## Summaries and assessments of selected studies

In the period from August to October 2016, 79 new publications have been identified, and eight of these were discussed in depth by BERENIS. Based on the selection criteria, four of these publications were selected as the most relevant ones. Their summaries and assessments are provided below.

### *1) Experimental animal and cell studies*

*Extremely low frequency and radiofrequency electromagnetic fields and potential health effects – a meta-analysis of existing datasets (Parham* et al. *2016)*

In the publication of Parham *et al.* (2016) data from existing gene expression studies were used to investigate linkages between exposure to extremely low frequency (ELF MF) and radiofrequency electromagnetic fields (RF EMF) and diseases as well as underlying signal transduction and metabolic pathways. Using a complex algorithm, a three-step process was applied, in which the genes obtained in the studies were linked to human diseases and to molecular signaling pathways. The three steps included: (a) linking genes associated with classes of human diseases to molecular signaling pathways, (b) linking molecular signaling pathways to ELF MF and RF EMF microarray data, and (c) identifying associations between human disease and EMF exposures by similarity of the affected signaling pathways. This algorithm evaluates the degree to which a given genetic signaling pathway is affected on the level of changes of gene expression or their products. Most signaling pathways found were associated with cellular or metabolic function. To link genes associated to diseases, the Gene Ontology Database (GAD) was used in the algorithm. ELF MF datasets were sporadically linked to human diseases, but no clear pattern emerged. Signaling pathway linkages indicated a potential association with cancer, metabolic disorders, and neurological development and function. These were more pronounced for ELF MF datasets than for RF EMF datasets. This methodological approach is a promising tool for the identification of future research areas. For instance, the topic of neurological function and disorders has been identified in this study.

*Impact of the static geomagnetic field on cell motility (Mo* et al. *2016)*

For once, the influence of the natural geomagnetic field (GMF) and not of manmade electromagnetic fields on molecular processes of cells was the topic of this well-done and interesting *in vitro* study by Mo *et al.* (2016). Corresponding to a 250-fold reduced GMF, the authors grew human neuroblastoma cells under hypomagnetic field (HMF) conditions for 3 hours up to seven days. First, the authors observed that cells cultured in the HMF for seven days exhibited a reduced cell adhesion to non-surface-coated culture dishes. This effect was found consistently and it could be reproduced after 3 days of HMF exposure, but was also observed occasionally after shorter culturing time (3 and 48 hours). Applying complex automated image analysis procedures, a restricted horizontal and vertical mobility as well as reduced motility of cells were described. Furthermore, the authors detected morphological alterations such as increases in cell volumes and protrusions, the latter playing a role in cellular movements and communication. Based on these observations, the authors speculated that there could be a connection between the HMF effects and the cytoskeleton comprising a complex network of filamentous cell structures. Localized predominantly in the proximity of the cell membrane and in cellular protrusions, actin fibers are part of the cytoskeleton. They provide not only

mechanical stability but are also involved in many processes at cell membranes. Cells can dynamically regulate the actin fibers by polymerization and de-polymerization. Based on this link, the authors assessed the actin filaments in a time-dependent manner and reported a reduction of global levels of actin filaments as well as fewer actin-containing cell protrusions after two days of cultivation under HMF conditions. Coincidently, the expression of a key regulator of actin polymerization was found to be significantly reduced, which may be causal for the reduction of actin filaments. Finally, the self-assembly of actin protein to filaments was assessed. Under HMF conditions, the kinetics was altered and the formation of thicker filaments as well as unphysiological aggregations were found. The findings presented in this publication suggest that the GMF directly influences the integrity of the cytoskeleton and thereby indirectly a multitude of cellular mechanisms. Although these observations only have limited health relevance, e.g. for astronauts or in respect to the use of medical devices with static MF, they could represent a considerable mechanistic aspect for the interaction of electromagnetic fields with cells. Indeed, actin filaments were proposed occasionally in the scientific literature to have an antenna function for non-natural EMFs.

### *2) Review articles*

*Exposure assessment of low frequency electric and magnetic fields in Europe (Gajšek* et al. *2016)*

Gajšek *et al.* (2016) reviewed the findings of exposure assessment studies done in European countries on the exposure of the general public to low frequency electric and magnetic fields. Frequencies of up to 10 MHz were considered as low frequencies in this study. The reviewed studies from the past three decades mainly applied three methods: i) in-situ measurements (indoor and outdoor spot measurements; measurements of magnetic fields around electric devices and household electric appliances); (ii) personal measurements with portable devices (exposimeters); (iii) modeling of exposures on the basis of the configuration of wiring systems. A large part of the studies focused on the exposure to high-voltage power lines. For residential exposure, the major sources of magnetic fields are household appliances, nearby power transformers and high-voltage transmission lines, and domestic appliances. The largest measurement study of residential exposure assessment was performed in Germany with measurements of magnetic fields at 50 Hz and 16 2/3 Hz[1]. Similar studies with a smaller number of measurement locations were carried out in Austria and in the UK. Spot measurements do not provide sufficient insight into the exposure levels of individuals who are moving through a variety of environments and who are exposed to multiple sources over different periods. For this reason, measurements with portable personal exposimeters carried by volunteers over a certain amount of time were conducted in some countries. The reviewed studies show that outdoor average ELF MF range between 0.05 and 0.2 µT in terms of flux densities. Higher values (of the order of a few µT) may occur directly beneath high-voltage power lines, at the walls of transformer buildings, and at the boundary fences of substations. In the indoor environment, the highest field values have been measured close to several domestic appliances (up to the mT range), some of which are held close to the body, such as hair dryers and electric shavers. Common sources of exposure to intermediate frequencies (300 Hz to 10 MHz) include induction cookers, compact fluorescent lamps, inductive charging systems for electric cars and security or anti-theft devices. No systematic measurement surveys for the intermediate frequency range have been carried out so far,

[1] Schüz J, Grigat JP, Störmer B, Rippin G, Brinkmann K, Michaelis J (2000): **Extremely low frequency magnetic fields in residences in Germany. Distribution of measurements, comparison of two methods for assessing exposure, and predictors for the occurrence of magnetic fields above background level.** Radiat Environ Biophys. 2000 Dec;39(4):233-40. https://www.ncbi.nlm.nih.gov/pubmed/11200967

and only a few reports on measurements of EMF around such devices are mentioned. For future risk assessment, the authors suggest three population exposure categories. These three categories comprise intermittent variable partial body exposure, continuous elevated level whole body exposure and continuous low level background exposure. The authors consider this classification to be a mandatory step in any future health risk assessment of EMF exposure.

*Thresholds of thermal damage – workshop report by an ICNIRP task group (Sienkiewicz* et al. *2016)*

Undisputedly, microwave radiation of wireless communication devices absorbed by humans is converted into heat. The international guidelines for limits account for these thermal effects and related health effects. Currently, the International Commission on Non-ionizing Radiation Protection (ICNIRP) is in the process of reviewing the limits regarding radiofrequency electromagnetic fields that are in place since 1998. In order to obtain an overview of the latest insights regarding the critical threshold for thermal damages, a workshop was held in Istanbul from May 26-28, 2015. The participating scientists indicated that the effects of heating caused by RF EMF are consistent with those from other sources, and that the information derived from those studies can be applied to radiofrequency-induced heating as well. It was concluded that absolute temperature of tissues was more important for thermal damage than temperature change. However, it was emphasized that any change of temperature can have a biological effect, and that some of the observed so-called “non-thermal” EMF effects are in fact attributable to small temperature changes. Thermoregulation is regulated by peripheral and central sensors, and is affected by a multitude of factors (e.g. sweating, clothing). Thermoregulation in older people and women is less efficient than in younger people and men. A testicular temperature higher than 35°C is considered detrimental. Relevant in this context are the posture (sitting vs. walking), clothing (clothed vs. being naked), and whether a person is asleep or awake. These factors may cause a variability of 1-2°C. RF EMF induced temperature increases in everyday life are relatively small. Occupational guidelines for exposed workplaces ensure that body core temperatures do not increase beyond 38-38.5 °C. In elderly people, a whole-body SAR of 4 W/kg causes an increase of the core temperature of 0.9 °C after 30 min. In younger adults, the temperature increase is significantly lower. Heat removal capacity of the eye is relatively low, which makes particularly the lens relatively sensitive to RF EMF. In general, the thresholds for damage are more difficult to determine for localized exposure compared to whole body exposure. Current limits are based on RF EMF induced temperature increase only, thus not taking into account exceedance of the critical core temperature. The workshop emphasizes that the interaction of heat and RF EMF may be critical. When exposure to heat is already high, additional heating by RF EMF can be critical and should thus be avoided.

## References

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Mo WC, Zhang ZJ, Wang DL, Liu Y, Bartlett PF, He RQ (2016**): Shielding of the Geomagnetic Field Alters Actin Assembly and Inhibits Cell Motility in Human Neuroblastoma Cells.** Sci Rep. 2016 Mar 31;6:22624. https://www.ncbi.nlm.nih.gov/pubmed/27029216

Parham F, Portier CJ, Chang X, Mevissen M (2016): **The Use of Signal-Transduction and Metabolic Pathways to Predict Human Disease Targets from Electric and Magnetic Fields Using in vitro Data in Human Cell Lines.** Front Public Health 4:193. http://journal.frontiersin.org/article/10.3389/fpubh.2016.00193/full

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

List of abbreviations (pdf)