# COMMISSION K: ELECTROMAGNETICS IN BIOLOGY AND MEDICINE

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## Introduction

The research activities on the biological effects of electromagnetic fields in Japan from 1999-2001 are reviewed. In vitro, in vivo, dosimetrical and epidemiological studies on DC and ELF electric fields, DC and ELF magnetic fields, RF and microwaves are discussed. Biomedical applications including magnetic stimulation, hyperthermia, thermal ablation, MEG, MCG, impedance MRI, current MRI, MRI, and radiometry are also introduced.

## K1 Biological Effects of Electromagnetic Fields

### K1.1 DC and ELF Electric Fields

On dosimetry, Hirata et al. calculated the spatial distribution of induced electric field and current density in a child and an adult bodies exposed to a 60 Hz electric field. They showed the difference in the induced electric field and the current density in various organs between a child and an adult [Hirata, 2001].

On instrumentation, Yamashita et al. have developed a technique to measure EEG and ECG at the subject exposed to a strong ELF electric field. The electrodes were carefully shielded and EEG and ECG could be measured by radio telemetry [Yamashita, 2001a,b].

On genetic effects, Ding et al. observed the increase in hypoxanthine-guanine phosphoribosyl transferase gene mutations in Chinese hamster ovary cells after the exposure to the electric field (10 V/m, 60 Hz) for 10 hours [Ding, 2001].

On cellular effects, Shimooka et al. reported the suppression of macrophage phagocytosis by electric current. Since this effect was caused by a displacement current as well, their results suggested the possibility of immunomodulation by electric field exposure [Shimooka, 2000, 2001]. Suda et al. demonstrated that the orientation of human red blood cells was controlled by an electric field as well as by a magnetic field [Suda, 1999]. Katsuki et al. showed that the growth activity of B. *Stearothermophilus* was affected by the pulsed electric field, while no remarkable lethal effect was observed in the range of up to 40 kV/cm [Katsuki, 2000].

In the experiments with human subjects, Kawada investigated the change in an EEG spectrum. He could not find any significant change in the EEG spectrum in the exposure of 3 kV/m electric field and 0.08 ? T magnetic field [Kawada, 2001]. Using the above mentioned telemetry system, Yamashita et al. have analyzed the changes in the heart rate variability (HRV) and the body surface temperature to investigate the effect on the autonomic nervous system. A 50 Hz electric field was exposed to a subject using the instrument designed for an electric therapy. Noticeable changes were observed in the spectral power of HRV and in the skin temperature at the back of the subject’s hand [Yamashita, 2000, 2001a,b]. Shimizu et al. analyzed the threshold of electric field perception with human subjects in detail. In an experimental study, various causes of the variation in the perception threshold were clarified. They also found the changes in peripheral blood flow at the body surface associated with the field perception [Shimizu, 1999a,b,c, 2000, 2001a,b].

### K1.2 DC Magnetic Field

### K1.2.1 In Vitro Studies

Studies on magnetic orientations of several kinds of floating cells and micro-creatures were reported. The summation of induced diamagnetic moments, which were of mainly lipid cell membrane, generated a torque force on the cell, and the cell rotated to orient in an aqueous solution. It was reported that red blood cells oriented parallel to external magnetic fields [Higashi T, 1998, Suda T, 1999].

The magnetic orientations of micro-creatures, such as bull sperms [Higashi T, 2000, Emura R, 1999 and 2001, Takeuchi T, 2002, Suga D, 2000], and *Euglena gracilis* [Tanimoto, 2001] were reported.

A functional change in red blood cells during floating and magnetically orienting under static magnetic fields was reported [Iwasaka M, 2001a]. The magnetic orientation of a red blood cell changed the spectrum profile of hemoglobin inside the cell. A floating cancer cell, lymphoma, showed the slowing growth rate under a magnetic field of 8 T [Ogiue-Ikeda M, 2001].

Drastic effects of static magnetic fields on the aggregation of floating blood cells were reported [Iino W, 2001]. Red blood cells under a 6.3 T magnetic field showed enhancements in both sedimentation and aggregation. Collagen stimulated blood platelets showed a rapid aggregation under magnetic fields of up to 14 T [Iwasaka M, 2000]. Diamagnetic torque forces of 14 T magnetic field modulated the cleavage pattern of early embryos of *Xenopus laevis*, [Iwasaka M, 2002a].

Based on the previous studies on magnetic orientation of collagen and fibrin, recent studies reported a new approach to manipulate cells in a non-contact condition using magnetically aligned protein polymers. The orientation of bone cells, which were embedded on magnetically oriented collagen gel, was reported [Kotani H, 2000]. The magnetically aligned collagen fibers provided ordered cell layers of endothelial cells and smooth muscle cells, which were applicable to an artificial blood vessel [Iwasaka M, 2002b].

The alignment of adherent cell assembly without adding any proteins under a magnetic field was reported [Iwasaka M, 1999a]. Smooth muscle cells directed their long axis parallel to a static high magnetic field of 8 T. Rat smooth muscle cell (A7r5) was cultured in a polystyrene flask for weeks in magnetic fields of up to 8 T. The alignment of smooth muscle cell was analyzed quantitatively using an order parameter [Umeno A, 2001].

Strong static magnetic fields have an effect on the orientation of adherent mammalian cells. However, no distinct effect was observed in cell growths. Two types of mammalian cells, mouse leukemia cells, P388, and Chinese hamster fibroblast cells, V79, showed no change in cell growth and DNA distribution by a 7.4 Tesla magnetic field [Sakurai H, 1999]. Also, the cell cycle distribution and cell growth in Chinese hamster ovary (CHO)-K1 cells were not changed by a 10 T magnetic field [Nakahara T, 2002]. In contrast, it was reported that static magnetic fields of milli-tesla order affected on metabolic activity of mitochondria [Yamashita K, 2000] and on cell cycle [Saito D, 2000].

Magneto-mechanical effects with the energy exceeding thermal agitation were observed in a cellular level. Diamagnetic torque rotation in cytoskeleton was detected by means of the linearly polarized light transmission measurement [Iwasaka M, 2002c]. Magnetic beads, which had strong magnetism and were injected into a cell, accelerated the cell differentiation of myoblasts under a magnetic field [Yuge L, 2000]. Spatial gradient magnetic fields of 90 T/m under 10 T fields exhibited magneto-phoreses of smooth muscle cells, blood platelets and yeasts [Iwasaka M, 2001b].

Behaviors of a bacteria, *Escherichia coli*, under static magnetic fields of several teslas were

observed [Shoda M, 1999]. It was reported that 5.2-6.1 tesla high magnetic field enhanced a stationary phase-specific transcription activity of *Escherichia coli* [Tsuchiya K, 1999 ]. Also, a suppression of *Escherichia coli* death was observed in the stationary phase [Ishizaki Y, 2001], and it was suggested that the *rpoS* gene was the target of magnetic field effect [Horiuchi S, 2001]. These effects were larger under gradient magnetic fie lds than under homogeneous magnetic fields [Okuno K, 2000, Okuno K, 2001].
Another study reported a synergetic activity of a 5 T static magnetic field on chemical mutagen in *Escherichia coli*. Mutagenicity of ENNG in the bacterial mutation assay was enhanced under the magnetic field exposure at 5 T [Ikehata, 1999a,b].
And also, 5 T static magnetic field exposure inducedgene conversion in yeast *S. cerevisiae* tester strain [Ikehata M, 2001]. *S. cerevisiae*, was also used as a test system to obtain a possible cell response to a static magnetic field exposure in transcriptome. Recently developed DNA micro array system was used for screening expression change in whole genes and several specific genes, which were up-regulated by a magnetic field exposure at 14 T was reported. [Ikehata M, 2001].

**K1.2.2 In Vivo Studies**
Genetic and physiological effects of static magnetic fields on biological systems *in vivo* have been studied by several research groups. Dr. Ohkubo of the National Institute of Public Health has conducted intensive studies on the effects of static magnetic field exposure to blood pressure and cutaneous microcirculation in rabbits. Using microphotoelectric plethysmography technique, they found that exposure of the animals to a 1mT magnetic field cancelled the pharmacologically induced high or low blood pressure [Okano, 1999a and 2001a]. Ichioka et al. [2000] exposed anaesthetized rats to a much higher intensity field (8T). They reported that the exposure caused a decrease in the microcirculation and, therefore, in subcutaneous temperature. Kawakubo et al. [1999], on the other hand, exposed human volunteers to 0.45 or 1.2T static fields and found an increase in skin temperature. It seems the latter finding is consistent with the results of Nakagawa who found volunteers exposed to 1T field fell into a vagotonic state [2000]. However, he presumed that the volunteers' anxiety at being exposed to a strong magnetic field caused an increase in the synpathetic tone. Effects of static fields up to 1.5T on neuroconduction [Osuga, 1999] and muscle tension [Satow, 2001] were also studied.
Genetic effects of a strong static field have been revealed by Takashima et al. [2000, 2001], using DNA repair defective mutants of fruit fly *Drosophila melanogaster*. In a post-replication repair defective mutant, exposure to a 5T magnetic field caused somatic recombination. In a excision repair defective strain, on the other hand, mutations resulting from chromosomal non-disjuntion or deletion increased while somatic recombination frequency was not affected. These findings suggest some mechanisms of carcinogenic action of magnetic fields. It is possible that exposure to static magnetic fields causes at least two kinds of DNA damage which, in repair proficient flies, are repaired by the excision repair and post-replication repair mechanisms, respectively. Defects in the excision repair results in deletion or non-disjunction, while defects in the post-replication repair causes somatic recombination. We are eager to learn about further observations on the relationship of magnetic field exposure and DNA repair mechanisms.

**K1.2.3 Other Studies**
The mechanism studies of DC magnetic field effects tended to focus on the physical and chemical effects of strong static magnetic fields and their relation to biological phenomena.

Three kinds of categories for the DC magnetic field effects are proposed; i) spatial gradient magnetic field effects on a mechanical property of material, ii) diamagnetic torque force dependent effects, such as magnetic orientation, and iii) biochemical studies respecting radical species. Concerning strong magnetic particles, magnetite, the gene responsible for the magnetite formation in magneto-tactic bacteria was investigated.

Recently, the techniques for making strong magnetic fields proceeded significantly [Kindo K, 2001]. Superconducting magnets with a room temperature bore of 10 Tesla order were introduced into many laboratories, and many effects of DC magnetic fields were observed.

Nakagawa, J., et al. [1999] reported that the gradient magnetic forces acting on paramagnetic oxygen molecules and water enhanced the water vaporization form a water pool under strong magnetic fields. Hirota, N., et al. [1999] presented the multiplication of the gravity and the diamagnetic force in horizontal direction affected the germination of plants. Yano, A, et al. [2001] found an effect of static magnetic fields of milli-tesla order on radish's root orientation. The magnetic forces, which were the products of magnetic flux density B and their spatial gradient dB/dx, were responsible for the effects on plant behaviors.

An application of both magnetic forces, rotational force of diamagnetic torque and gradient force, for the controlling biological macromolecular liquid crystals was exhibited, by utilizing a compact permanent magnetic circuit [Hirai M, 2001].

A slight change in the structure of water molecules under 14T magnetic field was reported by Iwasaka, M., et al. [1999b]. Diamagnetic energy generated in a liquid state material under external strong magnetic field, and it possibly affected the structure of molecular assembly.

Although the effects of magnetic fields on enzymatic reactions containing radical species were mainly investigated spectro-photometrically, Yoita, M. [2001], and Iwasaka, M. [2001c], et al., also observed magnetically disturbed activities of catalase and peroxidase, which were immobilized on an platinum black electrode.

Discoveries of new magnetic phenomenon under strong static magnetic fields and understanding the linkage of individual mechanisms will provide a new approach for studies on milli-tesla to micro-tesla magnetic fields, and also for time-varying magnetic fields.

## K1.3 - ELF Magnetic Field

### K1.3.1 In vitro Studies

Regarding the effects of extremely low frequency (ELF) magnetic field at the cellular level, many studies using *E. coli* and mammalian cells at various magnetic density have been published. Some of them are introduced in this section. In the studies using cell-free system, the rate and fidelity of DNA polymerase catalyzed DNA synthesis, as well as of RNA polymerase RNA synthesis, were not significantly affected by 60 Hz 0.25-0.5 T magnetic fields [Harada, 2001]. A 50 Hz, 14 mT circularly polarized magnetic field had no detectable mutagenic or co-mutagenic potential in bacterial tester strains [Nakasono, 2000]. Exposure to a switched, time-varying 1.7 T magnetic field partly suppressed $K^+$ influx, which may be mediated by $Ca^{2+}$-dependent $K^+$ channels [Ikehara, 2000]. The effect of ELF magnetic field on mutation was not observed in the CHO-K1 cells after 6-week exposure at 50 Hz and 5 mT, however, X-ray-induced mutation was increased [Miyakoshi, 1999a]. The wild-type p53 gene expression suppressed the increase in mutation caused by the exposure to 50 Hz, 400 mT ELF magnetic field [Miyakoshi, 1998b]. Also X-ray-induced strand breaks were potentiated by the exposure to 400 mT ELF magnetic field [Miyakoshi, 2000a]. In the study using both Mitomycin C (MMC) and the ELF magnetic field, an increase in chromatid-type chromosomal aberrations was observed in mouse m5S cells [Yaguchi, 2000]. Heat shock protein 70 (hsp70) expression was not affected by exposure to the ELF magnetic field alone, however, expression of heat-induced hsp70 protein was potentiated by repetitive pulsed magnetic stimulation (RPMS) [Tsurita, 1999] and suppressed by exposure to 60Hz, 50 m ELF magnetic field [Miyakoshi, 2000c]. X-ray-induced apoptosis was transiently suppressed by exposure to 60 Hz, 5 mT ELF magnetic field [Ding, 2001].

### K1.3.2 In Vivo Studies

A series of studies have been made in National Institute of Public Health. Ohkubo et al investigated the biological effects of static magnetic field and ELF-MF on microcirculation in animals [Ohkubo 1999a 1999b 2001; Ushiyama 1998 2001a 2001b; Xu 1998 2000]. As one of these studies, they investigated the acute and subchronic exposure effects of ELF-MF on leukocyte behavior in mice. In order to do this study, they developed a dorsal skinfold chamber technique and a cranial window system for measuring the behavior of intra-microvascular leukocytes in the cutaneous and cerebral microcirculation. Using this in vivo system, the results showed that ELF-MF exposure influence cell to cell interaction between venular endothelial cells and leukocytes.

The mutagenicity is the main issues in the study of ELF-EMF effects. Three papers were published by Koana et al [1999 2001a 2001b]. They examined the possible carcinogenic and /or mutagenic activity of ELF-MF using somatic mutation and recombination test system of *Drosophila melanogaster*. As a result, if larvae were exposed to a magnetic field in an annular dish, flies from the outer ring showed more mutant spots compared to those from the inner ring. They concluded that results suggest the eddy current induced in culture medium causes mutation, rather than the magnetic field itself.

Miyakawa et al [2001] examined the responses of the heat shock protein, hsp-16 in *Caenorhabditis elegans* to ELF-MF. They found the gene, hsp-16-lacZ, was induced by ELF-MF and concluded that *C.elegans* perceives ELF-MF as stress. In order to check the effects of ELF magnetic fields on swimming behavior, Nakaoka et al [2000] used *Paramecium* multimicronucleatum as a model. With discussion of the gravitaxis and thermotaxis of *Paramecium*, they suggest that the magnetic field may amplify to a large extent the negative gravitaxis of *Paramecium* and discuss the effects of induced electric field on the swimming behavior.

The above mentioned laboratory studies play an essential role in understanding the effects of ELF MF on various systems. More fundamental studies are needed.

Apart from animal exposure experiments, Takimoto et al [2001] showed the very interesting study about the effects of ELF-MF on the germination of plant seeds under the saturated humidity conditions. Their results suggest that exposure to EMF-MF might remove the inhibitory effect of saturated humidity on process of seed germination of *Arabidopsis*.

### K1.3.3 Other Studies

As a human exposure study, Hong et al [2001] investigated the possible effects of repeated exposure to ELF-MF with electric sheet at night time on melatonin in male subjects. The experiment consists of 16 week which has pre-, during and post-exposure periods. The urine samples are collected and analyzed. 24h rhythms are extracted for each subject by the method of complex cosine curve fitting. Peak height, acrophase and total daily amount of melatonin were characterized. These results did not reveal that any statistically significant different between exposure periods and non-exposure periods. They finally indicate that the effect of

magnetic field on the nocturnal melatonin production and its circadian rhythm is unlikely.
In order to provide the risk perception of EMF and compare the risk perception of EMF with other environmental factors, Yaguchi et al [2000] analyzed the response from undergraduate students in four universities in Kyoto. They used a questionnaire concerning risk perception and knowledge about EMF and health problems. Their results suggest that student's vague fear of EMF may not be based on accurate knowledge of the risk, but based on their own experience of health problems associated with the uses of household appliance and cellular phone. The clarification and resolution of the risk perception, risk assessment and risk communication are next step in understanding the EMF issues.
Ohkubo presented a series of review papers focusing on the electromagnetic fields and health [Ohkubo 2000a 2000b]. He emphasized also the necessity and application of electromagnetic fields phenomena in medicine [2000c]. Shigemitsu et al [2000] reviewed the progress and final evaluation of US-EMF-RAPID Program Nakagawa also pointed out the safety standards of EMF in electric industries [1998].

**K1.4 - RF and Microwaves**

Experimental systems were developed for animals to expose microwaves and SAR inside animals with those systems were evaluated [Wake, 2001a,b,c,d; Watanabe, 1999a,b,c, 2000a,c]. Exposure setup for in vitro experiment on biological effects of microwaves was also developed [Taki, 1999a].

The effects on blood brain barrier (BBB) by 1439 MHz time division multiple access (TDMA) signals for the personal digital cellular (PDC) Japanese cellular telephone standard system were studied using SD rats at Tokyo University [Tsurita, 2000; Nagawa, 1999, 2001]. They showed that there were no effects on BBB by the exposure without thermal effects. Studies on the microcirculation of rat's brain locally exposed to PDC signal were made by researcher of National Institute of Public Health [Masuda, 2000, 2001a, 2001b]. The exposure which brain average SAR was lower than 7.5 W/kg did not significantly influenced microcirculation of rat brain. The effects on memory and learning of rats were also studied at Tokyo University [Yamaguchi, 2000, 2001a,b,c]. Although the extremely high-level exposure which induced whole body temperature elevation of 2 degree changed memory of rats, the exposure of 7.5 W/kg brain average SAR did not cause changes in memory.

DNA damage and changes on heat shock protein exposed to 2.45 GHz electromagnetic fields were studied by in vitro experiment at Kyoto University [Miyakoshi, 1999c, 2001; Tian, 2002]. In these experiments, they reported that only high SAR (more than 20 W/kg) induced hsp70.

**K2 - Tissue Properties, Materials, and Phantoms**

Human body impedance is an important parameter to estimate the contact current in the LF to HF band. Kamimura et al., recently reported the measured contact impedance of Japanese people and investigated the equivalent circuit parameters [Kamimura, 2001a].
Cytomagnetometry is used to investigate intracellular movements of organelles such as phagosomes. Nemoto and his colleagues developed a noninvasive observation method by introducing magnetic particles into cells by phagocytosis, magnetizing them and measuring the field from the cells. This method can measure the rheological properties of the cytoplasm and the energy responsible for rotational random movements of the phagosomes. [Nemot, 1999, 2000, 2001, and Moeller 2000].
Hoshina et al., studied on an open-ended coaxial probe, which is widely used for complex

permittivity measurement at high frequencies. They investigated the measurement region experimentally and numerically and reported that the region extends to about 5.4 mm under the probe surface [Hoshina, 2000 and 2001].

Various phantoms for SAR measurement were studied. Ito and his colleagues developed tissue-equivalent solid materials optimized for thermographic dosimetry [Ito, 1998 and Okano, 2000a]. Basic investigation to improve accuracy of thermographic measurement using solid phantoms was also performed [Watanabe, 2000b]. Kobayashi et al., developed alcohol-base liquid phantom used at UHF band [Kobayashi, 1999]. Similar materials are recently proposed for standard head SAR measurement methods issued by IEEE, CENELEC, ARIB, and so on.

The shape of the phantom for determining the peak spatial-average SAR in the human head was recently standardized internationally. Watanabe and his colleagues studied the effect of the shape of the head phantom on the measured SAR values. They reported that the ear shape was crucial factor of the peak SAR values [Watanabe, 1999d, 1999e, and 1999f], but that the different size between the European/American base standard (large) head phantom and the Japanese averaged (small) head phantom hardly affects the peak SAR values [Watanabe, 2001a and 2001b].

## K3 - Field Measurement and Exposure Assessment

### K3.1 DC and ELF Fields

Studies on estimating ELF electrically and magnetically induced current inside living bodies have been actively conducted in some laboratories.

The induced current density is numerically analyzed during exposure to an ELF magnetic field, using a realistic MRI-based rat model, by means of the impedance method [Wake, 2000]. In the study, special focus was placed on both specific tissues, i.e., pineal gland and retina, and polarization of the magnetic field, for comparison with the result obtained from animal studies.

Electrically induced currents inside a human model, which was ungrounded or standing on an insulated plate, were calculated using the finite-element method (FEM). Here the human model was assumed to be axis-symmetric and homogeneous [Chiba, 1999, 2000]. Induced current inside a homogeneous sphere and spheroid was analyzed under the condition of simultaneous exposure to both electric and magnetic fields [Matsumoto, 1999, 2000]. A thin layer representing the bio-membrane inside a human body was incorporated in the multi-medium spherical model for magnetically induced current calculation using the semi-analytical solution developed for the model [Tarao, 2000].

Two studies were conducted using a simple human model taking into consideration five major spheroidal organs: i.e., the brain, heart, lungs, liver, and intestine. The boundary element method (BEM) was adopted to calculate exposure to electric [Techaumnat, 2000] and magnetic fields [Techaumnat, 2001]. In an other study, the surface charge method was adopted to clarify the effect of conductivity of each organ and the difference between human models [Yamazaki, 2000a,c, 2001a].

A simple characterization of the magnetic fields generated by electrical appliances was performed using an equivalent magnetic dipole moment incorporating harmonics [Yamazaki, 2001b]. A low stray magnetic field generator was developed for use in biological cell exposure studies [Yamazaki, 2000b].

### K3.2 RF and MW

A series of studies on the numerical dosimetry at frequencies for cellular phones with various antenna types [Fujiwara, 2000a; Wang, 1999d, 2000b] were conducted in Nagoya Institute of Technology. Based on the consideration that a localized SAR exposure limit should be determined from the resultant temperature-rises, the temperature-rises in human head were calculated by using the FDTD (finite-difference time-domain) method [Wang and Fujiwara, 1999e; Wang, 2000a]. Comparison of the peak SARs were made in adult and infant-size head models, and an increase of peak SAR or peak temperature-rise in the infant head, although the level is much less than the threshold that causes physiological damage to the brain tissue, was observed [Fujiwara 2000b]. The tissue structure dependence in numerical dosimetry and the uncertainty in one-gram-tissue average procedure were also investigated [Wang, 1999a, 2001a; Ushimoto, 2000]. In addition, an FDTD model for predicting the EMI (electromagnetic interference) of implanted cardiac pacemaker by cellular phones was developed and applied to the evaluation of EMI suppression effects [Wang, 2000c, 2001b].

For establishing a head phantom for SAR compliance evaluation, a detailed study of the earlobe effect on the peak SAR was conducted in Communication Research Laboratory and Tokyo Metropolitan University [Watanabe, 1999d, 1999e, 1999f]. The peak SAR in various homogeneous head models with different shapes was also investigated [Watanabe, 2001a, 2001b]. The European-American head model was found to give an overestimate on the peak SAR in comparison with the Japanese head model.

For dosimetry evaluation, an easy handling SAR meter was developed for cellular phones [Nojima, 1999, 2001; Iyama, 2001], and a spectrum analyzer based electric field meter was also developed for base stations [Tarusawa, 2001] in NTT DoCoMo Inc.

The frequency dependence of SAR in multiplayer spherical models for near-field exposure was analyzed [Kamimura, 1999, 2001d]. By using tissue-equivalent solid phantoms developed in Chiba University, experimental SAR evaluation also for near-field exposure was made with a thermographic method [Ito, 1999, 2001a; Koyanagi, 2001; Okano, 1999, 2000a, 2000b]. In addition, permittivity measurement techniques of phantom construction materials, for example, the standing wave method, were investigated for phantom design [Miyakawa, 2000, 2001a, 2001b].

## K4 - BioMedical Applications

### K4.1 Magnetic Stimulation

After Ueno et al. developed a method of localized magnetic stimulation of the brain with a pair of opposing pulsed magnetic fields produced by a figure-eight coil in 1988, the localized magnetic stimulation progressed and became one of essential techniques [Ueno S, 1999a] for the brain science research of 21 century.

Recently, many clinical studies reported on the application of the transcranial magnetic stimulation for functional mapping of human cortex [Shiga Y, 2002]. Kamida T, et al. [1998] measured motor evoked potentials in rat brain, which was induced by transcranial magnetic stimulation, and found that extrapyramidal activities and locomotor function were affected. Effects of magnetic stimulation on an experimental animal were studied using forced swimming test. Tsutsumi T, et al. [2002] reported that a repetitive transcranial magnetic stimulation on rat had a similar effect to electroconvulsive shock (ECS).

A clinical study investigated on neurologic effects of magnetic stimulation, and showed a therapeutic effect, such as pain relief [Sato T, 2002]. Also, a therapeutic study was carried out in the purpose of controlling the stress incontinence by Fujishiro T, et al. [2000]. Magnetic stimulation was applied to induce nerve stimulation in sacral roots.

Fujiki M, et al., [2001] exhibited a detailed functional brain mapping by transcranial magnetic stimulation by observing corticospinal D and I waves. Also, the induced neuronal modulation probably caused a change in gene expression. For example in 1997, Fujiki, M., et al. presented the evidence that the transcranial magnetic stimulation at 25 Hz on mouse upregulated the astroglial gene expression. They observed a distinct there increases in the levels of glial fibrillary acidic protein (GFAP) messenger-RNA in hippocampal dentate gyrus, after the 25Hz of magnetic stimulation on mouse brain. Tsurita G., et al., [1999] studied possible effects of repetitive pulsed magnetic stimulation on cell proliferation and expression of heat shock protein 70, however, no-significant effects were observed.

Numerical studies were proceeded to clarify the efficiency of magnetic stimulation in living tissue models. Hiwaki O, et al., [2000] reported that the threshold for peripheral nerve excitation became lowest when the angle of figure-of-eight coil's junction was parallel and perpendicular to nerve the fiber. In order to find an efficient condition for the magnetic stimulation using the figure-eight coil, Liu R, et al., [2000] calculated the activating function of nerve excitation in inhomogeneous volume conductor during magnetic stimulation using the finite element method. They found that the interface between conductors of different conductivities affected the nerve excitation by magnetic stimulation.

**K4.2 Hyperthermia and Thermal ablation**

In recent years, various types of medical applications of microwaves have been investigated. Among them, minimally invasive microwave thermal therapies are of great interest. They are interstitial hyperthermia and microwave coagulation therapy for thermal treatment for cancer, cardiac catheter ablation for ventricular arrhythmia treatment, and so on. Ito and his colleagues at Chiba University have been studying the heating characteristics of thin coaxial antennas by using the FDTD (Finite Difference Time Domain) method and the FDM (Finite Difference Method). Heating performances (SAR and temperature distributions) of an array applicator for the hyperthermic treatment are calculated by numerical analyses. The array applicator is composed of a few coaxial-slot antennas and is fed with a 430 MHz generator. Firstly, the SAR distributions around the applicator were calculated by the FDTD method. Next, the temperature distributions around the applicator were analyzed by solving the bioheat transfer equation based on the resultant SAR distributions. After confirmation of the validity of the numerical calculation, the temperature distributions inside the multilayered media, such as skin-fat-muscle, are described. [Ito, *et al.* 1999]. Microwave coagulation therapy (MCT) has been used mainly for the treatment of small size tumor. In the treatment, a thin microwave antenna is inserted into the tumor, and the microwave energy provided by the antenna heats up to the tumor at least 60 deg. C. to produce the coagulated region including the cancer cells for a few minutes or longer. There are some problems that need to be improved for conventional MCT antennas. There is a problem that we have not generated a sufficient coagulated region in the perpendicular direction of the antenna, as one of the problems. Therefore, Saito et al. [2000a] developed a novel technique to expand the coagulated region. The temperature distributions inside the human body were generated by an array applicator and an array spacing was optimized theoretically by using the numerical calculations to generate a desirable coagulated volume. The conventional MCT antennas have a problem that the coagulated region becomes long and uncontrollable in the antenna insertion direction. Therefore, Saito et al. [2000b] improved the shape of the coagulated region by introducing the coaxial-dipole antenna. This antenna has two sleeves on both sides of the slot.

An inductive regional heating system for breast hyperthermia is developed. This system consists of a pair of ferrite cores and realizes controlling the shape of the heating region at the breast part by changing the position of the ferrite cores. In order to find a method of controlling heating region vertically or horizontally, magnetic field distribution was analyzed using the three-dimensional (3-D) finite element method (FEM) taking eddy current into consideration. Some experimental investigations were carried out using an agar phantom and rabbits. On the basis of investigations, an applicator system has been developed. In this system, the operating frequency is 4.0 MHz and the output power is 600 W. Efficiency heating results have been obtained using an agar phantom and rabbits without heating fatty tissue by using the developed system [Kotsuka, 2000].

The soft heating method is an inductive heating method that uses as a heating element a thermosensitive magnetic material, which has low Curie temperature. The heating sources are hysteresis loss of the magnetic material and eddy current loss of the metal ring. In order to sufficiently heat the thermosensitive magnetic heating element, the generation magnetic field was 6 mT at 100 mm from the handy circular excitation coil at 100 kHz. As a result, the terminal voltage of the coil can be reduced 2.6 kV by using focused cooling. In addition, by changing the target point from 100 mm to 50 mm, the terminal voltage was reduced to 392 V, which is a realizable value [Jojo, 2001b].

A treatment system combining interstitial microwave hyperthermia and interstitial radiation therapy is investigated. It is considered that the combined method is effective for treatment of radiation-resistive tumor. This treatment system is realized by using the same catheter between the interstitial hyperthermia and the interstitial radiation therapy. In this system, firstly, thin microwave antennas such as coaxial-slot antennas with catheters heat the tumor. After heating only antennas are pulled out of the catheter. Then radiation sources such as the iridium 192 are automatically inserted into the catheter by a "high dose rate afterloading system". In order to evaluate the heating performances of the array applicator for heating, the SAR distributions and temperature distributions in and around the applicators are calculated numerically. It is considered that the results are useful for clinical trial [Ito, 2001b].

### K4.3 Medical Diagnosis

#### K4.3.1 Magnetoencephalography and Magnetocardiography

Uchida et al. [2000a] measured the magnetocardiogram in normal and abnormal rat which has ischemic myocardial muscles and obtained the current source imaging using a high resolution SQUID system. They obtained the results that the current distribution significantly increased at the ischemic area in the ST segment, and the direction of the current distribution shifted to the left thorax in the T wave. They also compared the iterative minimum norm estimation and current dipole estimation for magnetic field measurements from small animals [Uchida, 2000b].

Iwaki et al. [1999a] investigated the dynamic properties of the distributed cortical activity related to mental rotation processes at high temporal resolution by means of brain magnetic field measurements and a linear inversion algorithm. Iwasaki [2001] measured the somatosensory evoked magnetic fields to evaluate the cortical function quantitatively in patients in the chronic phase of severe traumatic brain injury. It was observed that middle-latency SEFs may be applicable as a cortical functional measure for patients with severe traumatic brain injury.

#### K4.3.2 Impedance MRI current distribution MRI

Yukawa et al. [1999] proposed a new and noninvasive method for imaging electrical properties such as conductivity and impedance based on MRI techniques. The basic idea is to use the shielding effects of induced eddy currents in the body on spin precession. Two types of methods are introduced; (i) a large flip angle method, and (ii) a third coil method. Kamei developed new methods to visualize neuronal current distribution and electrical-impedance distribution. The basic principle is to erase the effects of local spin interaction T2* by subtracting MRI signals with different polarities of gradient magnetic fields. Measurements were made with an echo planar imaging (EPI) sequence at 1.5 T. MRI tapping of the neuronal currents in the brain during middle finger and thumb tapping was clearly observed [Kamei, 1999].

**K4.3.3 MRI**

Iramina [1999b, 2001b] has compared the characteristic between fMRI and MEG by the somatosensory stimulation. Kanzaki [1998, 2001] has analyzed the NMR Fresnel transform imaging and the NMR Phase scrambled Fourier imaging. Yamada [1998], Kanzaki [1999] and Ito [2000b, 2001] have reported on the application of the holographic reconstruction technique in the above MRI. Ito [2000a] has proposed 3D Fresnel diffractive imaging technique for the MR angiography. Yamaguchi [1999] has investigated the MRI thermometry using artifact of thermo-sensitive magnetic material.

**K4.3.4 Radiometry**

Maruyama et al. [2000] conducted the feasibility study of noninvasive measurement of deep brain temperature in newborn infants by multi frequency MRW. They showed that the proposed technique is feasible, that it is expected to provide a good estimate of the temperature profile within the cooled baby-head. Mukumoto et al. [2001] developed a five-band microwave radiometer system for non-invasive measurement of deep brain temperatures.

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