns have been raised about the bio-effect of the microwave. Central nervous system (CNS) is the most sensitive part to the microwave radiation. This review is about the effect of microwave on CNS in the aspects of dosimetry, characteristic and regularity of injury, relationship between dose and effect, mechanism, brain tumor, diagnosis, prevention and cure.

1. Dosimetry of microwave radiation:

The commonly used parameter: (1) frequency (f): the times of vibrations in a second. Its unit is hertz (Hz). (2) wavelength (λ): the distance of electromagnetic wave spread in one cycle. Its unit is meter (m). (3) power density (Pd): the radiant energy per unit square which is proportional to the spread direction. Its unit is W/m². (4) special absorption rate (SAR): the energy absorbed per unit tissue. Its unit is W/kg.

Microwave can be classified into pulsed microwave and continuous microwave due to emission pattern. It can also be divided into ultra high frequency (300-3000MHz), super high frequency (3-30GHz) and extreme high frequency (30-300GHz). Because microwave was used in radar first, we often use the classification in radar technology. P frequency range is between 300 and 1000MHz, L frequency range is 1-2GHz, S frequency range is 2-4GHz, C frequency range is 4-8GHz, X frequency range is 8-12.5GHz, Ku frequency range is 12.5-18GHz, K frequency range is 18-26.5GHz, Karequency range is 18-26.5GHz.

2. characteristic and regularity of microwave injury

(1) Material: There are three kinds of materials as following: experimental animal, vitro cultured tissue

and brain slice. Brain slice is the common and special model in the research of CNS function and disease. It has been widely used in neuroscience research according to its advantages.

(2) Effect on behavior and learning: The most obvious effect on CNS is its damage to learning and memory. Some epidemic study show that microwave induce fatigue, headache, excitement, dreamy and memory damage et al. The incidence of Alzheimer's disease is greatly increased in the people exposed to microwave for a long time. when exposed to high power microwave, people can even catch mental confusion, behavioral error etc. animal experiment such as maze, long term potentiation (LTP) and electroencephalograph (EEG) also identified microwave damage on behavior, cognition, learning and memory.

(3) Pathologic changes in brain after microwave radiation: Microwave radiation can induce the morphology change in brain. When the rat exposed in $50\text{mW}/\text{cm}^2$ pulsed microwave, the nerve cells in hypothalamus and subthalamus may swell, cytoplasm vacuolation and chromosome resolution. In electron microscope, the rough endoplasmic reticulum (RER) and ribosome decreased in the nerve cells above mentioned. When over $50\text{mW}/\text{cm}^2$, brain hyperemia, nerve cells degeneration and microglia proliferation will happen. Exposed to $3\text{-}5.8\text{W}/\text{cm}^2$ see even more obvious tissue damage such as cerebral vessels hyperemia, hemorrhage, neuron swelling, resolution, nuclear membrane focal disruption, astrocyte rarefaction, nuclear membrane disruption or cytoplasm vacuole.

3. Dose and effect relationship

It is known that the effect of microwave radiation can be divided into heating effect and non-heating effect. The main effect of continuous microwave is heating effect, while the pulsed microwave is non-heating effect. The dose and effect relationship of heating effect is clear. The lethal and wounding effect show direct ratio to P_d , radiation time, tissue temperature, and show inverse ratio to radiation distance. The essence is direct ratio to the energy absorbed. In addition, big animals can endure heating effect more than small animals. It is unclear about the dose and effect relationship of non-heating effect. Someone suggest that there exist window effect, including frequency window and power window etc, and that window effect may relate to the resonance between electromagnetic wave and ion and protein in vivo. But the window effects are not reported in high frequency wave but in extreme low frequency. The dose and effect relationship remain to be solved.

4. The mechanism of microwave radiation effect

(1). Microwave and blood brain barrier

In 1970th, it is reported that microwave can affect the permeability of blood brain barrier (BBB). Rats exposed to 1.3GHz microwave for 20 minutes can cause the manicol permeated into brain which can not happen in normal condition. Recently, a vitro experiment has identified the idea. The effect has no relationship to the heating effect.

(2) Microwave and gene transcription

It has been a focus to investigate the effect of electromagnetic radiation on CNS on gene level. Microwave radiation can up-regulate HSP and c-fos expression, which may relate to cell damage and learning and memory disorder.

(3) Microwave and neurotransmitter

Electromagnetic wave can deduce the release of Ach in hippocampus and the activity of M-Ach receptor, and increase the expression of δ -opium receptor and mRNA in rat hippocampus, which depended on the dose and time of radiation.

(4) Microwave and signal transduction

Microwave can decrease the NMDA receptor activity, regulate Ca^{2+} flow in Ca^2 passage, reinforce the NO induced oxidative stress reaction, enhance the expression of iNOS and increase the binding activity of NF-K B.

5. Microwave radiation and brain tumor

Epidemic research exposed that microwave radiation is related to the brain tumor. But some researchers consider there are some defect in these research such as insufficient samples and unsure radiation dose. So the results remain to be confirmed. As to the mechanism of the relation between microwave and brain tumor, it is accepted that microwave can not damage DNA directly. It can not induce DNA break in non-heating condition. Its energy is not able to damage the chemical link. Someone suggested that microwave can produce lots of free radical which can affect the repair of DNA so as to

promote tumor occurrence. Other researchers investigated the cooperation of microwave to carcinogen and the effect of microwave on growth and proliferation of tumor cells, but show no significant difference to control group. The idea that microwave is the dangerous factor of brain tumor hasn't been accepted widely. The relationship remained to be studied.

6. Diagnosis, prevention and cure of microwave radiation

The bio-effect of microwave radiation is still not elucidated, so that the promptly and effective diagnosis is impossible. The treatment to the microwave damage is according to the disease. As to the prevention and cure, it is suggested to avoid being exposed to microwave, and safety dose of microwave radiation are ruled all over the world.

7. Perspective

It is well known that microwave can do harm to CNS, especially to behavior and cognition, but there are still some problems in the area: (1) The mechanism of the bio-effect is not clear. Some experiments can't be repeated, and the results are doubted. (2) The non-heating effect of the pulsed microwave and its mechanism are still not exposed. (3) The dose and effect relationship is still a question. (4) The diagnosis and cure of the microwave damage is to be solved. Above all, there is still a long way to go, and need more researchers to make their effort on it.

II-5

STUDIES ON THE INJURY EFFECTS OF HEMATOPOIETIC CELLS IN MACAQUES BONE MARROW INDUCED BY ELECTROMAGNETIC PULSE (EMP) IRRADIATION

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Background: Electromagnetic radiation is widespread present in people's daily life and work environment and people have pay close attention to it for being new environment pollution. Electromagnetic radiation may not only interference and destroy electron telecommunication equipment, but also injure the organs. The finished study showed that electromagnetic radiation may induce the changes of the structure and fuction of multi-organs including nerves, endocrine, blood circulation, hematopoietic, immune and genital system. But up to now, it has not been reported that the injury effects of hematopoietic cells in macaques bone marrow induced by electromagnetic irradiation The aim of the present study is to observe the injury effects of bone marrow hematopoietic cells induced by electromagnetic irradiation. It may be offerred the direct evidence for clarified the organnism damage effects for EMP .

Methods: 5 adult health monkeys, 2 male and 3 female. The body weight was 3.5~8.5kg, All animals were whole body irradiated with 6×10^4 V/m EMP, pulse rise time was 20ns, the pulse wide was 30us, the frequency of waves was 6 times/min and the total time of irradiation was 5 minutes. The bone marrow was abstracted through superior extremity of femur under anesthetization, separated the karyotes and smear before radiation and day 1,3,7,14,28 and 90 respectively after radiation. By means of light microscope (Gimsa, AgNOR and Feulgen staining), electron microscope and flow cytometry, the injury effects of the hematopoietic cells were studied.

Results: The hematopoietic cells and their DNA and AgNOR contents were more and more decreased and the morphology was abnormal in day 1 to 14 after injury, especially immature cells. The apoptotic hematopoietic cells were obviously increased and the characteristics of apoptosis were the chromatin condensation, margination and karyopyknosis in day 7 to 14 after injury. The number, morphology, DNA and AgNOR contents of hematopoietic cells were recovered gradually to normal condition in day 28 to months 3 after injury.

Conclusion: (1) EMP radiation may induce the number of hematopoietic cells decreased and the structure abnormal. (2) EMP radiation may induced hematopoietic cells occurred apoptosis. (3) The contents of DNA and Ag-nor were decreased after EMP radiation, and recoved at 3months. (4) EMP irradiation may decreased the ability of it in macaques bone marrow.

II-6

EFFECTS OF 9000MHZ PULSED MICROWAVE IRRADIATION ON ATP CONTENT AND Ca^{2+} , Mg^{2+} -ATPASE ACTIVITY OF MICE BRAIN

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Background With the development of aerospace undertaking and the increase of pulsed microwave application in this area, effects of pulsed microwave on human are more concerned. Some studies has shown that brain was sensitive to microwave, and ATP and Ca^{2+} , Mg^{2+} -ATPase of brain were keys to brain metabolism and signal transduction pathway, and Ca^{2+} , Mg^{2+} -ATPase was also target molecular in cell exposed to exchanged electric field. However reports of pulsed microwave effects in these areas were rare. So we decide to study how pulsed microwave affects metabolism and enzyme by researching mice brain ATP content and cortex, hippocampus and thalamus Ca^{2+} , Mg^{2+} -ATPase activity.

Methods Kunming mice were used as experiment animal and 9000MHz pulsed microwave were irradiation resource. Mice were divided into control and radiation groups which were divided into $1mW/cm^2$, $5mW/cm^2$, $10mW/cm^2$ group again. The indexes were ATP content of mice brain and Ca^{2+} , Mg^{2+} -ATPase activity of cortex, hippocampus and thalamus. They were measured by bioluminary and histochemical method respectively.

Results 9000MHz pulsed microwave at $1,5,10mW/cm^2$ decreased activity of Ca^{2+} , Mg^{2+} -ATPase significantly ($P<0.05$). ATP content of $5,10mW/cm^2$ group was increased significantly ($P<0.05$).

Conclusions Pulsed microwave could affect metabolism and signal transduction, which would injure brain issue.

RESEARCH ON THE PROLIFERATION AND DIFFERENTIATION OF RAT BONE MARROW MESENCHYMAL STEM CELLS WITH EXPOSURE TO MAGNETIC FIELDS

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Abstract A preliminary experimental research on the proliferation and differentiation of rat bone marrow mesenchymal stem cells with exposure to 50-Hz magnetic fields is done. The experimental results can be well repeated and show that 50-Hz magnetic fields can evidently affect the proliferation and differentiation of rat bone marrow mesenchymal stem cells(MSCs), besides, the results are not linear with the amplitude of magnetic fields, but existing a 'window' phenomenon. At the end of this paper, the domestic and overseas development of the research is discussed on how to cure the bone fracture with the help of magnetic fields, and our investigative thoughts are also presented.

Key words 50-Hz magnetic fields Mesenchymal stem cells(MSCs) Proliferation Differentiation

EFFECTS ON NOCICEPTION OF RAT EXPOSED TO EXTREMELY LOW FREQUENCY MAGNETIC FIELDS

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Background: Extremely low frequency (ELF) magnetic fields exert a diversity of biological effects, with the central nervous system (CNS) being their most liking site of action. But the magnetic fields sensing/transduction mechanism still remains to be identified. The mechanism of pain is a very complex process, in which serotonin (5-HT) plays an important role. Many works have approved the analgesia of magnetic fields, but the biological mechanism is still unknown. This effect on CNS has been shown to be dependent on both field strength and exposure duration. The present study was undertaken in order to examine the relationship of these exposure parameters of magnetic fields exposure, the content of 5-HT and pain threshold. This information can provide further insight into the mechanism of action of these fields. Our experiment was to study the bio-effect of magnetic fields on analgesia of rat, and to further discuss analgesia mechanism of ELF magnetic fields.

Methods:

1. Magnetic fields conditions: ELF apparatus was made for the present study. The length and diameter of the coil are respectively 42cm and 19cm with adjustable frequency, amplitude and wave type that can generate 5-500Hz, 5-20mT magnetic fields. In this experiment, 55.6Hz, 8mT ELF with triangular wave was chosen for study. Both the sham and ELF magnetic fields exposure were carried out in the same room, and the apparatus in same shape except that in the sham exposure the coil was removed from the apparatus that produced the ELF.

2. Subjects: Male Sprague-Dawley rats weighing 90-100g.

3. Test for nociception: Analgesia was assessed with tail-flick apparatus 6 hours later after exposed to ELF magnetic fields for 7 days, 6 hours each day, with the room temperature keeping at $23 \pm 2^\circ\text{C}$. To measure tail-flick latency (TFL), each rat was restrained in a polyethylene tube, and the light source, positioned below the tail, was focused at a point 1/4 distant from the tip of the tail. Each test rat had a 30min habituation trial in the tube before TFLs were assessed. A cut-off time of 15s was used to prevent lesion to the tail. And the latency to a brisk reflect movement of the tail was recorded. The pain threshold was measured every 10min for three times, and the average of the values denoted pain threshold. The time at which pain threshold was measured was fixed. The equation used for calculating change rate is: $\text{CPT} = (\text{PT} - \text{BPT}) / \text{BPT} \times 100\%$ (CPT: change rate of pain threshold; PT: value of pain threshold; BPT: base value of pain threshold).

4. Measurement of 5-HT: Rats were decapitated in turn at the selected time points 0, 2, 4, 6 hours after 7 days, 6 hours each day exposure to the ELF magnetic fields, and the whole brain was quickly removed and frozen immediately on ice, the hypothalamus was dissected thereafter, tissue samples were stored at -80°C until assay. 5-HT was measured according to the method described by G. Curzon. F-4500 fluorescence spectrophotometer was used; the excitation wavelength/emission wavelength is 350/475.

5. Statistical analysis: Statistical analysis for the data was performed using Student's *t*-test and ANOVA. All hypothesis tests used a criterion level of $\alpha = 0.05$.

Results:

1. The effect of ELF magnetic fields on analgesia.

After 7-day exposure to 55.6Hz, 8mT magnetic fields, TFL were assessed with tail-flick apparatus. CPT was calculated according to the equation described before. There was a significant ($P < 0.05$) increase of CPT in rats (Fig1).

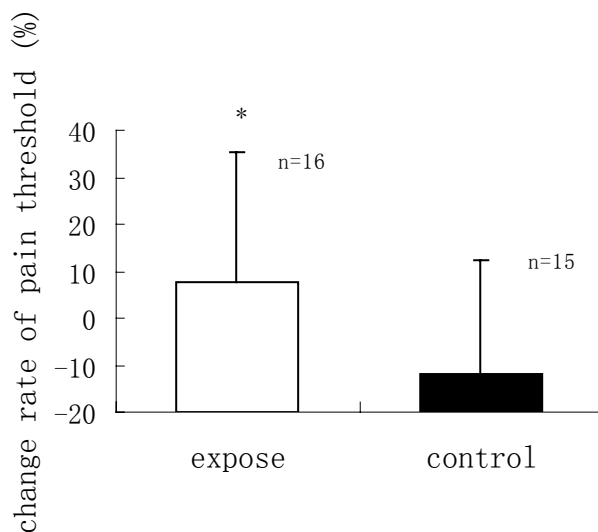


Fig1. Exposing the rats to ELF magnetic fields led to a significant ($P < 0.05$) increase of CPT in rats. The CPT was higher in control group than that in expose group.

2. The content of 5-HT in hypothalamus after exposed to ELF.

No significance ($P > 0.05$) was found in the time points 0, 2, 4, 6 hours after exposed to ELF between each expose group and control group (Fig 2); Comparing the content of 5-HT in hypothalamus in different time points after exposed to ELF, there was no obvious tendency of increasing or decreasing among the four selected time points ($P > 0.05$) (Fig 3).

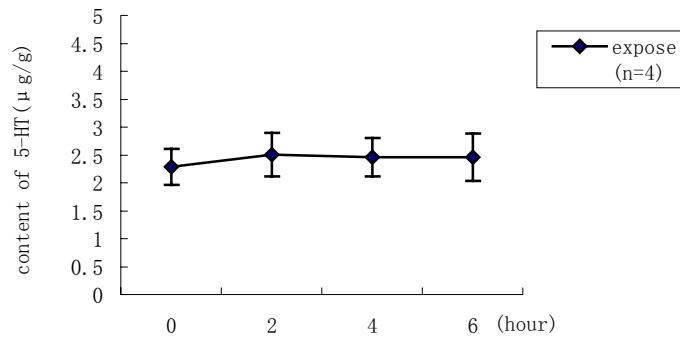


Fig2. Rats were decapitated after exposed to ELF for 7 days 6 hours each day, and 5-HT was measured by F-4500 fluorescence spectrophotometer. No significance ($P>0.05$) was found between each expose group and control group of 0, 2, 4, 6 hours.

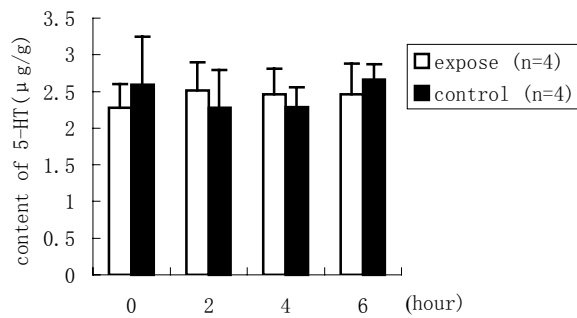


Fig3. To compare the content of 5-HT in hypothalamus in different time points after exposed to ELF, 0, 2, 4, 6 hours were selected, there was no increasing or decreasing tendency ($P>0.05$) among the four selected time points.

Conclusions:

1. There were some analgesia effects on rats exposed to 55.6Hz, 8mT magnetic fields for 7 days, 6 hours each day.
2. In our present study, there was no obvious variance of 5-HT in hypothalamus of rats. To further study the analgesia mechanism, the next step is to assay β -endorphin, which has close relationship to analgesia.

GENE EXPRESSION PROFILING OF HUMAN BREAST CANCER CELL (MCF-7) IN RESPONSE TO ELF MAGNETIC FIELDS (MFs) EXPOSURE

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BACKGROUND: The biological effects and mechanism of action of extremely low frequency magnetic fields (ELF MFs) has been widely studied, especially the relationship between ELF MFs and tumorigenesis, since epidemiological studies indicated that exposure to ELF-EMF may lead to an increased risk of certain types of adult and childhood cancers. But most of them focused on single gene or protein, not at the genomic or proteomic level, and contradictory data still remains in the literature.

OBJECTIVE: In this study, we are using genome analysis techniques to screen genes in response to ELF MFs exposure.

METHODS: 1. The exposure system consists of three groups of square copper coils (36 cm x 36 cm) placed inside an incubator (Model 3164, Forma). A 50-Hz sinusoidal magnetic fields was generated by feeding a line current to the coils. Magnetic flux densities were measured using a Model EFA2 meter (Wandel & Goltermann Co., Germany). When energized and adjusted, a very uniform (0.1%) 0.4 mT magnetic field can be generated in the center ($10 \times 10 \times 10 \text{ cm}^3$) of the coils where cell culture dishes were placed. During exposure, the incubator was aired with 5% humidified CO₂ air and maintained at 37°C. Temperature in the incubator was monitored and kept at $37.0 \pm 0.2^\circ\text{C}$ through out the entire experiment. Two groups were conducted: a) sham exposure, b) 0.4mT MF exposure. The exposure time was 24hr.

2. MCF-7 cells were grown in Dulbecco's modified Eagle's medium supplemented with 10% FBS in 5% humidified CO₂ at 37°C. The total RNAs were extracted by using QIAGEN's RNeasy mini Total RNA Isolation Kit. RNA yield was quantified by spectrophotometric analysis (Smart Spec™3000) using the convention that 1 absorbance unit at 260 nm equals 40 µg RNA per ml.

3. Genome U95A gene-chip (Affymetrix Co., USA) was applied to analyze gene expression level, which contains 12,000 known human genes, some of them related to diseases.

RESULT: The data of cDNA array Analysis demonstrated that comparing with control, there are more than 90% genes whose expression levels remain stable. And there were 98 genes whose expression levels were changed more than 2.5-fold, including 77 up-regulated genes and 21 down-regulated genes. The data showed that the levels of most of oncogenes (such as int-1, c-myc) or proto-oncogenes (such as c-fos, c-jun) were unchanged, but *BRC A2*, a gene involved in DNA recombination and repair pathway, was changed.

CONCLUSION: The genome expression levels will be changed after exposure to 50 Hz 0.4mT ELF-MF for 24 hours. It is suggested that ELF-MF might be a co-carcinogen through *BRC A2*-mediated pathway, which participates in DNA recombination and repair. In order to elucidate the relation between ELF-MF and breast carcinogenesis, further studies should be conducted to determine the expression patten and relationship with tumorigenesis for these ELF-MF response genes.

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No translation

EFFECTS OF LOW FREQUENCY PULSED MAGNETIC FIELD ON THE PROLIFERATION AND DIFFERENTIATION OF HEPG2 CELLS

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Background: Many investigations have been carried out regarding the influence of low-frequency electromagnetic field on cell proliferation within the mT range of magnetic flux density. In 1987, Adey et al. reported significant neurological effects be produced by modulation of microwave-frequency carrier at 16 Hz. This finding, as it was called “frequency window”, has been demonstrated by several other studies since. In this paper, we choose two frequencies (16Hz and 80Hz) to study the effect of magnetic fields on the cell proliferation and AFP secretion of HepG2 cells.

Methods:

1. ELF exposure system: The pulsed magnetic fields consist of a pulsed power and one cylindrical solenoid polarized magnetic fields, having frequencies of 5~200 Hz and effective magnetic field strengths of 0~6 mT, square waves, the solenoid inner size is 19cm in diameter. Our exposure field was characterized by two frequencies (16Hz and 80Hz) and a magnetic flux density of 1.55mT.

2. Cell culture: Human hepatoma-derived cell line HepG2. The cells were grown at 37°C in an atmosphere of 5%CO₂ incubators in MEM, supplemented with 10% fetal bovine serum.

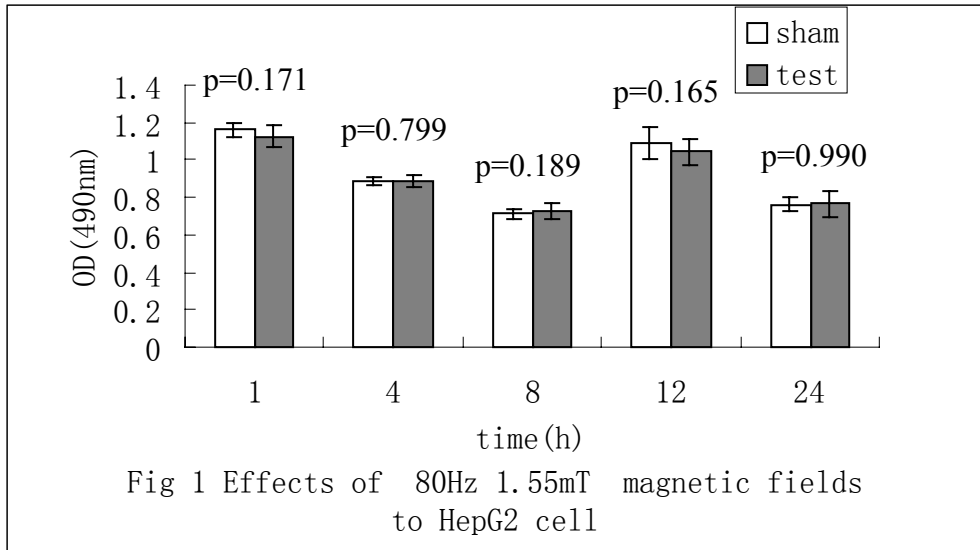
3. Determination of cell proliferation: Use MTS colorimetry method to determine the cell proliferation. Use ELISA assay to determine the content of alpha-fetoprotein (AFP) as the indicator of cell differentiation.

4. Data Analysis: Statistical analysis for the data was performed using Student’s *t*-test, used a criterion level of $\alpha=0.05$.

Results

1. Effects of the 80 Hz pulsed magnetic fields:

Incubated the inoculum cell size of 1×10^4 cells/ml for 24h at 37°C, 5%CO₂ when the cell growth turned into logarithmic phase. The cell culture was exposed for low frequency pulsed magnetic fields at 80Hz, 1.55mT for 1h, 4h, 8h, 12h and 24h, respectively. The exposed cells were then allowed to grow for another 24h in the incubator. At the end of incubation, the cell proliferation was determined by MTS method. The results showed that the sham and the magnetic field treatment were indicated no significantly different ($P>0.05$) by *t* test (Fig.1).



2. Effects of the 16 Hz pulsed magnetic fields:

The cell suspensions of 2×10^4 cells/ml were added to the wells of a 96-well culture plate. After 24h of incubation at 37°C , $5\%\text{CO}_2$, the plates were treated under the pulsed magnetic fields for 1h, 4h, 8h and 24h, respectively. At the end of incubation, cell proliferation was determined by MTS method, AFP was assayed by ELISA. The results showed that there were no significant difference between sham and treatments on cell proliferation and AFP secretion under the exposure to 16 Hz pulsed magnetic fields by t-test ($P > 0.05$) (Table 1).

Table 1. Results of MTS and AFP determination in exposure to 16 Hz Magnetic Fields ($\bar{X} \pm s$)

		Exposure time			
		1h	4h	8h	24h
MTS	Sham	0.621 ± 0.058	0.541 ± 0.031	0.621 ± 0.036	0.753 ± 0.023
	Exposure	0.638 ± 0.047	0.528 ± 0.023	0.609 ± 0.038	0.737 ± 0.026
AFP	Sham	1.503 ± 0.090	0.792 ± 0.085	1.837 ± 0.071	1.052 ± 0.056
	Exposure	1.514 ± 0.068	0.811 ± 0.091	1.803 ± 0.047	1.098 ± 0.072
P value	MTS	0.376	0.222	0.380	0.073
	AFP	0.723	0.607	0.214	0.094

Conclusion:

In this study, there were no significant effects of magnetic fields observed at 80 Hz, 1.55mT on cell proliferation for 1h, 4h, 8h, 12h and 24h, respectively. Likewise, there were no significant effects of magnetic fields observed at 16Hz, 1.55mT on cell proliferation and AFP secretion, the latter which was used as indicator of cell differentiation for 1h, 4h, 8h, 12h and 24h, respectively. Many investigations revealed that the release of cellular calcium ion responded to the modulation frequency as 'window' effect, meaning a largest response occurring around the frequency of 16Hz. However, it was not identified as such in this paper. Other investigations regarding the effects of 16Hz, 1.55mT magnetic field on HepG2 cells will be attempted for further progresses.

II-12

INJURIES OF EMP AND HPMW ON RABBIT OPTICAL SYSTEM

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Objective: There are transparent fibrotic tissues in the eye, more water and fewer blood vessels in it. So eye is a sensitive target organ of EMP and HPM on human body. Little systematic and dynamic reports were found about the effect of EMP and HPM on optical system. Using a rabbit model, we studied the dose-effect relation-ship, pathological changes and their mechanism.

Methods: Rabbits were irradiated with EMP and HPM to set up animal models. Slit lamp, ophthalmoscop, fluorescence fundus angiography, electroretinogram, colour doppler flow imaging, routine pathology, histochemistry staining, EM, Immunohistochemistry, Confocal Microscopy, image analysis and In Situ Hybridization were used to study the changes in 110 eyes systematically, dynamically, and long-termly.

Results: In EMP group, the death rate was 35.71% (5/14) during day 0~180 after irradiation, and the more radiation dosage, the more severe pathological changes. In HPM group, the death rate was 22.86% (8/35). The death rate was 0% in control group. In HPM group, the more irradiation dosage, the more severely pathological changes were found. In the EMP and HPM induced optical system injuries, lens was the most important part, and cataract could be present. Opacity could happen in the posterior surface of lens. anterior capsule of lens thickened, epithelial cell arranged disorderly, degeneration happened, and the number of epithelial cells was decreased. The fiber in lens was arranged disorderly. The pathological changes in cornea were less severely than in lens. Cornea fluorescence staining was positive. Vasodilatation was found in bulbar conjunctiva. Epithelial cells in cornea were arranged disorderly, and degeneration happened. Parenchymal layer were found edema. Pathological changes in retina were lightly.

Conclusion: In EMP and HPM induced optical system injuries, lens is the most serious one, cornea secondly, and retina thirdly. The injury degree are related to irradiation dosage. The more radiation doses, the more severe pathological changes were found.

II-13

PRELIMINARY STUDIES ON THE EFFECTS AND IT'S MECHANISMS OF ELECTROMAGNETIC PULSE ON MEMORY CAPABILITY OF RATS

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Objective To investigate the effects of electromagnetic pulse (EMP) on defensive conditioned reflex of rats and to explore the mechanisms responsible for the effects through observing the lesion of brain tissues induced by EMP exposure.

Methods

1. Behavioral testing At first, Fifteen adult Wistar rats were trained 40 times/day for a succession of 10

days with two-way active-avoidance shuttleboxes. Electric shock served as the unconditional stimulus(UCS) and white pilot lamps were used as conditional stimulus(CS). Programming of events in the experiment and recording of data were under control of a computer. Eleven rats which got a over 80% correctness of active avoidance response in the task were selected and to exposure to a high field strength EMP irradiation (6×10^4 v/m, rise time 20ns, pulse width 30 μ s, 5 pulse in 2 minute). Then repeated measurement were taken with shuttleboxes at different time points after exposure respectively(immediately, 3h, 6h, 12h, 24h after exposure). The scores of each rat's performance in different phase were collected for statistical analysis.

2. Morphological observation of hippocampus tissues Ten rats were used in morphological examination. At 3 hours and 6 hours after EMP exposure, rats were decapitated and brain tissues were prepared into paraffin-embedded sections. Those sections were stained with Hematoxylin-Eosin(H-E) and Toluidine Blue(TB) respectively for light microscopy examination. Control group were examined simultaneously.

3. Culture of primary hippocampus neuron Hippocampus neurons were isolated from brain tissues of the newly born rats and cultured for about 10 days. The mature cells were exposed to EMP irradiation. Pathologic changes were observed under inverted phase contrast microscope as well as the cell apoptosis ratio were measured with flow cytometer.

Results:

1. The achievement of behavioral testing were composed of four different variables. They were active avoidance response(AV), passive escape response(ESC), active avoidance response latency(AVLAT) and passive escape response latency(ESCLAT). Self-control and random block design were used in statistic analysis. Multivariable analysis of variance were made with SAS8.2. software. It was found that all the rats examined were possessed of a significantly lower AV tite immediately after exposure while compare with that before radiation ($F=19.20, P<0.01$), then it tended to recover at 3h after exposure; Contrarily, ESC tite rised markedly after exposure while compare with that before exposure ($F=14.49, P<0.01$) and tended to recover at 3h after exposure as well. There were no difference in AVLAT and ESCLAT tite between that before and after irradiation. ($F=0.93$ and 1.04 respectively, $P>0.05$; see Tab1)

2. Morphological examination: Such following pathologic changes were found in different regions of brain, especially in hippocampus: congestion of brain meninges, edema of brain parenchyma and derangement of hippocampus nerons. Cell degeneration occurred in both granular cells and pyramidal cells. Nissel bodies decreased markedly, especially in granular cells. Shrinkage of neuron were seen frequently: nerons became triangular which with deep-blue color and curved axon, microstructure of them could not be discerned either.

Tab1. Results of shuttlebox measurement in different time points (n=11, Mean \pm SD)

result	-2d	-1d	0h	3h	6h	12h	24h
AV	32.45 ± 1.97	33.64 ± 2.73	22.18 $\pm 5.34^{**}$	31.45 ± 3.62	30.27 ± 3.77	31.82 ± 3.16	33.18 ± 3.79
ESC	7.55 ± 1.97	6.27 ± 2.69	16.27 $\pm 5.02^{**}$	8.55 ± 3.62	9.27 ± 3.90	8.18 ± 3.16	6.64 ± 3.78
AVLAT	4.16 ± 0.76	3.95 ± 0.71	3.94 ± 0.54	4.26 ± 0.79	4.33 ± 0.82	4.22 ± 0.76	4.04 ± 0.80
ESCLAT	10.56 ± 0.16	10.43 ± 0.06	10.52 ± 0.07	10.53 ± 0.18	10.49 ± 0.11	10.54 ± 0.12	10.51 ± 0.15

** $P<0.01$ vs preradiation;

3. After EMP exposure, cultured cells took on a higer refractive powe. Liquefaction of neuron could be described as following: Cytoplasm of swelled cells show many minute vacuoles and the nucleus appears dissolution. Some neurons are spherical shape and agglomerate of death cells can be seen everywhere in visual field; The recoiled, degenerative neurite looks like beads. Neuropil fragmentated and became sparse gradually. What interest us is that neuroglial cells which support and nourish neurons are also sensitive to EMP radiation, a few of them degenerated and necrosed prior to neurons. The results of flow cytometry test: In the 2 hours after exposure, the apoptosis ratio of exposure cells is 31.37% which is significantly higher than that of sham-exposure cells(0.02%).

Conclusion

1. EMP irradiation may result in a temporary lost of acquired conditioned reflex in rats which exhibited declining of response correctness ratio, but those effects disappeared in a short period of time; AVLAT and ESCLAT of rats in the behavioral testing were not influenced by EMP irradiation.
2. Damages such as cell degeneration, apoptosis, necrosis and blood circulatory disorder can be seen in hippocampus tissues and ex vivo cultured neurons after EMP irradiation. Such pathologic changes may be partly responsible for the temporary memory impairment of rats. Farther investigation on the effects and its molecular mechanisms is in progress.

II-14

EFFECTS AND MECHANISMS OF ELECTROMAGNETIC PULSE ON RHESUS MONKEY LYMPHOCYTES

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Background: It has been shown that electromagnetic pulse (EMP) is non-ionizing irradiation with wide frequency and high energy. However, people usually pay more attention to the destructive power of EMP on the electronic equipment. Few studies have been reported on the definite biological effects of EMP, only in recent years, scientists have began to pay attention to the effects of EMP on biological bodies. In the experiment, we observed the effects and mechanisms of electromagnetic pulse on rhesus monkey lymphocytes.

Materials and Methods: 5 Rhesus monkey weighing 5.5 ± 1.8 Kg (male 2 and female 3) were used in the experiment. The animals were irradiated by electromagnetic pulse (EMP) simulator made by our Institute. The radiation field strength is 6×10^4 V/m, and the animals were irradiated for 30 times successively within 5 minutes. Width of pulse is 25-30 ns and wave bank with single pulse is 20ns.

Results: 1. After repeated irradiation 30 times of 6×10^4 V/m ($30 \times 6 \times 10^4$ V/m), the lymphocyte apoptosis began to increase on 1 day, and reached the maximal on day 3, 7, 14, the lymphocyte apoptosis were 2.2, 2.5 and 2.2 times respectively when compared that of control group. 2. At the same time, after same radiation field strength, the percentage of lymphocyte in peripheral blood were decreased markedly, which is about 74%, 77% and 79% as compared with that of control group. 3. On the other hand, after EMP irradiation, the Bax proteins in lymphocytes were increased and reached the peak value on day 7, the Bax-positive lymphocyte was about 3.1 times that of control group. On the contrary, the Bcl-2 proteins were decreased and showed the lowest value on day 7. The regular changes of Bax and Bcl-2 suggested that they played an important role in the regulation of lymphocyte apoptosis.

Conclusions: On the condition of this experiment, EMP could induced abundant peripheral lymphocyte apoptosis in rhesus monkey. It confirms that lymphocyte apoptosis might be the major cause of lymphocyte decrement and immunological function depression after EMP radiation. Bax could promote apoptosis and Bcl-2 suppress apoptosis of lymphocyte, both of them played an important role in the regulation of lymphocytes apoptosis. It is suggested that people should pay more attention to the injury caused by EMP, especially the effects of immunological function of the body.

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MILLIMETER WAVES AFFECT CRYSTAL OF AMINO ACIDS IN SOLUTION

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Background: We focus not only on the interactions between electromagnetic field and a single cell but also on those between electromagnetic field and organisms composed by all kinds of biological tissue. As known, the living systems are made up of those chemical elements such as carbon, hydrogen, oxygen, nitrogen, phosphorus, sulfur, iron etc..All these elements exist as kinds of compounds, for example, inorganic compound (including salt and water) and organic compound (including protein and DNA). And proteins are the basal structures of organisms, however proteins are made up of amino acids. As a result, we have to study amino acids before we continue to study organism.

There are essential differences between amino acids and original abio-molecules, whereas, when they crystal under some conditions they both play the same commonly regularity rules. Crystalline process of amino acids is sequence process just like other small molecules, that is, molecules in random order in solution turn into solid in regular arrange. At the beginning of the process there must be some nucleus and then molecules can link to the nucleus and then become crystals. Amino acids solution can become over-saturated and new steady chemical bond(subbond)come into being then the whole energy of the system is reduced and crystals produced. During the process it is easy to be influenced by environments, for instance, PH, temperature, and MMWs irradiation, and the conformation of amino acids will be changed and pearl line effects may be observed^[1].

Methods:Refer to saturation of amino acids^[2] and make 10ml saturated solution of one kind of amino acid. Take two tissue culture dishes and inject 2ml saturated solution in each dish. Take one of the dishes as experiment team and put it on the trumpet of the 8mm/36.36GHz WWMs' system, 8 hours/day, with the density of power 3.3mW/cm². The other is put nearby without MMWs irradiation. Every afternoon after the irradiation, we observe the two dishes under the same upside-down microscopes and take pictures with Smartscape Bio-image analyzing System, analyse the pictures at last.

Conclusion: MMWs can affect some kinds of amino acids while they are in solution. We can see pearl line effect —the amino acid crystals become a line after the irradiation. At the same time we can observe that conformation of amino acid crystal has been changed after the irradiation. Maybe we can explain some phenomena in MMWs' biological effects if we continue to study the experiment.

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DOWN-REGULATION IN NESTIN MRNA EXPRESSION IN HIPPOCAMPUS OF ADULT RATS BEING EXPOSED TO ELECTROMAGNETIC FIELD

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Key Word: Electromagnetic radiation, hippocampus, nestin, RT-PCR

Previous evidence has indicated that neural proliferation and differentiation actively exist in certain brain regions, e.g. the hippocampal structure and subventricular zone of adult mammals. It is also found that neuron production and differentiation in dentate gyrus of hippocampus persist through the lifetime of animals, and constitute the basis of neural structural and function plasticity in hippocampus. The mechanism involving in the modulation of neuronal proliferation, however, is not clear. In the present study, therefore, the influence of electromagnetic radiation on the neurogenesis in hippocampus was investigated in the rats. Male Sprague-Dawley rats weighing 240-250g were exposed in electromagnetic field and samples of hippocampus were picked up at 12h and 24h after electromagnetic exposure. The expression levels of nestin mRNA in the hippocampus were examined with semi-quantitative reverse transcription-polymerase chain reaction PCR (RT-PCR) at 12h- and 24h-radiated groups. In these hippocampus of 12h and 24h-radiated animals, nestin mRNA expression levels significantly decreased compared with that of controls. It is well known that nestin, an embryonic intermediate filament, represent a neural precursor marker, and expression of nestin protein reflects the differentiation or proliferation state of neural precursors during prenatal and postnatal developing brains. The results suggested that neurogenesis in hippocampus may be inhibited by electromagnetic radiation in the early period. Further study will be need to elucidate the characterization or differentiation of nestin-expressing cells, such as their expression of glial fibrillary acid protein (astrocyte marker), neuronal nuclear specific protein (neuronal marker), and their physiological and pathophysiological functions in electromagnetic exposure.

OBSERVATION ON LOW ELECTROMAGNETIC RADIATION POLLUTION ON ANIMAL EXPERIMENT

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Background: Electromagnetic radiation is one of the environment pollution however it is unknown whether low electromagnetic radiation is harmful. Broadcast radiation was done on animal to discuss its effect on living body.

Methods: The method adopted a broad-band electromagnetic wave radiation (XG-27) which frequency is 510--515KHz decimeter. The 45 rats (Wistar) were averagely divided in three groups according to the radiation intensity they undergo: high (1.28w/m^2), media (0.27w/m^2) and low (0.07w/m^2). Among those three there were significantly different ($F_{0.01} 2.41=5.18$ $p<0.01$).

Results:

There were significantly different among three groups underwent the experiment:

	Without animals(w/m ²)	with animals(w/m ²)	P
high	12.90±0.240	7.770±+0.168	<0.001
media	0.31±0.019	0.165±0.024	<0.001
low	0.12±0.091	0.065±0.043	<0.05

the absolute absorb rate of each group are:0.52, 0.10, 0.03; the relative absorb rate(%)of each one are:40.6, 37.0, 33.3. The electromagnetic radeation on animal can be absorb by the medium,then transfer into heating effect together with energy through the magnetic field. In our test,it produce non-heating effect besides heating effect.It's due to electromagnetic radiation and electromagnetic force though we use low intension. Changes are caused in many fields such as biophysics, biochemisty, immunology and genetics. The absolute absorb rate on animal are rising accompany with the increasingly radiation intensity whatever in which group.

Conclusion: There lies significantly different when different radiation intensity on animals.Only after absorbing the definite amount of electromagnetic radiation can produce biological effect.It appears abnormal effect on animals in different fields as the increasingly serious environmental radiation pollution.So it is important to control the electromagnetic radition.

II-18

No Translation

II-19

REAL-TIME EFFECTS OF 900 MHZ ELECTROMAGNETIC FIELD OF MOBILE TELEPHONE ON THE STRUCTURE AND FUNCTION OF HEMOGLOBIN IN SINGLE INTACT LIVING HUMAN ERYTHROCYTE

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Background: With the development of the technology of digital communication, effects of electromagnetic field of mobile telephone on human health have increasingly come to attention. Lots of studies on biological and medical effects of exposure to electromagnetic field, and many data were accumulated. But, the real-time effects of electromagnetic wave on cells were not observed, while the real-time effects were one of keys to study biological effects of electromagnetic wave. In this research, the real-time effect of exposure to electromagnetic field of mobile telephone on the structure and function of intracellular hemoglobin (Hb) in single intact living human erythrocyte was studied in situ with non-invasive by employing a fast multi-channel micro-spectrophotometer.

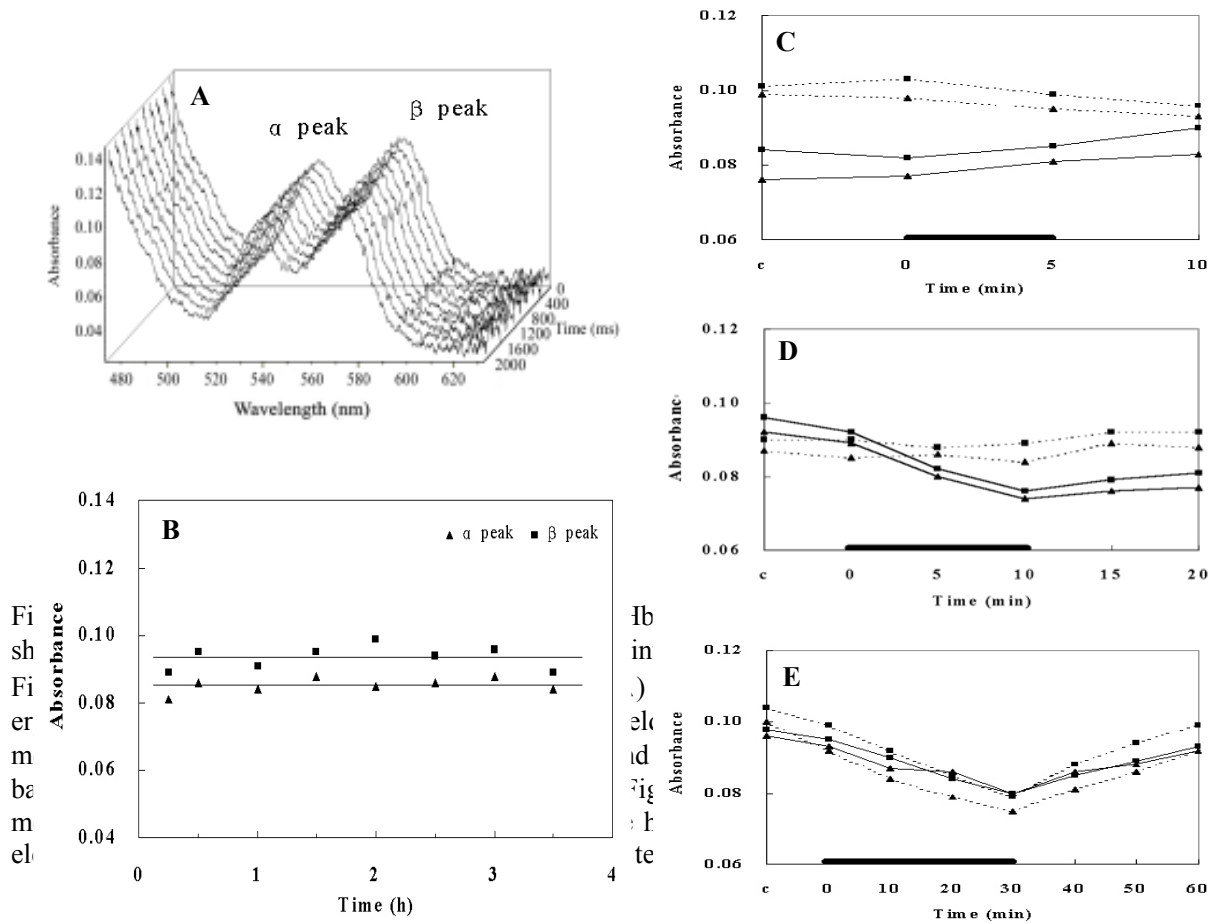
Methods: Two well-known types mobile telephone M and mobile telephone E were used as exposure source. The frequency of two types mobile telephone M and E was all 900 MHz. During the experiment,

normal communication of mobile telephone was simulated. The distance between the antenna and irradiated cells was 1 cm. The average electromagnetic field strengths of mobile telephone M and mobile telephone E were 10.70 V/m and 7.21 V/m, while the average power densities of mobile telephone M and mobile telephone E were $30.87 \mu\text{W}/\text{cm}^2$ and $14.87 \mu\text{W}/\text{cm}^2$ separately. The data of electromagnetic field of mobile telephone were determined using PMM8503A electromagnetic radiation analyzer (PMM Corp., Italy) and the measure probe was EP330S. Vein blood from health adult men were taken out and poured into heparinized tubes and immediately centrifuged at $2,000 \times g$ for 10 min at 4°C to remove the buffy coat. Subsequently, erythrocytes were washed in PBS (pH 7.4) three times by centrifugation. The washed erythrocytes were incubated in PBS with various pH at 37°C for 1 h, then kept cold until being used on the same day. All preparation of cell suspension were carried out at room temperature and all measurements were carried out at 37°C . Erythrocytes sample was assessed by a phase contrast microscopy (NIKON TE300) on glass slide, which was put into a special mini-cell culture pool. Erythrocyte was exposed to 900 MHz electromagnetic field of mobile telephone M and E directly. The absorption spectra of intracellular Hb of single intact living human erythrocyte were measured by means of a fast multi-channel micro-spectrophotometer. In this experiment, ten absorption spectra of intracellular Hb in single erythrocyte in 2 seconds (Fig. A) were recorded at the beginning of mobile telephones turn-on and at different moments of radiation. The content and structure of intracellular Hb in single erythrocyte can be determined by the heights and positions of absorption peaks respectively.

Results: 1. Under physiological conditions (37°C , pH 7.4), the positions and heights of two characteristic absorption peaks of Hb at wavelength around 540 nm (α peak) and 575 nm (β peak) were not altered within 4 hours (Fig.B). It suggested that the structure and function of intracellular Hb in normal erythrocytes were not affected within 4 hours. 2. The positions of two absorption peaks of Hb in erythrocyte were not altered before and after continuous exposure to 900 MHz electromagnetic field of mobile telephone M and mobile telephone E for 5, 10 or 30 min at a time. This suggested that the molecular structure of intracellular Hb was not affected by exposure to mobile telephone under this experimental condition. 3. The heights of two absorption peaks of intracellular Hb at the beginning of radiation of both two mobile telephones (point 0 min at the horizontal bar), shown in Fig.C, Fig.D, and Fig.E, was not altered significantly compared with those at the moment of 5 min or 10 min before radiation (point c at the horizontal bar, $p > 0.05$). When the radiation of mobile telephone M lasted 10 min, the heights of two absorption peaks of intracellular Hb were significantly lower than those at the moment of 10 min before radiation (Fig.D, $p < 0.05$). But they were not changed significantly when exposure to mobile telephone E for 10 min. When the radiation of mobile telephone M and mobile telephone E lasted 30 min, the heights of two absorption peaks of intracellular Hb were significantly lower than those at the moment of 10 min before radiation (Fig.E, $p < 0.05$), and they all rose gradually after stop radiation.

Conclusions: 1. There are two characteristic absorption peaks of Hb at wavelength around 540 nm (α peak) and 575 nm (β peak) under physiological conditions (37°C , pH 7.4) (shown in Fig.A). The heights of the two peaks are correlated not only with the content of intracellular Hb, but also with the physical and chemical properties of Hb such as solubility, stability, oxidation state and so on; while the positions of the two peaks reflect the molecular structure of Hb with different oxygen carrying capacity. In this experiment, the configuration of intracellular Hb was not affected by exposed to both mobile telephone M and E. 2. In this experiment, the heights of two peaks in the spectra of Hb in single living cell were decreased significantly after exposed to 900 MHz electromagnetic field of mobile telephone M and E. This suggests a significant decrease of the intracellular Hb content took place by exposure to 900 MHz electromagnetic field of mobile telephone.

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II-20

PRIMARY INVESTIGATION ON THE OFFSPRING'S INTELLIGENCE AND SEX RATIO AFFECTED BY THE OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION

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Background: This investigation is based on that large dose of microwave radiation can cause chromosome aberration in biological cells.

Methods:

11 microwave stations from the Bureau of Provincial Communication, radio and TV broadcasting, electricity control were selected in the investigation. 118 male and 12 female workers who exposed to 0.9GHz or above microwave at least 1 year before their babies born were chosen in the investigation. IQ

test, sex ratio and malformation were induced to the 6 to 15-year-old children whose parents worked in the microwave-related operation room for transmission, adjusting and repairing. Children from the same district, same school, same sex, same age and the same background of their parents were applied as the control. Persons who had obvious genetic disorders or family history, obvious injuries were excluded in the investigation. The microwave intensities were measured in the working environment. Intelligence test was performed with form CRT-RC₂ in grouped children. A relatively detailed instruction was made to the junior (1st grade) pupil.

Results:

Measurement result: 13 equipment rooms and 27 transmitters which microwave radiation frequency was within the range of 0.9GHz to 12GHz were measured. The maximum microwave leakage was 300, 46 and 100 μ W/cm² in front of the transmitters, in the duty room and under antennas respectively. The results showed that 7 sites exceeded the national hygienic standard (50 μ W/cm²). Microwave intensities in duty rooms were all below the standard limit.

Sex ratio and intelligence examination to the offspring of the workers exposed to microwave: The investigation involved 11 microwave communication stations in the province, 130 exposures and their children. The result demonstrated that, of 132 children, 55 were male and 77 were female. The sex ratio (male : female) was 1:1.4. In the intelligence test, 38 6- to 13-year-old children in one group were studied with a case-control method. The result showed that, in the exposure group, 18.4%, 68.4%, 10.5% and 2.6% children had a "excellent", "good", "medium" and "below medium" intelligence level respectively, while 26.3%, 23.7%, 39.5% and 10.5% in the control group respectively. There are statistic differences between two groups.

Conclusion: It is concluded that the sex ratio between the offspring of the microwave exposed workers and those of the controls. Female are more than male. Intelligence level of the offspring is probably affected by microwave. Because the sample we investigated was small, the actual effects remain to be studied.

II-21

EFFECTS OF 900 MHZ ELECTROMAGNETIC FIELD OF MOBILE TELEPHONE ON THE ELECTROKINETIC PROPERTIES OF LIVING HUMAN ERYTHROCYTES

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Background: With the development of the technology of digital communication, effects of electromagnetic field of mobile telephone on human health have increasingly come to attention. The structure and function of the surface of erythrocyte membrane, especial surface charges, is not only closely related to adherence, aggregation, metabolism and immunity of erythrocyte, but also closely related to cells deformation and flowing through capillary vessels. So, it is very important to study effects of electromagnetic radiation of mobile telephones on surface charges and electrokinetic properties of erythrocytes.

Methods: Two well-known types mobile telephone M and mobile telephone E were used as exposure source. The frequencies of two types mobile telephone M and E were all 900 MHz. During the experiment, normal communication of mobile telephone was simulated. The distance between the antenna and irradiated cells was 1 cm. The average electromagnetic field strengths of mobile telephone M and mobile telephone E were 10.70 V/m and 7.21 V/m, while the average power densities of mobile telephone M and

mobile telephone E were $30.87 \mu\text{W}/\text{cm}^2$ and $14.87 \mu\text{W}/\text{cm}^2$ separately. The data of electromagnetic field of mobile telephone were determined using PMM8503A electromagnetic radiation analyzer (PMM Corp., Italy) and measure probe was EP330S. Vein blood from health adult men were taken out and poured into heparinized tubes and immediately centrifuged at $2,000 \times g$ for 10 min at 4°C to remove the buffy coat. Subsequently, erythrocytes were washed in PBS (pH 7.4) three times by centrifugation. The washed erythrocytes were incubated in PBS with various pH at 37°C for 1 h, then kept cold in polyethylene tube until being used on the same day. All preparation of cell suspension were carried out at room temperature and all measurements were carried out at 37°C . Erythrocytes in polyethylene tube were exposed to 900 MHz electromagnetic field of mobile telephone M and mobile telephone E for 60 min respectively. The Zeta potential and the electrophoretic mobility (EPM) of erythrocytes were determined at different radiation time by use of Zeta Plus Analyzer (Brookhaven Instruments Corp., USA).

Results: The Zeta potential and EPM of erythrocytes at different radiation time were shown in Fig.A and Fig.B respectively. Both the Zeta potential and the EPM of erythrocytes decreased significantly when cells exposed to 900 MHz electromagnetic field of mobile telephone M and mobile telephone E for 15 min ($p < 0.05$). But when the radiation is continued for 60 min, both the Zeta potential and the EPM of erythrocytes all increased with the extension of exposure time. They reached the largest at the exposure time of 60 min and were significantly more than that before exposure. At the same time, both the Zeta potential and the EPM of control erythrocytes were not altered.

Conclusions: The electrophoretic mobility reflects the motion velocity of cells in impressed electric field, while the Zeta potential reflects the character, distribution and density of surface charges of intact cells. Our results showed that both the electrophoretic mobility and the Zeta potential of erythrocytes could be changed by exposure to 900 MHz electromagnetic field of mobile telephone. The structure and function of cell surface was affected because of the alteration of the number of surface charges and their distribution on the surface of erythrocyte membrane. The repulsive force among cells decreased and the chance of cells adherence and aggregation increased. The flow of erythrocytes through capillary vessels was affected by the change of the electrophoretic mobility. Those all would influence the transportation of oxygen and carbon dioxide, the substance exchange across the membrane, and therefore the viscosity and flowing property of whole blood. It is significant to cardiovascular system.

Acknowledgements: This work was supported partly by Guangdong Province Scientific Funds in China (No. 010420).

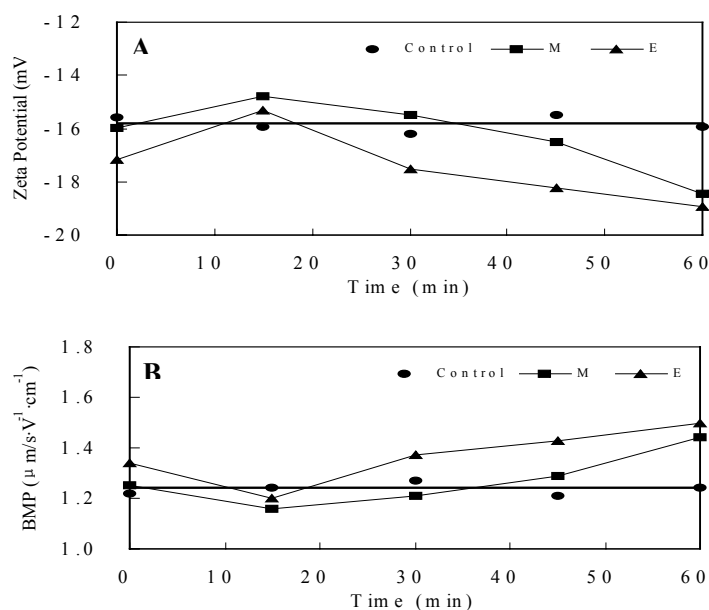


Fig. Influence of exposure to 900MHz electricmagnetic field of mobile telephone M and mobile telephone E for 60 min on the Zeta potential and the electrophoretic mobility . (n=6)

II-22

No translation

II-23

No translation

O-1

No translation

O-2

SIMULATED EQUATIONS OF HUMAN BODY TISSUE IN A WIDE FREQUENCY BAND*

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Background: Due to the research development of the effects and its mechanisms of electromagnetic waves on human body, the need for extensive permittivity data of each tissue is greatly increased because these parameters are essential in determining the specific absorption rate (SAR) and SAR's distribution in human body.

Methods: Generally used permittivity is consist of a pair of values: electrical conductivity σ and relative dielectric ε_r . At present the permittivity data at discrete frequency of different tissues is scattered in reports and it's not convenient for reference purpose. Because the data are from the given point frequencies, the purpose of this paper is to simulate the permittivity equations of different tissues based on these measured data from the given point frequencies and presents them in such forms that would be convenient to acquire the data needed for research work. The measured electrical properties of fifty-eight kinds of tissues (brain, muscle, intestine, heart, bone, etc) between a wide frequency band (10Hz—100GHz) were obtained from relative documents.

Results: Firstly, we take the logarithm of measured permittivity data of different tissues and the measured frequencies between 10Hz and 100GH. Then the equations matching to the measured data were simulated by Matlab program. Here an example of skin is given as follows. Obviously the simulated curves are in accordance with original data in Fig1. The simulated equations of skin based on the measured data were given as follows. Based on this equation, it is easy to calculate σ and ε_r values for that tissue at any frequency between the range mentioned above .

$$\lg \sigma = 10^3 \times [-0.0002(\lg f)^{11} + 0.0006(\lg f)^{10} - 0.0010(\lg f)^9 - 0.0063(\lg f)^8 + 0.0551(\lg f)^7 - 0.2265(\lg f)^6 + 0.5984(\lg f)^5 - 1.0736(\lg f)^4 + 1.3021(\lg f)^3 - 1.0208(\lg f)^2 + 0.4659(\lg f) - 0.0971]$$

$$\lg \varepsilon_r = 0.0002(\lg f)^{14} - 0.0029(\lg f)^{13} + 0.0302(\lg f)^{12} - 0.2327(\lg f)^{11} + 1.3434(\lg f)^{10} - 5.7384(\lg f)^9 + 17.4742(\lg f)^8 - 34.1887(\lg f)^7 + 25.6022(\lg f)^6 + 70.8677(\lg f)^5 - 273.4312(\lg f)^4 + 451.6176(\lg f)^3 - 423.2214(\lg f)^2 + 217.5148(\lg f) - 42.8692$$

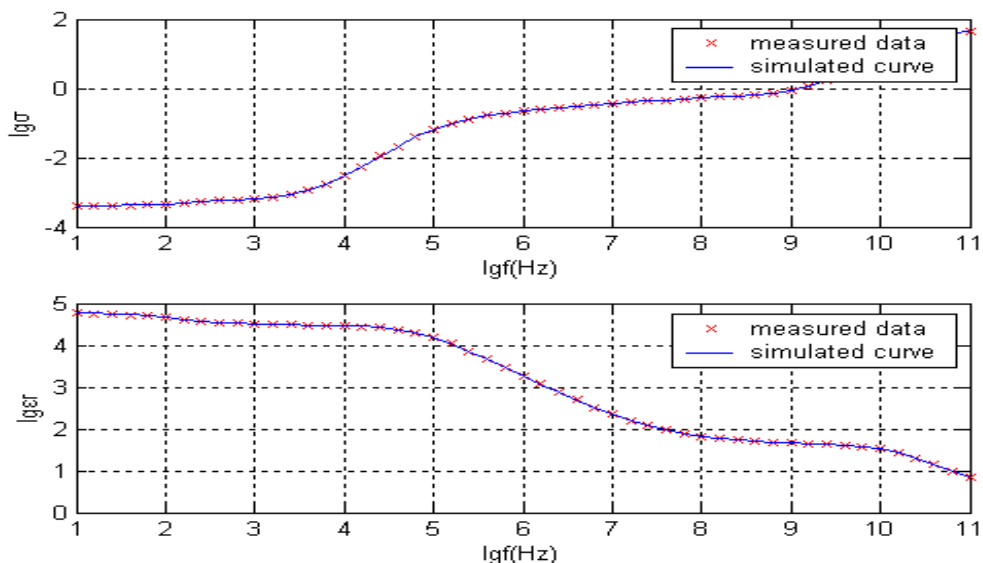


Fig 1: simulated permittivity curves of skin

Conclusion: In order to verify the correctness of the equations, the permittivity of skin was calculated by the equations at $f=1000\text{MHz}$. The result is: $\sigma=0.8767$, $\epsilon_r=45.472$. Compared to the original data: $\sigma=0.8818$, $\epsilon_r=45.711$, obviously they are in excellent agreement and the error can be neglected.

* The Project Supported by National Natural Science Foundation of China

O-3

THE NUMERICAL 3-D RECONSTRUCTION OF HUMAN BODY ELECTROMAGNETIC MODEL*

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Background: The need for accurate human body numerical electromagnetic model is frequently and strongly felt among the researchers involved in the interactions of electromagnetic fields and human body. The process of 3-D reconstruction was discussed in this paper.

Methods: This process includes two steps: human body structure model and electromagnetic model. Firstly, a millimeter-resolution model configured from CT and MRI cross-sectional scans of a male was built (Fig 1). These scans involving 47 tissue types were performed at 2mm intervals and the positioning of the interior structure can be acquired. Using the functions of image 3-D reconstruction in Matlab, as incised model displayed in Fig 2, the scans were converted into continuous 3-D model.

Results: From this precise model the other demanded model can be obtained easily. Because it is impossible to run the $293 \times 170 \times 939\text{mm}$ -resolution model of the whole body with the computer memories when calculating SAR distributions, according to the calculation demands, another coarse 1.77m model made up of $38 \times 95 \times 187$ 1cm cells along the x, y and z directions respectively was built. The cross-sectional scans were taken with a resolution of 1cm along the height of the body and totally 16 kinds of tissues are involved in this model. After the reconstruction of structure model, it was processed to numerical electromagnetic model.

Conclusion: Using Photoshop, the images were processed and different tissues were displayed by different colors (Fig3). Then the processed images were read by Matlab program and different colors were endowed with different codes (Fig4). For example, muscle express as 2. Finally, the electrical conductivities and dielectric constants of the tissues have been assigned to the codes. With that, the human body structure model was converted to human body electromagnetic model.

* The Project Supported by National Natural Science Foundation of China

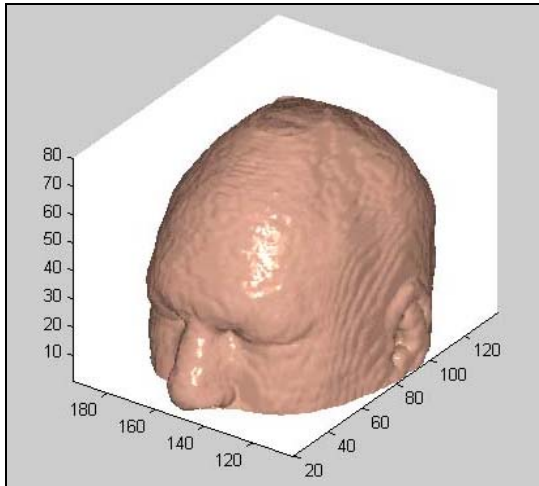


Fig1 3-D reconstruction human head model

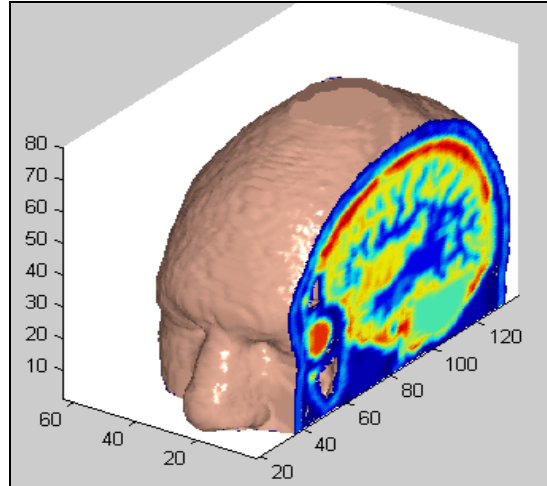


Fig2 incised 3-D reconstruction model



Fig3 thorax color map

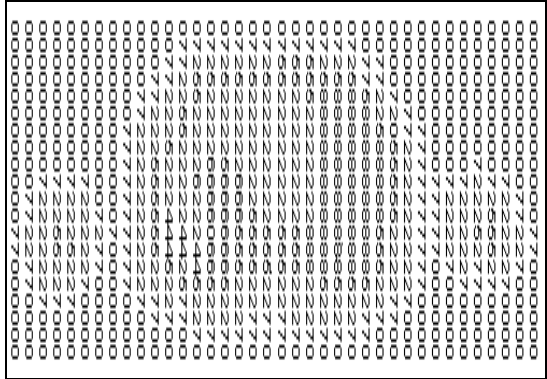


Fig 4 numerical display of thorax

FOR RADIATION OF PULSE ELECTROMAGNETIC WAVE*

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Background: A great deal of progress has been made in dosimetry of bioelectromagnetic fields in the last decades years and the high-power electromagnetic advices were used widely. So the problem of interactions between high-power electromagnetic fields and human body is getting significant. In this paper it was discussed that the electromagnetic power is absorbed by human body, and the average specific absorption rates (SAR_{av}) of different human body tissue is compared when exposed to pulse electromagnetic wave. According to the result, the important protective tissues and place in human body are pointed out. The research is important both in theory and in practice. It can offer database not only for establishing the non-ionization electromagnetic radiation hygienic standard but also for evaluating whether the electromagnetic pulse radiation will do harm to human health.

Methods: Firstly, FDTD method calculated the electromagnetic power absorbed by human body was used. The calculation program was compiled and verified. Then the time-domain map based on about 1000 measured data of electromagnetic pulse is transformed to the frequency-domain by discrete Fourier transform to find the field distribution at several frequencies of interest. The pulse electromagnetic wave is from a real environment. The human body structural and electromagnetic model involving 16 kinds of tissues used in this paper is made up of $38 \times 95 \times 187 = 675070$ 1cm^3 cells. The incidence electromagnetic pulse waves is E polarized (parallel to the long axis of the model and the power-flux density is $1\text{mw}/\text{cm}^2$) and it is frontally radiated to the model.

Results: Four methods were used to display the results: (1) SAR_{a1} , it means the average SAR distributions in a cell/gram/ cm^3 , when the power-flux density is $1\text{mw}/\text{cm}^2$. (2) SAR_{av1} , it means the average SAR distributions within given tissues throughout the frequency range, when the power-flux density is $1\text{mw}/\text{cm}^2$. Moreover, the max value and min value and their places of SAR_{av1} are also pointed out. (3) $SAR_{av/s}$, it means the layer average SAR along the body model, when the power-flux density is $1\text{mw}/\text{cm}^2$. (4) SAR_{av} , it means the average SAR distributions in given organs, when the model is radiated to the electromagnetic pulse.

Conclusion: From the row result of SAR_{av1} shown in Table 1 it can be seen that even when there is not much difference in $SAR_{av/s}$, there can be significant difference in the internal SAR distributions. It shows significant increase occurred in the skin and eye when the frequency is increase, but it is decrease in the tissues inside the body model, such as muscle, intestine and heart. Compare the results of SAR_{av1} in different tissues at the same frequency, it can be seen the values of skin are significant. The SAR_{av1} values of brain are maximal at the frequency of 200, 400 and 600MHz. While the frequency is larger than 800MHz, the SAR_{av1} values of eye and skin are maximal. This is due to the fact that the higher rate of energy absorption for a high frequency does not allow much energy to penetrate to an organ that is located inside the body. From the whole point of view, it is further shown that the SAR_{av1} distributions of some tissues are very high in some specific frequencies, such as SAR_{av1} distributions of lung and spleen at 600MHz. This specific absorption is due to the wavecrest produced by the traveling waves and standing waves reflected on the tissue surface. Table 2 gives the SAR_{av} distributions in different tissues at different frequencies when exposed to the high-power electromagnetic pulse. It shows SAR_{av} distributions of brain, intestine, heart, stomach, pancreas, spleen, kidney and gall focus on the low frequencies. From the results displayed above, the perfect protective frequency band is 100-1000MHz. Moreover, because the greatly uneven SAR_{av1} distribution in the human body, more attention should be focused on SAR_{av1} than the whole body averaged SAR (WBA-SAR) when establishing the non-ionization electromagnetic radiation hygienic standard and for evaluating whether the electromagnetic pulse radiation will do harm to human health.

Table 1. SAR_{av1} in different tissues at different frequencies

f(MHz)	100	200	400	600	800	1000	1200	1400	1600
brain	.055938	.245882	.034128	.114282	.024880	.067074	.012436	.019682	.008112
muscle	.059145	.064102	.021200	.051854	.015408	.032440	.009675	.012444	.008922
intestine	.133157	.075232	.007880	.004038	.002134	.001172	.000183	.000249	.000122
heart	.051011	.022291	.001347	.002300	.001534	.000473	.000082	.000161	.000110
bone	.039405	.026866	.007128	.018998	.007047	.017781	.008054	.012902	.010731
liver	.040271	.012536	.003918	.010022	.001942	.002748	.000433	.000153	.000069
skin	.068127	.103100	.031045	.082611	.035137	.123767	.065305	.202954	.230672
lung	.010624	.005424	.001204	.007259	.001260	.000943	.000048	.000027	.000018
stomach	.040391	.022634	.004967	.004671	.008197	.000758	.002044	.000315	.000674
pancreas	.027804	.025952	.006331	.008071	.001043	.000679	.000020	.000063	.000029
spleen	.006827	.010233	.005909	.050118	.003214	.011413	.000318	.000128	.000020
kidney	.039320	.028465	.004946	.005530	.001120	.000598	.000047	.000096	.000049
gall	.030303	.017833	.005904	.003853	.000894	.000463	.000029	.000056	.000026
eye	.083635	.098547	.014361	.016041	.086469	.015523	.224337	.122217	.560671
testis	.130411	.027201	.010050	.034668	.022033	.049122	.055530	.056120	.270210
bladder	.139836	.005645	.010883	.006614	.004801	.002716	.003553	.002175	.003131

O-5

ANALYZING THE ELECTROMAGNETIC PARAMETERS OF THE AMINO ACIDS AND BASES VIA HARTREE-FOCK MODEL

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Background: One of hot point of research is the mechanism and target of athermal bio-effect of electromagnetic field. Nowadays, there are a lot of experiments to testify athermal bio-effect of electromagnetic field and existence of the frequency-window and power-window. For the living creature is nonlinear complicated system and can adjust itself, there exist lots of problems when we explain the electromagnetic power's transportation and exhaustion in living creature, and it is hard for us to set up the mathematical model and explain clearly the athermal bio-effect of electromagnetic field. However, the premise of the research for bio-effect of electromagnetic field is to disclose the principle and process of interaction between electromagnetic field and biological tissue, cell and molecule. For the basic research, besides analyzing frequency of electromagnetic field, direction of polarizability and power, it is very important for us to study the target of electromagnetic field. As we know, living creature consists of cells. In the cell the important macromolecule-proteins consist of amino acids and the base is the basal unit of nucleic acid structure. So, it is important to study the electromagnetism parameter of these basic biological molecules.

Method:

Adopting the Closed-Shell Restricted Hartree-Fock model(choose the STO-3G (5D, 7F) as the standard basis function and the environment of imitation is gas phase), we calculated the polarization volume, dipole moment and rotation frequency of twenty kinds of amino acids and five kinds of base.

Results:

Table 1: the electromagnetic parameters of base

	Categ -ory	Molecular weight	Polarizability volume $\times 10^{(-30)}\text{m}^3$	Dipole moment (Debye)	Rotation frequency (GHZ)	energy (Hartree)
Base	C	111.102	10.82	4.7974	3.9356076 1.9628891 1.3096943	-387.501879893
	U	112.087	9.91	3.0760	3.8843197 2.0834882 1.3561098	-407.061536535
	A	135.127	14.68	3.5931	2.2068687 1.4232288 0.8715968	-458.407707065
	T	126.113	11.77	2.9881	3.1253119 1.4534901 0.9986021	-445.645283195
	G	151.126	14.06	5.7331	2.0171446 1.0237488 0.6831990	-532.093850906

Note:1 Hartree=4.3597482 e⁽⁻¹⁸⁾ Joules=27.2116 eV。 In the item of Rotation frequency, the datum from top to bottom is X, Y, Z respectively direction.

Table 2: the electromagnetic parameters of amino acids

	Categ -ory	Molecular weight	Polarization volume $\times 10^{(-30)}\text{m}^3$	Dipole moment (Debye)	Rotation frequency (GHZ)	Energy (Hartree)
	Gly	75.067	6.50	2.4261	28.7246695 4.5120998 4.2942533	-205.237179506
	Ala	89.093	8.32	2.5468	8.2261996 3.7229673 2.8700136	-243.820717607
	Pro	115.131	11.06	2.3005	5.9095071 1.8274441 1.5959001	-319.827962883
	Leu	115.174	13.27	2.3867	2.7395432 1.2897650 1.0444554	-359.552986607
	Val	117.146	11.98	2.4272	3.4892710 2.0574865 1.4162579	-320.974266588

	Ile	131.173	13.82	2.4287	3.3653704 1.2135205 0.9559556	-359.551080440
	Phe	165.189	18.03	2.3454	2.1760278 0.7005088 0.6452237	-470.564034702
Unseparated polar amino acid	Ser	105.093	8.93	2.4226	5.2708312 2.6088082 2.0931244	-317.640974905
	Thr	119.119	10.75	2.4002	4.0702259 1.7386160 1.6072047	-356.221674593
	Cys	121.159	11.45	3.2160	3.7512063 2.0643515 1.4133542	-636.986705900
	Asn	132.118	11.57	4.7785	3.0601038 1.5835554 1.1351725	-409.360439261
	Gln	146.145	13.41	1.4085	2.8236995 0.8156737 0.6646149	-447.943610750
	Met	149.212	15.17	1.6841	3.0996816 0.7394155 0.6214766	-714.151223577
	Tyr	181.189	18.78	3.1589	2.1164356 0.5022722 0.4708404	-544.402950847
	Trp	204.225	22.90	3.9850	1.3144550 0.4586584 0.4128862	-599.658865484
Separated polar amino acid	Asp	133.103	10.78	1.7131	3.1856141 1.4405039 1.2165187	-428.903328162
	Lys	146.188	15.23	2.2738	3.2888132 0.5836440 0.5144785	-413.862875290
	Glu	147.129	12.62	1.4792	2.8747038 0.7983702 0.6524568	-467.479486730
	His	155.155	15.07	5.6560	2.6401617 0.9135344 0.7775251	-464.618157703
	Arg	174.201	16.13	14.1251	2.1401988 0.3973517 0.3688482	-521.789156381

Conclusion: According to the datum in the table, we come into the following conclusions:

1. By use of the polarizability volume and related formula, we can calculate molecular polarizability, and reckon macromolecular polarizability and dielectric constant of tissue;
2. By use of the dipole moment and related formula , we can reckon dipole moment of macromolecule;
3. Molecular rotational frequency is be fallen into the band of microwave. If the low-intensity microwave can activate these molecules and alter the molecular spectrums, we believe that athermal bio-effect of electromagnetic field would happen.

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O-6

ANALYZING THE ELECTROMAGNETIC PARAMETERS OF THE AMINO ACIDS AND BASES BASED ON DFT

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Background: One of hot point of research is the mechanism and effect sites of bio-effects of electromagnetic field. Nowadays, there are a lot of experiment data^[1-3] to testify existence of bio-effect of electromagnetic field and find the frequency-window and power-window. For the living creature is nonlinear complicated system and can adjust itself , there exists lots of problems when we explain the electromagnetic power's transportation and exhaustion in living creature, and it is hard for us to set up the mathematical model and explain clearly the bio-effect of electromagnetic field. However, the premise of the research for bio-effect of electromagnetic field is to disclose the principle and process of interaction when biological tissue, cell and molecule are exposed by electromagnetic field. To progress the basic research, besides analyzing frequency of electromagnetic field, direction of polarizability and power, it is very important for us to study the effect sites of electromagnetic field. As we know, living creature consists of cells. Moreover in the cell, the important macromolecule-proteins consist of amino acids and the base is the basal unit of nucleic acid structure. So, it is important to study the electromagnetism parameter of these basic biological molecules.

Method of calculation: In this paper, we calculate and analyse the molecule by Becke31yp method of Density Function Theory(DFT)^[4] of quantum chemistry.

Density Function Theory(DFT) is a kind of approximate method to simulate electron correlation by building function of electron density when used to solve Schrodinger equation. DFT calculates electronic energy by dividing the energy into four parts: kinetic energy, attracting energy between electron and nucleus, Coulomb repulsion energy and exchange-correlation energy. Therefore, the total energy of n electrons is expressed as follows:

$$E_{el} = -\frac{1}{2} \sum_i \int \phi_i(r_1) \nabla^2 \phi_i(r_1) dr_1 + \sum_A \frac{Z_A}{|R_A - r_1|} \rho(r_1) dr_1 + \frac{1}{2} \int \frac{\rho(r_1)\rho(r_2)}{|r_1 - r_2|} dr_1 dr_2 + E^{XC} \quad (1)$$

The terminal item E^{XC} in the Eq.1 can be broken into exchange energy E^X and correlation energy

E^C . Here, E^X and E^C correspond individually to interaction of the same self-spin and the mixed self-spin. Therefore, the calculation of DFT combines exchange function and correlation function. The B3LYP method used in our paper adopts exchange function included gradient correction and correlation function of Lee, Yang and Parr also included gradient correction. Meanwhile, local correlation function is disposed extensively by local self-spin density of Vosko, Wilk and Nusair. Therefore, The Becke function that having three parameters is got as follows:

$$E_{B3LYP}^{XC} = E_{LDA}^X + C_o(E_{HF}^X - E_{LDA}^X) + C_x \Delta E_{B88}^X + E_{VWN3}^C + C_c(E_{LYP}^C - E_{VWN3}^C) \quad (2)$$

From Eq.2, we can adjust three parameters C_o , C_x and C_c , then optimize and control the correction of exchange energy and correlation energy. In addition, according to function form of Becke3LYP in Eq.2, our paper adopts self-consistent DFT calculation, which is similar to iterative method of self-consistent field. The condition of calculation is supposed to gaseous phase.

Results of calculation:

Table 1 the electromagnetic parameters of amino acids

	Category	Molecular weight	Polarization volume $\times 10^{(-30)}m^3$	Dipole moment (Debye)	Rotation frequency (GHZ)		
					X	Y	Z
Nonpolar hydrophobic amino acid	Gly	75	6.5	2.42	28.72	4.51	4.29
	Ala	89	8.3	2.54	8.23	3.72	2.87
	Pro	115	11.1	2.30	5.91	1.82	1.60
	Leu	115	13.2	2.39	2.74	1.28	1.04
	Val	117	11.9	2.43	3.49	2.06	1.42
	Ile	131	13.8	2.43	3.36	1.21	0.95
	Phe	165	18.0	2.34	2.18	0.70	0.64
Unseparated polar amino acid	Ser	105	8.9	2.43	5.27	2.61	2.09
	Thr	119	10.7	2.40	4.07	1.74	1.61
	Cys	121	11.3	3.22	3.75	2.06	1.41
	Asn	132	11.9	4.78	3.06	1.58	1.13
	Gln	146	13.4	1.41	2.82	0.81	0.66
	Met	149	15.2	1.68	3.10	0.74	0.62
	Tyr	181	18.8	3.16	2.11	0.50	0.47
Trp	204	22.9	3.98	1.31	0.46	0.41	
Separated polar amino acid	Asp	133	10.8	1.71	3.18	1.44	1.21
	Lys	146	15.2	2.27	3.29	0.58	0.51
	Glu	147	12.6	1.45	2.87	0.79	0.65
	His	155	15.1	5.66	2.64	0.91	0.78
	Arg	174	16.1	14.13	2.14	0.40	0.37

Table 2 the electromagnetic parameters of bases

	Category	Molecular weight	Polarization volume $\times 10^{(-30)}m^3$	Dipole moment (Debye)	Rotation frequency (GHZ)		
					X	Y	Z
Ba	C	111	10.8	4.79	3.93	1.96	1.31
	U	112	9.9	3.08	3.88	2.08	1.36

A	135	14.7	3.59	2.21	1.42	0.87
T	126	11.8	2.99	3.12	1.45	0.99
G	151	14.1	5.73	2.02	1.02	0.68

Conclusion: We take the H₂O for example to validate the feasibility of the method. The dipole moment and polarization volume are respectively 1.78 Debye and $1.5 \times 10^{(-30)} \text{m}^3$, compared with the corresponding experiment data 1.84 Debye and $1.5 \times 10^{(-30)} \text{m}^3$ respectively.

From the results above of calculation and analysis, it can be seen that these amino acids and bases have biggish dipole moments. These molecules will vibrate ceaselessly to and fro when exposed to microwave radiation and then release heat energy because of friction. Distinctly thermal bio-effect of microwave is possible to be produced.

Because the rotational spectra of these molecules fall into the band of microwave, their rotational levels can be excited when exposed to microwave radiation of certain frequency. What is more important is that micowave field can influence selectively on degree-of-freedom of molecules. That is, the rotation frequencies of X,Y and Z direction fall particularly into a certain frequency, which can be thought to be sensitive to a certain frequency of EMF. When microwave quantum act on these molecules, the molecules can be excited. Farther, microwave radiation influences the characteristics of proteins and nucleic acids. Moreover, the structure and function of proteins and gene expression can be influenced.

Preferrence

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O-7

ANALYSIS OF Ca^{2+} OSCILLATION OF CELLS EXPOSURE TO ELF

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Background: In the study of Ca^{2+} oscillation on cells, the increasing of Ca^{2+} concentration can be found in time domain, but the information about frequency domain is ignorance. In this paper, the study of effect of ELF on cells will be performed in time-frequency domain.

Methods: Calcium ions are widely concerned with life action, which control cells metabolism and have relation with duplication of DNA and regulation of transduction. The information can be transfered by dissociative calcium ions in cells. The research shows that the difference of Ca^{2+} concentration between two sides of cytoplasm membrane or cells one play an important regulation roles in conformation and function of membrane protein, especially in participant and maintaining the answer to the stimulation from outside and realizing the information transferred between the membrane. Calcium balance of intercellular is regulated and controlled by a physiological action, and the concentration of Ca^{2+} in cytochylema is maintained in low level. The variation of calcium ions is result in transport between the membrane and the release or ingester by calcium depository. The destroying of calcium steadystate will reduce the cell variation. So, any factor which introduce continuance change of calcium ions will spoiled the metabolism

of cells, even cause death. Some researches indicate that many diseases accompany with abnormality concentration of calcium ions in occurring and developing.

Calcium oscillation depends on the variation with the time and the space, so it is necessary to detect the static or dynamic concentration of Ca^{2+} . In this paper, the method of fluorescent symbol (Fluo-3) was used to express the concentrations of Ca^{2+} . Combining with Ca^{2+} , the fluoresce intensity increases 40 times, which was detected with the laser scanning confocal microscope.

Introduction to analysis of time-frequency: The signals in biomedicine area are almost non-steadystate signal, so the analysis of time-frequency is widely used. Fourier transform is often used in signal analysis, which is obvious to find the character of signal in some case. But Fourier transform is defined on the whole time axes, and the frequency spectrum indicates the energy information of every frequency component in whole time but not a moment. In the analysis of such non-steadystate signal, which statistical character varies with time, it is necessary to know not only the waveform in some moment but also the related spectrum character. Such method combined time domain with frequency domain is called time-frequency analysis.

Time-frequency distribution were studied by Wignor and Cabor first, then Cohen brought forward a definition of a kind of time-frequency distributions which are called Cohen genus, from which different property distribution can be obtained. Time-frequency distribution is mapping the function of time $x(t)$ to the function of time-frequency $C_x(t, \omega)$, as follows:

Time-frequency distributins can be divide into several classes, such as Short Time Fourier Transform (STFT), Wavelet Transform (WT), Spectrogram, Wigner Distribution, Chio-Willams Distribution, Zhao-Atlas-Marks Distribution, Gabor Expansion, ext.Pseudo-Margenau-Hill distribution was used in this paper, which is

$$PMH_x(t, \nu) = \int_{-\infty}^{\infty} \frac{h(\tau)}{2} (x(t+\tau)x^*(t) + x^*(t)x(t-\tau)) e^{-j2\pi\nu\tau} d\tau$$

Analysis on the fluoresce intensity with PMH distribution: In Fig. 1, the fluoresce intensity varied with time was shown, condition that modulation with 16Hz pulse, 53v/m. The graph on top shows that the fluoresce intensity of the control group varies with time, the bottom one shows the fluoresce intensity of the exposure group does. The most underside line is the fluoresce intensity of background. From the two graphs, the fluoresce intensity changes so much after exposure in time domain. Fig.2 is the graph after the time-frequency analysis.

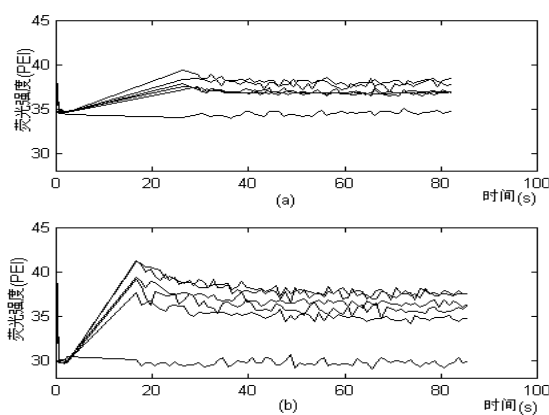


Fig. 1

Fig.2

The abscissa is time axes, and the ordinate is frequency axes. The graphs are contour map, the left one is the control group, the right one is the exposure group. After compare, we find the components in the middle are lower after exposure.

In other examinations, such as (16Hz,26v/m), (16Hz,53v/m), similarity changes can't be find, but in 16Hz,42.5v/m, continuous wave exposure, the similitude result can be found.

Conclusion: Exposure to the electromagnetic wave which is modulated in 16Hz, Ca^{2+} Oscillation of cells will happen in some energy spot, which proves there exists the athermal effect. Exposure to the same continuous wave, the same effect will take place. It is necessary to perform a deeper study..

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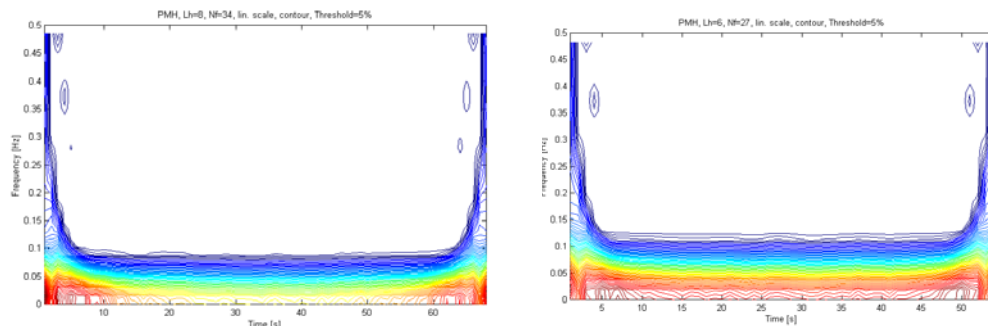
EFFECT OF ELECTROMAGNETIC PULSE IRRADIATION ON LEYDIG CELLS IN MICE

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Objective Electromagnetic irradiation has become the most environmental pollutant at present, effect of electromagnetic irradiation on human reproduction hse been one of widespread interesting hot spot. Electromagnetic pulse (EMP) is a kind of high-energy, ultra-wideband electromagnetic wave which belongs to electromagnetic pollutant in normal time. Changes of structure and function in leydig cells in three month after electromagnetic pulse irradiation has been observed to explore effect of EMP irradiation on sexual function and sperm production.

Methods 138 male Kunming mice were randomly divided into irradiated group and control groups, serum follicle-stimulating hormone(FSH), luteinizing hormone(LH), testosterone (T) and estradiol (E2) were measured dynamically by radioimmunoassay , organizational and ultrastructural changes of leydig cells were observed at 6h, 1d, 3d, 7d, 14d, 28d and 90d after mice irradiated generally by 8×10^3 v/m, 2×10^4 v/m and 6×10^4 v/m EMP (rise time 20 nsec, pulse width 30 μ sec) respectively for five times within two minutes.

Results Compared with normal controls, all of Serum T was decreased differently in 90 days, and decreased significantly at 6 h ~ 14d, 6 h ~ 7d and 1d ~ 28d after 8×10^3 v/m, 2×10^4 v/m and 6×10^4 v/m EMP irradiation respectively ($P < 0.05$ or $P < 0.01$), but EMP irradiation caused no significant changes in serum FSH , LH and E2. Main pathological changes was observed by light microscope to be edema and



vacuolation, nuclei deformation, nuclei volume diminution, chromatin agglutination and deep staining, dissociation of karyoplasms in leydig cells in 28 days after EMP radiation. There was apparent

mitochondrial swelling, reduce of mitochondrial ridge and decrease of matrix electron density, dilatation of endoplasmic reticulum, decrease of most of electron density and shallow staining in lipid droplet, complete cavitation of part lipid droplet at 6 hour after irradiation. There was clouding and focal lysis of nuclear membrane, swelling of mitochondria, striking dilatation of endoplasmic reticulum, agglutination or marginal translocation of chromatin, excludation of lipid droplet, decrease of electron density and shallow staining in most of lipid droplet, increase of crescent-shaped and annular electron density in few lipid droplet, or concentration and deep staining in whole lipid droplet, appear of dense granules, adhesion, hourglass or dumb bell shape fusion of lipid droplet in 1d ~14d after irradiation. Whole excludation of lipid droplet in most leydig cells appeared in 28d ~ 90d after irradiation.

Table 2. SAR_{av} in different tissues at different frequencies when exposed to electromagnetic pulse

f(MHz)	100	200	400	600	800	1000	1200	1400	1600	总和
brain	3.703	749.178	270.922	576.987	158.891	235.624	13.169	7.544	0.537	2016.6
muscle	3.915	195.312	168.299	261.799	98.398	113.956	10.245	4.770	0.591	857.3
intestine	8.815	229.223	62.556	20.385	13.628	4.118	0.194	0.095	0.008	339.0
heart	3.377	67.918	10.694	11.610	9.795	1.660	0.086	0.062	0.007	105.2
bone	2.609	81.859	56.587	95.917	45.006	62.463	8.529	4.945	0.710	358.6
liver	2.666	38.195	31.104	50.600	12.401	9.653	0.458	0.059	0.005	145.1
skin	4.510	314.135	246.457	417.087	224.390	434.781	69.152	77.792	15.271	1803.6
lung	0.703	16.527	9.561	36.649	8.043	3.314	0.051	0.011	0.001	74.9
stomach	2.674	68.964	39.434	23.581	52.347	2.664	2.164	0.121	0.045	192.0
pancreas	1.841	79.073	50.262	40.749	6.663	2.386	0.021	0.024	0.002	181.0
spleen	0.452	31.177	46.908	253.034	20.522	40.091	0.337	0.049	0.001	392.6
kidney	2.603	86.730	39.265	27.922	7.147	2.101	0.049	0.037	0.003	165.9
gall	2.006	54.336	46.868	19.454	5.710	1.625	0.030	0.021	0.002	130.1
eye	5.537	300.261	114.005	80.989	552.200	54.530	237.550	46.846	37.116	1429
testis	8.633	82.878	79.782	175.030	140.704	172.561	58.801	21.511	17.888	757.8
bladder	9.257	17.200	86.398	33.393	30.657	9.541	3.762	0.834	0.207	191.2

Conclusion The results suggest that leydig cells is one of the most susceptible cells ,EMP irradiation may cause significant injury in leydig cell structure and function in mice, which will be bound to affect sexual function and sperm production owing to its earlier period and continuous effect.

Key words electromagnetic pulse ,leydig cell

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Thermally Biological effects and its Medical Functions of the Infrared Rays absorbed by living systems

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Background: Scientists and people pay always give attention to the biological effect of infrared light, this is due to important relation of the infrared lights with growth and live of human beings and animals and plants. The infrared lights come from sunshine and various thermal radiators and equipments, and so on, in general case. At present, a variety of infrared medical-instruments and health-protection- equipments and materials containing infrared lamps, underwear, trousers and belts and a lot of thermal-radiators have extensively been used for curing sickness in the hospitals and family. Some of these instruments are effective, which have very well medical functions, but other are not so. Why is this? In such a case it is very necessary to know mechanism and properties of biological effect of the infrared lights absorbed. Nowadays, we knew already that the infrared lights have two different kind of biological effects, thermal and nonthermal effects. As far as mechanism of the nonthermally biological effect is concerned, it is proposed by us and can be summarized as follows[1]. The infrared light absorbed by the living systems can cause the quantum vibrations of amide-Is in protein molecules, the vibrational quanta (excitons) can become as soliton by the self-trapping interaction with deformations of amino acid lattice. The soliton with energy acquired from the infrared lights can transport from one place to other by dipole-dipole interaction between neighbouring amides to generate a series of biological effects. Also, the infrared light can also participate some biological chemical reactions, for example, $\text{CO}_2 + 6\text{H}_2\text{O} + h\nu \rightarrow \text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2$ (photosynthesis reactions) and the reaction between ADP(adenosine biphosphate) and ATP(adenosine triphosphate), $\text{H}_3\text{PO}_4 + \text{ADP} + h\nu \rightarrow \text{ATP} + \text{H}_2\text{O}$, etc.. This is just nonthermally biological effect of the infrared lights. However, the mechanism and properties of the thermally biological effect of infrared light is not exposed up to now. This is very sorrowful. This question is quite important in life sciences and biological medical engineering. Thus it quite worth to study.

METHOD: A great number of experiments shows that main influences of infrared lights on living systems are a thermal effect, i. e., absorbed infrared lights can result in lifting of bodied temperature. We can confirm that this thermally biological effect is a result produced by disorder motions of bio-water molecules, instead of protein, DNA and other bio-molecules, in the living system, the liquid water is heated by absorbing infrared lights due to four following reasons: (1) essence of heat, or speaking, reason producing heat; (2) experimental fact of the infrared light which can heat water; (3) features of molecular structure of water and its distribution in the living system; (4) theory of molecular physics and principle of resonant absorption. From theories of thermodynamics and statistics we know that the heat is a result of disorder motion of a large number of microparticles. There are a great number of water molecules in living systems, water is an important component, and also a microscopic small-molecules for the living bodies. Animal organisms consists of nearly two thirds waters. The human embryo contains about 93% waters during the first month. Therefore, there is a large number of water in the living system. Waters in the living systems are distributed in cell-membrane, cytoplasm, cytoblast and blood and lymph liquid and space between cells, i.e., there is waters in all biological organizations. Experimental measurements show that waters are about 45% in blood liquid, 8% in membrane, 80% in cytoplasm. Therefore its disorder motion can generate heat. Meanwhile, the water molecules in living system are polarized and have certainly electric dipolar-moment, Hence it can interact with the infrared light with electromagnetic feature. Also, vibration of molecule can radiate or absorb infrared lights according to theory of molecular physics[2]. we knew. Therefore, infrared light absorbed can result in vibrations of water molecules, i. e., liquid water can absorb infrared lights according to the principle of resonant absorption and Herzberg et al's and Jiang Yijian et al's Raman experiments which show that the liquid waters can absorb the infrared lights with 3540cm^{-1} and 3617cm^{-1} wavelengths. Again according to the feature of individual distribution of water molecules, in which there is not an organization to transport the energy absorbed from infrared light to other place from one in the living systems, and the knowledges for the infrared light to can heat water in

everyday livings, we can confirm that the energy absorbed by bio-water molecules transforms the thermal energy of its disorder motion, thus the waters are heated. However, in order to explain the thermally biological effect of the infrared lights, we must farther study which frequencies of the infrared light can be absorbed by water molecules and what biological effects are generated by heating bio-water. These problems can be solved by calculating. vibrational energy –spectra of bio-water molecules in nonlinear quantum theory and by investigating biological function of water in the living systems.

The biological functions of the biowater are as follows. (1) The hydration of ions, hydrophobic and hydrophilic effects and hydrogen bonded structure of waters determine essentially the secondary structure and conformations of protein molecules and structure of cellular and intracellular membranes without which there would be no individual cells and many biological processes important for life. It is the hydrophobic interaction which are responsible for the fact that living organisms are insoluble in water although they are two thirds water. (2) Water forms the basic medium in which all bio-chemical reactions take place in the cell. Water is practically a bed of activity and living of bio-zymic, which can facilitate the bio-chemical feaction to occur.(3) Water can participate in a lot of bio-chemical reactions, for example, ATP hydrolysis. $ATP^{-4} + H_2O \Leftrightarrow ADP^{-3} + H_3PO_4^2 + H^+ + 0.43ev$ and glucose oxidation; $C_6H_{12}O_6 + 38ADP + 38H_3PO_4 \rightarrow 6CO_2 + 6H_2O + 38ATP$, and so on .(4) Water is essential for digestion because the decomposition of carbohyorates, proteins and fats take place by a addition of water molecules.(5) A large number of waters are involves in plasma. It forms the liquid part of the blood and the lymph. Therefore water is a bed or motor for the circulation or microcirculation of blood and for the flow of lymph.(6) Circulation of water between interior of the living systems and external environment can ensure and retain the physiological temperature of the living systems about 300-310K which is a foundations of normal growth for life. (7) Breeding and fecundity of cell, differentiation and reproduction of macrobiomolecules and variation of conforma- tion and bio-functions for the protein molecules depend on waters. The cell is in death, biological functions of DNA and protein molecules eliminate or desist without waters. Because bio-water molecules exist are polarized, in which hydrogen-bonded system for the water molecules are formed as mentioned above. This is a nonlinear system. Thus we can calculated the vibrational energy- spectra of HOH or OH bonds by using classical discrete self-trapping equation in nonlinear quantum theory for a system is in the form of $(i\frac{d}{dt} - \omega_0)\bar{A} + \lambda diag(|A_i|^2)\bar{A} + \varepsilon M\bar{A} = 0$, to calculate the vibrational energy spectra of OH stretching of H₂O in liquid phases through choosing a set of optimal values .In table 1 we list calculated result ($1 \leq n \leq 9$) together with some experimental data.

CONCLUSION: From table 3 we see clearly that bio-water can absorb the infrared light with wavelengths from $3549.42cm^{-1}$ to $14538.8cm^{-1}$ or $0.6 \mu m - 6 \mu m$. This energy absorbed can cause the quantum vibrations of OH or HOH bonds in waters. This effect can result in the destruction of the hydrogen bonds of the water and disorder thermal-motion of individual water molecules due to the fact that there is not bio-organization to transport the vibrational energy to other place from one in the liquid water. Thermal energy of motions of water molecules is transformed from its vibrational energy.Thus the temperature of the liquid water increases in such a case. This is just thermal effect of the infrared lights. This mechanism can be confirmed by our experiments. We measured the infrared absorption of 20 different amino acid molecular crystals, constructing the protein, under exposure of infrared lights with 2—12 μm wavelengths We found are different. Surprisingly, shape and confor-

Table 1 quantum vibrational energy-spectra for water molecules

H ₂ O(liquid): (a) $\omega_0=3460.20\text{cm}^{-1}$, $\lambda=135.0\text{cm}^{-1}$ $\epsilon=84.50\text{cm}^{-1}$								
n	cal.	exp.	n	cal.	exp.	n	cal.	exp.
1	3240.70 3409.70	3241.00 3415.00	4	12408.97		7	20379.51	
				12429.54			20379.60	
				12730.14			21139.87	
				12957.06			21162.65	
				13278.28			21543.47	
							21787.86	
							22144.76	
							22553.49	
2	6515.40 6764.88		5	15207.03		8	22761.07	
				15211.54			22761.08	
				15631.77			23675.22	
				15783.58			23679.77	
				16085.70			24209.48	
				16436.38			24358.49	
							24700.23	
							25077.06	
							25512.01	
3	9466.27 9526.28 9775.93 10053.92		6	17862.11		9	25007.24	
				17862.82			25007.24	
				18450.63			26064.22	
				18524.55			26064.89	
				18833.81			26782.09	
				19146.23			26844.13	
				19528.25			27213.32	
							27526.57	
	27944.63							
							28403.66	

that these amino acid molecules can all absorb infrared lights, although their absorption coefficients mation of these amino acid crystals was changed, but its temperature are not altered after exposure of the infrared lights. This shows that the energy absorbed by these amino acids transforms not as the energy of their thermal motion, but changes their conformations. However, if inserting water into these amino acids to form their hydrations, we discover that the temperature of the hydration of amino acid in water was raised from 25.6°C to 27.2 °C under exposure of infrared light about 10 minutes through measurement by thermal sensors with high-accuracy. This result shows that the water in these hydrations absorbed the infrared lights, but the energy absorbed can only transform as that of thermal motions of the water molecules in them. Thus the temperature of the hydrations in liquid water was raised. This result confirm experimatally the above mechanism. Thus we can suppose that heating bio-water can cause changes of the following biological phenomena.(1) Because waters are a basic medium in which bio-chemical reactions take place. Therefore, heating bio-water can not only accelerate the speed and evolution of bio-chemical reactions related with waters due to increasing the velocity of motion of the molecules jonining the chemical reaction, but also increase the speed of bio-zymes escoping from zymogen (a zyme source) and reduce the times of motion of the zymes between zymes and substrate, although it affects not the modulated effect of zymes to substructure.(2) Heating water can increase the rate of breeding of the cell because its biological activity depend closely on the status of water. We observed experimentally that the breeding and fecundity of the cell was enhanced about 40-50% under exposure of infrared light produced by Zhou Lin's spectrum-instrument when compared with that under no exposure of infrared light. This demonstrated experimentally that this conclusion is correct.(3) Heating water change the envorenment condition of protein molecules and DNA, thus it can increase also interaction of the protein and DNA with envorenments. Therefore variations of conformations and states of hydrophilic and hydrohobic protein molecules and DNA are enhanced. Then their functions change also.(4) Heating water enhances speeds of motion of water molecules, changes also these conformations of hydrophilic and hydrohobic protein molecules and combinations degrees of the protein molecules with waters and hydrocarbon. Thus biological activity and recognition of cell and its membrane are changed. Because functions and conformation of cell membrane change, the speed and capacities of passive and forced translates and transport of ions including Na⁺, K⁺, Ca⁺⁺ and Mg⁺⁺ and Cl⁻ on the membrane and the rate of molecules across cell membrane are enhanced, then coefficients of diffusion and translation of the ions increase on the membranes.(5) Heating water expodite the circulation and microcirculation of bloods and flow of lymph liquid in living systems. Because the water forms the liquid parts of the blood and lymph, when the temperature of water increases, then the speed of the circulation and microcirculation of bloods and of flow of lymph increase also. Meanwhile, because the naemoglobin molecule and myoglobin molecules stored and transported oxygen and carbon dioxide (CO₂).[4] are in the plasma in blood, therefore, when water is

heated, the ability of transport and store of oxygen and CO₂ changes also.

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IN VITRO STUDIES RELATED TO MOBILE TELEPHONY, PERFORMED AT THE PIOM LABORATORY IN BORDEAUX, FRANCE

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The PIOM (Physics of Wave-Matter Interaction) laboratory has been involved for several years in experimental bioelectromagnetic research. Since 1997, the “wire-patch antenna” has been used to expose cultured cells to mobile phone related radiofrequency radiation (RFR, 217-Hz modulated GSM-900 signals). This set-up was designed and numerically characterized at the IRCOM laboratory in Limoges (Philippe Lévêque and coll.) and the experimental dosimetry performed in our laboratory and at IT’IS in Switzerland (Niels Kuster and coll.). To avoid the occurrence of temperature gradients at the cell level within the Petri dishes, we chose to use two CO₂ incubators for sham- and GSM-exposure.

Within national and international programs, we have performed studies on several relevant endpoints for the evaluation of the in-vitro toxicity of GSM-900 microwaves:

(i) *Apoptosis*: Apoptosis, or programmed cell death, is a major mechanism of protection against genotoxic agents. However, it is known that excessive apoptosis can contribute to neurodegenerative diseases whereas default in apoptosis is involved in cancer or autoimmune diseases. There is to date only a few reports on the effect of signals from the mobile telephony on cellular apoptosis. We focused our research on the investigation of the role of GSM-900 on apoptosis in immune, nerve and skin cells.

(ii) *HSP*: Heat shock proteins can be used as markers for many environmental insults and have been shown by several groups to respond to low level GSM-exposure. Since the brain is one of the main targets of RFR emitted by mobile phone, we chose to follow the expression of the 70-kDa heat shock protein family (the major form of stress proteins in the brain) in neuronal and glial cell cultures after exposure to the GSM-900 signal.

(iii) *NOS₂*: Production of nitric oxide (NO) by glial cells after stimulation has been shown to be responsible for neuronal cell death. Moreover, an increase in the rate of cell death in the adult nervous system is involved in neurodegenerative diseases. We investigated whether exposure to GSM-900 microwaves could elicit the expression of the inducible isoform of the Nitric Oxide Synthase (*NOS₂*) or interfere with lipopolysaccharide plus cytokine-induced *NOS₂* expression in C6 rat glial cells.

(iv) *ODC*: Ornithine DeCarboxylase (*ODC*) plays a pivotal role in the synthesis of polyamines that are essential for cell growth. Recent reports have shown that *ODC* overexpression may be involved, not only in cell neoplastic transformation but also in cancer cell invasiveness. by the Litovitz group. reported a temporary increase in *ODC* activity in L929 fibroblasts after exposure to RFR emitted by North American mobile phones (Penafiel *et al.*, 1997, *Bioelectromagnetics*, 18, 132-141). Only modulated RF had an effect on *ODC* by contrast to continuous wave signals. Such an increase in *ODC* activity might indicate that RFR could act as a non-genotoxic carcinogen. We are involved in a replication study of the results published by this group.

Data available in our group show that to date none of the endpoints investigated so far (i to iii) was shown to be affected after exposure to GSM-900 microwaves. Further investigations are ongoing (iv).

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THE SPECIES SPECIFICITY AND SENSITIVE TARGET ORGANS OF INJURY INDUCED BY ELECTROMAGNETIC RADIATION (BIOEFFECTS OF EMP AND HPM)

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Electromagnetic radiation (EMR) widely exists in daily life and military applications. The experimental investigation and epidemiological survey have confirmed that EMR can induce human injury and health risks, even fatal effect. Through study on the injury effect induced by electromagnetic pulse (EMP) and high power microwave (HPM) in several experimental animals, we found that injury degree was different between monkeys, dogs, rabbits, rats and mice, and the sensitive degree was also discrepant in various organs. In this paper, by means of observation of behavior, physiology, hematology, biochemical, immunology, pathology and especially, death percentage during one year, we explored the species specificity and sensitive target organs of injury induced by EMR.

Methods: All of experimental animals were irradiated by electromagnetic pulse (EMP, $2 \times 10^4 \sim 6 \times 10^4$ V/m, rise times 20ns, pulse width 30 μ s), including 5 monkeys (6×10^4 V/m), 15 dogs (2×10^4 V/m and 6×10^4 V/m), 43 rabbits (6×10^4 V/m), 100 Wistar rats (2×10^4 V/m and 6×10^4 V/m) and 108 mice (2×10^4 V/m and 6×10^4 V/m). At same time in every species group, 5~10 corresponding animals were as control. The observative period was one year. The behaviors, physiology (EEG, ECG), hematology (WBC, PLT, HB, Clotting function), biochemical (enzymes, ions, et al), immunology (T lymphocyte, B lymphocyte, et al), pathology (systematical autopsy, microscopy, electromicroscopy, immunohistochemistry and molecular pathological techniques were carried out in died and killed animals) and death rate were respectively observed and measured dynamically at 0h, 1h, 1d, 3d, 7d, 14d, 30d, 90d, 180d, and 365d after irradiation.

Results and discussion:

1. Mortality: The mortality of irradiated monkeys was highest, below in proper order dog, rabbit, mice, rat, (Table 1). The death times were at 1st~265thd after irradiation.

2. The death causes: The main death causes were different. In earlier phase (within 1 to 7 days), the main causes were coma and shock; in metaphase (within 8 to 30 days), most animals died of infection and/or hemorrhage complications (mainly involved lung); in late phase (more than 1 month), the main death causes were extremely emaciation, and then dyscrasia, some animals died of infection (particularly pulmonary or disseminated infection).

Table 1 Mortalities of various animals irradiated by EMP

Animals	Field intensity (V/m)	No. of animals	No. of death	Death rate (%)	Time of death(d)
Monkey	6×10^4	5	4	80.0	30~265
Dog	$2 \times 10^4, 6 \times 10^4$	15	9	60.0	1~83
Rabbit	6×10^4	43	14	27.1	3~180
Mouse	$2 \times 10^4, 6 \times 10^4$	108	10	9.3	10~156
Rat	$2 \times 10^4, 6 \times 10^4$	100	5	5.0	7~120

3. In dead animals, the main pathological changes included systemic (multi-organs) blood circulation disturbance (congestion, edema, hemorrhage, et al), severe degeneration, apoptosis (observed by TUNEL and FACS) and necrosis of parenchyma cells (brain, heart, endocrine gland, gonad, bone marrow, lymph tissue crystalline lens), infection complication (mainly in lung) and dyscrasia.
4. In killed animals within 9~12 months, the main pathological changes included lens opacity and cataract, atrophy of brain, hypoplasia of hemopoietic and lymph tissue, disturbance of spermatogenesis, ovigenesis, atrophy of testis and tumor (hepatocarcinoma, thyroid cancer, et al)
5. The main injured organs included brain (particularly hippocampus), endocrine glands (hypothalamus, hypophysis, thyroid gland, suprarenal gland), heart (mainly conductive system), gonad (testis and ovary, particularly spermatogenic epithelium and Leydig cell), eye (especially lens), lymph tissue (spleen, thymus gland, lymph node and mucous lymph tissue), bone marrow. Damage of other organs was light.
6. The physiological findings: mental disorder (first inhibition and then restlessness), learning and memory capability depress, LTP delayed, waveform of EEG abnormal, the main ECG changes were T wave upside down and conduction block, cardiac rhythm disordered and so on.
7. The hematological examination: WBC decreased, T lymphocyte and B lymphocyte reduced, apoptotic rate of lymphocytes in peripheral blood increased about 5 times, clotting mechanisms disturbance (TT and APTT prolong and FIB decreased).
8. Biochemical examinations: Serum AST, CHE, LDH and BUN significantly increased, testo decreased, and so on.

Conclusions:

1. According to the mortality and symptoms, pathologic changes, the injury degree induced by EMP has species specificity in mammal, that is, primate (monkey) most sensitive, below in proper order dog, rabbit, mice, and rat.
2. According to the character and degree of damages and influence for organism, the sensitive targets could be divided into 5 types: extremely sensitive (brain), high sensitive (gonad, endocrine gland, heart-conductive fiber, lymph tissue, bone marrow and crystalline lens) moderate sensitive (lung, liver, kidney), low sensitive (stomach, intestine, esophagus) and non-sensitive (bone, cartilage, muscle, connective tissue).

COMPARATION OF BIO-EFFECTS OF EMP AND HPM

The main bio-effects of EMP and HPM are the similar, however, the bio-effects of HPM have some special characteristics.

1. The similarities of bio-effects of EMP and HPM

- (1) There are similar physiological effects (including behavior and cognition, learning and memory ability);
- (2) There are similar biochemical and blood alternations (including Serum AST, CHE, LDH and BUN significantly increased, testo decreased, and so on);
- (3) There are similar pathological changes (including basic pathological damages, target organs, death causes, and so on);
- (4) There are similar damage mechanisms (such as electroporation of cell membranes, free radical, cell factors, and gene expression participated in it);
- (5) There are similar protective materials and diagnostic methods.

2. The special characteristics of bio-effects of HPM

- (1) The damage degree of HPM is more severe than that of EMP;
- (2) In the injury mechanism of HPM, the number of electroporation of cell membrane is more, the diameter is larger, the degree of depth is deeper, the shape is more irregular;
- (3) The nature of damage effects of HPM: thermal effects and non-thermal effects are co-exist generally;

ENVIRONMENTAL INVESTIGATION ON THE ELECTROMAGNETIC FIELD LEVELS IN THE URBAN AREA OF ROME (ITALY)

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Background: It is presented the work carried out by the Laboratory of Radiation and Ultrasounds Pollution of the National Institute of Occupation Safety and Prevention (ISPESL) about the measurement of radiofrequency and microwave electromagnetic field in the urban area of Rome (Italy) from 1999 to 2001. The measurements have been carried out within the framework of the technical and scientific advice paid by ISPESL to the public authority and to the companies to implement the cellular networks in TACS, GSM and DCS technologies.

Methods: It is presented the results of approximately 500 wide band measurements of the electromagnetic field background in the urban area of Rome, carried out near the sites selected for the installation of new base stations. It is presented the results of the theoretical estimate of the electromagnetic field, carried out by using simulation models applied in correspondence of selected areas for density of population or maximum concentration of emitting systems; in particular it has been evaluated the total electromagnetic impact assuming all the operative base stations and the new ones, all included in the area, working at the maximum power. The results of the electromagnetic measurements have been compared with the electric field levels (6 V/m) fixed in 1998 by the Italian law to prevent hazardous due to long term people exposure to the electromagnetic field sources with frequency between 100 kHz-300 GHz.

Results: The results of the measurements show that only a small percentage of the examined sites exhibits electromagnetic field levels equal or higher than that fixed by the Italian law. In general, a large percentage of the examined sites shows electromagnetic levels lower than half of the quality target.

Conclusions: The results of the simulations show that in the urban area of Rome it is not expected an important rise in the electromagnetic background for long term people exposure due to the presence in the area of old and new base stations.

Reference: Italian law :D.I. n. 381/98

RADIOFREQUENCY ELECTROMAGNETIC FIELDS (GSM SIGNALS) AFFECT GENE EXPRESSION LEVELS ON RAT NEURONS

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BACKGROUND: The recent increase in personal mobile communications has heightened public awareness and concern about the possible biological and health effects posed by exposure to radiofrequency(RF) electromagnetic fields(EMF) radiation. However, no precise health hazards have been identified with exposure to RF EMF. But most of them focused on single gene or protein. In this paper, the response genes to RF EMF were studied with high-throughput genechip analysis techniques

OBJECTIVE: In order to determine sensitive gene of RF EMF, we Investigate the global change of gene expression pattern induced by 1.8GHz RF EMF using genechip.

METHODS: 1. Primary culture of neurons: neurons of cortex and hippocampus tissue from new-borned SD rat were seeded in 35mm dishes as a density of 10^6 cells/ml . With mixture medium (containing 10% fetal bovine serum, 5% horse serum, 0.2mol/L L-glutamine, 1% N₂, 2% B₂₇) culture neurons. 5 days later, Ara-C (cytosine arabinoside) was added to inhibit the over-growth of glial cells. The incubator was at 37 °C in 5% CO₂/95% air. All cultured cells were used at 12 days in vitro.

2. Identification of neuron: Utilize immunohistochemistry to identify the neurons by the first antibody against the neuron-specific enolase. Neurons cultured for 12 days were observed. Count the number of the neurons under fluorescence microscopy. The bodies with green fluorescence were neurons. It was observed that more than 90% of the cells were primary neurons.

3. RF EMF irradiation: The neurons were exposed to RF EMF (GSM 217) as a pattern of 5min on/10 min off for 24 hours at the 12th day. The carrier frequency was 1.8GHz with pulse modulation at 217Hz, and the SAR levels at the location of the cell layer was 2W/kg. Sham exposure was used as a control. The exposure set-up was the sXc-1800 System (made in the ETH Zurich, Switzerland.)

4. Extraction of total RNA: The total RNA of neurons were extracted immediately after exposure to RF EMF with RNeasy Mini Kit (QIAGEN). The quality and quantity of RNA were analyzed by spectrophotometric set Smart SpecTM3000.

5. Gene chip: The RNA was analyzed by Rat Neurobiology U34 array (Affymetrix) which containing more than 1200 gene related to neurobiology.

RESULT: The data showed that totally 24 genes were up-regulated and 10 genes were down-regulated in respond to RF EMF. The function of those genes including regulation of ion channels of the cell membrane, regulation of transcript, signal transduction, constitution of the cell framework, cell movement, immunity, metabolism and etc..

CONCLUSION: It was feasible to screen the genes susceptible to radiofrequency using gene chip; it was the result of the change of several genes that RF affected the bodies. The most important thing was that we found the change of transcript factor AP-1 and CREB-related genes (jun-b c-fos p300), and it was consistent to the previous researches.

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STUDY ON THE EFFECTS OF HEMP ON HEPATOCELLULAR DNA CONTENT AND PLOIDY IN MICE

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OBJECTIVE To observe the changes of high power electromagnetic pulse (HEMP) on DNA content and DNA ploidy of mice hepatocellular nuclear and explore the biological effects of electromagnetic radiation on liver.

METHODS Kunming mice were exposed to whole body irradiation by HEMP generator at field strength of 8×10^3 V/m, 2×10^4 V/m, 6×10^4 V/m, respectively. The main relative technological parameter of generator: pulse increase time is 20ns, pulse width is 30μ s, irradiation frequency is 5 times/2min. The changes of hepatocellular nuclear DNA content in mice were analyzed for 365 days including 10 time phases (n=6) by using Feulgen staining in liver tissue section. DNA content quantitation and DNA ploidy were measured by IBAS microscopical digital image analysis system from German.

RESULTS Within 90 days after HEMP irradiation, the hepatocellular DNA content of mice were similar to controls and the 2C were in dominant. At day 180 after irradiation, the higher DNA content ($p < 0.05$) and more 4C, 6C than control in 8×10^3 V/m group were found. At day 270 and 365, in all of irradiation groups, the highest DNA content ($p < 0.01$) and most 4C were presented than the others.

CONCLUSION The results suggested that the DNA content and ploidy of hepatocyte in mice can be altered by HEMP and thus may be the long-term effects. It is purposed that the hepatocellular nucleic acid may be a key target for the biological effects of electromagnetic fields. The data provide basic information for studying on the effects and mechanisms of EMP. Moreover, the investigation demonstrated that the long-term observation must be emphasized in order to keep the integrality and reliability of results.

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THE DEVELOPMENT OF GUIDANCE ON PROTECTION BY ICNIRP

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The International Commission on Non-Ionizing Radiation Protection (ICNIRP) is an independent group of experts established ten years ago to evaluate the state of knowledge about the effects of non-ionizing radiation (NIR) on human health and well being and to provide science-based advice on protection against harmful effects of NIR.

ICNIRP provides scientific advice to the World Health Organization (WHO) on all aspects of NIR and health. ICNIRP recognizes that the acceptability and adoption of a complete system of protection also requires data and evaluations based on social, economic and political considerations. It is ICNIRP's view that these matters are more appropriate to the functions of national governments and their designated authorities. ICNIRP and other scientific advisory bodies may, however, provide background information of relevance for such evaluations. Whereas ICNIRP provides general practical information on measurable levels that are derived from basic restrictions on exposure, it recognizes the need for further technical

advice on special exposure situations. This requires physics and engineering expertise to develop practical measures to assess and/or to enable assessment of compliance with ICNIRP exposure guidelines. This includes guidance on the principles and practice of measurements, design of equipment and/or shielding to reduce exposure, and, where appropriate, setting emission limits for specific types of devices. ICNIRP considers that these matters are more appropriate to the functions of international, regional and national technical standards bodies.

The evaluation of the many scientific research reports that exist requires expertise from different medical and scientific disciplines. ICNIRP is the recognized international non-governmental organization that evaluates the results of such research and provides guidance and advice on the health hazards of non-ionizing radiation. Any single observation or study may indicate the possibility of a health risk related to a specific exposure. However, risk assessment requires information from studies that meet quality criteria. Peer reviewed literature usually provides information to judge the extent to which these criteria are met. Assessment of established risks normally requires consistent information from several such studies. I

ICNIRP, in carrying out its critical reviews, monitors the accumulation of new evidence, leading, as appropriate, to updating health risk assessments. These are based on the totality of the science, not just on the added information. The evaluation process used by ICNIRP consists of three steps. It is inevitable that parts of this process are a matter of scientific judgment, and that details of the process may vary depending on the question addressed. Hence, the description below provides overall guidelines, not strict rules. The three steps are:

- Evaluating single studies in terms of their relevance to the health effects being considered and of the quality of methods used. Evaluation criteria are described in ICNIRP's statement on General Approach to Protection against Non-Ionizing Radiation and these can be used as guidance in this evaluation. This may result in the exclusion of some studies from further use, or assigning different weights to studies, depending on their methodological quality. Such judgments should be made in light of the hypothesis to be evaluated, as the ability of a study to contribute to this evaluation may vary depending on the hypothesis.
- For each health effect evaluated, a review of all relevant information is required. At first, this review is normally done separately for epidemiological studies, for human laboratory, for animal studies and for in vitro studies, with further separations as appropriate for the hypothesis.
- Finally, the outcomes of these steps need to be combined into an overall evaluation including an evaluation of consistency of human data, animal data and in vitro data.

ICNIRP's Standing Committees, with support from Consulting Members as appropriate, normally perform the first two steps of this process, while the full Commission in collaboration with the Standing Committees performs the last step.

Risk assessment demands that an effect is confirmed and that it is detrimental to human health.

Ideally, advice on guidance on protection to NIR can be developed based upon a quantitative relationship between the exposure and the adverse effect. In many cases, such a quantitative relationship could take the form of a threshold and it may then be possible to state a level of exposure below which the adverse effect can be avoided. If available data permit the identification of an adverse effect, but not the detection of a threshold, other risk reducing strategies may be employed. The role of ICNIRP as a scientific body would be to analyze the risk in terms of levels of consequences that could be quantified. The acceptability of such risks would, however, be based also on social and economic considerations, and as such, fall outside the remit of ICNIRP.

In developing the guidelines, ICNIRP considers direct and indirect, acute and chronic health effects. Safety (reduction) factors are included, to account for quantitative uncertainties in the scientific database and biological variability in response.

In respect of exposure limits, the general strategy of ICNIRP is to define a basic restriction in terms of the biologically effective quantity, and then, if necessary, to relate this to reference levels expressed in terms of a directly measurable external exposure (e.g. irradiance, power density, and field strength). Protection against adverse health effects is ensured by compliance with the basic restrictions on exposure.

ICNIRP is currently working on writing a blue book on biological and health effects of radiofrequency radiation. This will take about two years and will be in phase with the WHO document that will be issued later. The next step for ICNIRP will be to update the RF guidelines.