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Literature on intermediate frequency RFR

Aerts S, Calderon C, Valič B, Maslanyj M, Addison D, Mee T, Goiceanu C, Verloock L, Van van den Bossche M, Gajšek P, Vermeulen R, Röösli M, Cardis E, Martens L, Joseph W. Measurements of intermediate-frequency electric and magnetic fields in households. Environ Res 154:160-170, 2017.

Historically, assessment of human exposure to electric and magnetic fields has focused on the extremely-low-frequency (ELF) and radiofrequency (RF) ranges. However, research on the typically emitted fields in the intermediate-frequency (IF) range (300Hz to 1MHz) as well as potential effects of IF fields on the human body remains limited, although the range of household appliances with electrical components working in the IF range has grown significantly (e.g., induction cookers and compact fluorescent lighting). In this study, an extensive measurement survey was performed on the levels of electric and magnetic fields in the IF range typically present in residences as well as emitted by a wide range of household appliances under real-life circumstances. Using spot measurements, residential IF field levels were found to be generally low, while the use of certain appliances at close distance (20cm) may result in a relatively high exposure. Overall, appliance emissions contained either harmonic signals, with fundamental frequencies between 6kHz and 300kHz, which were sometimes accompanied by regions in the IF spectrum of rather noisy, elevated field strengths, or much more capricious spectra, dominated by 50Hz harmonics emanating far in the IF domain. The maximum peak field strengths recorded at 20cm were 41.5V/m and 2.7A/m, both from induction cookers. Finally, none of the appliance emissions in the IF range exceeded the exposure summation rules recommended by the International Commission on Non-Ionizing Radiation Protection guidelines and the International Electrotechnical Commission (IEC 62233) standard at 20cm and beyond (maximum exposure quotients EQ_E 1.0 and $_EQ_H$ 0.13).

Bi J, Jing H, Zhou CL, Gao P, Han F, Li G, Zhang S. Regulation of skeletal myogenesis in C2C12 cells through modulation of Pax7, MyoD, and myogenin via different low-frequency electromagnetic field energies. Technol Health Care 2022;30(S1):371-382.

Background: A low-frequency electromagnetic field (LF-EMF) exerts important biological effects on the human body. **Objective:** We previously studied the immunity and atrophy of gastrocnemius muscles in rats with spinal cord injuries and found that LF-EMF with a magnetic flux density of 1.5 mT exerted excellent therapeutic and preventive effects on reducing myotubes and increasing spatium intermusculare. However, the effects of LF-EMF on all stages of skeletal myogenesis, such as activation, proliferation, differentiation, and fusion of satellite cells to myotubes as stimulated by myogenic regulatoryfactors (MRFs), have not been fully elucidated. **Methods:** This study investigated the optimal LF-EMF magnetic flux density that exerted maximal effects on all stages of C2C12 cell skeletal myogenesis as well as its impact on regulatory MRFs. **Results:** The results showed that an LF-EMF with a magnetic flux density of 2.0 mT could activate C2C12 cells and upregulate the proliferation-promoting transcription factor PAX7. On the other hand, 1.5 mT EMF could upregulate the expression of MyoD and

myogenin. **Conclusion:** LF-EMF could prevent the disappearance of myotubes, with different magnetic flux densities of LF-EMF exerting independent and positive effects on skeletal myogenesis such as satellite cell activation and proliferation, muscle cell differentiation, and myocyte fusion.

Bodewein L, Schmiedchen K, Dechent D, Stunder D, Graefrath D, Winter L, Kraus T, Driessen S. 2019. Systematic review on the biological effects of electric, magnetic and electromagnetic fields in the intermediate frequency range (300 Hz to 1 MHz). Environmental research.
171:247-259. (Review)

Background: Many novel technologies, including induction cookers or wireless power transfer, produce electric fields (EF), magnetic fields (MF) or electromagnetic fields (EMF) in the intermediate frequency (IF) range. The effects of such fields on biological systems, however, have been poorly investigated. The aim of this systematic review was to provide an update of the state of research and to evaluate the potential for adverse effects of EF, MF and EMF in the IF range (300 Hz to 1 MHz) on biological systems. **Methods:** The review was prepared in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Methodical limitations in individual studies were assessed using the Office of Health Assessment and Translation (OHAT) Risk of Bias Rating Tool for Human and Animal Studies. **Results:** Fifty-six studies exposing humans, animals or in vitro systems were eligible for this review. In these studies, many different endpoints were examined and most of the findings were obtained in studies with exposure to MF. For most endpoints, however, the reviewed studies yielded inconsistent results, with some studies indicating no effect and some linking IF exposure with adverse effects. In the majority of the included studies, the applied field strengths were above the International Commission on Non-Ionizing Radiation Protection (ICNIRP) reference levels for the general public and the applied frequencies were mainly below 100 kHz. Furthermore, many of the reviewed studies suffered from methodical limitations which lowered the credibility of the reported results. **Conclusion:** Due to the large heterogeneity in study designs, endpoints and exposed systems, as well as the inconsistent results and methodical limitations in many studies, the quality of evidence for adverse effects remains inadequate for drawing a conclusion on investigated biological effects of IF fields for most endpoints. We recommend that in future studies, effects of EF, MF and EMF in the IF range should be investigated more systematically, i.e., studies should consider various frequencies to identify potential frequency-dependent effects and apply different field strengths, especially if threshold-dependent effects are expected. Priority should be given to the investigation of acute effects, like induction of phosphenes, perception, excitation of nerves or muscles and thermal effects. This would be an important step towards the validation of the reference levels recommended by ICNIRP. Furthermore, we recommend that any new studies aim at implementing high quality dosimetry and minimizing sources of risk of bias.

Brech A, Kubinyi G, Németh Z, Bakos J, Fiocchi S, Thuróczy G. Genotoxic effects of intermediate frequency magnetic fields on blood leukocytes in vitro. Mutat Res Genet Toxicol Environ Mutagen 845:403060, 2019.

The widespread presence of electromagnetic sources in daily life has initiated several studies on the effects of radiofrequency and power frequency fields. Only few investigations on the genotoxic effects of exposure to intermediate frequency magnetic fields (IF-MF) have been done so far. Therefore, the aim of this study was to evaluate possible genotoxic effects of exposure to 123.90 kHz and 250.80 kHz IF-MF on canine and human blood. Blood was exposed to IF-MF at 630 A/m (0.79 mT) and 80 A/m (0.10 m T) with exposure durations of 1-5 h (hourly), 20 and 24 h. Cylindrically divided Petri dish system was developed for in vitro exposures where different induced current could be achieved in the samples at the same magnetic flux density level. For the assessment of genotoxicity the alkaline comet assay was applied. We detected a statistically significant increase in DNA damage only following 20 h exposure to IF-MF.

Chen J-S, Tsai L-K, Yeh T-Y, Li T-S, Li C-H, Wei Z-H, Lo N-W, Ju J-C. Effects of electromagnetic waves on oocyte maturation and embryonic development in pigs. J Reprod Dev 67(6):392-401, 2021.

Our living environment has been full of electromagnetic radiation (EMR) due to the prevailing electronic devices and equipment. Intermediate frequency electromagnetic field (IF-EMF) or waves constitute a significant part of EMR; therefore, an increasing number of household electrical appliances have become a source of IF-EMF, and concerns about IF-EMF on health are gaining more attention. However, little information is available about its impact on female reproductive traits, such as germ cell viability and early embryonic development, particularly at the cellular and molecular levels. In this study, we used porcine oocytes as a model system to explore the effect of IF-EMF at various intensities on the in vitro maturation (IVM) of oocytes and their subsequent embryonic development. Our results showed that no difference in oocyte maturation rates was detected among groups, but the cleavage and blastocyst rates of parthenotes derived from EMF-treated oocytes decreased with the weaker IF-EMF intensity (25 and 50 Gauss) groups compared to the control group ($P < 0.05$). For cytoplasmic maturation, the weaker IF-EMF intensity groups also showed a peripheral pattern of mitochondrial distribution resembling that of immature oocytes and increased autophagy activity. No obvious differences in cytoskeletal distribution and total cell numbers of blastocysts were investigated in the four IF-EMF treatments compared to those in the control group. Although the underlying mechanism associated with EMF effects on oocytes and embryos is still elusive, we have demonstrated that low intensity IF-EMF exerts harmful effects on porcine oocytes during the maturation stage, carrying over such effects to their subsequent embryonic development.

Chiang H, Wu R, Shao B, Fu Y, Yao G, Lu D. 1995. Pulsed magnetic field from video display terminals enhances teratogenic effects of cytosine arabinoside in mice. Bioelectromagnetics. 16(1):70- 74.

Eighty-nine Swiss Webster mice were randomly divided into four groups: a control group, a pulsed magnetic field (PMF) group, a cytosine arabinoside (ara-C, a teratogen) group, and a combined PMF + ara-C group. Mice in the PMF and PMF + ara-C groups were irradiated with a PMF (a sawtooth waveform with 52 microseconds rise time, 12 microseconds decay time, and 15.6 kHz frequency) at a peak magnetic flux density of 40 microT for 4 hours daily on days 6-17 of gestation. The mice in the ara-C and the PMF + ara-C groups were injected intraperitoneally on day 9 of gestation with 10 mg/kg of ara-C. The incidence of resorption and dead fetuses was

not affected by PMF but was increased by ara-C injection. The malformation incidence of cleft palate (CP) and/or cleft lip (CL) was significantly higher in all three of the treated groups than in the control group ($P < 0.05$). If, however, statistical analyses had been done on litters rather than on individual fetuses, they would show that the incidence of CP and/or CL in the PMF group is not significantly greater than that in the control group. A significantly higher incidence of CP and/or CL was found in the PMF + ara-C group (49%) than the ara-C alone group (26.1%). These data suggest that PMF might enhance the development of ara-C-induced CP and/or CL. The incidence of minor variations in skeletal development, including reduction of skeletal calcification and loss of skeleton, was not statistically significant in the PMF group.

Dawson BV, Robertson IG, Wilson WR, Zwi LJ, Boys JT, Green AW. 1998. Evaluation of potential health effects of 10 kHz magnetic fields: a rodent reproductive study. Bioelectromagnetics. 19(3):162-171.

New technology involving the use of high-frequency inductive power distribution (HID) has recently been developed for use in materials handling and personnel transfer. Sinusoidal magnetic fields at a frequency of 10 kHz with field intensities of approximately 0.2 mT are generated directly between the current-carrying coils of this equipment. Effects of 10 kHz magnetic fields on cell division, migration, and differentiation have never been previously investigated. To evaluate potential effects on these parameters, a rodent reproductive study was undertaken using Wistar rats. Exposures were at 0.095, 0.24, and 0.95 mT with a background exposure of 5-10 microT. Three sets of parental rats were exposed continuously for 20-23.5 h/day to the fields: maternal rats during gestation, paternal rats for at least 45 days prior to mating and maternal rats 1 month prior to mating. Exposure phases thus covered spermatogenesis, maturation of the ovum and ovulation, fertilization, implantation, embryogenesis, organogenesis, and maturation of the fetus immediately prior to parturition. In all experiments pregnancy outcome was assessed. These studies failed to demonstrate any reproductive toxicity resulting from maternal or fetal exposure during gestation or following paternal or maternal exposure for several weeks prior to mating. No quantitative or qualitative effects on spermatogenesis occurred after exposure, and no effects on the estrous cycle or ovulation could be demonstrably linked to the 10 kHz magnetic field exposure at 0.095, 0.25, or 0.95 mT. Where possible, parental clinical chemistry and hematology were also examined. As in mouse toxicology studies previously reported, minor differences were observed between control and treated groups. These were regarded as statistically, but not biologically, significant and could not categorically be attributed to magnetic field exposure.

de Kleijn S, Ferwerda G, Wiese M, Trentelman J, Cuppen J, Kozicz T, de Jager L, Hermans PW, Verburg-van Kemenade BM. 2016. A short-term extremely low frequency electromagnetic field exposure increases circulating leukocyte numbers and affects HPA-axis signaling in mice. Bioelectromagnetics. 37(7):433-443.

There is still uncertainty whether extremely low frequency electromagnetic fields (ELF-EMF) can induce health effects like immunomodulation. Despite evidence obtained in vitro, an unambiguous association has not yet been established in vivo. Here, mice were exposed to ELF-EMF for 1, 4, and 24 h/day in a short-term (1 week) and long-term (15 weeks) set-up to investigate whole body effects on the level of stress regulation and immune response. ELF-EMF

signal contained multiple frequencies (20-5000 Hz) and a magnetic flux density of 10 μT. After exposure, blood was analyzed for leukocyte numbers (short-term and long-term) and adrenocorticotropic hormone concentration (short-term only). Furthermore, in the short-term experiment, stress-related parameters, corticotropin-releasing hormone, proopiomelanocortin (POMC) and CYP11A1 gene-expression, respectively, were determined in the hypothalamic paraventricular nucleus, pituitary, and adrenal glands. In the short-term but not long-term experiment, leukocyte counts were significantly higher in the 24 h-exposed group compared with controls, mainly represented by increased neutrophils and CD4 ± lymphocytes. POMC expression and plasma adrenocorticotropic hormone were significantly lower compared with unexposed control mice. In conclusion, short-term ELF-EMF exposure may affect hypothalamic-pituitary-adrenal axis activation in mice. Changes in stress hormone release may explain changes in circulating leukocyte numbers and composition.

Deweyert A, Iredale E, Xu H, Wong E, Schmid S, Hebb MO. Diffuse intrinsic pontine glioma cells are vulnerable to low intensity electric fields delivered by intratumoral modulation therapy. J Neurooncol 143(1):49-56, 2019.

Introduction: Diffuse intrinsic pontine glioma (DIPG) is a high fatality pediatric brain cancer without effective treatment. The field of electrotherapeutics offers new potential for other forms of glioma but the efficacy of this strategy has not been reported for DIPG. This pilot study evaluated the susceptibility of patient-derived DIPG cells to low intensity electric fields delivered using a developing technology called intratumoral modulation therapy (IMT). **Methods:** DIPG cells from autopsy specimens were treated with a custom-designed, in vitro IMT system. Computer-generated electric field simulation was performed to quantify IMT amplitude and distribution using continuous, low intensity, intermediate frequency stimulation parameters. Treatment groups included sham, IMT, temozolomide (TMZ) chemotherapy and radiation therapy (RT). The impact of single and multi-modality therapy was compared using spectrophotometric and flow cytometry viability analyses. **Results:** DIPG cells exhibited robust, consistent susceptibility to IMT fields that significantly reduced cell viability compared to untreated control levels. The ratio of viable:non-viable DIPG cells transformed from ~ 6:1 in sham-treated to ~ 1.5:1 in IMT-treated conditions. The impact of IMT was similar to that of dual modality TMZ-RT therapy and the addition of IMT to this treatment combination dramatically reduced DIPG cell viability to ~ 20% of control values. **Conclusions:** This proof-of-concept study provides a novel demonstration of marked DIPG cell susceptibility to low intensity electric fields delivered using IMT. The potent impact as a monotherapy and when integrated into multi-modality treatment platforms justifies further investigations into the potential of IMT as a critically needed biomedical innovation for DIPG.

Dimberg Y. 1995. Neurochemical effects of a 20 kHz magnetic field on the central nervous system in prenatally exposed mice. Bioelectromagnetics. 16(4):263-267.

C57/B1 mice were exposed during pregnancy (gestation days 0-19) to a 20 kHz magnetic field (MF). The asymmetric sawtooth-waveform magnetic field in the exposed racks had a flux density of 15 microT (peak to peak). After 19 days, the exposure was terminated, and the mice were housed individually under normal laboratory conditions. On postnatal day (PD) 1, PD21,

and PD308, various neurochemical markers in the brains of the offspring were investigated and the brains weighed. No significant difference was found in the whole brain weight at PD1 or PD21 between exposed offspring and control animals. However, on PD308, a significant decrease in weight of the whole brain was detected in exposed animals. No significant differences were found in the weight of cortex, hippocampus, septum, or cerebellum on any of the sampling occasions, nor were any significant differences detected in protein-, DNA-level, nerve growth factor (NGF), acetylcholine esterase- (AChE), or 2',3'-cyclic nucleotide 3'-phosphodiesterase- (CNP; marker for oligodendrocytes) activities on PD21 in cerebellum. Cortex showed a more complex pattern of response to MF: MF treatment resulted in a decrease in DNA level and increases in the activities of CNP, AChE, and NGF protein. On PD308, the amount of DNA was significantly reduced in MF-treated cerebellum and CNP activity was still enhanced in MF-treated cortex compared to controls. Most of the effects of MF treatment during the embryonic period were similar to those induced by ionizing radiation but much weaker. However, the duration of the exposure required to elucidate the response of different markers to MF seems to be greater and effects appear later during development compared to responses to ionizing radiation.

Frölen H, Svedenstål BM, Paulsson LE. 1993. Effects of pulsed magnetic fields on the developing mouse embryo. Bioelectromagnetics. 14(3):197-204.

The influence of a pulsed magnetic field (PMF; sawtooth with 45-microseconds linear rise time and 5-microseconds decay time, peak strength of 15 microT, and frequency 20000 pps) [corrected] on the embryogenesis of CBA/S mice was investigated in five experiments based on a total of 707 exposed and 543 unexposed primigravidas. Sham and PMF exposures began on day 1 of gestation (experiments 1 and 2), on day 2 (experiment 3), on day 5 (experiment 4), and on day 7 (experiment 5); all exposures continued until day 19 post conception (p.c.), when they were terminated, at which time the following variables were measured: number of implants; number of placental resorptions; number of living fetuses; number of dead fetuses; number of malformations in living and dead fetuses; and length and body mass of living fetuses. Control dams were sham-exposed concurrently with corresponding, PMF-exposed dams. With the exception of experiment 5, in which exposure to PMF started on day 7 p.c., all groups of exposed mice had significantly more placental resorptions when compared with concurrent controls. The increased resorption rate was not reflected in a reduction in litter size or in the number of litters. A significant increase in malformed fetuses was not seen in any of the exposed groups, or when groups were pooled. Only in experiment 1 was the number of dead fetuses affected by exposure to PMF. The effect of PMF on the implantation rate was not significant. Body mass and length of exposed fetuses were significantly reduced only when the PMF treatment began on day 7 p.c.

Gryz K, Karpowicz J, Zradziński P. Evaluation of the Influence of Magnetic Field on Female Users of an Induction Hob in Ergonomically Sound Exposure Situations. Bioelectromagnetics 41(7):500-510, 2020

The hypothesis being tested was that the exposure of female workers to the electromagnetic field (EMF) emitted by an induction hob (IHb) meeting public exposure limitations (evaluated according to EN/IEC 62233) is also compliant with European Directive 2013/35/EU on workers' protection. The electric field induced in three female models in a realistic ergonomically

comfortable posture near IHb was evaluated using numerical models of 25 kHz EMF sources (IHb covered by cooking vessels). It was found that, in analyzed ergonomically comfortable exposure situations, the electric field induced in the user's body may exceed public and workers' limits when the vessels do not match the dimensions of IHb's heating zone. This can even be the case when IHb complies with Conformité Européenne labeling requirements (i.e. EMF exposure falls below public limits 30 cm away from IHb edge). In the 36 exposure scenarios analyzed, statistically significant differences were found when the distances from IHb and vessel dimension, and the height and body mass index of models in exposure scenarios varied, but not between the use of models of pregnant and nonpregnant women. The use of IHb complying with European requirements on general public protection does not ensure that EMF exposure to workers complies with the relevant limits. Adequate protection measures need to address these occupational environmental hazards.

Herrala M, Kumari K, Koivisto H, Luukkonen J, Tanila H, Naarala J, Juutilainen J. 2018. Genotoxicity of intermediate frequency magnetic fields in vitro and in vivo. Environ Res. 167:759-769.

We assessed genotoxic effects of intermediate frequency magnetic fields (MF) in vitro and in vivo. Rat primary astrocytes were exposed for 24 h to a 7.5 kHz MF at a magnetic flux density of 30 or 300 μT. Male C57BL/6 J mice were exposed continuously for 5 weeks to a 7.5 kHz MF at 12 or 120 μT, and blood samples were collected for the genotoxicity assays. To evaluate possible co-genotoxicity, the in vitro experiments included combined exposure with menadione (an agent that induces mitochondrial superoxide production and DNA damage) and methyl methanesulfonate (an alkylating agent). DNA damage and DNA repair (in vitro) were measured using the alkaline Comet assay and formation of micronuclei was assessed microscopically (in vivo) or using flow cytometry (in vitro). The results did not support genotoxicity or co-genotoxicity of 7.5 kHz MFs at magnetic flux densities up to 300 μT in vitro or in vivo. On the contrary, there was some evidence that exposure to 7.5 kHz MFs might reduce the level of genetic damage. Strongest indication of any biological effects was obtained from measurements of relative cell number, which was significantly and consistently increased after MF exposure in all in vitro experiments. Health implications of this finding are unclear, but it suggests that 7.5 kHz MFs may stimulate cell proliferation or suppress cell death.

Herrala M, Naarala J, Juutilainen J. Assessment of induced genomic instability in rat primary astrocytes exposed to intermediate frequency magnetic fields. Environ Res 173:112-116, 2019.

We investigated whether exposure to intermediate frequency magnetic fields (IF MFs) could induce or enhance genomic instability in primary astrocytes. Rat primary astrocytes were exposed to vertical or horizontal 7.5 kHz, 300 μT MF for 24 h. To study possible combined effects with known genotoxic agents, the cells were exposed for 3 h to menadione or methyl methanesulfonate after the MF treatment. Induced genomic instability was evaluated 36 days after exposures using the Comet assay and flow cytometric scoring of micronuclei. Exposure to 7.5 kHz, 300 μT MF did not induce genomic instability alone or in combination with chemicals in measurements performed several cell generations after exposure.

Huuskonen H, Juutilainen J, Julkunen A, Mäki-Paakkanen J, Komulainen H. 1998a. Effects of gestational exposure to a video display terminal-like magnetic field (20-kHz) on CBA/S mice. Teratology. 58(5):190-196.

Possible adverse effects of magnetic fields (MFs) on reproduction have been an open question. To verify the embryo-lethal effect of pulsed MF of the type emitted by video display terminals (VDTs) reported previously in CBA/S mice, a developmental toxicity study was conducted in animals of the same origin. Mated CBA/S mice (80-86 pregnant animals per group) were exposed to a 20-kHz MF with sawtooth waveform continuously from gestational day 0-18. The flux density of the vertical MF was 15 microT peak-to-peak (150 mG). This field was previously reported to increase the number of resorptions in CBA/S mice. On gestational day 18, the dams were killed and blood and bone marrow samples were taken for hematology and micronuclei analysis, respectively. The number of corpora lutea was counted and the content of the uterus examined. There were no statistically significant differences in maternal or fetal body weights, number of corpora lutea, implantations, resorptions, dead and live fetuses, or external and skeletal malformations. MF did not alter the number of blood cells or cause micronuclei in bone marrow erythrocytes in the dams. The mean number of resorptions was slightly but not statistically significantly, higher in the MF group than in controls. The results do not indicate marked developmental, hematological, or clastogenic effects of 20-kHz MFs.

Huuskonen H, Juutilainen J, Julkunen A, Mäki-Paakkanen J, Komulainen H. 1998b. Effects of lowfrequency magnetic fields on fetal development in CBA/Ca mice. Bioelectromagnetics. 19(8):477-485.

Effects of alternating magnetic fields (MFs) on the embryonic and fetal development in CBA/Ca mice were studied. Mated females were exposed continuously to a sinusoidal 50 Hz (13 microT or 0.13 mT root mean square) or a sawtooth 20 kHz (15 microT peak-to-peak) MF from day 0 to day 18 of pregnancy for 24 h/day until necropsied on day 18. Control animals were kept under the same conditions without the MF. MFs did not cause maternal toxicity. No adverse effects were seen in maternal hematology and the frequency of micronuclei in maternal bone marrow erythrocytes did not change. The MFs did not increase the number of resorptions or fetuses with major or minor malformations in any exposure group. The mean number of implantations and living fetuses per litter were similar in all groups. The corrected weight gain (weight gain without uterine content) of dams, pregnancy rates, incidences of resorptions and late fetal deaths, and fetal body weights were similar in all groups. There was, however, a statistically significant increase in the incidence of fetuses with at least three skeletal variations in all groups exposed to MFs. In conclusion, the 50 Hz or 20 kHz MFs did not increase incidences of malformations or resorptions in CBA/Ca mice, but increased skeletal variations consistently in all exposure groups.

Huuskonen H, Juutilainen J, Komulainen H. 1993. Effects of low-frequency magnetic fields on fetal development in rats. Bioelectromagnetics. 14(3):205-213.

We studied effects of alternating magnetic fields on the embryonic and fetal development of rats. Mated females of the Han:Wistar-strain were sham exposed or exposed continuously to a 50-Hz field or to a 20,000 pulse-per-second (pps) sawtooth magnetic field from day 0 to day 20 of pregnancy for 24 h/day until necropsied on day 20. The respective peak-to-peak intensities of the fields were 35.6 microT (sinewave) and 15.0 microT (sawtooth). Each treatment group contained 72 bred females. Control animals were kept under the same conditions without the magnetic field. No adverse effects were seen in the dams. The mean numbers of implantations and living fetuses per litter were statistically significantly increased in the 50-Hz group. There were, however, three total resorptions of litters in dams of the control group, which contributed to the difference in the number of living fetuses. The corrected body-mass gains (gains without uterine content) of dams were similar in all groups. Pregnancy rates, incidences of resorptions, late fetal deaths, and fetal body masses were similar in all groups. The incidence of fetuses with minor skeletal anomalies was statistically significantly increased in both exposed groups. Only one serious malformation (anophthalmia, sawtooth-exposed group) and a few minor visceral malformations were found. In conclusion, the magnetic fields used in this study did not increase the incidence of major malformations or resorptions in Wistar rats. The increased number of skeletal anomalies and implantations we observed indicates, however, that some developmental effects in rats may attend exposure to time-varying magnetic fields.

Ikuyo M, Esaki K, Aimoto A, Wake K, Yamaguchi Sekino S, Kojimahara N, Suzuki Y, Masao Taki M. Measurement and Exposure Assessment of Intermediate Frequency Magnetic Fields From Electronic Article Surveillance (EAS) Gates in Libraries. Front Public Health 2022 May 12;10:871134.

Exposure to magnetic fields from the electronic article surveillance (EAS) gate was evaluated in consideration of the application to epidemiological studies of library workers who are exposed continually to intermediate frequency magnetic fields from the EAS gate. Two types of exposures were investigated. One was transient exposure due to passing through or beside the gate and another was chronic exposure in the room. We measured magnetic fields from five EAS gate models which were commonly used in libraries in Japan. Detailed measurements were performed for two of them in consideration of the phase difference of vector components of magnetic flux density. The polarization of the magnetic field in the gate was investigated with the index of ellipticity. The induced electric field in a human body was numerically calculated for exposures to magnetic fields of the two gate models. The results provide a quantitative understanding of exposures during passing through or by the EAS gate. Magnetic field distribution was measured in a large room for one gate model to quantify the chronic exposure of library workers during the work at the desk. It was found that the magnetic field was distributed as a function of the horizontal distance to the nearest gatepost. The 45-point average value B_{IEC} defined by the IEC standard was suggested to be a useful quantity to characterize the magnitude of the magnetic field from the EAS gate. Exposures to different EAS gates are expected to be compared through this quantity without detailed measurements. These results are expected to provide useful means for exposure assessment of epidemiological studies on the association between the IF-EMF exposure and possible health outcomes.

Jones TH, Song JW, Abushahin L. Tumor treating fields: An emerging treatment modality for thoracic and abdominal cavity cancers. Transl Oncol 15(1):101296, 2022.

Tumor treating fields (TTFields)-an intermediate-frequency, electric field therapy-has emerged as a promising alternative therapy for the treatment of solid cancers. Since the first publication describing the anticancer effects of TTFields in 2004 there have been numerous follow-up studies by other groups, either to confirm the efficacy of TTFields or to study the primary mechanism of interaction. The overwhelming conclusion from these in vitro studies is that TTFields reduce the viability of aggressively replicating cell lines. However, there is still speculation as to the primary mechanism for this effect; moreover, observations both in vitro and in vivo of inhibited migration and metastases have been made, which may be unrelated to the originally proposed hypothesis of replication stress. Adding to this, the in vivo environment is much more complex spatially, structurally, and involves intricate networks of cell signaling, all of which could change the efficacy of TTFields in the same way pharmaceutical interventions often struggle transitioning in vivo. Despite this, TTFields have shown promise in clinical practice on multiple cancer types, which begs the question: has the primary mechanism carried over from in vitro to in vivo or are there new mechanisms at play? The goal of this review is to highlight the current proposed mechanism of action of TTFields based primarily on in vitro experiments and animal models, provide a summary of the clinical efficacy of TTFields, and finally, propose future directions of research to identify all possible mechanisms in vivo utilizing novel tumor-on-a-chip platforms.

Juutilainen J, Björk E, Saali K. Epilepsy and electromagnetic fields: effects of simulated atmospherics and 100-Hz magnetic fields on audiogenic seizure in rats. Int J Biometeorol 1988; 32: 17-20.

No abstract available.

Juutilainen J, Huuskonen H, Komulainen H. 1997. Increased resorptions in CBA mice exposed to low frequency magnetic fields: an attempt to replicate earlier observations. Bioelectromagnetics.18(6):410-417.

This paper has two aims. First, it reports the findings of a study on the effects of low-frequency magnetic fields on reproduction. Second, it serves as an example of an attempt to replicate the results of an experimental study in an independent laboratory and discusses some of the problems of replication studies. To try to replicate the findings of a study reporting increased resorptions (fetal loss) in mice exposed to 20 kHz magnetic fields with sawtooth waveform and to study the possible effects of 50 Hz sinusoidal fields, pregnant mice were exposed to magnetic fields from day 0 to 18 of pregnancy, 24 h per day. The flux densities of the vertical magnetic fields were 15 microT (peak-to-peak) at 20 kHz and 13 or 130 microT (root mean square) at 50 Hz. Two strains of animals were used: CBA/S mice imported from the laboratory reporting the original observations, and a closely related strain CBA/Ca. The CBA/S mice were cleaned of pathogenic microbes and parasites before they were imported into our laboratory. The magnetic field exposures did not affect resorption rate in CBA/Ca mice. In CBA/S, the frequency of resorptions was higher in the exposed mice than in the control group. However, the increase was

not significantly different from either the no-effect hypothesis or the results of the original study we were attempting to replicate. Differences between the two studies and difficulties in interpreting the results are discussed. It is concluded that the results tend more to support than argue against increased resorptions in CBA/S mice exposed to the 20 kHz magnetic field. The results demonstrate that animal strain is an important variable in bioelectromagnetics research: even closely related strains may show different responses to magnetic field exposure.

Kim SH, Lee HJ, Choi SY, Gimm YM, Pack JK, Choi HD, Lee YS. 2006. Toxicity bioassay in Sprague- Dawley rats exposed to 20 kHz triangular magnetic field for 90 days. Bioelectromagnetics. 27(2):105-111.

Sprague-Dawley rats (10 each of male and female per group for sham and magnetic field exposed) were exposed in a carrousel irradiator to 20 kHz intermediate frequency (IF) magnetic field at 6.25 microT rms for 8 h/day, 5 days/week for 90 days. Urine analysis (pH, serum glucose, protein, ketone bodies, RBC, WBC, bilirubin, urobilinogen, and specific gravity), blood analysis [WBC, RBC, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), thrombocyte count, and leucocyte count], blood biochemistry (total protein, blood urea nitrogen, creatinine, glucose, total bilirubin, total cholesterol, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and lactate dehydrogenase), and histopathological analysis for organs such as liver, kidney, testis, ovary, spleen, brain, heart, and lung were performed on day 90. Results showed no significant differences in the above analyses between IF magnetic field exposed and sham control rats. Therefore, we conclude that there were no significant toxicities in rats exposed to 20 kHz IF triangular magnetic field-exposure for 90 days.

Kim SH, Song JE, Kim SR, Oh H, Gimm YM, Yoo DS, Pack JK, Lee YS. 2004. Teratological studies of prenatal exposure of mice to a 20 kHz sawtooth magnetic field. Bioelectromagnetics. 25(2):114-117.

In order to evaluate the importance of gestational age in possible effects due to exposure to a 20 kHz sawtooth magnetic field, pregnant ICR mice at gestational 2.5-15.5 days post-coitus, which is the most sensitive stage for the induction of major congenital malformations, were exposed in a carrousel irradiator. The mice were exposed to a 20 kHz intermediate frequency (IF) sawtooth magnetic field had a 6.5 microT peak intensity for 8 h/day. The animals were sacrificed on the 18th day of gestation; and the fetuses were examined for mortality, growth retardation, changes in head size, and other morphological abnormalities. From the above conditions, it is concluded that the exposure to a 20 kHz sawtooth magnetic field with 6.5 microT peak intensity does not inflict any adverse effect on fetuses of pregnant mice.

Kitajima T, Joachim Schüz , Akemi Morita , Wakaha Ikeda , Hirokazu Tanaka , Kayo Togawa , Esteban C Gabazza , Masao Taki , Kuniaki Toriyabe , Tomoaki Ikeda , Shigeru Sokejima. Measurement of Intermediate Frequency Magnetic Fields Generated by Household Induction Cookers for Epidemiological Studies and Development of an Exposure Estimation Model. Int J Environ Res Public Health 2022 Sep 21;19(19):11912

Introduction: Exposure assessment of intermediate frequency (IF) electromagnetic fields (EMFs) is difficult and epidemiological studies are limited. In the present study, we aimed to estimate the exposure of pregnant women to IF-EMFs generated by induction cookers in the household using a questionnaire and discussed its applicability to epidemiological studies. **Method:** Two main home-visit surveys were conducted: a Phase 1 survey to develop an estimation model and a Phase 2 survey to validate the model. The estimation model included the following variables: wattage, cookware diameter, and distance from the hob center (center of the stove). Four models were constructed to determine the importance of each variable and the general applicability for epidemiological studies. In addition, estimated exposure values were calculated based on the Phase 2 survey questionnaire responses and compared with the actual measured values using the Spearman rank correlation coefficient. **Result:** The average value of the magnetic field measured in the Phase 1 survey was 0.23 μT (variance: 0.13) at a horizontal distance of 30 cm at the height of the cooking table. The highest validity model was inputted distance from the hob center to the body surface that is variable (correlation coefficient = 0.54, 95% confidence interval: 0.22-0.75). No clear differences were identified in the correlation coefficients for each model (z-value: 0.09-0.18, *p*-value: 0.86-0.93). **Discussion and conclusions:** No differences were found in the validity of the four models. This could be due to the biased wattage of the validation population, and for versatility it would be preferable to use three variables (distance, wattage, and estimation using the diameter of the cookware) whenever possible. To our knowledge, this is the first systematic measurement of magnetic fields generated by more than 70 induction cookers in a real household environment. This study will contribute to finding dose-response relationships in epidemiological studies of intermediate-frequency exposure without the use of instrumentation. One of the limitations of this study is it estimates instantaneous exposure in place during cooking only.

Kos B, Valič B, Miklavčič D, Kotnik T, Gajšek P. Pre- and post-natal exposure of children to EMF generated by domestic induction cookers. Phys Med Biol 56(19):6149-6160, 2011.

Induction cookers are a type of cooking appliance that uses an intermediate-frequency magnetic field to heat the cooking vessel. The magnetic flux density produced by an induction cooker during operation was measured according to the EN 62233 standard, and the measured values were below the limits set in the standard. The measurements were used to validate a numerical model consisting of three vertically displaced coaxial current loops at 35 kHz. The numerical model was then used to compute the electric field (E) and induced current (J) in 26 and 30 weeks pregnant women and 6 and 11 year old children. Both E and J were found to be below the basic restrictions of the 2010 low-frequency and 1998 ICNRIP guidelines. The maximum computed E fields in the whole body were 0.11 and 0.66 V m(-1) in the 26 and 30 weeks pregnant women and 0.28 and 2.28 V m(-1) in the 6 and 11 year old children (ICNIRP basic restriction 4.25 V m(-1)). The maximum computed J fields in the whole body were 46 and 42 mA m(-2) in the 26 and 30 weeks pregnant women and 27 and 16 mA m(-2) in the 6 and 11 year old children (ICNIRP basic restriction 70 mA m(-2)).

Kumari K, Capstick M, Cassara AM, Herrala M, Koivisto H, Naarala J, Tanila H, Viluksela M, Juutilainen J. 2017. Effects of intermediate frequency magnetic fields on male fertility indicators in mice. Environ Res. 157:64-70.

Human exposure to intermediate frequency (IF) fields is increasing due to new applications such as electronic article surveillance systems, wireless power transfer and induction heating cookers. However, limited data is available on effects of IF magnetic fields (MF) on male fertility function. This study was conducted to assess possible effects on fertility indicators from exposure to IF MF. Male C57BL/6J mice were exposed continuously for 5 weeks to 7.5kHz MF at 12 and 120μT. Sperm cells from cauda epididymis were analysed for motility, total sperm counts, and head abnormalities. Motile sperm cells were classified as progressive or non-progressive. Testicular spermatid heads were counted as well. The body weight development and reproductive tissue weights were not affected. No exposure-related differences were observed in sperm counts or sperm head abnormalities. Proportion of non-motile cells was significantly decreased in the 120μT group, and a corresponding increase was seen in the percentage of motile cells (significant in non-progressive motile cells). In conclusion, no adverse effects on fertility indicators were observed. Increased sperm motility is an interesting finding that needs to be confirmed in further studies.

Kumari K, Koivisto H, Viluksela M, Paldanius KMA, Marttinen M, Hiltunen M, Naarala J, Tanila H, Juutilainen J. 2017. Behavioral testing of mice exposed to intermediate frequency magnetic fields indicates mild memory impairment. PLoS One. 12(12):e0188880.

Human exposure to intermediate frequency magnetic fields (MF) is increasing due to applications like electronic article surveillance systems and induction heating cooking hobs. However, limited data is available on their possible health effects. The present study assessed behavioral and histopathological consequences of exposing mice to 7.5 kHz MF at 12 or 120 μT for 5 weeks. No effects were observed on body weight, spontaneous activity, motor coordination, level of anxiety or aggression. In the Morris swim task, mice in the 120 μT group showed less steep learning curve than the other groups, but did not differ from controls in their search bias in the probe test. The passive avoidance task indicated a clear impairment of memory over 48 h in the 120 μT group. No effects on astroglial activation or neurogenesis were observed in the hippocampus. The mRNA expression of brain-derived neurotrophic factor did not change but expression of the proinflammatory cytokine tumor necrosis factor alpha mRNA was significantly increased in the 120 μT group. These findings suggest that 7.5 kHz MF exposure may lead to mild learning and memory impairment, possibly through an inflammatory reaction in the hippocampus.

Kumari K, Koivisto H, Capstick M, Naarala J, Viluksela M, Tanila H, Juutilainen J. 2018. Behavioural phenotypes in mice after prenatal and early postnatal exposure to intermediate frequency magnetic fields. Environmental Research. 162:27-34.

Electromagnetic fields are ubiquitous in the environment. Human exposure to intermediate frequency (IF) fields is increasing due to applications like electronic article surveillance systems, wireless power transfer, and induction heating cooking hobs. However, there are limited data on possible health effects of exposure to IF magnetic fields (MF). In the present study, we set out to assess cognitive and behavioural effects of IF MF in mice exposed during prenatal and early postnatal periods. Pregnant female mice were exposed continuously to 7.5kHz MFs at 12 and 120μT, from mating until weaning of pups. Sham exposed pregnant mice were used as a control

group. A behavioural teratology study was conducted on the male offspring at two months of age to detect possible effects on the developing nervous system. Body weight development did not differ between the exposure groups. The exposure did not alter spontaneous motor activity when exploring a novel cage or anxiety in novelty-suppressed feeding or marble burying tests. Improved performance in the Rotarod task was observed in the 12μT group, while the 120μT exposure group swam more slowly than the sham exposed group in the Morris swim navigation task. However, indices of learning and memory (path length and escape latency during task acquisition and search bias during the probe test) did not differ between the exposure groups. Furthermore, the passive avoidance task did not indicate any impairment of long-term memory over a 48h interval in the exposed groups. In a post-mortem histopathological analysis, there was no evidence for an effect of IF MF exposure on astroglial reactivity or hippocampal neurogenesis. The results suggest that the IF MF used did not have detrimental effects on spatial learning and memory or histological markers of tissue reaction. The two statistically significant findings that were observed (improved performance in the Rotarod task in the 12μT group and decreased swimming speed in the 120μT group) are likely to be chance findings, as they do not form an internally consistent, dose-dependent pattern indicative of specific developmental effects.

Lerchl A, Karen Drees Née Grote, Isabel Gronau, Dirk Fischer, Julia Bauch, Axel Hoppe. Effects of Long-Term Exposure of Intermediate Frequency Magnetic Fields (20 kHz, 360 µT) on the Development, Pathological Findings, and Behavior of Female Mice. Bioelectromagnetics 2021 42(4):309-316.

The use of magnetic fields in the intermediate-frequency (IF) range to wirelessly charge electric cars with power transfer in the kilowatt range has become increasingly widespread, leading to unavoidable stray fields in the microtesla range. Only a handful of studies have assessed the potential biological risks associated with exposure to such fields. We exposed female mice (n = 80 per group) to either 20 kHz, 360 µT (rms), or sham in Helmholtz coils to conduct a blind design study. Exposure started at 3 months of age (24 h/day). Body mass was recorded every 1-2 weeks. At 10 months of age, three behavioral tests were performed on 24 animals per group. Three months later, the mice were sacrificed and organs (brain, liver, kidney, spleen, and lung) were removed and prepared for microscopic analysis. Our findings demonstrate no differences in the development of body mass and survival rates (96% and 89%, respectively). Similarly, no significant differences were observed in tumor incidence rates. When it comes to behavioral tests, the 8-arm maze results revealed no significant differences. In contrast, the Rotarod data were significantly ($P < 0.001$) different with longer retention times seen in the exposed mice. In the open field, the number of supported rears was significantly lower ($P < 0.01$), whereas the other endpoints did not show any differences. Overall, our data reveal no adverse effects of exposure to 20 kHz, 360 µT on the development and tumor incidences, while the significant differences in the behavioral tests may indicate higher levels of alertness in mice.

Lee HJ, Choi SY, Jang JJ, Gimm YM, Pack JK, Choi HD, Kim N, Lee YS. 2007. Lack of promotion of mammary, lung and skin tumorigenesis by 20 kHz triangular magnetic fields. Bioelectromagnetics. 28(6):446-453.

In order to evaluate possible tumorigenic effects of a 20 kHz intermediate frequency triangular magnetic field (IF), a frequency emitted from TV and PC monitors at 6.25 microT rms, which is the regulated exposure limit of magnetic field for the public in Korea, mammary tumors were produced in female Sprague-Dawley rats by oral intubation of dimethylbenz(a)anthracene (DMBA), lung tumors in ICR mice by scapular region injection of benzo(a)pyrene (BP), and skin tumors in female ICR mice by topical application of DMBA and tetradecanoylphorbol ester (TPA). IF was applied 8 h/day for 14 weeks beginning the day after DMBA treatment for mammary tumor experiment, for 6 weeks after weaning for lung tumor, and for 20 weeks beginning 1 week after DMBA application for skin tumor experiment. For skin tumors, TPA was applied once a week for 19 weeks. Results showed no significant differences in tumor incidence, mean tumor number and volume, and histological patterns between IF magnetic-field exposed and sham control rats in the above three tumor models. Therefore, we conclude that within the limitation or number of animals and the experimental conditions, 20 kHz IF triangular magnetic field exposure of 6.25 microT does not appear to be a strong co-tumorigenic agent in the chosen murine mammary, lung and skin models.

Lee HJ, Gimm YM, Choi HD, Kim N, Kim SH, Lee YS. 2010. Chronic exposure of Sprague-Dawley rats to 20 kHz triangular magnetic fields. Int J Radiat Biol. 86(5):384-389.

Purpose: As a continuing study of 20 kHz triangular magnetic fields (MF) [Lee et al. 2006], we investigated the chronic toxicity and possible health effects of exposure to 20 kHz MF at the flux density of 30 microT, which is the limit standard for the occupational population in South Korea, with the use of Sprague-Dawley rats. **Materials and methods:** Rats were exposed to 20 kHz triangular MF at 30 microT Root Mean Square for 8 h/day for 18 months. Body and organ weights were measured and urinalysis, hematological and blood biochemistry analyses were performed in individual animals. Histopathological evaluation was also performed for the brain, thymus, lung, heart, liver, kidney, intestine and reproductive organs, including tumour tissue. **Results:** The mortality patterns in male or female rats exposed to magnetic fields were compared to the mortality patterns found in sex-matched sham control animals. Significant alteration of body weight was not observed with MF exposure. No significant differences were seen in sham-exposed and MF-exposed animals based on urological factors, hematological factors and blood biochemistry. Total tumour incidence was not different between sham-exposed and MF-exposed animals. **Conclusion:** Our results suggest that chronic exposure to 20 kHz triangular MF with 30 microT flux density did not increase toxicity in rats.

Lee HJ, Kim SH, Choi SY, Gimm YM, Pack JK, Choi HD, Lee YS. 2006. Long-term exposure of Sprague Dawley rats to 20 kHz triangular magnetic fields. Int J Radiat Biol. 82(4):285-291.

Purpose: There are only a few reports on harmful effects of 20 kHz sine waves; however, it is essential to comprehensively evaluate the potentially harmful effect of triangular signals at the same frequency. Therefore, in this study, effects of long-term exposure to 20 kHz magnetic fields was examined. **Materials and methods:** Eighty Sprague Dawley rats were divided into

two groups (half male and female in each sham and exposed groups), and they were exposed to 20 kHz triangular magnetic fields at 6.25 microT rms for 8 h/day for 12 or 18 months. Urinalysis [pH, glucose, protein, ketone bodies, red blood cells (RBC), nitrogen, bilirubin, urobilinogen, and specific gravity], hematological analysis (RBC, hemoglobin, hematocrit, thrombocyte count, and leucocyte count), blood biochemistry (total protein, blood urea nitrogen, creatinine, glucose, total bilirubin, total cholesterol, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase), and histopathological analysis of organs (thymus, stomach, intestine, liver, kidney, testis, ovary, spleen, brain, heart, and lung) were performed. **Results:** No significant differences were seen between 20 kHz magnetic-fields exposed rats and sham-exposed rats in body and organ weights, hematological analysis, blood biochemistry, urinalysis data, and histopathological examination, except for the numbers of neutrophiles and lymphocytes in female rats. The number of neutrophiles was significantly increased in female rats on the 12th month after exposure, and the number of lymphocytes in female rats was significantly decreased on the 18th month. **Conclusion:** Long-term exposure of rats to 20 kHz triangular magnetic fields did not induce any significantly harmful effects, except changes in neutrophiles at 12 months and lymphocytes at 18 months of exposure in female rats. These hematological changes need to be investigated again at a higher intensity of 20 kHz magnetic fields.

Lee HJ, Pack JK, Gimm YM, Choi HD, Kim N, Kim SH, Lee YS. 2009. Teratological evaluation of mouse fetuses exposed to a 20 kHz EMF. Bioelectromagnetics. 30(4):330-333.

As a continuation of our previous study, we performed a teratological evaluation of the importance of gestational age with regards to the exposure of 20 kHz intermediate frequency magnetic field (IF) on pregnant ICR mice. The pregnant mice were exposed to a 20 kHz IF magnetic field for 8 h/day in a carousel irradiator at 30 microT which is the limit standard for occupational population in Korea. The animals were sacrificed on the 18th day of gestation and the fetuses were examined for mortality, growth retardation, changes in head size and other morphological abnormalities. We concluded that exposure to 30 microT with 20 kHz IF did not cause any observable adverse effects on mouse fetuses.

Lee H-J, Hee Jin , Young Hwan Ahn , Nam Kim , Jeong Ki Pack , Hyung-Do Choi , Yun-Sil Lee. Effects of intermediate frequency electromagnetic fields: a review of animal studies. Int J Radiat Biol 99(2):166-182, 2023.

Purpose: Many novel devices such as induction cookers or wireless power transfer produce electromagnetic fields (EMFs) in the intermediate frequency (IF) range (300 Hz to 10 MHz) and it is very meaningful for summarizing the bioeffects of IF-EMF research, particularly animal studies. This review takes into account experimental studies that used murine models to study the health effects of exposure to IF-EMF. The analyses included here use data available in the literature published from January 1988 to August 2021 including the animal studies about general adverse effects, tumorigenic effects, and effects on developmental stages. The studies that linked IF-EMF exposure during pregnancy or neonatal stage to behavioral and cognition changes were included. Additionally, this review also covers the effects of IF-EMF on gene expression patterns in the brain, behavior patterns associated with learning and memory, and immune function. **Conclusions:** Although most studies have suggested that IF-EMF is harmless, some adverse effects have been reported after exposure at developmental stages and prolonged

exposure. Compared to extremely low frequency (ELF) or radiofrequency (RF) EMF bands, studies on health effects with more diverse perspectives of IF-EMF have not been conducted. Therefore, performing more research should be necessary using the latest biomedical tools. From this point of view, a comprehensive review of IF-EMF studies, particularly animal studies, will provide a valuable basis for further risk analysis in humans.

Lerchl A, Drees Née Grote K, Gronau I, Fischer D, Bauch J, Hoppe A. 2021. Effects of Long-Term Exposure of Intermediate Frequency Magnetic Fields (20 kHz, 360 µT) on the Development, Pathological Findings, and Behavior of Female Mice. Bioelectromagnetics. 42(4):309-316.

The use of magnetic fields in the intermediate-frequency (IF) range to wirelessly charge electric cars with power transfer in the kilowatt range has become increasingly widespread, leading to unavoidable stray fields in the microtesla range. Only a handful of studies have assessed the potential biological risks associated with exposure to such fields. We exposed female mice (n = 80 per group) to either 20 kHz, 360 µT (rms), or sham in Helmholtz coils to conduct a blind design study. Exposure started at 3 months of age (24 h/day). Body mass was recorded every 1-2 weeks. At 10 months of age, three behavioral tests were performed on 24 animals per group. Three months later, the mice were sacrificed and organs (brain, liver, kidney, spleen, and lung) were removed and prepared for microscopic analysis. Our findings demonstrate no differences in the development of body mass and survival rates (96% and 89%, respectively). Similarly, no significant differences were observed in tumor incidence rates. When it comes to behavioral tests, the 8-arm maze results revealed no significant differences. In contrast, the Rotarod data were significantly ($P < 0.001$) different with longer retention times seen in the exposed mice. In the open field, the number of supported rears was significantly lower ($P < 0.01$), whereas the other endpoints did not show any differences. Overall, our data reveal no adverse effects of exposure to 20 kHz, 360 µT on the development and tumor incidences, while the significant differences in the behavioral tests may indicate higher levels of alertness in mice.

Li X, Yang F, Rubinsky B. A Correlation Between Electric Fields That Target the Cell Membrane Potential and Dividing HeLa Cancer Cell Growth Inhibition. IEEE Trans Biomed Eng 68(6):1951-1956, 2021.

Objective: Clinical studies show that low intensity (single V/cm), intermediate-frequency (100 kHz-300 kHz) electric fields inhibit the growth of cancer cells, while the mechanism is not yet understood. We examine the hypothesis that electric fields modify the cell membrane potential of dividing cancer cells in a way that correlates with cells growth inhibition. **Methods:** A Schwan based mathematical model calculates the changes in HeLa cells membrane potential due to single V/cm electric fields and frequencies from 0.1 to 1 MHz. An experimental study examines the effect of these electric fields on the inhibition of HeLa cells growth in an incubator. **Results:** The theoretical calculation shows that the effects of these electric fields on cell membrane potential decrease with an increase in frequency. The HeLa cells experiments verified the inhibitory effect of these fields on cell growth. The inhibitory effect is decreasing with an increase in frequency, in a way that is similar to the frequency dependent effect of these fields on the cell membrane potential. **Conclusions:** The superposition of the theoretical results and the experimental results

suggest a correlation between the effect of these fields on the cell membrane potential and inhibition of cancer cell growth. It should be emphasized that correlations do not prove causality, however, they suggest an area for future research. **Significance:** These findings have value for the understanding of the mechanisms of cancer cells growth inhibition with electric fields and suggest an interesting area of research on the interaction between electromagnetic fields and cancer cells.

Maaroufi K, Save E, Poucet B, Sakly M, Abdelmelek H, Had-Aissouni L. 2011. Oxidative stress and prevention of the adaptive response to chronic iron overload in the brain of young adult rats exposed to a 150 kilohertz electromagnetic field. Neuroscience. 186:39-47.

Iron surcharge may induce an oxidative stress-based decline in several neurological functions. In addition, electromagnetic fields (EMF) of frequencies up to about 100 kHz, emitted by electric/electronic devices, have been suggested to enhance free radical production through an iron dependent pathway. The purpose of this study was therefore to determine a possible relationship between iron status, exposure to EMF, and brain oxidative stress in young adult rats. Samples were micro-dissected from prefrontal cortex, hippocampus, striatum, and cerebellum after chronic saline or iron overload (IO) as well as after chronic sham exposure or exposure to a 150 kHz EMF or after combining EMF exposure with IO. The brain samples were used to monitor oxidative stress-induced lipid peroxidation and activity of the antioxidant enzymes superoxide dismutase and catalase. While IO did not induce any oxidative stress in young adult rats, it stimulated antioxidant defenses in the cerebellum and prefrontal cortex in particular. On the contrary, EMF exposure stimulated lipid peroxidation mainly in the cerebellum, without affecting antioxidant defenses. When EMF was coapplied with IO, lipid peroxidation was further increased as compared to EMF alone while the increase in antioxidant defenses triggered by the sole IO was abolished. These data suggest that EMF exposure may be harmful in young adults by impairing the antioxidant defenses directed at preventing iron-induced oxidative stress.

Mamaghaniyeh R, Zandieh A, Goliaei B, Nezamtaheri MS, Shariatpanahi SP. Effects of exposure to alternating low-intensity, intermediate-frequency electric fields on the differentiation of human leukemic cell line U937. Bioelectromagnetics 2023 Oct 23. doi: 10.1002/bem.22487. Online ahead of print.

Studying the bioeffects of electric fields have been the subject of ongoing research which led to promising therapeutic effect, particularly in cancer treatment. Here, we investigated the impact of low-intensity, intermediate-frequency alternating electric fields on the differentiation of human myeloid leukemia cell line U937. The results showed a near twofold increase in differentiation of U937 cells treated for 24 h by alternating 600 kHz, 150 V/m electric fields, in comparison to their control groups. This measure was evaluated by latex bead phagocytosis assay, nitro blue tetrazolium test, and cell cycle analysis which revealed a significant shift in the number of cells from G2 +M to G0 +G1 phases. The simulation result for the intracellular field intensity showed around 50% attenuation with respect to the applied external field for our setup which ruled out masking of the applied field by the internal electric noise of the cell. Based on previous studies we postulate a possible calcium-related effect for the observed differentiation,

yet the exact underlying mechanism requires further investigation. Finally, our results may offer a potential therapeutic method for leukemia in the future.

Mohammed S, Sundaram V, Venkata CRA, Zyuzikov .N, Polycystic ovary rat model exposure to 150 kHz intermediate frequency: hypothalamic-pituitary-ovarian axis at the receptor, cellular, tissue, and hormone levels. J Ovarian Res 14(1):173, 2021.

Introduction: The hypothalamic-pituitary-ovarian (HPO) axis is the principal regulator of the reproductive system. The neurons in the arcuate nucleus of the hypothalamus signal the basophilic cells of the anterior pituitary to release luteinizing hormone (LH) and follicle stimulating hormone (FSH), which bind to the granulosa and theca cells of a follicle in the ovary to promote healthy follicular development. Disruption of this process at any time can lead to polycystic ovaries and, if left untreated, can lead to Polycystic Ovarian Syndrome (PCOS), one of the leading causes of infertility. A novel treatment option using 150 kHz Intermediate Frequency (IF) Electromagnetic Radiation (EMR) has been proposed to monitor the effect of this frequency during cystic development. **Methods:** To prove this, an experiment was conducted to study the effect of whole-body exposure to 150 kHz EMR for 8 weeks at receptor, cellular, tissue and hormonal levels on the HPO axis of 25 young cyclic female rats. **Results:** The results showed that 150 kHz EMR did not affect the histoarchitecture of neurons of arcuate nucleus of the hypothalamus of PCO-induced rats. It was also found that the number of basophilic cells of the pituitary gland was increased and the immunoreactivity of LH and FSH secretion increased. This EMR field also decreased the development of follicular cysts in the ovary and possibly increased the immunoreactivity of the LH and FSH receptors as well on the theca and granulosa cells of follicles in the ovary. **Conclusion:** There are still many limitations to this study. If properly evaluated, the results of this experiment could help develop a new non-invasive treatment option for women with PCOS in the near future.

Nishimura I, Oshima A, Shibuya K, Negishi T. 2011. Lack of teratological effects in rats exposed to 20 or 60 kHz magnetic fields. Birth Defects Res B Dev Reprod Toxicol. 92(5):469-477.

Background: A risk assessment of magnetic field (MF) exposure conducted by the World Health Organization indicated the need for biological studies on primary hazard identification and quantitative risk evaluation of intermediate frequency (300 Hz-100 kHz) MFs. Because induction heating cookers generate such MFs for cooking, reproductive and developmental effects are a concern due to the close proximity of the fields' source to a cook's abdomen. **Methods:** Pregnant Crl:CD(SD) rats (25/group) were exposed to a 20 kHz, 0.2 mT(rms) or 60 kHz, 0.1 mT(rms) sinusoidal MF or sham-exposed for 22 hr/day during organogenesis, and their fetuses were examined for malformations on gestation day 20. All teratological evaluations were conducted in a blind fashion, and experiments were duplicated for each frequency to confirm consistency of experimental outcomes. **Results:** No exposure-related changes were found in clinical signs, gross pathology, or number of implantation losses. The number of live fetuses and low-body-weight fetuses as well as the incidence of external, visceral, and skeletal malformations in the fetuses did not indicate significant differences between MF-exposed and

sham-exposed groups. Although some fetuses showed isolated changes in sex ratio and skeletal variation and ossification, such changes were neither reproduced in duplicate experiments nor were they common to specific field frequencies. **Conclusions:** Exposure of rats to MFs during organogenesis did not show significant reproducible teratogenicity under experimental conditions. Present findings do not support the hypothesis that intermediate frequency MF exposure after implantation carries a significant risk for developing mammalian fetuses.

Nishimura I, Oshima A, Shibuya K, Mitani T, Negishi T. 2012. Absence of reproductive and developmental toxicity in rats following exposure to a 20-kHz or 60-kHz magnetic field. Regul Toxicol Pharmacol. 64(3):394-401.

The use of intermediate frequency (IF) magnetic fields (MFs) in occupational equipment and domestic appliances, such as inductive heating cookers, is increasing. The WHO indicated a lack of scientific evidence needed to assess the health risk of exposure to IF MFs. Male and female rats (24/group) were exposed to a 20 kHz, 0.2 mT(rms) or 60 kHz, 0.1 mT(rms) sinusoidal MF for 22 h/day from 14 days prior to and during mating. Copulated females were exposed until gestation day 7 and sacrificed thereafter. Mated males were sacrificed to examine MF exposure effects on spermatogenesis. Reproductive examinations were blinded, and experiments were duplicated per frequency to ensure reproducibility. No statistically significant, exposure-related changes were found in the estrous cycle, copulation and fertility indices, numbers of corpora lutea and implantation sites, or pre- and postimplantation loss. No reproducible changes were observed in sperm count, motility, or morphological abnormality, or in the weights of testes and epididymides after MF exposure. No significant abnormalities were observed in gross pathology or histopathology of the uterus, ovary, testis, and epididymis in the MF- or sham-exposed groups. MF exposure during the preimplantation period was not toxic to fertility or early embryogenesis under the experimental conditions.

Nishimura I, Oshima A, Shibuya K, Mitani T, Negishi T. 2016. Acute and subchronic toxicity of 20 kHz and 60 kHz magnetic fields in rats. J Appl Toxicol. 36(2):199-210.

Despite increasing use of intermediate frequency (IF) magnetic fields (MFs) in occupational and domestic settings, scientific evidence necessary for health risk assessments of IF MF is insufficient. Male and female Crl:CD(SD) rats (12 per sex per group) were exposed to 20 kHz, 0.20 mT(root mean square, rms) or 60 kHz, 0.10 mT(rms) sinusoidal MFs for 22 h day(-1) for 14 days (acute) or 13 weeks (subchronic). Experiments were duplicated for each frequency to ensure outcome reproducibility, and examinations were blinded for quality assurance. All rats survived without significant clinical signs until the end of experiments. Some changes in body weight between the MF-exposed and control groups were observed over the course of exposure, although the directions of the changes were inconsistent and not statistically significant after subchronic exposure. There were significant differences between MF-exposed and control groups in some organ weights and parameters in hematology and clinical chemistry, but these were minor in magnitude and not repeated in duplicate experiments. Histopathological findings reflecting toxicity were sporadic. Frequencies of other findings were similar to historic data in this rat strain, and findings had no specific relationship to changes in organ weight or parameters of hematology and clinical chemistry in each animal. The changes observed throughout this

study were considered biologically isolated and were attributable to chance associations rather than to MF exposure. The results, in particular the histopathological evidence, indicate an absence of toxicity in IF MF-exposed rats and do not support the hypothesis that IF MF exposure produces significant toxicity.

Nishimura I, Doi Y, Imai N, Kawabe M, Mera Y, Shiina T. 2019. Carcinogenicity of intermediate frequency magnetic field in Tg.rasH2 mice. Bioelectromagnetics. 40(3):160-169.

Although the likelihood of exposure to leaking intermediate frequency magnetic fields (MFs) from electronic devices, such as induction-heating and wireless power transfer systems, has increased, biological data assessing the health risks associated with human exposure remain insufficient. We examined the carcinogenicity of a 20 kHz MF, a typical frequency produced by induction-heating cookers, using a transgenic rasH2 mouse model. Twenty-five male and female CByB6F1-Tg(HRAS)2Jic mice were exposed to a 0.20 mT, 20 kHz MF (22 h/day) or sham-exposed for 26 weeks. As a positive control, 10 male and female rasH2 mice from the same batch were administered a single intraperitoneal injection of 75 mg/kg N-methyl-N-nitrosourea. A blinded histopathological evaluation was performed, and the same experiments were conducted twice, independently, to confirm the reproducibility of the results. Histopathological examination revealed that spontaneous neoplastic lesions, such as splenic hemangiosarcomas and gastric squamous cell papillomas, were less (1-3 per group) in the MF- and sham-exposed groups. The frequency of the neoplastic lesions was not significantly different between the groups. Eight to ten mice in each positive-control group exhibited malignant lymphoma. The outcomes were consistent between duplicated experiments, which indicates lack of carcinogenicity of 20 kHz MF in the rasH2 mouse model.

Ohtani S, Ushiyama A, Maeda M, Wada K, Suzuki Y, Hattori K, Kunugita N, Ishii K. 2019. Global Analysis of Transcriptional Expression in Mice Exposed to Intermediate Frequency Magnetic Fields Utilized for Wireless Power Transfer Systems. Int J Environ Res Public Health. 16(10).

Background: Intermediate frequency magnetic fields (IF-MFs) at around 85 kHz are a component of wireless power transfer systems used for charging electrical vehicles. However, limited data exist on the potential health effects of IF-MFs. We performed a comprehensive analysis of transcriptional expression in mice after IF-MF exposure. **Materials and methods:** We developed an IF-MF exposure system to generate a high magnetic flux density (25.3 mT). The system can expose the IF-MF for a mouse whole-body without considering thermal effects. After 10 days (1 h/day) of exposure, a comprehensive expression analysis was performed using microarray data from both the brain and liver. **Results:** No significant differences in transcriptional expression were detected in the 35,240 probe-sets when controlling the false discovery rate (FDR) under a fold change cutoff >1.5. However, several differential expressions were detected without FDR-adjustment, but these were not confirmed by RT-PCR analysis. **Conclusions:** To our knowledge, this is the first in vivo study to evaluate the biological effects of IF-MF exposure with an intense magnetic flux density 253 times higher than the occupational restriction level defined by the International Commission on Non-Ionizing

Radiation Protection guidelines. However, our findings indicate that transcriptional responses in the living body are not affected under these conditions.

Ohtani S, Ushiyama A, Wada K, Suzuki Y, Ishii K, Hattori K. No evidence for genotoxicity in mice due to exposure to intermediate-frequency magnetic fields used for wireless powertransfer systems. Mutation Research/Genetic Toxicology and Environmental Mutagenesis. 863:503310, 2021.

Time varying magnetic fields (MFs) are used for the wireless power-transfer (WPT) technology. Especially, 85 kHz band MFs, which are included in the intermediate frequency (IF) band (300 Hz - 10 MHz), are commonly used WPT system for charging electric vehicles. Those applications of WPT technology have elicited public concern about health effects of IF-MF. However, existing data from health risk assessments are insufficient and additional data are needed. We assessed the genotoxic effects of IF-MF exposure on erythroid differentiation in mice. A high-intensity IF-MF mouse exposure system was constructed to induce an average whole-body electric field of 54.1 V/m. Blood samples were obtained from male mice before and after a 2-week IF-MF exposure (1 h/day, total: 10 h); X-irradiated mice were used as positive controls. We analyzed the blood samples with the micronucleus (MN) test and the Pig-a mutation assay. No significant differences were seen between IF-MF-exposed and sham-exposed mice in the frequencies of either MN or Pig-a mutations in mature erythrocytes and reticulocytes. IF-MF exposure did not induce genotoxicity in vivo under the study conditions (2.36× the basic restriction for occupational exposure, 22.9 V/m, in the International Commission on Non-Ionizing Radiation Protection (ICNIRP) guidelines). The absence of significant biological effects due to IF-MF exposure supports the practical application of this technology.

Ohtani S, Ushiyama A, Wada K, Suzuki Y, Hattori K. In vivo genotoxicity of high-intensity intermediate frequency magnetic fields in somatic cells and germ cells. J Radiat Res. 2022 Dec 29:rrac081. doi: 10.1093/jrr/rrac081.

Intermediate frequency magnetic fields (IF-MFs) at ~85 kHz are one of the components of wireless power transfer (WPT) systems. However, the available data needed for the assessment of the safety of organisms from IF-MF exposure are scarce. Thus, there is an imminent need to accumulate evidence-based assessment data. In particular, if humans are exposed to IF-MF due to an accident or trouble, they are at increased risk of being exposed to high-intensity IF-MF within a short period. The already existing exposure system was improved to a system that could intermittently expose animals at 3 s intervals. This system allows the exposure of a mouse to high-intensity IF-MF (frequency: 82.3 kHz; induced electric field: 87 V/m, which was 3.8 times the basic restriction level for occupational exposure in the ICNIRP guideline), while regulating the heat generated by the coil. In vivo genotoxicity after IF-MF exposure was assessed using micronucleus (MN) test, Pig-a assay, and gpt assay. The results of MN test and Pig-a assay in hematopoietic cells revealed that neither the reticulocytes nor the mature erythrocytes exhibited significant increases in the IF-MF-exposed group compared with that in the sham-exposed group. In germ cells, MN test and gpt assay outcomes showed that IF-MF exposure did not cause any genetic or chromosomal abnormality. Based on these data, there was no genotoxic effect of

our set IF-MF exposure on somatic and germ cells. These findings can contribute to the widespread use of WPT systems as effective data of IF-MF safety assessment.

Robertson IG, Wilson WR, Dawson BV, Zwi LJ, Green AW, Boys JT. 1996. Evaluation of potential health effects of 10 kHz magnetic fields: a short-term mouse toxicology study. Bioelectromagnetics. 17(2):111-122.

A high-frequency inductive power distribution (HID) technology has been developed that generates sinusoidal magnetic fields at a frequency of 10 kHz. In typical industrial applications, field intensities in the order of 0.2 mT can be expected between the current-carrying coils. Because the possible health effects of 10 kHz sinusoidal magnetic fields of this type had never been investigated, a broad evaluation of possible effects on animal health was made in a preliminary 14 day acute study and in a 90 day subchronic study using male and female B6C3F1 mice. Exposures were at 0.08, 0.28, and 1.0 mT vs. a background exposure of 3.7 microT and were essentially continuous. These studies failed to demonstrate any health effects that can be clearly related to the magnetic field exposure. No changes in animal behaviour or indications of morbidity were detected during the initial exposure to the fields. There were no significant differences in body weight between exposed and unexposed (control) mice at any time in the study, and the clinical chemistry and hematology parameters were essentially unchanged. Although minor differences in some clinical chemistry and hematology parameters were seen between control and exposure groups, the lack of exposure dependence, the lack of consistency between sexes, and the lack of correspondence with the results of the two studies all suggest that these were chance associations. Even if the changes were real, the magnitude of the changes was very small and does not indicate serious biological effects. Finally, all organs were macroscopically and microscopically normal except for isolated, generally mild, histological lesions and lesions that were ascribed to fighting among males. There was no obvious association with field intensity.

Rusovan A, Kanje M, Mild KH. 1992. The stimulatory effect of magnetic fields on regeneration of the rat sciatic nerve is frequency dependent. Exp Neurol. 117(1):81-84.

The effects of exposure to sinusoidal magnetic fields on regeneration of the rat sciatic nerve were studied. Regeneration distances were measured after a crush lesion. The rats were exposed to a 0.1-mT magnetic field of various frequencies (50-2000 Hz) inside a pair of Helmholtz coils for various periods of time. Regeneration was measured by the pinch test or by immunocytochemical staining for neurofilaments 3, 4, or 6 days after the lesioning. Frequencies of 250, 500, and 1000 Hz significantly increased the regeneration distance. Higher (2000 Hz) and lower (50 Hz) frequencies had no effect. Maximal stimulation was obtained at 1000 Hz. At this frequency the rate of regeneration was increased by 24%. The results suggest that a broad frequency window exists within which the regeneration processes are sensitive to perturbation by magnetic fields and/or currents induced in the animal.

Sachiko Yamaguchi-Sekino S, Masao Taki , Miwa Ikuyo , Kaoru Esaki , Atsuko Aimoto, Kanako Wake, Noriko Kojimahara. Assessment of combined exposure to intermediate-frequency electromagnetic fields and pulsed electromagnetic fields among library workers in Japan. Front Public Health 2022 Jul 28;10:870784.

Objective: To assess exposure levels to electromagnetic fields (EMFs) among library workers in Japan, focusing on co-exposure to intermediate-frequency EMF (IF-EMF) and pulsed EMF, to propose a new epidemiological research methodology. **Methods:** The evaluated exposure sources were an electromagnetic type-electronic article surveillance gate (EM-EAS, IF-EMF (operating frequency 220 Hz-14 kHz)) and an activator/deactivator of anti-theft tags termed as "book check unit" (BCU, pulsed EMF). Short-term exposures were: (E1) whole-body exposure from the EAS gate when sitting within 3 m; (E2) local exposure to transient IF-EMF while passing through or beside the EAS gate; and (E3) local exposure to a pulsed magnetic field on BCU use. E1-E3 were evaluated based on exposure levels relative to magnetic flux density at the occupational reference level (RL; E1) or as per occupational basic restrictions (BR; E2 and E3) delineated by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) 2010 guidelines. Exposure indices based on mid-term exposure (D1-D3), assuming exposure according to employment on a weekly basis, were used to assess exposure in actual working conditions. D1 represents continuous exposure from an EAS gate when sitting within 3 m of the gate. D2 and D3 represent repeated transient exposures occurring during gate pass or on the operation of a BCU. A link to a web-based questionnaire was distributed to librarians working at all libraries where the authors had mailed institutional questionnaires (4,073 libraries). Four exposure patterns were defined according to various exposure scenarios. **Results:** We obtained information on exposure parameters and working conditions from the 548 completed questionnaires. The ICNIRP guideline levels were not exceeded in any of the E1-E3 scenarios. Median of the D1 (% ICNIRP RL × hour/week) was 1, and >85% respondents had values <10. However, the maximum value was 513. Altogether, these results indicate that continuous exposure was low in most cases. The same tendency was observed regarding repeated transient exposure from EM-EAS gates (i.e., the median value for D2 (% ICNIRP BR × gate pass) was 5). However, there were several cases in which D1 and D2 values were >10 times the median. The median of D3 (% ICNIRP BR × BCU operation) was 10, and most respondents' D3 values were greater than their D2 values, although the derived results depended on the assumptions made for the estimation. **Conclusion:** We conducted an assessment of combined exposures to IF-EMF and pulsed EMF among library workers in Japan by evaluating both short-term exposures (E1-E3) and exposure indices based on mid-term exposures (D1-D3) assuming actual working conditions per questionnaire results. These results provide useful information for future epidemiological studies.

Sato Y, Kiyohara K, Takehara S, Kojimahara N. Ecological study on the penetration of induction heating cookers and birth outcomes in Japan. AIMS Public Health 7(2):336-343, 2020.

In recent years, equipment that generates intermediate-frequency electromagnetic fields (IF-EMFs) has become increasingly prevalent, and the influence of IF-EMFs on human health is thus attracting increasing attention. The present study was conducted with the aim of analyzing whether there is a relationship between the penetration of induction heating cookers and birth outcomes using an ecological study design at the prefectural level. We created data sets for all 47 prefectures in Japan using previously published statistics. Spontaneous fetal death rate, fetal death rate after 22 weeks of pregnancy, perinatal mortality rate, and proportion of newborns weighing less than 2500 g were used as birth outcomes in correlation analysis. A weak positive

association was observed between the penetration of induction heating cookers and the fetal death rate after the 22nd week of pregnancy (r = 0.27, p = 0.07), but it was not statistically significant. In addition, a weak negative association was observed between the penetration of induction heating cookers and the spontaneous fetal death rate (r = -0.27, p = 0.07), but it was not statistically significant. In the present ecological study, no statistically significant association were shown between the penetration of induction heating cookers and birth outcomes. To demonstrate further the safety of induction heating cooker use, observations in epidemiological studies of other designs should be considered.

Stuchly MA, Ruddick J, Villeneuve D, Robinson K, Reed B, Lecuyer DW, Tan K, Wong J. 1988. Teratological assessment of exposure to time-varying magnetic field. Teratology. 38(5):461- 466.

A teratological assessment was performed using rats that were exposed to an alternating magnetic field. The magnetic field had a sawtooth waveform similar to that produced by video display terminals (VDTs). Female rats were exposed 2 weeks prior to and throughout pregnancy at a rate of 7 h/day. Three intensities of magnetic field (5.7, 23 or 66 microT) were used. All of these field intensities were much greater than those to which VDT users are exposed. A slight but statistically significant decrease in maternal lymphocyte count for the highest intensity field was found as compared with the control group. However, the lymphocyte count was within the normal range, and the observed changes in hematological parameters were considered mild. No other maternal or fetal parameters that were examined showed a significant difference for any of the three field intensities. Where minor variations in skeleton development were observed they were known to be the common "noise" that appears in every teratological evaluation.

Sundaram V, Mohammed S, Zyuzikov N. Effects of 150 kHz intermediate frequency electromagnetic radiation on fertility indicators in male rats. Heliyon. 8(12). 2022. doi: 10.1016/j.heliyon.2022.e12228.

Background The present study aimed to evaluate the effects of whole-body exposure to 150 kHz Intermediate-frequency electromagnetic radiation (IF EMR) on fertility indicators of male rats since human exposure to this frequency has increased in recent years. Fourteen adult male Sprague-Dawley rats were used in this study. The rats were randomly divided into a control and an EMR group (n = 7/group). The EMR group was continuously irradiated with 150 kHz EMR for 8 weeks. Male fertility indicators, body mass, testicular mass, rectal temperature, testicular histology, histometry, sperm analysis, and serum gonadotrophic hormone levels were evaluated. Results The study showed no negative effect on body mass (grams) (323.78 ± 37.09 to 305.09 ± 26.36; p = 0.72), rectal temperature (Control: 34.5 °C–35.8 °C; EMR: 34.4 °C–36.1 °C; p < 0.05), and testicular histology. There were significant reductions in left and right testicular mass (1.04 ± 0.10 to 0.96 ± 0.32: p = 0.03 and 1.02 ± 0.08 to 0.96 ± 0.35 p = 0.04, respectively), interstitial cell count/1000 μm2 (5.33 ± 0.56 to 4.47 ± 0.48; p = 0.01), sperm motility trajectories (p = 0.05) and sperm distal cytoplasmic droplet (%) (2.27 ± 2.28 to 6.84 ± 5.01; p = 0.05). A significant increase in follicle-stimulating hormone levels was observed (13.44 ± 6.38 IU/ml to 26.96 ± 8.07 IU/ml; p = 0.01). Conclusions Most male fertility parameters of rats in the present study were not affected by 8 weeks of whole-body exposure to 150 kHz EMR. However,

significant decreases in testicular mass, interstitial cell count/1000 μm2, sperm motility trajectories, and distal cytoplasmic droplets were observed, as well as an increase in FSH level.

Svedenstål BM, Johanson K-J. 1998. Leukocytes and micronucleated erythrocytes in peripheral bloodfrom mice exposed to 50-Hz or 20-kHz magnetic fields. Electro-and magnetobiology. 17(2):127-143.

CBNS and CBNCa mice were exposed to 50-Hz, 14-μT peak-to-peak (p-p) or 20-kHz, 15-μT pp magnetic fields (MFs) for various periods in 5 experiments. Numbers of leukocytes and erythrocytes, as well as of micronucleated erythrocytes, were studied in peripheral blood. Statistically significant decreases in the number of lymphocytes occurred with nearly the same frequency as increases. The variation in the numbers of leukocytes was more time dependent in MF-exposed than in sham-exposed control animals. The ratio between the immature and mature erythrocytes increased significantly only in mice exposed for 90 days to a 50-Hz MF. The 50-Hz MF did not increase micronuclei in peripheral erythrocytes during 90-day exposure. Taken together, the results do not indicate any strong effects of MFs on leukocyte and erythrocyte formation in CBA mice. If there were slight effects on blood leukocytes, they need further confirmation with larger numbers of animals.

Svedenstål BM, Holmberg B. 1993. Lymphoma development among mice exposed to X-rays and pulsed magnetic fields. Int J Radiat Biol. 64(1):119-125.

CBA mice were exposed to a total of 5.24 Gy X-rays (260 kV, 11 mA, 0.45 Gy/min), divided into four exposures, and to saw-tooth 15 microT (peak to peak) pulsed vertical 200 kHz magnetic fields for their life-time. In parallel, series with magnetic fields only or non-exposed animals were run. The animals were observed for their life-time. The frequency of lymphomas was 65.7% in the X-ray group and 71.4% in the groups exposed to both X-ray and magnetic field. Of the non-exposed control animals, and of the animals exposed to magnetic fields only 6.4 and 5.7% had lymphomas, respectively. There were no statistically significant differences between the magnetic field series and the corresponding controls for lymphomas. Blood cell counts and haemoglobin data did not show differences between the X-irradiated, and X-ray and magnetic field-exposed groups. Mononuclear cells and total leukocytes were elevated for pulsed magnetic fields-exposed animals compared with the non-exposed controls. This difference was due to two animals with extreme values. In the pulsed magnetic fields treated group there was a statistically significant increase of the carcass weight compared with the non-treated control group.

Svedenstål BM, Johanson KJ. 1995. Fetal loss in mice exposed to magnetic fields during early pregnancy. Bioelectromagnetics. 16(5):284-289.

The effects of low-frequency magnetic fields (MFs) on early pregnancy were studied in CBA/S mice. The magnetic field was a 20 kHz, 15 microT sawtooth. Pregnant females were divided into four groups, two control groups and two exposed groups. One group was exposed to MFs continuously from day 1 postconception (pc) until day 5.5 pc, and the other group was exposed continuously until day 7 pc. All animals were sacrificed on day 19 pc, the day before partus, and

their uterine contents were analyzed. No significant increase in the resorption (early fetal death) rate was found in the exposed animals compared to the sham controls. In the group exposed during days 1.0-5.5 pc, the body weight and length of the living fetuses were significantly decreased. Except on day 3 pc (progesterone) and day 13 pc (calcium) in the treated groups, there were no significant differences in progesterone and calcium levels in peripheral blood. Implantation occurred on the same day in MF-treated and control animals.

Tokinobu A, Tanaka K, Arakawa M, Miyake Y. Maternal Use of Induction Heating Cookers During Pregnancy and Birth Outcomes: The Kyushu Okinawa Maternal and Child Health Study. Bioelectromagnetics 42(4):329-335, 2021.

The effects of exposure to intermediate-frequency electromagnetic fields (IF-EMFs) during pregnancy on birth outcomes are uncertain. We investigated the association between the use of induction heating (IH) cookers, which are major sources of IF-EMFs, during pregnancy and preterm birth (PTB), low birth weight (LBW), small-for-gestational-age (SGA), and birth weight, using data from a prebirth cohort study in Japan. Study participants were 1,565 mothers with singleton pregnancies and the babies born from these pregnancies. We collected the data presented here using self-administered questionnaires. An adjustment was made for maternal age, region of residence, number of children, family structure, maternal education, maternal employment, maternal alcohol intake, smoking during pregnancy, maternal body mass index, baby's sex, and gestational age at birth. IH cooker use during pregnancy was independently associated with a reduced risk of PTB: the adjusted odds ratio was 0.28 (95% confidence interval: 0.07-0.78). IH cooker use during pregnancy was not associated with LBW, SGA, or birth weight. This is the first study to show that IH cooker use during pregnancy is independently inversely associated with PTB.

Uehara S, Yuasa A, Ushizawa K, Kodera S, Kamimura Y, Hirata A, Otaka Y. Characteristics of current perception produced by intermediate-frequency contact currents in healthy adults. Front Neurosci 17:1145505, 2023.

Introduction: Contact electrical currents in humans stimulate peripheral nerves at frequencies of <100 kHz, producing sensations such as tingling. At frequencies above 100 kHz, heating becomes dominant, resulting in a sensation of warmth. When the current amplitude exceeds the threshold, the sensation results in discomfort or pain. In international guidelines and standards for human protection from electromagnetic fields, the limit for the contact current amplitude has been prescribed. Although the types of sensations produced by contact current at low frequencies, i.e., approximately 50-60 Hz, and the corresponding perception thresholds have been investigated, there is a lack of knowledge about those in the intermediate-frequency band-particularly from 100 kHz to 10 MHz. **Methods:** In this study, we investigated the current-perception threshold and types of sensations for 88 healthy adults (range: 20-79 years old) with a fingertip exposed to contact currents at 100 kHz, 300 kHz, 1 MHz, 3 MHz, and 10 MHz. **Results:** The current perception thresholds at frequencies ranging from 300 kHz to 10 MHz were 20-30% higher than those at 100 kHz ($p < 0.001$). In addition, a statistical analysis revealed that the perception thresholds were correlated with the age or finger circumference: older participants and those with larger finger circumferences exhibited higher thresholds. At frequencies of ≥300

kHz, the contact current mainly produced a warmth sensation, which differed from the tingling/pricking sensation produced by the current at 100 kHz. **Discussion:** These results indicate that there exists a transition of the produced sensations and their perception threshold between 100 kHz and 300 kHz. The findings of this study are useful for revising the international guidelines and standards for contact currents at intermediate frequencies.

Ushiyama A, Ohtani S, Suzuki Y, Wada K, Kunugita N, Ohkubo C. 2014. Effects of 21-kHz intermediate frequency magnetic fields on blood properties and immune systems of juvenile rats. Int J Radiat Biol. 90(12):1211-1217.

Purpose: Due to a lack of science-based evidence, we explored the effects of exposure to intermediate frequency magnetic fields (IF-MF) on experimental animals. We assessed several immunological parameters to determine the effect of exposure of the whole body to IF-MF. **Materials and methods:** Male Sprague-Dawley rats (4-5 weeks old) were divided into three groups: Cage-control, sham, and 3.8-mT (rms) exposure groups. The animals were exposed to IF-MF at 21 kHz under fixed conditions in an acrylic holder. Exposure was performed for 1 h/day for 14 consecutive days. On the 15th day following the exposure, biochemical and hematological parameters in blood were analyzed. The effects of the exposure on immunological functions such as the cytotoxic activity of lymphocytes, chemotactic and phagocytic activity of granulocytes, and T (cluster of differentiation 4 [CD4] and cluster of differentiation 8 [CD8])-cell frequency were also examined. **Results:** Hematological parameters were not affected by IF-MF exposure. Other immune functions such as the cytotoxic activity and phagocytic activity were not affected. Populations of T cells after exposure also did not show any significant differences. In blood biochemistry, there was significant difference in inorganic phosphorus level between sham and exposure group. However, this will not induce any pathophysiological status, because they were still within physiological range. Overall, no significant effect by exposure of IF-MF was observed under our experimental conditions. **Conclusions:** Our results suggest that exposure to 21-kHz sinusoidal IF-MF at 3.8 mT for 1 h/day for 14 days did not affect immune function in juvenile rats.

Wiley MJ, Corey P, Kavet R, Charry J, Harvey S, Agnew D, Walsh M. 1992. The effects of continuous exposure to 20-kHz sawtooth magnetic fields on the litters of CD-1 mice. Teratology. 46(4):391-398.

Mated CD-1 mice were exposed to 20-kHz sawtooth magnetic fields similar to those associated with video display terminals (VDT). Four groups of animals were continuously exposed from day 1 to day 18 of pregnancy to field strengths of 0, 3.6, 17, or 200 microT. There were no less than 185 mated dams in each exposure group. On day 18, the dams were sacrificed and assessed for weight gain and pregnancy. The litters were evaluated for numbers of implantations, fetal deaths and resorptions, gross external, visceral and skeletal malformations, and fetal weights. There were no less than 140 pregnant females in each group, and there were no significant differences between any of the exposure groups and the sham group (0 microT) for any of the end points. The results of this study do not support the hypothesis that the 20-kHz VLF magnetic fields associated with video display terminals are teratogenic in mammals.

Win-Shwe TT, Ohtani S, Ushiyama A, Fujimaki H, Kunugita N. 2013. Can intermediate-frequency magnetic fields affect memory function-related gene expressions in hippocampus of C57BL/6J mice? J Toxicol Sci. 38(2):169-176.

Recently, a cooking appliance based on the principle of electromagnetic induction has come to be used domestically on a widespread basis; this induction heating cooking hob mainly generates intermediate-frequency magnetic fields (IF-MF). However, whether electromagnetic fields originating from household appliances represent a health risk remains uncertain. We investigated the effect of IF-MF on the expressions of memory function-related genes and related transduction molecules in the mouse hippocampus. Male and female C57BL/6J mice were allotted to a control (sham-exposed), an exposure, or a recovery (one week after exposure) group and were exposed to IF-MF (21 kHz, 3.8 mT) one hour per day for 2 weeks. Twenty-four hour after final exposure, the expression levels of memory function-related genes and the mRNA levels for signal transduction pathway molecules in the hippocampi were examined using real-time RT-PCR. The relative mRNA expression levels of the N-methyl-D aspartate (NMDA) receptor subunits NR1, NR2A, and NR2B as well as transcription factors (calcium/calmodulin-dependent protein kinase (CaMK) -IV, cyclic AMP responsive element binding protein (CREB) -1) and neurotrophins (nerve growth factor (NGF), and brain-derived neurotrophic factors (BDNF)) were not significantly altered in the IF-MF-exposed mice. We also examined the morphology of the hippocampus using a histological analysis, but no changes in the IF-MF-exposed mice were seen. This is the first in vivo study to show that IF-MF exposure did not affect the expression levels of memory function-related genes in the hippocampus of C57BL/6J mice. The present findings suggest that IF-MF exposure may not affect cognitive function in the present animal model.

Win-Shwe TT, Ohtani S, Ushiyama A, Kunugita N. 2015. Early exposure to intermediate-frequency magnetic fields alters brain biomarkers without histopathological changes in adult mice. Int J Environ Res Public Health. 12(4):4406-4421.

Recently we have reported that intermediate-frequency magnetic field (IF-MF) exposure transiently altered the mRNA expression levels of memory function-related genes in the hippocampi of adult male mice. However, the effects of IF-MF exposure during brain development on neurological biomarkers have not yet been clarified. In the present study, we investigated the effect of IF-MF exposure during development on neurological and immunological markers in the mouse hippocampus in 3- and 7-week-old male mice. Pregnant C57BL/6J mice were exposed to IF-MF (21 kHz, 3.8 mT) for one hour per day from organogenesis period day 7 to 17. At adolescence, some IF-MF-exposed mice were further divided into exposure, recovery, and sham-exposure groups. The adolescent-exposure groups were exposed again to IF-MF from postnatal day 27 to 48. The expression of mRNA in the hippocampi was examined using a real-time RT-PCR method, and microglia activation was examined by immunohistochemical analysis. The expression levels of NR1 and NR2B as well as transcription factors (CaMKIV, CREB1), inflammatory mediators (COX2, IL-1 b,TNF-α), and the oxidative stress marker heme-oxygenase (HO)-1 were significantly increased in the IF-MF-exposed mice, compared with the control group, in the 7-week-old mice, but not in the 3-week-old mice. Microglia activation was not different between the control and other groups. This study provides the first evidence that early exposure to IF-MF reversibly affects the NMDA receptor,

its related signaling pathways, and inflammatory mediators in the hippocampus of young adult mice; these changes are transient and recover after termination of exposure without histopathological changes.

Yamazaki K, Taki M, Ohkubo C. 2016. Safety assessment of human exposure to intermediate frequency electromagnetic fields. Electrical Engineering in Japan. 197(4):3-11.

The “intermediate frequency” electromagnetic fields in the context of protecting human exposure have received public concerns in recent years. This is mainly due to the growing emergence of technology or products using those fields, such as induction heating (IH) cookers and wireless power transfer (WPT) systems. This paper reviews the trend of studies and guidelines for human protection related to safety assessment of human exposure to such fields.

Zhao J, Wu Z, Yang T, Zhao Y, Wang L. 2020. Electromagnetic Biological Effect on Mice in Wireless Power Transmission System. IEEE Access. 8:205558-205567.