Summaries and assessments of selected studies

In the period from early November 2017 to mid of January 2018, 65 new publications have been identified, and eight of these were discussed in depth by BERENIS. Based on the selection criteria, three of these publications were selected as the most relevant ones. Their summaries and assessments are provided below.

1) Experimental animal and cell studies

Radiofrequency exposure, mitochondrial oxidative stress, apoptosis and altered calcium concentration in rats (Ertilav et al*., 2018)*

The *in vivo* study by Ertilav *et al.* (2018) investigated a possible impact on the TRPV1 (transient receptor potential) channel in neurons of the hippocampus and the dorsal root ganglion in rats intermittently exposed to RF EMF (900 and 1800 MHz) for one year. The TRPV1 channel belongs to the calcium-permeable TRP superfamily and is activated by different stimuli such as high temperature, capsaicin (contained in chili peppers), oxidative stress and acidic pH. Activation of this channel by oxidative mitochondrial stress causes increased calcium levels in neurons involved in physiological as well as pathological processes such as apoptosis (programmed cell death). In neurons of the hippocampus and the dorsal root ganglion, the levels of this protein are particularly high. TRPV1 is thus probably involved in pain signaling and hippocampal injury.

At the age of 12 weeks, female Wistar rats (n=8+8) were exposed to radiofrequency radiation at 900 or 1800 MHz (60 minutes/day, five days/week) for a period of one year. The respective control group (n=8) was not exposed. The average whole body SAR was stated as 0.1 W/kg. Within the animal, the SAR varied between 0.001-1.1 W/kg, with the highest values found in the head area. Twelve hours after the last exposure, tissue from the brain and the spinal cord was removed and examined. Electrical currents were measured by electrophysiological methods (patch clamp) on isolated hippocampal neurons or isolated dorsal root ganglia. The neurons were stimulated with capsaicin, triggering the entry of calcium into the cell. Calcium was analyzed spectrofluorometrically by using fluorescent dyes. Furthermore, the intracellular amount of reactive oxygen species (ROS) and the mitochondrial membrane depolarization were measured, and the activity of the apoptosis markers caspase 3 and 9 was determined.

The results show that exposure at 900 and 1800 MHz significantly increased TRPV1 currents, intracellular calcium concentrations, ROS production, mitochondrial membrane depolarization, and apoptotic marker activity in a frequency-dependent manner. The authors conclude that both frequencies initiate oxidative stress in the mitochondria, apoptosis, and calcium entry into the cell through activation of the TRPV1 channels in a frequency-dependent way. Furthermore, the authors suggest that this channel may be a potential target protein for pharmacological treatment of 900 and 1800 MHz EMF-induced apoptosis as well as a target for peripheral pain in rat models.

The results are interesting because dorsal root ganglia are involved in pain transmission. However, with regard to pain, no experiments have been performed so far and thus the relevance for humans remains open. The results regarding the hippocampus are potentially important for behavior and cognitive functions; however, no further memory tests have been performed. Measurements or calculations of SAR values in the brain and the spinal cord were not presented and therefore the exposure level in these tissues is unclear.

2) Epidemiological studies

Extremely low frequency magnetic field exposure during pregnancy and potential effects on premature birth rate and neonatal size (Migault et al. *2017)*

A French cohort study (Migault *et al.* 2017) investigated whether maternal ELF-MF exposure during pregnancy has an impact on the likelihood of moderate prematurity (birth between 33-37 completed weeks of gestation) or the size of newborns. This study is based on data from the Elfe cohort, a prospective birth cohort aiming at investigating the influence of environmental factors, nutrition, family situation and socio-cultural influences on development up to the age of 20 years. The study included 18,329 newborns born in the 33rd week of pregnancy or later. Exposure was assessed by using the ISCO-88 standard classification and the revised INTEROCC job exposure matrix. This matrix also includes an estimate of the average ELF-MF exposure in non-professional situations such as housewives, students, as well as unemployed and retired individuals. Based on the employment situation of the mothers during pregnancy, cumulative exposure was estimated in microTesla days. The epidemiological analysis has been adjusted for a variety of confounders including smoking, hypertension, mother's body mass index before pregnancy and family income. No association was observed between cumulative magnetic field exposure and the likelihood of moderate premature birth. The size of newborns was also not related to maternal magnetic field exposure during pregnancy. The overall quality of the study is high, and the size of the cohort is relatively large. The epidemiological analysis took into account important confounding factors. Exposure was assessed systematically, and both occupational as well as non-occupational exposure was considered. Nevertheless, such exposure estimates always include uncertainties. For example, residential exposure assessment relied on mean values only, and it was not explored whether the mothers lived near a relevant source of exposure (e.g. power line or transformer). The proportion of the study population in the highest exposure category was relatively small (6.8%). The highest category was defined as ≥41 µT days (cumulative). This corresponds to a mean exposure of about 0.18 µT during the first 33 weeks of pregnancy, which was taken into account for the exposure calculation. Therefore, the study cannot make any statement regarding mothers who were exposed frequently and/or for a long time to significantly higher magnetic fields than 0.18 µT during pregnancy. The results are consistent with those of a survey in 140,000 newborns in England (De Vocht *et al.* 2014, De Vocht & Lee 2014; see Newsletter Nr. 1, March 2015) which found no increased risk of premature birth and delayed growth of infants in the offspring of mothers residing near power lines.

3) Dosimetric studies

Modeling of the absorbance of sub-terahertz radiation by human skin (Betzalel et al.*, 2017)*

In numerical studies of the absorption of electromagnetic waves in humans, the skin is typically modeled as an absorbent, homogeneous medium with a specified content of water. Up to now, any details such as the different layers of the skin and other structures contained therein have usually not been considered. In most cases, this is justified by the fact that the wavelength is much greater than the dimensions of the tissue structures. By assuming a corresponding mix structure, tissue can be approximated as a homogeneous medium. However, for analyzing the absorption of higher frequency bands that will soon be used by 5G technology, such an approximation is increasingly insufficient. In the publication by Betzalel *et al.* (2017), the influence of the structure of sweat glands

on absorption is investigated. By using optical coherence tomography, it has been shown that sweat ducts have a helical structure. This structure is assumed to be distinctly more conductive than the surrounding tissue, since sweat has a much higher salt content, and thus a higher ion concentration. In the so-called sub-terahertz bands (frequencies above 30 GHz, wavelength in the tissue in the range of 1 mm) such structures become relevant for the modeling of the absorption of the tissue. The present study uses a more detailed model of the skin that contains two layers, the dermis and the epidermis. The respective layers are sinusoidally interlocked and contain helical sweat ducts. Since measurement data of the respective tissue in this frequency range is not yet available, the physical tissue parameters were estimated based on the water content of the individual layers.

The results of the modeling show that at sub-terahertz frequencies, the topology and finer structures of the skin have a significant impact on absorption in the skin. When considering sweat ducts in the model, the maximum local SAR in the skin is 1,000 to 10,000 times higher as compared to a model that does not consider sweat ducts. The sweat ducts thus stand out as microstructures with a very high absorption capacity. The results of the study should now be verified and validated, and the respective tissue parameters should be measured. It would also be interesting to include tissue structures other than sweat glands in the model, and to extend the modeling to lower frequency ranges.

References

Betzalel N, Feldman Y, Ishai PB (2017): **The Modeling of the Absorbance of Sub-THz Radiation by Human Skin.** IEEE Transactions on Terahertz Science and Technology 7(5): 521-528. http://ieeexplore.ieee.org/document/8016593/

De Vocht F, Hannam K, Baker P, Agius R (2014): **Maternal residential proximity to sources of extremely low frequency electromagnetic fields and adverse birth outcomes in a UK cohort.** Bioelectromagnetics, 35: 201–209. https://www.ncbi.nlm.nih.gov/pubmed/24482293

De Vocht F, Lee B (2014): **Residential proximity to electromagnetic field sources and birth weight: Minimizing residual confounding using multiple imputation and propensity score matching.** Environ Int 2014; 69: 51 – 57. http://www.ncbi.nlm.nih.gov/pubmed/24815339

Ertilav K, Uslusoy F, Ataizi S, Nazıroğlu M (2018): **Long term exposure to cell phone frequencies (900 and 1800 MHz) induces apoptosis, mitochondrial oxidative stress and TRPV1 channel activation in the hippocampus and dorsal root ganglion of rats.** Metab Brain Dis. 2018 Jan 13. https://www.ncbi.nlm.nih.gov/pubmed/29332300

Migault L, Piel C, Carles C, Delva F, Lacourt A, Cardis E, Zaros C, de Seze R, Baldi I, Bouvier G (2017): **Maternal cumulative exposure to extremely low frequency electromagnetic fields and pregnancy outcomes in the Elfe cohort.** Environ Int. 2017 Dec 20;112:165-173. https://www.ncbi.nlm.nih.gov/pubmed/29275242

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BERENIS - Swiss expert group on electromagnetic fields and non-ionising radiation

List of abbreviations (pdf)