Dr. Joel Moskowitz (Director, Center for Family and Community Health, School of Public Health University of California, Berkeley, <u>https://www.facebook.com/SaferEMR</u>) has posted 20 New papers on EMF, biology or health on his blog <u>https://www.saferemr.com/2018/04/recent-research.html</u> Below are some of those studies and excerpts from that page. Studies show effects on liver (hepatic),heart, kidney, adrenal glands, brain, testes and sperm. Also papers on measurements of radiation and EMFs in the environment.

Bio-physical effects of RF EMR on blood parameters, spermatozoa, liver, kidney and heart of albino rats

Adebayo EA, Adeeyo AO, Ogundiran MA, Olabisi O. Bio-physical effects of radiofrequency electromagnetic radiation (rf-emr) on blood parameters, spermatozoa, liver, kidney and heart of albino rats. Journal of King Saud University - Science. 15 Nov 2018. <u>https://doi.org/10.1016/j.jksus.2018.11.007</u>.

Abstract

Current study aimed at determining the consequence of Radiofrequency (≈1800 MHz) electromagnetic radiation (RF-EMR) on the histological, hematological and histochemical properties of selected tissues of rat and to assess morphological changes associated with such exposures. Three groups of thirty rats of which two groups of twenty rats were subjected to average radiation of \approx 1.40 mW/cm2 at 24 m from the base of two different telecommunications network mast for 5 weeks. Histochemical, haematological and histological analyses of the rats were afterward carried out on selected tissues of the experimental animals using standard procedures. Impacts of radiation were noted in the exposed groups of rats. There was rise in white blood cells with variations in other blood parameters; the sperm motility and sperm count of the exposed rats is lower than the control; the **liver** of the exposed rats shows pronounced dilated sinusoids, distorted architecture, hyperchromatic nuclei, congested central vein, with change of hepatocytes structure; the **heart** shows gross distortion of cardiac muscular architecture with distorted irregular cardiac muscle fibres and wider interfibres spaces; kidney showing hyperchromatic nuclei, gradual loss and degeneration of flattened squamous epithelial cells lining and **testis** shows grossly distorted seminiferous tubules and epididymis with loss of cellular structure and an area of inflammatory changes with complete absence of spermatozoa, which may lead to low fertility. This study shows that radiofrequency electromagnetic radiation may induce morphological changes in various tissues of living systems in rat.

Conclusion

From the data presented in this study, it can be observed that **impact of RF-EMR from telecommunication base stations are reasonably manifested on internal organs in a similar manner observed in ionizing radiation studies.** Some of the organs examined showed histological, hematological and histochemical changes which are different from normal. The study established that the reproductive organs of male rats were seriously impaired, which may have similar effect on higher mammal. It is recommended that further research to study the long term effect of RF-EMR from telecommunication on living systems in Nigeria be intensified.

Open access paper: https://www.sciencedirect.com/science/article/pii/S1018364717308789

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2.45 GHz microwave radiation impairs learning, memory, and hippocampal synaptic plasticity in the rat

Karimi N, Bayat M, Haghani M, Saadi H, Ghazipour GR. 2.45 GHz microwave radiation impairs learning, memory, and hippocampal synaptic plasticity in the rat. Toxicol Ind Health. 2018 Oct 21:748233718798976. doi: 10.1177/0748233718798976

Abstract

Microwave (MW) radiation has a close relationship with neurobehavioral disorders. Due to the widespread usage of MW radiation, especially in our homes, it is essential to investigate the direct effect of MW radiation on the central nervous system. Therefore, this study was carried out to determine the effect of MW radiation on memory and hippocampal synaptic plasticity. The rats were exposed to 2.45 GHz MW radiation (continuous wave with overall average power density of 0.016 mW/cm2 and overall average whole-body specific absorption rate value of 0.017 W/kg) for 2 h/day over a period of 40 days. Spatial learning and memory were tested by radial maze and passive avoidance tests. We evaluated the synaptic plasticity and hippocampal neuronal cells number by field potential recording and Giemsa staining, respectively. Our results showed that MW radiation exposure decreased the learning and memory performance that was associated with decrement of long-term potentiation induction and excitability of CA1 neurons. However, MW radiation did not have any effects on short-term plasticity and paired-pulse ratio as a good indirect index for measurement of glutamate release probability. The evaluation of hippocampal morphology indicated that the neuronal density in the hippocampal CA1 area was significantly decreased by MW.

https://www.ncbi.nlm.nih.gov/pubmed/30345889

Maternal cell phone use during pregnancy and child cognition at age 5 years in 3 birth cohorts

Sudan M, Birks LE, Aurrekoetxea JJ, Ferrero A, Gallastegi M, Guxens M, Ha M, Lim H, Olsen J, González-Safont L, Vrijheid M, Kheifets L. Maternal cell phone use during pregnancy and child cognition at age 5 years in 3 birth cohorts.Environ Int. 2018 Nov;120:155-162. doi: 10.1016/j.envint.2018.07.043. Highlights

- Prenatal maternal cell phone use may be related to child cognition.
- Cognition scores are slightly lower in relation to higher frequency use, although

imprecise.

• The causal mechanisms are unknown at this time.

• The association is likely affected by social and behavioral factors. Abstract

METHODS: This study included data from 3 birth cohorts: the Danish National Birth Cohort (DNBC) (n = 1209), Spanish Environment and Childhood Project (INMA) (n = 1383), and Korean Mothers and Children's Environment Health Study (MOCEH) (n = 497). All cohorts collected information about maternal cell phone use during pregnancy and cognitive performance in children at age 5. We performed linear regression to compute mean differences (MD) and 95% confidence intervals (CI) in children's general, verbal, and non-verbal cognition scores comparing frequency of maternal prenatal cell phone use with adjustments for numerous potential confounding factors. Models were computed separately for each cohort and using pooled data in meta-analysis.

RESULTS: No associations were detected between frequency of prenatal cell phone use and children's cognition scores. Scores tended to be lower in the highest frequency of use category; MD (mean differences) (95% CI) in general cognition scores were 0.78 (-0.76, 2.33) for none, 0.11 (-0.81, 1.03) for medium, and -0.41 (-1.54, 0.73) for high compared to low frequency of use. This pattern was seen across all cognitive dimensions, but the results were imprecise overall.

CONCLUSION: We observed patterns of lower mean cognition scores among children in relation to high frequency maternal prenatal cell phone use. The causal nature and mechanism of this relationship remain unknown. https://www.ncbi.nlm.nih.gov/pubmed/30096609

Radiations and male fertility

Kesari KK, Agarwal A, Henkel R. Radiations and male fertility. Reprod Biol Endocrinol. 2018 Dec 9;16(1):118. doi: 10.1186/s12958-018-0431-1. Abstract

During recent years, an increasing percentage of male infertility has to be attributed to an array of environmental, health and lifestyle factors. Male infertility is likely to be affected by the intense exposure to heat and extreme exposure to pesticides, radiations, radioactivity and other hazardous substances. We are surrounded by several types of ionizing and non-ionizing radiations and both have recognized causative effects on spermatogenesis. Since it is impossible to cover all types of radiation sources and their biological effects under a single title, this review is focusing on radiation deriving from cell phones, laptops, Wi-Fi and microwave ovens, as these are the most common sources of non-ionizing radiations, which may contribute to the cause of infertility by exploring the effect of exposure to radiofrequency radiations on the male fertility pattern. From currently available studies it is clear that radiofrequency electromagnetic fields (RF-EMF) have deleterious effects on sperm parameters (like sperm count, morphology, motility), affects the role of kinases in cellular metabolism and the endocrine system, and produces genotoxicity, genomic instability and oxidative stress. This is followed with protective measures for these radiations and future recommendations. The study concludes that the RF-EMF may induce oxidative stress with an increased level of reactive oxygen species, which may lead to infertility. This has been concluded based on available evidences from in vitro and in vivo studies suggesting that RF-EMF exposure negatively affects sperm quality. Open access paper: <u>https://rbej.biomedcentral.com/articles/10.1186/s12958-018-0431-1</u>

Peculiar Effects of Electromagnetic Millimeter Waves on Tumor Development in BALB/c Mice

Bantysh BB, Krylov AY, Subbotina TI, Khadartsev AA, Ivanov DV, Yashin AA. Peculiar Effects of Electromagnetic Millimeter Waves on Tumor Development in BALB/c Mice. Bull Exp Biol Med. 2018 Sep;165(5):692-694. doi: 10.1007/s10517-018-4243-2.

Abstract

The study examined the effects of millimeter electromagnetic waves at a frequency of 130 GHz corresponding to the molecular absorption and radiation spectra of NO and O2 with the total exposition time of 6 h on tumor morphogenesis in 3- and 6-month-old tumor-prone BALB/c mice of both sexes. In experimental mice exposed to electromagnetic radiation, the development of cancer process was slowed down throughout the observation period; moreover, no macroscopic signs of the tumors were revealed. However, in contrast to control mice, experimental animals demonstrated the formation of pathological reactions reflected by hepatic biochemical indices accompanied by the development of dystrophic and microcirculatory alterations in the liver tissue.

https://www.ncbi.nlm.nih.gov/pubmed/30225701

Exposure to cell phone radiofrequency changes corticotrophin hormone levels and histology of the brain and adrenal glands in male Wistar rat

Shahabi S, Taji IM, Hoseinnezhaddarzi M, Mousavi F, Shirchi S, Nazari A, Zarei H, Pourabdolhossein F.Exposure to cell phone radiofrequency changes corticotrophin hormone levels and histology of the brain and adrenal glands in male Wistar rat. Iranian J Basic Medical Sciences. 21(12):1269-1274. DOI: 10.22038/ijbms.2018.29567.7133

Abstract

Objective(s): Nowadays, the electromagnetic field-emitting devices are used routinely in our lives. Controversial reports exist concerning the effects of mobile radiofrequency (RF) on different parts of the body, especially stress hormones. The main goal of the present work was to study the long-term effects of mobile RF900 MHz exposure with special focus on the adrenal

gland pathophysiology and function.

Materials and Methods: Adult male Wistar rats were exposed to mobile RF 6 hr daily for 4-8 weeks. Intact and switched-off exposed animals were considered as controls. Plasma ACTH and cortisol levels were measured by the ELISA method. At the end of the experiment, a histological study was done on adrenal gland and brain tissues by hematoxylin and eosin staining. The thickness of the fasciculate layer of the adrenal gland, and its cell count and perimeter were measured using the Fiji software.

Results: Enhanced plasma ACTH and cortisol levels were found after prolonged exposure to mobile RE The fasciculata layer of adrenal cortex eventually thickened following mobile RF radiation. While the number of cells in zona fasciculata remained constant, the cell size and perimeter increased during RF exposure. Finally, we found that vacuolization in brain tissue and the number and size of vacuoles considerably increased during two months of RF exposure.

Conclusion: Cell phone RF exposure induced significant hormonal and structural changes in adrenal gland and brain tissues. Therefore, the public should be aware and limit their exposure as much as possible.

http://ijbms.mums.ac.ir/article_11712.html

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Changes in testicular morphology & oxidative stress in 60-day-old rats following exposure to continuous 900-MHz EMF throughout adolescence

Hanci H, Kerimoğlu G, Mercantepe T, Odacı E. Changes in testicular morphology and oxidative stress biomarkers in 60-day-old Sprague Dawley rats following exposure to continuous 900-MHz electromagnetic field for 1 h a day throughout adolescence. Reprod Toxicol. 2018 Oct;81:71-78. doi: 10.1016/j.reprotox.2018.07.002.

Abstract

The purpose of this study was to investigate the 60-day-old male rat testis following exposure to continuous 900-megahertz (MHz) electromagnetic field (EMF) throughout the adolescent period using histopathological and biochemical analysis methods. Twenty-four Sprague Dawley rats aged 21 days were randomly and equally (n = 8) divided into three groups. No procedure was performed on the control group rats. The sham group rats were held in an EMF-cage without exposure to EMF. The EMF group rats were exposed to continuous 900-MHz EMF for 1 h each day inside the EMF-cage during adolescence. On postnatal day 60 the testes were extracted and divided into right and left halves. The right half was used for histopathological evaluation and the left half for biochemical analyses. Our results show that changes may occur in morphology and oxidative stress biomarkers in the rat testis following exposure to continuous 900-MHz EMF throughout the adolescent period.

https://www.ncbi.nlm.nih.gov/pubmed/30009952

The effects of radiofrequency radiation on mice fetus weight, length and tissues

Alimohammadi I, Ahtarinezhad A, Mohamadzadeh Asl B, Masruri B, Moghadasi N. The effects of radiofrequency radiation on mice fetus weight, length and tissues. Data in Brief. 19:2189-2194. August 2018. <u>https://doi.org/10.1016/j.dib.2018.06.107</u>.

Value of data

• The result of this study is useful for workers and users that are exposed to radiofrequency radiation as a physical agent.

• Investigation of radiofrequency radiation effects in organogenesis period during pregnancy and protective role of vitamin C as a water-soluble antioxidant in body tissues and fluids are the innovation of this study.

• These data showed changes of growth parameters and abnormalities in tissues as the result of radiofrequency radiation exposure which could be useful for some organization such as Ministry of Health and Medical Education to recognize possible risks in vulnerable groups like pregnant women and their embryos and protect them more effective.

Abstract

The public concern of harmful effects of radiofrequency radiation exposure, especially with rapid increase in the use of wireless and telecommunication devices, is increasing. Some studies show fetal and developmental abnormalities as the result of radiofrequency radiation exposure. We aimed to investigate possible teratogenic effects of radiofrequency in 915 MHz on mice fetus and protective role of vitamin C. 21 pregnant mice were divided into 3 groups. Control group was in normal condition without any stressor agent. Exposure group was exposed to 915 MHz RFR (8 h/day for 10 days) and 0.045 µw/cm2 power density. The exposure plus vitamin C group received 200 mg/kg vitamin C by gavage and was exposed to 915 MHz RFR (8 h/day for 10 days) and 0.045 μ w/cm2 power density. The fetus weight, C-R length were measured by digital balance and caliper. Tissues were assessed after staining with H & E. Our results showed significant increase in fetus weight and C-R length and also enlarged liver, tail deformation in mice fetus in exposure group. Although usage of vitamin C caused significant decrease in mentioned parameters. The outcome of this study confirms the effects of radiofrequency radiation on growth parameters such as body weight, length and some tissues in mice fetuses and protective effect of vitamin C. However more studies on non-ionization radiation in different frequencies and severity, during pregnancy are needed to clarify the exact mechanisms of these changes and better protection.

Open access paper: https://www.sciencedirect.com/science/article/pii/S2352340918307583

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Thermal effects of mobile phones on human auricle region

Bauer J, O'Mahony C, Drahomir Chovan, John Mulcahy, Christophe Silien and Syed A.M. Tofail. Thermal effects of mobile phones on human auricle region. Journal of Thermal Biology. <u>https://doi.org/10.1016/j.jtherbio.2018.11.008</u> Highlights

• An in silico model of thermal heating of human auricle region due to mobile phone has been developed from first principle and using a COMSOL Multiphysics

• The model allowed determination of the impact of battery discharge rate, battery capacity, battery cathode material, biological tissue distance, antenna radio-wave frequency and intensity.

• Mobile phone heating during a typical call has been simulated and compared with experimental infrared thermographic imaging.

• 1800MHz frequency of data transmission showed the highest temperature increase in the fat/water phantom

• Heating process is generally dominated by the CPU heat although antenna heat can penetrate deeper and can still be a cause of concern.

• The proposed model can be used for the understanding of negative mobile phones impact on human health, including prediction and comprehension of eventual long and short-term side effects

• This new model will aid designing of mobile phones to prevent causing potential negative thermal effect.

Abstract

Mobile phones have become an indispensable utility to modern society, with international use increasing dramatically each year. The GSM signal operates at 900 MHz, 1800MHz and 2250 MHz, may potentially cause harm to human tissue. Yet there is no in silico model to aid design these devices to protect from causing potential thermal effect. Here we present a model of sources of heating in a mobile phone device with experimental verification during the phone call. We have developed this mobile phone thermal model using first principles on COMSOL® Multiphysics modelling platform to simulate heating effect in human auricle region due to mobile phone use. In particular, our model considered both radiative and non-radiative heating from components such as the lithium ion battery, CPU circuitry and the antenna. The model showed the distribution and effect of the heating effect due to mobile phone use and considered impact of battery discharge rate, battery capacity, battery cathode material, biological tissue distance, antenna radio-wave frequency and intensity. Furthermore, the lithium ion battery heating was validated during experiments using temperature sensors with an excellent agreement between simulated and experimental data (<1% variation). Mobile phone heating during a typical call has also been simulated and compared with experimental infrared thermographic imaging. Importantly, we found that 1800MHz frequency of data transmission showed the highest temperature increase in the fat/water phantom used in this simulation. We also successfully compared heating distribution in human auricle region during mobile phone use with clinical thermographic images with reasonable gualitative and guantitative agreements. In summary, our model provides a foundation to conceive thermal and other physical effects caused by mobile

phone use and allow for the understanding of potential negative health effects thus supporting and promoting personalized and preventive medicine using thermography. Excerpt

For the frequencies active in mobile phones, 900MHz, 1800MHz and 2250MHz, 1800MHz showed the highest temperature increase in the fat/water phantom used in this simulation. 900MHz and 2250MHz showed similar heating, but below 1 degree C. Varying the distance of the complete mobile phone model from the phantom cube, the temperature increased by a factor of 10 from contact with the phantom compared to 50 mm away. The model shows that the temperature was dominated by the CPU heat, conduction from and exceeded the contributions to the heating from the antenna and the battery. The antenna heat, however, has more penetrative properties. This allowed for temperature changes to travel deeper and cause much serious temperature effect on soft tissues and brain.

https://www.sciencedirect.com/science/article/pii/S0306456518304431

Theoretical & numerical assessment of maximally allowable power-density averaging area for EMF exposure assessment above 6 GHz

Neufeld E, Carrasco E, Murbach M, Balzano Q, Christ A, Kuster N. Theoretical and numerical assessment of maximally allowable power-density averaging area for conservative electromagnetic exposure assessment above 6 GHz. Bioelectromagnetics. 01 November 2018. <u>https://doi.org/10.1002/bem.22147</u>

Abstract

The objective of this paper is to determine a maximum averaging area for power density (PD) that limits the maximum temperature increase to a given threshold for frequencies above 6 GHz. This maximum area should be conservative for any transmitter at any distance >2 mm from the primary transmitting antennas or secondary field-generating sources. To derive a generically valid maximum averaging area, an analytical approximation for the peak temperature increase caused by localized exposure was derived. The results for a threshold value of 1 K temperature rise were validated against simulations of a series of sources composed of electrical and magnetic elements (dipoles, slots, patches, and arrays) that represented the spectrum of relevant transmitters. The validation was successful for frequencies in which the power deposition occurred superficially (i.e., >10 GHz). In conclusion, the averaging area for a PD limit of 10 W/m² that conservatively limits the temperature increase in the skin to less than 1 K at any distance >2 mm from the transmitters is frequency dependent, increases with distance, and ranges from 3 cm² at <10 GHz to 1.9 cm² at 100 GHz. In the far-field, the area depends additionally on distance and the antenna array aperture. The correlation was found to be worse at lower frequencies (<10 GHz) and very close to the source, the systematic evaluation of which is part of another study to investigate the effect of different coupling mechanisms in the reactive near-field on the ratio of temperature increase to incident power density. The presented model can be directly applied to any other PD and temperature thresholds.

Excerpts

Standardization The results presented herein have important consequences for safety standards, as they demonstrate a need to use smaller and potentially frequency-dependent averaging areas. The maximal area at a source distance of 2 mm ranges from <2 cm2 at 100 GHz to ≥3 cm2 at <10 GHz. These conditions could be relaxed, should a temperature threshold >1 K be selected or for larger distances from the source. The suggested areas are smaller but comparable to the 4 cm2 previously suggested by Hashimoto et al. [2017] based on computational modeling of localized exposure-

induced heating.

Further Investigations The current investigation assumed stationary exposure. However, time-averaged limits are foreseen by the standards to allow for pulsed exposures. The presented investigation can be readily extended to transient exposures by application of 4D rather than 3D Green's functions [Yeung and Atalar, 2001]. In the absence of a steady-state temperature increase, the 1 K criterion could be replaced, for example, with a criterion based on thermal dose [Van Rhoon et al., 2013].

CONCLUSIONS Analytical relationships for localized exposure in the 5G frequency range that permit estimation of temperature increase and of conservative limits on the acceptable power density averaging area have been established, ensuring exposure safety for devices positioned as close as 2 mm from the body. The predictions have been validated against simulations of conservative layered skin configurations exposed to a range of single antennas and antenna arrays in the frequency range of 10–100 GHz. For frequencies >30 GHz, the analytical predictions of temperature increase generally deviated from the simulation results by less than 25%. The results demonstrate that a conservative averaging area can be expressed as function of frequency, distance from the transmitter, and—in the far-field—antenna aperture (see Eq. for a simple approximation at a distance of 2 mm from the source).

https://onlinelibrary.wiley.com/doi/full/10.1002/bem.22147

Environmental RF exposure in Stockholm Old Town compared with tumour risks in rats in the Ramazzini Study

Hardell L, Carlberg M. Hedendahl L, Koppel T, Ahonen M. (2018) Environmental radiofrequency radiation at the Järntorget Square in Stockholm Old Town, Sweden in May, 2018 compared with results on brain and heart tumour risks in rats exposed to 1.8 GHz base station environmental emissions. World Academy of Sciences Journal. January-February 2019. DOI: 10.3892/wasj.2018.5

Abstract

Radiofrequency (RF) radiation in the frequency range 30 kHz to 300 GHz was evaluated in 2011 by the International Agency for Research on Cancer (IARC) at WHO to be a 'possible human carcinogen' Group 2B. The conclusion was based on human epidemiological studies on an increased risk of glioma and acoustic neuroma.

In previous measurement studies, we found high environmental RF radiation levels at certain public places and also in an apartment in Stockholm, Sweden. One such place was the Järntorget square in the Stockholm Old Town. The EME Spy exposimeter was used for these studies.

We have now conducted a field spatial distribution measurement with a radiofrequency broadband analyser. The maximum E-field topped at 11.6 V/m at the centre of the square, where the antenna was focused. Järntorget's mean value was 5.2 V/m, median 5.0 V/m, range 1.2-11.6 V/m.

Of interest is that this level can be compared to a lifespan carcinogenicity study on rats exposed to 1.8 GHz GSM environmental radiation performed at the Ramazzini Institute

(RI) in Italy. A statistically significant increase in the incidence of malignant schwannoma in the heart was found in male rats at the highest dose, 50 V/m. In treated female rats at the highest dose, the incidence of malignant glial tumours was increased, although this was not statistically significant.

On the whole, the findings of this study showed that RF radiation levels at one square, Järntorget, in Sweden, were only one order of magnitude lower than those showing an increased incidence of tumours in the RI animal study. An increased cancer risk cannot be excluded for those working in the proximity of Järntorget for longer time periods.

PDF: http://worldacademyofsciences.com/journal/WASJ-104_HARDELL.pdf

Analysis of relationship between EMR characteristics and urban functions in highly populated urban areas

Tang C, Yang C, Cai RS, Ye H, Duan L, Zhang Z, Shi Z, Lin K, Song J, Huang X, Zhang H, Yang J, Cai P. Analysis of the relationship between electromagnetic radiation characteristics and urban functions in highly populated urban areas. Sci Total Environ. 2018 Nov 10;654:535-540. doi: 10.1016/j.scitotenv.2018.11.143. Abstract

The electromagnetic environment (EME) in cities is becoming increasingly complex, and the resulting potential health hazards have attracted widespread attention. Large-scale field observations and monitoring of electromagnetic fields were performed in Xiamen Island over the past six years. The results show that the integrated electric field intensity in Xiamen Island ranged from 0.32 V/m to 1.70 V/m, while the integrated magnetic flux density ranged from 0.11 µT to 0.50 µT; where more electric power facilities and electronic equipment are present in the island, the electric and magnetic field strengths are higher; the radiation power of 2nd Generation mobile communication (2G) is higher than that of 3rd Generation mobile communication (3G) and 4th Generation mobile communication (4G), the coverage of the 3G signal was more uniform than the others and the 4G communication signal's coverage is still developing. The relationship between the EME characteristics and urban functions has been analyzed in this study. Results showed that electric field intensity had no correlation with urban functional areas, magnetic flux density had a positive correlation with residential area (q = 0.29); 2G and 4G radiation power are positively related to the educational (Edu) function area (960 MHz q = 0.22, 1.8 GHz q = 0.47, 2.61 GHz q = 0.28); there was a positive relationship between 2G (1.8 GHz) radiation power and residential area (q = 0.2). We concluded that there is a strong link between the Xiamen Island's EME and the distribution of electromagnetic radiation (EMR) sources, the denser and wider distributed EMR sources lead to a more complicated urban EME.

https://www.ncbi.nlm.nih.gov/pubmed/30447592