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Introduction

The research activities on the biological effects of electromagnetic fields in Japan from 2007 to 2010 are reviewed. In vivo, in vitro, dosimetrical studies on DC electric and magnetic fields, extremely low frequency (ELF) electric and magnetic fields, intermediate frequency (IF) magnetic fields, radio frequency (RF) and microwaves are discussed. Biomedical applications including magnetic stimulation, hyperthermia, thermal ablation, MEG, MCG, current distribution MRI, fMRI and radiometry, contactless power transmission, and electromagnetic interference (EMI) are also introduced.

This report does not describe every paper of the member of Japanese Commission K that has been carried out during 2007-2010. It begins with a section describing the recent published papers of the biological effects of electromagnetic fields. Next section reviews the results of electromagnetic field measurement, dosimetry and exposure assessment. Third and forth sections provide a state-of-the-art review of biomedical applications using thermal therapy, hyperthermia with soft-and inductive-heating, MRI, and current distribution MRI, and further discuss some of the EMI issue on implantable medical devices.

K1 Biological Effects of Electromagnetic Fields

K1.1 Static magnetic field

K1.1.1 *In vivo* study

Kimura *et al* [2008] reported the effect of high strength static magnetic fields and ionizing radiation on gene expression and DNA damage in *Caenorhabditis elegans.* They demonstrate that genes involved in motor activity, actin binding, cell adhesion, and cuticles are transiently and specifically induced following exposure to 3 or 5 T SMF They suggest that the response of *C. elegans* to high SMFs is unique and capable of adjustment during long exposure, and that this treatment may be less hazardous than other therapeutic tools.

Nakaoka *et al* [2010] reported about orientation of *Paramecium* swimming in a static magnetic field in a static magnetic field (0.78 T). Results of measurements of membrane lipid fluidity obtained using fluorescence image analysis with the lipophilic dye, laurdan (6-lauroyl-2-dimethylaminonaphtalene), showed that the degree of membrane lipid fluidity was correlated with the differences in magnetic orientation between syngens. That is, the syngens with decreased membrane fluidity showed an increased degree of magnetic orientation. Therefore, the membrane lipid order is a key factor in the magnetic orientation of

Paramecium swimming.

Furuno, *et al.,* investigated effects of strong magnetic fields on amphibian. Oocyte maturation, fetal development and gene expression were affected by exposure to over 10 T static magnetic field of *Silurana tropicalis* [Furuno, *et al.,* 2007, 2010 and Kashiwagi, *et al.,* 2010].

Xu, *et al.*, reported recovery effects of static magnetic field on bone mineral density in ovariectomized rats. 180 mT static magnetic field enhanced recovery of bone mineral density of osteoporotic lumbar vertebrae in the rats [Xu, *et al.*, 2011].

K1.1.2 *In vitro* study

Egami *et al* [2010] reported the effect of static magnetic fields on the budding of single yeast cells, Saccharomyces cerevisiae. The budding angle was clearly affected by the direction of the homogeneous and inhomogeneous magnetic fields strong magnetic field. In the homogeneous magnetic field, the budding direction of daughter yeast cells was mainly oriented in the direction of magnetic field B at 2.93 T.

Ikehara *et al.* reported that Effects of exposure to a time-varying 1.5 T magnetic field on the neurotransmitter-activated increase in intracellular Ca (2+) in relation to actin fiber and mitochondrial functions in bovine adrenal chromaffin cells. They measured the physiological functions of ER, actin protein, and mitochondria with respect to a neurotransmitter-induced increase in Ca(2+) in chromaffin cells exposed to the time-varying 1.5 T magnetic field for 2h.Results show the magnetic field-exposure influenced both the ER and mitochondria, but the inhibition of Ca(2+) release from ER was not due to mitochondria inhibition. The effect of eddy currents induced in the culture medium may indirectly influence intracellular actin and suppress the transient increase in [Ca(2+)] [Ikehara*, et al.,* 2010, 2011].

Research group of Railway Technical Research Institute (RTRI) (Ikehata and Yoshie) investigated mutagenicity of strong static magnetic field up to 13T in various *in vitro* test systems. In bacteria, SOD defective *Escherichia coli* was exposed to up to 13T static magnetic field for investigating effects of magnetic field on super oxide [Yoshie, 2007, 2008a]. In addition, plumbagin (super oxide producer) was treated during exposure period in the test system to investigate effect of magnetic field on mutagenesis by super oxide. In this test system, no effect was observed both experiments and concluded SOD related mutagenesis was not affected by exposure strong magnetic field. These results also indicated that mutagenic effect of strong static magnetic field in SOD deficient *E. coli* that was reported by Zhang's results did not confirmed in similar test system [Yoshie, 2008b]. In yeast cells, *Saccharomyces cerevisiae* was used to examine the effect of static magnetic field in various mutagenesis. In this system, point mutation was not induced but gene conversion/recombination was slightly increased by exposure to 5T magnetic field for 72 hr [Ikehata, 2007a, 2008b]. In culture cells, mouse lymphoma assay (MLA) conducted up to 5T magnetic field but no mutagenicity was observed in L5178Y $tk^{+/-}$ 3.7.2c cells that was generally used in this assay

[Ikehata, 2009]. Ikehata also reported evaluation of biological effect by exposure to combined magnetic field with static and 50Hz [Ikehata, 2007c, 2008c, 2008d]. No synergetic effect to combine magnetic field was found in their study.

In Prof. Miyakoshi's group, Monzen *et al* [2009] reported that effect of static magnetic field on human placental and umbilical cord blood. Results suggest that the 10 T SMF exposure may change gene expressions and result in the specific enhancement of megakaryocytic/erythroid progenitor (MEP) differentiation from pluripotent hematopoietic stem cells and/or the proliferation of bipotent MEP. Sakurai et al reported effect of strong static magnetic field on several secreting systems. Enhanced secretion of prostaglandin E2 from osteoblasts [Sakurai, 2008a], enhance of responsiveness to glucose stimulation and enhanced insulin secretion (only by exposure to gradient magnetic field) [Sakurai, 2009a, 2009f] were reported. Sakurai et al [2009c] also reported the effects of strong static magnetic fields on astrocyte differentiation. Terashima *et al* [2007] reported morphological changes of cultured cells by the medium convection under strong static magnetic fields.

Nakamichi *et al* [2009] reported the effects of static magnetic field on the functionality of neural progenitor cells. Static magnetism not only significantly decreased proliferation of neural progenitor cells without affecting cell viability, but also promoted differentiation into cells immunoreactive for MAP2 with a concomitant decrease in that for an astroglial marker in fetal rat brain.

Okano *et al* have been investigating effects of magnetic field on behavior, hypertension, angiogenesis, etc. They reported promotion of tubule formation by applying the peak gradient/force (1428 mT/m) using moderate magnetic field (120 mT) in endothelial tubular formation *in vitro* (Okano, 2008a).

K1.1.3 Other study

Effect of gradient static magnetic field on unstirred Belousov-Zhabotinsky reaction was investigated by Okano *et al* [Okano, 2008b, 2009] The ferroin-catalyzed BZ medium was exposed to the SMF for up to 16 min at 25 degrees C. The experiments demonstrated that the wave velocity was significantly accelerated primarily by the magnetic gradient. The propagation of the fastest wave front indicated a sigmoid increase along the peak magnetic gradient line, but not along the peak magnetic force product line. The underlying mechanisms of the SMF effects on the anomalous wave propagation could be attributed primarily to the increased concentration gradient of the paramagnetic iron ion complexes at the chemical wave fronts induced by the magnetic gradient.

Yanamoto, *et al.*, investigated repeated application of an electric field. The field increases BDNF in the brain, enhances spatial learning and induced infarct tolerance [Yanamoto, *et al.*, 2008].

K1.2 Extremely Low Frequency (ELF) magnetic field

K1.2.1 In vivo study

Negishi *et al.* [2008] belong to Central Research Institute of Electric Power Industry (CRIEPI), reported the promotion effects of 0 (sham-exposed), 7, 70, or

350 μT (rms) circularly polarized 50 Hz magnetic fields on 7, 12-dimethylenz (a) anthracene-induced malignant lymphoma/ lymphatic leukemia in mice. There is no evidence to support the hypothesis that power frequency MFs is a significant risk factor for hematopoietic neoplasia.

Nishimura *et al.* [2010] investigated the behavioral responses of a diurnal agamid lizard (Pogona vitticeps) to a sinusoidal ELF electromagnetic field (EMF; 6 and 8 Hz, peak magnetic field 2.6 μT, peak electric field 10 V/m). The average number of the tail lifts per individual per day was greater in the EMF group than in the control group. The tail-lifting response to the ELF-EMF disappeared, when the parietal eye of the lizards was covered with a small round aluminum 'cap' which could block light. These results suggest that lizards perceive the EMFs, and that the parietal eye may be involved in light-dependent magnetoreceptive responses.

Tanaka K., *et al.* [2010] reported the effect of power frequency MF (60-Hz, 0.05 μT - 60 mT) on acute, chronic, and genetic toxicities of fruit flies. Statistical analysis of the results showed that there was no obvious evidence that magnetic field level affects the behavior, longevity, and mutation of fruit flies.

K1.2.2 In vitro study

From Prof. Miyakoshi's group, four reports of the biological effect of the extremely low frequency (ELF) magnetic fields (MFs) were published. Koyama *et al.* [2008a] studied the effects of the ELF MFs on the number of apurinic/apyrimidinic (AP) sites in human glioma A172 cells. The results showed no difference in the number of AP sites between the cells exposed to the ELF MF and sham controls. Exposure to the ELF MF in combination with a genotoxic agents (MMS or H_2O_2) increased AP-site levels compared with the genotoxic agents alone. The results suggest that such exposure can enhance the activity or lengthen the lifetime of radical pairs. Sakurai *et al.* [2008b] reported the effect of ELF MFs (a sinusoidal magnetic field at a frequency of 60 Hz, 5 mT) on beta-cell survival and function of a hamster-derived insulin-secreting cell line (HIT-T15). The results showed the increase in cell number under apoptotic culture conditions by exposure to the ELF MF. Sakurai *et al.* [2008d] also investigated the effects of the ELF MF on cytokine-mediated dysfunction of insulin-secreting cells, RINm5F cells. Three days of continuous exposure at 5 mT enhanced cell dysfunction and insulin content. These results indicated that the increase in intracellular insulin concentration by the ELF MF would be useful for cell transplantation to cure diabetes mellitus. Sakurai *et al.* [2009d] studied the effects of extremely low frequency magnetic fields on adipogenesis in a preadipocyte cell line, 3T3-L1. The exposure to ELFMFs does not affect adipogenesis of 3T3-L1 cells and hence has no effect on patients suffering from obesity.

Soda *et al.* [2008] reported the effect of exposure to ELF MF (3 mT, 60 Hz) on differentiation of mouse osteoblast-like MC3T3-E1 cells. The results showed the exposure to the MF increased significantly the collagen, a marker of the differentiation, in the cells. Treatment with PD98059, an inhibitor of extracellular signal-regulated kinase 1/2 (ERK1/2) activation, did not prevent the increase in the collagen caused by ELF-EMF exposure. The insulin-like growth factor I (IGF-I) increased the collagen in the presence of the inhibitor. When phosphatidylinositol 3-kinase (PI3K) pathway was inhibited by LY294002, the increase in collagen induced by ELF-EMF exposure was accelerated, however, the increase in collagen observed by IGF-I addition was suppressed. Treatment with SB203580, an inhibitor of p38 mitogen-activated protein kinase (p38 MAPK), suppressed the increase in the collagen induced by ELF-EMF exposure, whereas IGF-I addition increased the collagen in the presence of the inhibitor. These results suggested that collagen synthesis stimulated by ELF-EMF exposure was carried out by the participation of p38 MAPK pathway, and that PI3K pathway may have the role to suppress the collagen synthesis induced by ELF-EMF exposure, and that the suppression of the PI3K pathway may allow the acceleration of the collagen synthesis.

From Prof. Jimbo's group, five reports of the biological effect of the ELF MFs were published. Saito A., *et al.* [2008] studied the effects of ELF MF (1 mT, 50 Hz, sinusoidal) exposure on differentiation and spontaneous activity of P19 embyonal carcinoma (P19EC) -derived neuronal cells. This report showed the changes of the size of EBs and spontaneous activities by long-term cultivation of P19EC-derived neuronal networks. At the 14 days after plating, the spontaneous activity and neuronal differentiation rate of exposed P19EC-derived neuronal networks were drop down compared to non-exposed one. Saito A., *et al.* [2009] [2010a] also reported the effects of the ELF MFs (1 mT or 10 mT, 50 Hz, sinusoidal) on the neuronal differentiation process of P19 embryonal carcinoma cells (P19 cells). The results showed the percentage of MAP2 positive cells and the spike frequencies were increased by 10 mT ELF-MF, and then the percentage of GFAP positive cells were reduced. However, these effects were not seen in 1 mT exposed cells. Saito et al. [2010b] studied the neuronal differentiation of P19EC cells by exposure to AC magnetic fields (50 Hz sinusoidal and the strength used 1, 5, 10, and 20 mT). The results showed that a slight rise (1, 5 mT) or reduction (10, 20 mT) of the spike firing rate were observed by repeated exposure to the MF for 60 sec. Saito *et al.* [2010c] also investigated the effects of AC magnetic fields on neuronal differentiation and network activities of P19EC cells. The results showed the neuronal marker (MAP2) positive cells and spike frequency recorded by microelectrode array (MEA) were increased by 10 mT AC-MFs (50 Hz, sinusoidal) exposure. And the percentage of positive cells and the size of embryoid bodies (EBs) which formed in the neuronal induction were correlated with intensities of induced current.

K1.2.3 Epidemiological study

Saito T. *et al.* [2010] reported the effect of power-frequency MF on childhood brain tumors. The population-based case-control study encompassed 54 % of Japanese children under 15 years of age. After excluding ineligible targeted children, 55 newly diagnosed brain tumor cases and 99 sex-, age-, and residential area-matched controls were included in the analyses. The result showed a positive association between high-level exposure-above 0.4 μT and the risk of brain tumors. This association could not be explained solely by confounding factors or selection bias.

K1.2.4 Other study

Mizuki *et al.* [2010] reported the activity of an enzyme immobilized on super-paramagnetic particles in a rotational MF of 1, 3, 5, 7, 10 and 30 Hz. The results showed that the activity of the enzyme molecules immobilized on super- para-magnetic particles increases in the rotational magnetic field and reaches maximum at a certain frequency (5 Hz). Enzyme reactions are enhanced even in a tiny volume of solution using the present method, which is very important for the development of efficient micro reactors and micro total analysis systems (mu-TAS).

K1.3 Intermediate Frequency (IF) magnetic field

K1.3.1 In vivo study

From CRIEPI group, Nishimura *et al.* [2009] investigated the chick embryo-toxicity after 20 kHz, 1.1 mT magnetic field exposure. White Leghorn fertile eggs (60/group) were either exposed to a 20 kHz, 1.1 mT (rms) sinusoidal magnetic field or sham-exposed during the first 2, 7, or 11 days of embryogenesis. Lower dose exposures at 0.011 and 0.11 mT (rms) for 2 days were also conducted to elucidate possible dose-response relationships. Additional eggs given all-trans-retinoic acid, a teratogen, were exposed to the 1.1 mT (rms) magnetic field for the same periods to investigate the modification of embryotoxicity. No exposure-related changes were found in any of the endpoints in intact embryos exposed to 1.1 mT (rms) or to the lower doses of 0.11 and 0.011 mT(rms) magnetic fields. Retinoic acid administration produced embryotoxic responses, which were embry-onic death and developmental abnormalities, in 40-60% of embryos in the sham-exposed groups. The magnitude of these responses was not changed significantly by the magnetic field exposures. Under the present experimental conditions, exposure to 20 kHz magnetic field up to 1.1 mT (rms) was not embryotoxic in the chick and did not potentiate the embryotoxic action of retinoic acid.

Sakai H *et al.* [2010] studied the effect of radiofrequency radiation at 40 kHz on the liver hepatic injury in Long-Evans Cinnamon (LEC) rats, an animal model for human Wilson disease. The activities of ALT and AST in serum of LEC rats exposed to the RF radiation for 2 weeks were approximately 3.8-fold and 2-fold higher than those in serum of sham-exposed rats, respectively. The result showed that the RF radiation at 40 kHz induced hepatic injury in LEC rats.

K1.3.2 In vitro study

From RTRI's group, six reports of the biological effect of the intermediate frequency magnetic fields (IF-MFs) were published. Ikehata *et al.* [2008a] [2008e] reported the mutagenicity of IF-MF of 2, 10 and 20 kHz at 0.8mT by mouse lymphoma assay (MLA) using L5178Y tk+/-3.7.2c cells. The result shows that no significant difference by exposure to any IF-MFs was observed in mutation frequency between unexposed control and exposed cells. Ikehata *et al.*[2009b]

[2010] [2010] also reported the effect of 2 mT, 21 kHz IF-MFs on growth in various DNA repair deficient cells (such as Ku86, DNA-PK, XRCC1), frequency of micronucleus in CHL/IU cells, and gene mutation frequency at hprt locus in CHO-K1 cells. The results showed no significant effect by exposure to 2 mT, 21 kHz IF-MF in all every experimental indexes. Additionally, Ikehata *et al.* [2010] studied the development of novel exposure system of IF-MFs for *in vitro* test systems, which is capable of generating 20 kHz, up to 3.9 mT IF-MF within exposure space (150mm×150mm×150mm) within ± 5% deviation. From the same group, Yoshie *et al.* [2010] investigated the effect of a IF-MF (20 kHz, 2 mT (rms)) on growth rate of various cell lines, which are deficient in DNA repair, and mutagenicity by HPRT mutation assay using CHO-K1 cells. The results showed that the IF-MF exposure does not affect cell growth regardless of the ability of DNA repair. In the HPRT mutation assay, the results indicated that the IF-MF exposure does not cause mutation.

Fujita *et al.* [2010] have developed novel exposure system for *in vitro* research, which can generate an IF MF of 6.25 mT (rms) at 23 kHz with a uniformity within ± 5 %. The authors examined the harmonics, coil shape, and heat generated in the medium by the high-strength MF. They confirmed the system can be used to evaluate the biological effects of the IF MF.

From Prof. Miyakoshi's group, four reports of the biological effect of the IF-MFs published. Miyakoshi *et al.* [2007] reported the effects of IF magnetic fields of 532 ± 20 μT at 23 kHz on growth, mutation and DNA strand break. The results showed the exposure to the IF MF for 2 h did not affect the growth of CHO-K1 cells or cellular genotoxicity in both bacteria and Chinese hamster cells. From the same group, Kiyokawa *et al.* [2008] [2009] reported the effect of an IF MF of 23kHz at 6 mTrms for 2 hours on cell growth, micronucleus formation, DNA strand breaks, HPRT gene mutation and expression of heat shock proteins. As a result, there was no significant difference between exposure and sham-exposure group in the experiments of each cellular criterion. Sakurai et al. [2009e] investigated the effects of the IF MF on cellular genotoxicity and stress responses. The authors did not detect any effects of the IF magnetic fields on cell growth, comet assay, micronucleus formation, HPRT gene mutation, expression of phosphorylated Hsp27, or nuclear translocation of Hsp27, 70 or 105. Overall results indicate that the exposure to an IF MF at 6.05 mT (rms) for 2 h does not cause detectable cellular genotoxicity, and does not induce detectable cellular stress.

From CRIEPI's group, six reports of the biological effect of the intermediate frequency magnetic fields published. Nakasono *et al.* [2008b] [2010a] [2010b] used bacterial mutation tests and yeast genotoxic test to evaluate the effects of intermediate frequency (IF) magnetic fields (MFs) on mutagenicity, co-mutagenicity and gene conversion. For the *in vitro* research, the authors constructed a Helmholtz type exposure system which can generate vertical and sinusoidal MFs, such as 0.91mT at 2 kHz, 1.1mT at 20 kHz and 0.11 mT at 60 kHz. The assays of mutagenicity, co-mutagenicity and gene conversion were carried out for the three MF exposure conditions. For the mutagenicity tests, four strains of *S.*

typhimurium (TA98, TA100, TA1535, TA1537) and two strains of *E. coli* (WP2 uvrA, WP2 uvrA/pKM101) were selected to cover a wide spectrum of point mutation. For co-mutagenicity tests, the authors used four sensitive test strains (TA98, TA100, WP2 uvrA, WP2 uvrA/pKM101), and five chemical mutagens, BH (hydroxyl radical precursor), AF2 and ENNG (DNA reactive reagents), BaP and 2AA (DNA reactive promutagens which were activated metabolically by rat S9mix). For the gene conversion tests, the authors used the yeast test strain, *S. cereviciae* XD83. The effects on the repair system of DNA damage caused by UV radiation were also tested. In statistical analysis for all above genotoxicity tests, neither significant nor reproducible difference was found between exposed and unexposed control groups. These results indicate that the IF MFs did not have mutagenic or co-mutagenic potentials for the chemical mutagens in the experimental conditions. These results also indicate that the IF MFs did not induce gene conversion and did not affect DNA damage repair system in eukaryotic cells. Nakasono *et al.* [2008a] [2010a] [2010b] also investigated the effects of the intermediate frequency (IF) magnetic fields (MFs) on micronucleus formation in a mammalian cell line. The Chinese hamster V79 cell was chosen to estimate the effects of the MF exposure on micronucleus formation and DNA damage repair caused by mitomycin C (MMC). The V79 cells were exposed to MFs of 0.91 mTrms at 2 kHz, 1.1mTrms at 20 kHz or 0.11mTrms at 60 kHz, for 24h in 5% CO_2. In statistical analysis, neither significant nor reproducible difference was found between the micronucleus formation rates for all MF exposure conditions. To examine the effect on DNA damage, V79 cells were exposed to MMC with/without above three MF conditions, which potentiate micronucleus formation. Some statistically significant differences were found between the rates for all MF exposure conditions, however, no reproducible difference was found. These results suggested that the strong IF MFs used in this study did not induce micronucleus formation and did not affect DNA damage by MMC or DNA damage repair system in mammalian cells. Nakasono *et al.* [2009] [2010a] [2010b] investigated the effects of the IF MFs on genotoxicity in Mouse Lymphoma Assay (MLA). The L5178Y tk+/- -3.7.2c cells were exposed the IF MF of 0.91mT at 2 kHz, 1.1mT at 20 kHz or 0.11 mT at 60 kHz. In statistical analysis, neither significant nor reproducible difference in the mutation frequencies was found between exposure and control groups under the all MF exposure conditions. To examine the effects on DNA damage, the cells were exposed to each MF with MMS that potentiates mutation. In statistical analysis, neither significant nor reproducible difference in the mutation frequencies was found between exposure and control groups under the all MF exposure conditions. The strong, sinusoidal IF MFs at 2 kHz (0.91 mT), 20 kHz (1.1 mT) or 60 kHz (0.11 mT) did not have genotoxic or promotion potentials by in vitro tests.

K1.4 RF Electromagnetic Field and Microwaves

K1.4.1 *In Vivo* Studies

Masuda *et al.* studied whether albumin leakage and dark neurons were present in rat brains 14 and 50 days after a single 2-h exposure to a 915 MHz electromagnetic field [Masuda, 2009]. The whole-body average specific absorption rates of 0, 0.02, 0.2 and 2.0 W/kg in TEM cells for 2 h were studied. No albumin immunoreactivity was observed in the exposed groups. Dark neurons were rarely present with any statistically significant difference between exposed and sham exposed animals. This study thus failed to confirm the results of Salford *et al.* (Environ. Health Perspect. 111, 881–883, 2003).

Ogawa *et al.* studied whether gestational exposure to an EMF targeting the head region, similar to that from cellular phones, might affect embryogenesis in rats [Ogawa*, et al.*, 2009]. A 1.95 GHz wideband code division multiple access (W-CDMA) signal, which is one applied for the International Mobile Telecommunication 2000 (IMT-2000) system and used for the freedom of mobile multi- media access (FOMA), was employed for exposure for gestational days 7–17. The exposure was performed for 90 min/day in the morning. The spatial average SAR for individual brains was designed to be 0.67 and 2.0 W/kg with peak brain SARs of 3.1 and 7.0 W/kg for low and high exposures, respectively, and a whole-body average SAR less than 0.4 W/kg so as not to cause thermal effects due to temperature elevation. There were no differences in maternal body weight gain. No adverse effects of EMF exposure were observed on any reproductive and embryotoxic parameters such as number of live, dead or resorbed embryos, placental weights, sex ratios, weights or external, visceral or skeletal abnormalities of live fetuses.

Takahashi, *et al.*, investigated effects of whole-body exposure to 2.1 GHz radio frequency EMF on the rat fetus. The data did not reveal any adverse effects of exposure to a 2.14 GHz W-CDMA signal for 20 h/day. Thus none of the experimental findings demonstrated any consistent adverse biological effects of whole body exposure to the electromagnetic field on gestation and lactation in either dams or F1 rats or in the F2 offspring [Takahashi, *et al.*, 2009].

Salama *et al.* investigated the effect of exposure to electromagnetic radiation emitted from the mobile phone on sperm motility using the adult rabbit as a model [Salama, 2009]. Rabbits were exposed to radio frequency emitted from a mobile phone (900 MHz) kept in standby mode and positioned adjacent to the genitalia for 8 h daily for 12 weeks. A significant drop in both fructose levels and number of motile sperms was observed in the phone group at the 10th week. However, no correlation was found between the two values. The stress control animals showed a similar but significantly less decline in motility. In conclusion, the pulsed radio frequency emitted by the mobile phone kept in the standby position longitudinally affected sperm motility and fructose but not citrate levels in rabbit semen.

Salama *et al.* studied the accumulating effects of exposure to electromagnetic radiation emitted by a conventional mobile phone (standby position) on the testicular function and structure [Salama *et al.,* 2010]. Rabbits were exposed to radio frequency emitted from the mobile phone (800 MHz) in a standby position opposite to that of testes for 8 h daily for 12 weeks. A drop in the sperm concentration appeared in the phone group at week 6. This became statistically significant at week 8, compared with the two control (stress and ordinary) groups.

Motile sperm population showed similarity amongst the three study groups until week 10 when it declined significantly, and thereafter in the phone and stress control groups, with more significant decline in the phone animals. Histological examination showed also a significant decrease in the diameter of seminiferous tubules in the phone group vs. the stress and ordinary controls. In conclusion, low intensity pulsed radio frequency emitted by a conventional mobile phone kept in the standby position could affect the testicular function and structure in the adult rabbit.

Yamashita *et al.* elucidated the possible effects of short-term exposure to a 1439 MHz electromagnetic field employing time division multiple access (TDMA), which is the basis of the Japanese Personal Digital Cellular system, on estrogenic activity in rats [Yamashita *et al.,* 2010]. Rats were exposed for 4 h per day on three consecutive days to the 1439 MHz TDMA signal that produced 5.5–6.1 and 0.88–0.99 W/kg average SARs in the brain and the whole body, respectively. The uterine wet mass and serum estradiol level significantly increased in the 17 beta-estradiol injected group, while there were no differences among the other groups. Although negative effects of long-term electromagnetic field exposure must be thoroughly investigated before a final conclusion can be reached, our results do not support the assumption that the high frequency electromagnetic field used in cellular phones exerts estrogenic activity.

Tanaka *et al.* investigated the effect of pulsed radiofrequency (PRF) current on mechanical allodynia induced with resiniferatoxin (RTX) in rats [Tanaka, 2010]. Adult male Sprague-Dawley rats received a single intraperitoneal injection of RTX (200 microg/kg). Rats in group S(2) were assigned to receive PRF current to the right sciatic nerve for 2 minutes 1 week after RTX treatment; rats in group M(2), PRF current for 2 minutes 3 weeks after RTX treatment; rats in group L(2), PRF current for 2 minutes 5 weeks after RTX treatment; rats in group S(4), PRF current for 4 minutes 1 week after RTX treatment; rats in group S(6), PRF current for 6 minutes 1 week after RTX treatment; and rats in group S(0), no PRF current was delivered. In groups S(2), S(4), S(6), and M(2), the ipsilateral paw withdrawal thresholds significantly increased. A statistically significant difference was detected between the PRF-treated and PRF-untreated hindpaws. The ipsilateral-contralateral paw withdrawal thresholds after PRF procedures in group S(2) were significantly higher than those in groups M(2) and L(2). Between groups M(2) and L(2), significant differences were found 1, 2, 4, and 5 weeks after PRF procedures. The ipsilateral-contralateral paw withdrawal thresholds in group S(6) were significantly higher than those in groups S(2) and S(4) 5 weeks after PRF procedures. No significant difference was found between groups S(2) and S(4) at any time. After PRF procedures, no difference in the withdrawal latency after heat stimulation and no motor disturbance were observed at any time in all groups. In conclusions, PRF treatment was more effective when applied in the early stages of mechanical allodynia (1 week) in rats. Increased exposure time to PRF current from 2 to 6 minutes showed a significant anti-allodynic effect without motor impairment. They propose the application of PRF current for 6 minutes adjacent to the nerve as soon as possible when allodynia appears.

A 1.95 GHz wide-band code division multiple access (W-CDMA) signal, which is used for the freedom of mobile multimedia access (FOMA), was employed for whole body exposure for 5 hours per day, 7 days a week for 5 weeks. Whole-body average specific absorption rates (SAR) for individuals were designed to be 0.4 and 0.08 W/kg respectively. There were no differences in body weight gain or weights of the testis, epididymis, seminal vesicles, and prostate among the groups. The number of sperm in the testis and epididymis were not decreased in the electromagnetic field (EMF) exposed groups, and, in fact, the testicular sperm count was significantly increased with the 0.4 SAR. Abnormalities of sperm motility or morphology and the histological appearance of seminiferous tubules, including the stage of the spermatogenic cycle, were not observed. Thus, under the present exposure conditions, no testicular toxicity was evident.

Hirota, *et al.*, investigated direct observation of microcirculatory parameters in rat brain using cranial window technique to estimate effects of local exposure to radio-frequency electromagnetic field [Hirota, *et al.*, 2009a].

K1.4.2 *In Vitro* Studies

Hirose *et al.* studied the effects of low-level radiofrequency (RF) fields from mobile radio base stations employing the International Mobile Telecommunication 2000 (IMT-2000) cellular system to test the hypothesis that modulated RF fields act to induce phosphorylation and overexpression of heat shock protein hsp27 [Hirose, 2007]. Human glioblastoma A172 cells were exposed to Wideband Code Division Multiple Access (W-CDMA) radiation at SARs of 80 and 800 mW/kg for 2–48 h, and continuous wave (CW) radiation at 80 mW/kg for 24 h. Human IMR-90 fibroblasts from fetal lungs were exposed to W-CDMA at 80 and 800 mW/kg for 2 or 28 h, and CW at 80 mW/kg for 28 h. No significant differences in the expression levels of phosphorylated hsp27 at serine 82 (hsp27 [pS82]) were observed between the test groups exposed to W-CDMA or CW signal and the sham-exposed negative controls, as evaluated immediately after the exposure periods by bead-based multiplex assays and no noticeable differences in the gene expression of hsps were observed between the test groups and the negative controls by DNA Chip analysis. Our results confirm that exposure to low-level RF field up to 800 mW/kg does not induce phosphorylation of hsp27 or expression of hsp gene family.

Koyama *et al.* examined the effects of 2.45 GHz electromagnetic fields at SARs from 5 to 200 W/kg on bacterial mutations and the hypoxanthine-guanine phosphoribosyl transferase (HPRT) gene mutations [Koyama *et al.,* 2007]. Bacteria were exposed to high-frequency electromagnetic fields (HFEMF) for 30 min in Ames test and CHO-K1 cells were exposed to HFEMF for 2 h in examination of mutations of the HPRT gene. In Ames test, there was no significant difference in the frequency of revertant colonies between sham exposure and HFEMF-exposed groups. In examination of mutations of the HPRT gene, we detected a combination effect of simultaneous exposure to HFEMF and bleomycin at the respective SARs. A statistically significant difference was observed between the cells exposed to HFEMF at the SAR of 200 W/kg. Cells treated with the combination of HFEMF at SARs from 50 to 200 W/kg and bleomycin exhibited increased HPRT mutations. As the exposure to HFEMF induced an increase in temperature, these increases of mutation frequency may be a result of activation of bleomycin by heat. We consider that the increase of mutation frequency may be due to a thermal effect.

Hirose *et al.* conducted a large-scale *in vitro* study focusing on low-level radio-frequency (RF) fields from mobile radio base stations employing the International Mobile Telecommunication 2000 (IMT-2000) cellular system to test the hypothesis that modulated RF fields affect malignant transformation or other cellular stress responses [Hirose, 2008]. BALB/3T3 cells were continuously exposed to 2.1425 GHz W-CDMA RF fields at specific absorption rates (SARs) of 80 and 800 mW/kg for 6 weeks and malignant cell transformation was assessed. In addition, 3-methylcholanthrene (MCA)-treated cells were exposed to RF fields in a similar fashion, to assess for effects on tumor promotion. Finally, the effect of RF fields on tumor co-promotion was assessed in cells initiated with MCA and co-exposed to 12-Otetradecanoylphorbol-13-acetate (TPA). No significant differences in transformation frequency were observed between the test groups exposed to RF signals and the sham-exposed negative controls in the non-, MCA-, or MCA plus TPA-treated cells. Our studies found no evidence to support the hypothesis that RF fields may affect malignant transformation. Our results suggest that exposure to low-level RF radiation of up to 800 mW/kg does not induce cell transformation, which causes tumor formation.

Matsui *et al.* investigated the effects of exposure to RF fields (UMTS/ IMT-2000; 1950 MHz) on micronucleus (MN) formation in HL-60 cells [Matsui *et al.,* 2008]. The experiments were performed, as follows: 1) RF exposure, 2) Sham-exposure, 3) Control groups that were incubated in a conventional incubator, and 4) Positive control groups that were irradiated by X-rays with 1 and 3 Gy. The exposure conditions for the RF field were as follows: 1) SAR; 0.2, 1.0, 1.3, 1.6, 2.0 and 3.0 W/kg for 24 hours, and 2) SAR; 1.3 W/kg for 6, 24 and 72 hours. No significant differences in the frequencies of MN formation were observed in the RF exposure group compared with the sham-exposure and control groups. We did not observed any increase in MN formation by exposure to UMTS/IMT-2000 (1950 MHz) RF field.

Hirose *et al.* investigated the effect of RF fields on microglial cells in the brain to examine any biological effects on the central nervous system (CNS) induced by 1950 MHz Wideband Code Division Multiple Access (W-CDMA) RF field, which are controlled by the International Mobile Telecommunication-2000 (IMT-2000) cellular system, at specific absorption rates (SARs) of 0.2, 0.8, and 2.0 W/kg for 2 h [Hirose *et al.,* 2010]. Assay samples obtained 24 and 72 h after exposure were processed in a blind manner. Results showed that the percentage of cells positive for major histocompatibility complex (MHC) class II was similar between cells exposed to W-CDMA radiation and sham-exposed controls. No statistically significant differences were observed between any of the RF field exposure groups and the sham-exposed controls in percentage of MHC class II positive cells.

Further, no remarkable differences in the production of tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6) were observed between the test groups exposed to W-CDMA signal and the sham- exposed negative controls. These findings suggest that exposure to RF fields up to 2 W/kg does not activate microglial cells *in vitro*.

Yoshie *et. al*. investigated thermal tolerance of budding yeast exposed to radio -frequency electromagnetic fields (RFs) under the active temperature regulation evaluating the expression of mRNA relating to stress response in yeast cells [Yoshie *et al.,* 2009]. 50 W/kg SAR of RF was exposed to yeast cells. Incubation temperature was kept at 25°C. Stress response of yeast cells were analyzed by survival rate after heat treatment at 47 or 48°C for 5 min and level of gene expression as quantity of mRNA of four stress response genes. The effect on expression of *hsp82* in *S. cerevisiae* following RF exposure (2.45 GHz, 50 W/kg) did not observed in this study. This suggests that stress response pathway regulated by HSF might little respond to RF exposure under the condition in this study.

Narita *et al*. investigated the influence of a high-frequency electromagnetic field (HFEMF) at 2.45 GHz on neurite outgrowth of PC12VG cells cultured for 7 days after exposure to HFEMF at average specific absorption rates (SARs) of 1 and 10 W/kg for 4h [Narita *et al.,* 2009]. We found that HFEMF exposure slightly inhibited the percentage of neurite-bearing cells. However, at the same time, the average length of all neurites per neurite-bearing cell and the longest neurite length increased by approximately 10% and 5%, respectively. Significant increases in the average length of neurites, the longest neurite length and the percentage of neurite-bearing cells were observed in PC12VG cells cultured in the presence of NGF. These data suggest that exposure to a HFEMF of 2.45 GHz for 4h has no significant effect on neurite outgrowth in PC12VG cells.

Sekijima *et al*. investigated the mechanisms by which radiofrequency (RF) fields exert their activity, and the changes in both cell proliferation and the gene expression profile in the human cell lines, A172 (glioblastoma), H4 (neuroglioma), and IMR-90 (fibroblasts from normal fetal lung) following exposure to 2.1425 GHz continuous wave (CW) and Wideband Code Division Multiple Access (W-CDMA) RF fields at three field levels [Sekijima *et al*., 2010]. During the incubation phase, cells were exposed at the specific absorption rates (SARs) of 80, 250, or 800 mW/kg with both CW and W-CDMA RF fields for up to 96 h. Heat shock treat-ment was used as the positive control. No significant differences in cell growth or viability were observed between any test group exposed to W-CDMA or CW radiation and the sham-exposed negative controls. Using the Affymetrix Human Genome Array, only a very small (< 1%) number of available genes (ca. 16,000 to 19,000) exhibited altered expression in each experiment. The results confirm that low-level exposure to 2.1425 GHz CW and W-CDMA RF fields for up to 96 h did not act as an acute cytotoxicant in either cell proliferation or the gene expression profile. These results suggest that RF exposure up to the limit of whole-body average SAR levels as specified in the ICNIRP guidelines is unlikely to elicit a general stress response in the tested cell lines under these conditions.

K1.4.3 Other Studies

Takebayashi *et al.* used a novel approach for estimating the specific absorption rate (SAR) inside the tumour, taking account of spatial relationships between tumour localisation and intracranial radiofrequency distribution in a case–control study in Japan of brain tumours in relation to mobile phone use [Takebayashi *et al.,* 2008]. Personal interviews were carried out with 88 patients with glioma, 132 with meningioma, and 102 with pituitary adenoma (322 cases in total), and with 683 individually matched controls. All maximal SAR values were below 0.1 Wkg 1, far lower than the level at which thermal effects may occur, the adjusted odds ratios (ORs) for regular mobile phone users being 1.22 (95% confidence interval (CI): 0.63–2.37) for glioma and 0.70 (0.42–1.16) for meningioma. When the maximal SAR value inside the tumour tissue was accounted for in the exposure indices, the overall OR was again not increased and there was no significant trend towards an increasing OR in relation to SAR-derived exposure indices. A non-significant increase in OR among glioma patients in the heavily exposed group may reflect recall bias.

Furubayashi *et al.* conducted a double-blind, cross-over provocation study to confirm whether subjects with mobile phone related symptoms (MPRS) are more susceptible than control subjects to the effect of electromagnetic fields (EMF) emitted from base stations [Furubayashi *et al.,* 2009]. There were four EMF exposure conditions, each of which lasted 30 min: continuous, intermittent, and sham exposure with and without noise. Subjects were exposed to EMF of 2.14 GHz, 10 V/m (W-CDMA), in a shielded room to simulate whole-body exposure to EMF from base stations. The MPRS group did not differ from the controls in their ability to detect exposure to EMF. The two groups did not differ in their responses to real or sham EMF exposure according to any psychological, cognitive or autonomic assessment. In conclusion, we found no evidence of any causal link between hypersensitivity symptoms and exposure to EMF from base stations. Mizuno *et al.* investigated the effects of the third generation system on regional cerebral blood flow (rCBF) in humans [Mizuno *et al.,* 2009]. They compared effects of the electromagnetic field (EMF) emitted from the Wideband Code Division Multiple Access (W-CDMA) cellular system versus sham control exposure on rCBF in humans after unilateral 30 min EMF exposure. The subtraction analysis revealed no significant rCBF changes caused by the EMF conditions compared with the sham exposure, suggesting that EMF emitted by a third generation mobile phone does not affect rCBF in humans.

Rongen *et al.* reviewed the effects of exposure to radiofrequency electromagnetic fields (EMF), specifically related to the use of mobile telephones, on the nervous system in humans [Rongen *et al.,* 2009]. Exposure to a GSM-type signal may result in minor effects on brain activity, but such changes have never been found to relate to any adverse health effects. No consistent significant effects on cognitive performance in adults have been observed. If anything, any effect is small and exposure seems to improve performance. Effects in children did not differ from those in healthy adults. Studies on auditory and vestibular function are more unequivocal: neither hearing nor the sense of balance is influenced by short-term exposure to mobile phone signals. Subjective symptoms over a wide range, including headaches and migraine, fatigue, and skin itches, have been attributed to various radiofrequency sources both at home and at work. However, in provocation studies a causal relation between EMF exposure and symptoms has never been demonstrated. There are clear indications, however, that psychological factors such as the conscious expectation of effect may play an important role in this condition.

Okano *et al.* investigated whether exposure to a pulsed high-frequency electromagnetic field (pulsed EMF) emitted by a mobile phone has short-term effects on the inhibitory control of saccades [Okano *et al.,* 2010]. A double-blind, counterbalanced crossover study design was employed. They assessed the performance of 10 normal subjects on antisaccade (AS) and cued saccade (CUED) tasks as well as two types of overlap saccade (OL1, OL2) task before and after 30 min of exposure to EMF emitted by a mobile phone or sham exposure. After EMF or sham exposure, we observed a slight but significant shortening of latency in the CUED and OL2 tasks. AS amplitude decreased as well as the saccade velocities in the AS, CUED, and OL1 tasks after exposure. These changes occurred regardless of whether exposure was real or sham. The frequencies of prosaccades in the AS task, saccades to cue in the CUED task, and prematurely initiated saccades in the overlap (OL2) task did not change significantly after real or sham EMF exposure. They concluded that thirty minutes of mobile phone exposure has no significant short-term effect on the inhibitory control of saccades.

Sato., *et al.* conducted a case–case study of mobile phone use and acoustic neuroma using a self-administered postal questionnaire [Sato *et al.,* 2010]. A total of 1589 cases identified in 22 hospitals throughout Japan were invited to participate, and 787 cases (51%) actually participated. Associations between laterality of mobile phone use prior to the reference dates (1 and 5 years before diagnosis) and tumor location were analyzed. The overall risk ratio was 1.08 (95 % confidence interval (CI), 0.93–1.28) for regular mobile phone use until 1 year before diagnosis and 1.14 (95 % CI, 0.96–1.40) for regular mobile phone use until 5 years before diagnosis. A significantly increased risk was identified for mobile phone use for >20 min/day on average, with risk ratios of 2.74 at 1 year before diagnosis, and 3.08 at 5 years before diagnosis. Cases with ipsilateral combination of tumor location and more frequently used ear were found to have tumors with smaller diameters, suggesting an effect of detection bias. Furthermore, analysis of the distribution of left and right tumors suggested an effect of tumor-side-related recall bias for recall of mobile phone use at 5 years before diagnosis. The increased risk identified for mobile phone users with average call duration >20 min/day should be interpreted with caution, taking into account the possibilities of detection and recall biases. However, we could not conclude that the increased risk was entirely explicable by these biases, leaving open the possibility that mobile phone use increased the risk of acoustic neuroma.

K1.5 Other higher frequencies and other studies.

K1.5.1 Millimeter wave

Kojima *et al* [2009c] reported about thermal ocular injuries by irradiated to 60 GHz electromagnetic field in rabbit eye. Three different antenna systems such as a horn antenna and two lens antennas (6 and 9 mm diameter; phi6, phi9) were used. Morphological changes were assessed by slit-lamp microscopy. The most reproducible injuries without concurrent eyelid edema and corneal desiccation were achieved using the phi6 lens antenna: irradiation for 6 min led to an elevation of the corneal surface temperature (reaching 54.2 ± 0.9 degrees C) plus corneal edema and epithelial cell loss and the three types of millimeter-wave antennas can cause thermal injuries of varying types and levels. The thermal effects induced by millimeter-waves can apparently penetrate below the surface of the eye.

K1.6 Contact currents

Kamimura *et al* [2008, 2009, 2010a] reported the study of tracking methods to monitor threshold of contact currents for perception. Some differences were found in the perception threshold for ELF, 100 kHz and VLF band currents while no difference was observed in 300 kHz and 1 MHz currents.

K2 Dosimetry

K2.1 Numerical dosimetry using voxel human models

Nagaoka and his colleagues have developed various voxel human models based on Japanese MRI. They have applied Free-Form Deformation (FFD) technique to voxel human models to develop child models based on an adult voxel model [Nagaoka 2008b] or to change the posture of a voxel human model [Nagaoka 2008a]. Recently they have also developed new techniques to change the posture of the voxel human models without anatomical knowledge [Nagaoka 2009b].

Dosimetry of pregnant woman models is one of the most important themes in EMF safety as described in 2006 WHO Research Agenda. Chiba University and NICT have developed 26-weeks pregnant woman model and applied it for numerical calculation of SAR and temperature due to a VHF-band professional transceiver [Akimoto *et al.*, 2008a, 2008b, 2009a, 2009b, 2009c, 2010a, 2010b, and 2010c]. Togashi *et al.*, have studied on the SAR in the pregnant woman model due to cellular phones [Togashi *et al.*, 2008]. Kawai et al., have also reported SAR characteristics of the embryo in a pregnant woman model during early stage and found that the maximum averaged SAR of the embryo with the incident power density of the ICNIRP reference level is lower than the basic restriction, i.e., 0.08 W/kg, from 10 MHz to 1.5 GHz [Kawai *et al.*, 2009].

Hirata *et al.*, have reported the temperature elevation due to human-body exposure to RF fields and compared between adults, children and laboratory animals [Hirata *et al.,* 2008c, 2009d]. They also investigated on the averaging mass for local SAR and the temperature elevation due to EMF from a dipole antenna [Hirata et al., 2008d and 2009e]. Onishi *et al.*, have numerically estimated the SAR and temperature elevation in a Japanese human model due to the use of body-worn wireless devices [Onishi *et al.*, 2009a, 2010a, and 2010b].

Furthermore Hirata *et al.*, have improved thermal parameters used for numerical simulations of temperature elevation and reported the importance of time variation of blood temperature [Hirata *et al.,* 2009a]. They have also proposed conservative models for whole-body averaged SAR based on the numerical calculations using the voxel human models [Hirata *et al.*, 2008e].

Various characteristics of whole-body averaged SAR which is used for the most important basic restriction for RF region have been investigated. Polarization of the EM wave have been reported as the important factor for human-body SAR and concluded that the horizontal polarization is the worst case at 2 GHz compared with the vertical polarization which is assumed for the worst condition at lower frequencies [Hirata *et al.*, 2009b and 2009f]. Hirata *et al.,* have also proposed the estimation formula for the whole-body averaged SAR for the resonant frequency region [Hirata *et al.,* 2010b].

Whole-body averaged SAR of children has been great concerns as ICNIRP Statement has pointed out in 2009. In Japan, Nagaoka *et al.,* have reported the whole-body averaged SAR of children [Nagaoka 2008a and 2009a].

Human SAR characteristics in complex environments have been investigated. Simba *et al.*, have reported the effect of SAR enhancement or passive exposure in an elevator where multiple reflection causes hot spots of EMF [Simba, et al., 2009a and 2009b]. Wang, *et al.*, have investigated human-body exposure to EMF when using wireless body-area network (WBAN) devices with UWB signals [Wang J.*, et al.*, 2009; Wang Q.*, et al.*, 2009a and 2009b]. Arima *et al.*, have developed a new modeling method for FDTD calculation of a human voxel model standing on lossy ground plane using the surface impedance technique [Arima *et al.*, 2009].

Applications of millimeter wave have recently increased while the needs for accurate dosimetry have also been growing. Kanezaki *et al.,* have conducted a fundamental investigation using a multi-layer flat model of human skin and subcutaneous tissues exposed to millimeter wave. They have reported the dependence of the SAR and temperature elevation due to the millimeter wave exposure on the electrical and thermal parameters [Kanezaki *et al.,* 2009 and 2010].

Numerical dosimetry using voxel human models have also been applied for EMF dosimetry in ELF frequency region. Hirata *et al.,* have conducted the detailed calculation of induced current and *in-situ* electric field strength in a human body exposed to ELF magnetic field [Hirata *et al.,* 2009c]. This study is referred in the revision of the ICNIRP guidelines issued in 2010. The averaging volume for *in-situ* electric field, used for the basic restrictions in the ICNIRP guidelines, has also been investigated [Hirata *et al.*, 2010c; Takano, *et al.,* 2010]. Inter-laboratory comparison has also been conducted among Japanese research group [Hirata *et al.*, 2010e; Yamazaki, *et al.*, 2009]. It is found from the comparison that differences in the maximal and 99th percentile value of the in situ electric field were less than 30 and 10 % except for the results of one group and that differences in the current density averaged over 1 cm^2 of the central nerve tissue are 10 % or less except for the results of one group. Kamimura has proposed high-speed calculation procedure for ELF dosimetry [Kamimura 2010b].

Yamazaki has reported a calculation of induced electric field and current for human-body exposure to magnetic field in the context of compliance testing [Yamazaki 2010].

Tarao *et al.*, have conducted numerical calculations of internal body resistance at power frequency and compared with experimental measurements. They found similar trend in electric potential distribution but significant difference in absolute resistance values between the numerical calculations and the experimental measurements.

Nagai *et al.*, have estimated *in situ* electric field causing electro-stimulation from conductor contact of charged human using a dispersive FDTD model and the indices used in international guidelines [Nagaoi et al., 2010].

Intermediate frequency region (300 Hz to 10 MHz) has also been great concerns in dosimetry research fields because of extensive growing new wireless systems operating in this frequency region, such as EAS/RFID, IH cooking systems, and wireless power transmission systems. Suzuki *et al.,* have conducted numerical estimation of induced current density and in-situ electric field strength in the pregnant woman model exposed to internal frequency magnetic field [Suzuki *et al.,* 2009].

K2.2 Compliance methods for EMF applications to EMF safety guidelines and exposure assessment

In order to evaluate the compliance of EMF applications with EMF safety guidelines, we need to estimate internal dose of a human body exposed to EMF, i.e., SAR or induced (*in-situ*) electric field strength, or incident electromagnetic field strength as reference levels described in safety guidelines. The research group of NTT DoCoMo and their colleagues has extensively studied on the evaluation methods for SAR by a cellular phone and for E-field radiated from a base station antenna.

Onishi with NTT DoCoMo also joined an international research group on the evaluation method of the compliance of multiple RF sources [Faraone, *et al.*, 2009]. Higashiyama and his colleagues have proposed a RF field measurement method around W-CDMA base stations and reported detailed characteristics of E-field distribution around the base station [Higashiyama, et al., 2009a, 2009b, 2010a, 2010b, and 2010c]. Iyama *et al.,* have proposed a novel SAR measurement method using multiple probes embedded in a flat phantom [Iyama *et al.,* 2008a and 2008b; Kiminami 2008a and 2008b; Onishi 2008a and 2009b]. They also developed three-axial electro-optic (EO) SAR probe [Iyama *et al.*, 2009a; Kiminami 2008c]. A novel SAR measurement procedure for multiple-antenna transmitter such as MIMO, which has recently been introduced into advanced wireless devices to realize high-speed data transmission, has been proposed [Iyama *et al.*, 2009b, 2010a, and 2010b; Onishi 2008b].

The researchers of National Institute of Information and Communications (NICT) have also conducted researches on the compliance procedures. Simple and fast measurement methods using a novel flat phantom have been proposed [Hamada*, et al.*, 2009a and 2009b]. They also studied on a novel calibration method for SAR probes using a small standard antenna in phantom liquid in cooperation with Niigata University [Watanabe T., *et al.*, 2009; Ishii, *et al.*, 2008].

Exposure assessment or experimental measurement of electric and magnetic field strength in low frequency region have also been investigated in Japan. Sato *et al.*, with his colleagues of Utsunomiya University have developed a free scanning method for measuring magnetic field using a magnetic tracker [Sato K *et al.,* 2009 and 2010]. Tanaka, et al., with his colleagues of Nagoya Institute of Technology has reported frequency spectrum of electromagnetic fields leaked form household appliance from 40 to 800 Hz [Tanaka K., *et al.*, 2009]. Hosono *et al.*, have developed array sensor system for intermediate-frequency magnetic field radiated from IH hob or EAS/RFID [Hosono *et al.*, 2010].

Very wide-frequency EMF measurement around the Large Helical Device (LHD) has also been reported [Uda, *et al.,* 2009]. It is shown that usual leakage of the static magnetic field strength was less than 0.1 mT, that the leakage of the electric and magnetic fields from the Ion Cyclotron Range of Frequency (ICRF) plasma heating sources of 25-100 MHz were less than occupational regulation levels, and that high-strength extremely-low-frequency (ELF) electromagnetic levels were measured near the magnetic coil power supply boxes.

K2.3 Development of exposure setups and dosimetry for medical and biological studies.

Arima *et al.,* have developed a local-exposure setup for the head of a rat. Applying this setup to a cranial window rat, real-time observation can be available. They have evaluated SAR of the rat fixed in the setup and found that the localized head exposure similar to the case of the mobile-phone use in the proximity of a human head can be realized [Usui *et al.,* 2010]. Wang, *et al.*, have developed *in vivo* exposure setup simulating whole-body exposure to RF signals from base stations [Wang *et al.*, 2008a and 2008c] and partial-body exposure to RF signal from cellular phones [Wang *et al.*, 2008b] for pregnant rats.

Wake *et al.*, has developed the estimation method for epidemiological studies on cellular-phone use and brain cancer, i.e., *INTERPHONE* study led by WHO/ IARC, [Cardis *et al.*, 2008; Varsier *et al.*, 2008a, 2008b and 2008c; Wake *et al.*, 2009]. Especially the development of a novel estimation procedure for actual dose around brain cancer region based on the categorization of cellular phones used by subjects provided more reliable estimation of the relationship between the brain cancer and cellular phone use for Japanese epidemiological study [Takebayashi, *et al.*, 2008].

Hirata *et al.,* have studied on temperature elevation of laboratory animals due to RF exposure. They found good agreement between the experimental measurement and the numerically calculation with optimized thermal parameters [Hirata 2008a and 2008b]. They have also investigated the thresholds for thermal stress for 2.45-GHz microwave exposure in rabbits [Hirata 2010d].

Kozai *et al.*, have conducted fine resolution E-field measurement from millimeter-wave lens antenna which have been used for thermal sensation human studies or ocular effects of rabbit eyes [Kozai *et al.,* 2009; Kouzai *et al.*, 2010].

Based on the measurement, they have reconstructed the millimeter-wave beam radiation from the lens antenna with plane-wave spectrum method and numerically calculated the SAR in the human skin.

IH cooking systems, RFID, EAS, wireless power transmission systems and so on operate in intermediate frequency (IF; 300 Hz to 10 MHz) region. Health effects of IF EMF are also important topics in Japan because those systems are very popular in public environment. Fujita *et al.*, have developed an exposure setup for *in vitro* studies on biological investigation in intermediate-frequency region. The system can realize 6.25 mT (rms) at 23 kHz with uniformity within 5 %. Ikehata *et al.,* have also developed an *in vitro* exposure setup for simulating the magnetic field (3.9 mT at 20 kHz) exposure from IH cooking systems with high-performance temperature control system (37±1℃). The research group has also developed a high-performance magnetic field generator at 20 kHz [Kogure *et al.*, 2009]. Shigemitsu *et al.*, have developed an exposure system for *in vivo* studies on 20 kHz magnetic-field exposure [Shigemitsu *et al.*, 2009a].

K2.4 Mechanism between biological tissues and EMF.

Koyama *et al.,* has conducted *in vivo* measurements for complex permittivities of human skin using time-domain reflectometry (TDR) method from 300 MHz to 6 GHz [Koyama *et al.,* 2010]. Sakai *et al.,* have recently reported complex permittivities of biological tissues and organs up to 50 GHz and also proposed a temperature-compensation technique based on the temperature characteristics of the water relaxation mechanism [Sakai T., *et al.*, 2010].

Sekino, *et al.*, have developed a magnetic resonance imaging of electric properties in living bodies [Sekino *et al.*, 2007 and 2008b]. Recently they also measured low-frequency conductivity tensor of rat brain tissue [Sekino *et al.*, 2009b; Imae *et al.*, 2008].

Cespedes *et al.,* have investigated the effects of radio frequency magnetic fields on iron release and uptake from and in cage proteins. They reported the radio frequency magnetic fields of 1 MHz and 30 μT can increase the release of iron ion from cage proteins up to a factor of 3 [Cespedes, *et al.*, 2009]. They also investigated the mechanism of this effect using Raman spectroscopy [Cespedes, *et al.*, 2010].

Hinou *et al.*, have investigated the effect of microwave (2.45 GHz) radiation on glycosylation promoted by solid super acid in supercritical carbon dioxide. They reported that microwave irradiation without alteration of the temperature of the reaction solution enhanced reaction yield when aliphatic acceptors were employed while no enhancement was observed when a phenolic acceptor was employed [Hinou, *et al.,* 2009].

K2.5 Dosimetry for medical application (see also K3)

Temperature elevation of a human body in a MRI system is required to be estimated, especially in a high-magnetic-field-strength MRI system introduced recently. Kikuchi *et al.,* have studied detailed SAR and temperature elevation of a pregnant woman in a MRI system [Kikuchi 2008a, 2008b, 2009a, 2009b, 2009b, and 2010]. They found that in a thermal equilibrium state, the temperature elevations in the intrinsic tissues of the woman and fetal tissues were 0.85 and 0.61 °C, respectively, at a whole-body averaged specific absorption rate of 2.0 W/kg, which is the restriction value of the International Electrotechnical Commission (IEC) for the normal operating mode although the maximum temperature elevation exceeded the recommendation described in ICNIRP statement on MRI issued in 2004.

Saito and his colleagues with Chiba University have investigated the application of the thermograph method to the temperature elevation in a human body exposed to high-strength RF fields radiated from a birdcage coil of 3-T MRI system [Kawamura *et al.,* 2009; Saito K., *et al.,* 2009]. Sekino *et al.*, with The University of Tokyo have also conducted FDTD simulation of RF electromagnetic field and signal inhomogeneities in ultra-high-field MRI system [Sekino *et al.*, 2008a].

Microwave radiometry is a promised technique for future medical treatment such as noninvasive temperature measurement during hypothermal neural rescue for newborns. Sugiura, *et al.*, have developed high-accurate radiometry system with five-band microwave signals [Sugiura *et al.,* 2010]. Hirata *et al.*, have investigated the validity of inverse coupler to improve temperature resolution of one-band microwave radiometer for non-invasive brain temperature monitoring [Hirata *et al.,* 2010a].

Higaki *et al.,* have evaluated the SAR and current density during the use of energy transmission for artificial hearts and compared with the ICNIRP guidelines [Higaki *et al.*, 2010]. Sato et al., have investigated the heating level due to a prototype charger system for a cardiac pacemaker and also developed a wireless communication system in real-time internal dose measurement system [Sato T *et al.*, 2008; Sato F., 2009]. Watanabe, *et al.*, have reported SAR enhancement in a human body with an implantable pacemaker using a cellular phone due to the reflection at the metal boundary of the household of the pacemaker [Watanabe *et al.,* 2010].

K3 Biomedical Applications

K3.1 Medical treatment

Hyperthermia has been one of the most important research fields on medical application of EMF. Prof. Ito with Chiba University and his colleagues have extensively studied on MW hyperthermia and coagulation with coaxial antennas [Saito K., et al., 2008a, 2008b, 2008c, 2010a, 2010b, 2010c, and 2010d]. They reported five clinical cases (four cases were supraclavicular or inguinal node metastasis and one was a soft palate primary lesion) [Aoyagi, *et al.*, 2008] and experimental evaluation of thermal treatment of bile duct carcinoma [Tsubouchi, *et al.*, 2010]. They also developed a circular loop antenna combined with high intensity focused ultrasound (HIFU) treatment system [Ishikawa, *et al.*, 2010a and 2010b]. They furthermore developed an external microwave hyperthermia system for treatment of pleural metastasis in orthotopic lung cancer model and evaluated the system in vitro and in vivo [Motomura, *et al.*, 2010].

Watanabe Y., *et al.*, have developed a second-generation radiofrequency ablation system. They used MgFe2O4 needles and introduced alternating magnetic field for human cancer therapy [Watanabe Y., *et al.*, 2009].

Prof. Matsuki with Tohoku University and his colleagues have also studied on the hyperthermia with magnetic field. They developed a novel method called as soft-heating medhot in which a small elongated element is implanted inside the body and heated by strong magnetic field excited by a coil [Furiya *et al.,* 2009]. They studied on the magnetic particle heated by incident magnetic field [Takura, et al., 2008a, 2008b, and 2009]. Other research group has also investigated the heat ability of the magnetic nanoparticles under AC magnetic field for cancer therapy [Motoyama, *et al.*, 2008].

Matsumine *et al.,* have reviewed the difficulty of the application of hyperthermia to bone tissues because of their deep location from the body surface and low conductivity. In order to overcome these difficulties, they developed a novel hyperthermia treatment for bone metastases using magnetic materials [Matsumine, *et al.*, 2011].

Takahashi *et al.*, have applied MW hyperthermia to osteoarthritis, one of the most frequency muscleoskeltal disorders in the elderly population, and reported that the MW heating can increase Hsp7 which protects the cartilage and inhibits the apoptosis of chondrocytes [Takahashi *et al.*, 2009].

Baba *et al.*, have studied on medical treatment of electrical stimulation to ischemia stroke. They conducted electric cortical stimulation (0 to 200 μA at 0 to 50 Hz) of adult Wistra rats and found that the electrical stimulation abrogated the ischemia-associated increase in apoptotic cells in the injured cortex [Baba *et al.*, 2009]. Kato *et al.*, have developed a novel functional electrical stimulation method using small implanted stimulators under the skin at a depth of 10—20 mm and a magnetic coupling system to transport stimulus energy and signals noninvasively. They developed a magnetic connective dual resonance (MCDR) antenna with two resonance circuit for the magnetic coupling system [Kato, *et al.*, 2009].

Nakajima *et al.*, have studied on the effect of electroacupuncture on the healing process of tibia fracture in a rat model. They used the electroacupuncture (50 Hz, 20 μA, 20 min) and reported that the treatment accelerated bone healing [Nakajima et al., 2010].

Transcranial magnetic stimulation has been developed and studied by Prof. Ueno and his colleague long time. Recently Tsuyama *et al.*, investigated the effects of coil parameters on the stimulation area by transcranial magnetic stimulation system [Tsuyama, *et al.,* 2009].

Wireless power transmission systems for implanted medical devices have been investigated. Prof. Matsuki and his colleagues have studied on a contactless power transmission for implantable medical devices [Tokuhara, *et al.*, 2008]. They pointed out that the eddy current (loss) caused by the metal case of the medical devices for magnetically energy coupling must be reduced [Komai, *et al.*, 2009]. Same research group has also developed a desktop contactless power station system using spiral coils [Miyamori, *et al,*, 2009]. MW is also used for the wireless power transmission. Kumagai *et al.,* have developed a small 915 MHz antenna for wireless power transmission for medical applications [Kumagai *et al.*, 2010].

Takura, *et al.*, have studied thermosensitive magnetic powder that was coated with Ag-paste for cancer therapy [Takura *et al.*, 2008a].

K3.2 Medical diagnosis

Hoshino *et al.*, have reported detailed measurement and analysis of magnet-cardiograms (MCG) and body surface potential maps (BSPMs) using 39-channnel superconducting quantum interface device (SQUID) [Hoshino, *et al.*, 2009].

Kotani *et al.*, have investigated measurement methods for respiratory sinus arrhythmia as a selective index of cardiac vagal activity under the condition of body motion (keyboard typing and mental arithmetic with touching panel). They reported that elastic chest band is suitable under the quiet condition, while thermistor is suitable under the condition of body motion [Kotani, *et al.*, 2007]. They also investigated the multiple effects of respiration on cardiovascular variability in different postures by analyzing respiratory sinus arrhythmia and respiratory-related blood pressure variations [Kotani , *et al.*, 2008].

Sekino, *et al.*, reported improvement method to detect transient changes in magnetic resonance signal intensity by neuronal electrical activities [Sekino, *et al.*, 2009a]

Sekino *et al.*, have studied on improvement of MRI system with an off-centered distribution of homogeneous magnetic field zone using superconducting magnet. They fabricated the sytem for a functional-MRI-based Benton visual retention test [Sekino, *et al.*, 2010].

Shinohe, *et al.,* have developed X-ray internal dosimeter using a wireless communication system similar to RFID. A signal transmission small coil with X-ray detector (CdTe) is implanted in a human body and 3-MHz magnetic field is used to read the information noninvasively [Shinohe, *et al.*, 2008 and 2009]. An equivalent human model has been developed for medical applications by Prof. Ito and his colleagues with Chiba University [Uno, *et al.,* 2010]. The same research group have also developed a dynamic phantom for evaluation for breath detection Doppler radar [Yonebayashi, *et al.*, 2010a and 2010b].

Sugiura *et al.,* have developed and improved the multi-frequency microwave radiometer system for measuring deep brain temperature in new born infants [Sugiura, *et al.*, 2009].

Hayami *et al.,* reported magnetic field variation of fiber loss on a peripheral nerve. The loss of nerve fibers, which is observed in some neuropathies, is considered as the cause of low amplitude and slow conduction of the wave [Hayami, *et al.*, 2008].

Sann *et al.,* investigated discriminating multiple source components of magnetocephalogram by time-frequency analysis [Sano, *et al.*, 2009].

Sato, *et al.*, reported variations and differences in evoked EEG by transcranial magnetic stimulation [Sato*, et al.*, 2008].

K3.3 Neuronal circuit development in vitro

Prof. Jimbo's group is active in artificial neuronal circuit development in vitro and studies its behavior. Goto, *et al.*, developed "Micropipette drawing" technique to develop micropatterning of neurite outgrowth and recording its electrical activity [Goto, *et al.*, 2009, 2010a, 2010b]. Hattori, *et al.*, reported direction control of information transfer between neuronal cells using asymmetric three-dimensional microstructure [Hattori, *et al.*, 2008]. Hirota, *et al.,* reported reconstruction of visual information processing system using retina cells and superior colliculus *in vitro* [Hirota, *et al.,* 2008, 2009b]. Moriguchi, *et al.*, investigated site-selective stimulation of neuronal networks that was constructed on micro-patterning electrode and recording of electric activity of the neuronal circuits [Moriguchi, *et al.*, 2008a, 2008b, 2008c, 2008d]. Suzurikawa, *et al.,* investigated methods for stimulation of cultured neurons using light-addressable electrode with hydrogenated amorphous silicon and low-conductive passivation layer [Suzurikawa, *et al.,* 2007a, 2007b, 2008a, 2008b, 2008c, 2009]. Takayama, *et al.*, used P19 embryonal carcinoma cells to establish functional neuronal network on microelectrode array and induced ensemble calcium oscillations within network [Takeyama, *et al.,* 2007, 2008a, 2008b, 2008c, 2009a, 2009b, 2009c, 2009d]. In addition, they showed interaction of hybrid in vitro neuronal network by co-culture of P19 cell-derived neuronal networks and mouse cortical networks [Takeyama *et al.,* 2010a, 2010b, 2010c]. Takeuchi*, et al.,* investigated developmental changes in spontaneous beating rhythm of cardiac myocytes [Takeuchi*, et al.*, 2008]. They developed semi-separated co-culture system for electrical stimulation and extracellular recording of sympathetic neuron and cardiomyocyte to investigate their relationship [Takeuchi, *et al.,* 2009a, 2009b, 2010a, 2010b, 2010c, 2010d]. Tonomura, *et al.,* applied MEMS device for electrophysiological measurement with micro channel array for cellular network analysis and parallel multipoint recording of aligned and cultured neurons [Tonomura, *et al.,* 2007, 2008].

K3.4 Medical instrumentation

Abe*, et al.,* developed high throughout automated bioscreening system using magnetic beads to elucidate molecular mechanisms of anticancer drugs [Abe*, et al.,* 2009]..

K3.5 Electromagnetic interference (EMI) of implanted medical devices.

EMI with a bipolar pacemaker in a patient with sick sinus syndrome by an IH rice cooker has also been investigated [Nagatomo, 2009].

Watanabe *et al.,* have investigated the interference voltage of a pacemaker embedded in a human phantom, which has been used for experimental investigation promoted by Ministry of Internal Affair and Communications, by a cellular phone model [Watanabe R *et al.,* 2009]. They found good agreement between the numerical calculation and the experimental measurement.

Kitagawa *et al.,* have investigated the E-field distribution inside of the elevator with humans with cellular phones [Kitagawa *et al.,* 2009]. The estimated data can be used for risk assessment of the EMI of implantable cardiac pacemakers.

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