Summaries and assessments of selected studies

In the period from end of October 2019 to mid of January 2020, 71 new publications have been identified, and ten of these were discussed in depth by BERENIS. Based on the selection criteria, five of these publications were selected as the most relevant ones. Their summaries and assessments are provided below.

1) Experimental animal and cell studies

Radiofrequency electromagnetic fields and sperm of mice (Houston et al. *2019)*

The study of Houston *et al.* (2020) investigated the effects of RF-EMF exposure on sperm quality and testicular tissue of adult male mice (C57BL/6). The mice were exposed in cages, in which they were able to roam freely (905 MHz, whole body exposure of 2.2 W/kg, 12 h/day for 1, 3 and 5 weeks). The testicular tissue was examined histologically. Oxidative stress and the generation of reactive oxygen species (ROS) were analysed by flow cytometry. DNA damage was determined by comet assay with the exception of oxidative base damage, which was determined by immunofluorescence. In addition, functional parameters such as motility, vitality and fertilisation competence of spermatozoa obtained from exposed and sham-exposed animals were analysed *in vitro*. Furthermore, the study investigated the RF-EMF impact on early embryonic development.

The results showed a reduced lifetime and motility of mature sperm, but no histopathological changes in the testicular tissue. After one week of RF-EMF exposure of the male mice, the mitochondrial ROS production in the sperm samples was increased. Moreover, elevated DNA oxidation and fragmentation of sperm DNA (single-strand breaks) was found at all three exposure times, with the strongest effect measured at the longest exposure duration of 5 weeks. The functional impairment of spermatozoa by RF-EMF exposure might be attributed to oxidative stress. On the one hand, the most pronounced impairment of sperm vitality was correlated with the highest ROS levels in the sperm cells. On the other hand, these effects were also correlated with the increase of another biomarker for oxidative stress (8_OH-dG) in the nuclei of the sperm cells. However, these changes did not affect fertilisation competence or early embryonic development.

The exposure system used is a cylindrical waveguide similar to the one used in previous studies. The calibration of the field strengths was performed in the empty waveguide. The resulting whole-body SAR was determined in relation to these field strengths using the factors calculated for other studies. In such an exposure system, the field distribution is strongly influenced by the animals and the cage. In the present study, thus, the extent of the SAR value variations in the animals with regard to the cage-equipped waveguide cannot be estimated adequately, requiring more measurements. Furthermore, a whole-body SAR of 2.2 W/kg (limit value: 0.08 W/kg) causes an increase in body core temperature. Thermal effects might therefore also play a role.

2) Human experimental studies

Effects of radiofrequency electromagnetic fields on sleep in healthy elderly males and females (Danker-Hopfe et al. *2020)*

The results of published human experimental studies on the effects of RF-EMF on sleep are heterogeneous and mainly derived from young adults. The aim of the study by Danker-Hopfe *et al.*

(2020) was to investigate the effects of RF-EMF exposure on the macrostructure of sleep (sleep stages and structure) in elderly persons (men and women aged 60-80 years) and to assess whether there are sex-specific effects. Thirty men and thirty women were exposed to two types of RF-EMF and a control condition without radiation for 30 minutes prior to sleep and for the whole night (7.5 hours): GSM900 (Global System for Mobile Communications; carrier frequency 915 MHz, modulation 217 Hz, duty cycle 0.125, maximum SAR 2 W/kg) and TETRA (Terrestrial Trunked Radio; carrier frequency 385 MHz, modulation 17.6 Hz, duty cycle 0.25, maximum SAR 6 W/kg). The study was conducted double-blind and randomised. Participants underwent each of the three exposure conditions on three occasions resulting in a total of nine study nights per participant. GSM900 and TETRA exposure resulted in a reduction of so-called "arousals" (i.e. brief wake-up reactions), as well as a shorter latency to deep sleep and a shorter self-reported time awake after falling asleep. The effects of RF-EMF exposure were depending on sex (higher number of significant effects in women) and different for GSM900 and TETRA exposure.

Nevertheless, no dose-response relationship was observed. TETRA radiation had a higher intensity and penetrates deeper into the brain due to the lower frequency. However, regardless of gender, the observed changes are not indicative of a sleep disturbing effect of RF-EMF exposure, and might on the contrary be interpreted as sleep-promoting in terms of more consolidated sleep.

3) Epidemiological studies

Mobile phone use, thyroid cancer and gene-environment interactions: results of a case-control study in the USA (Luo et al. *2020)*

The case-control study by Luo *et al.* (2020) investigated a potential association of mobile phone use and thyroid cancer. The thyroid gland is located in the throat below the larynx and is thus relatively close to the mobile phone when making a call. Thyroid hormones play an important role regarding growth, development and metabolic processes in the body. The study included all patients who were diagnosed with thyroid cancer in Connecticut between 2010 and 2011, and still alive by the time of interview. Control persons of the same age (±5 years) and sex were recruited from the population by random phone digit dialing. Data on mobile phone use and relevant confounders were collected through personal interviews. A total of 498 control persons (participation rate: 62%) and 462 patients (66%) aged between 21 and 84 years participated in the study. The main results of the study have already been reported in a previous publication (Luo *et al.* 2019)[1], indicating no association with mobile phone use, but a non-significant trend towards an increased risk for frequent users. In the new publication (Luo *et al.* 2020), possible gene-environment interactions were investigated. For this purpose, 823 genetic variations (polymorphisms) of 176 genes from regions involved in DNA repair were analysed. None of the polymorphisms studied was associated with the incidence of thyroid cancer. Ten polymorphisms in a total of seven different genes showed a statistically significant ($p<0.01$) interaction with mobile phone use and thyroid cancer.

This study uses an interesting approach to gain a better understanding of disease development caused by RF-EMF. However, it lacks a confirmation analysis, as is common in genetic studies. Ten significant results in a total of 1646 statistical tests are less than would be expected by chance, and it thus remains unclear whether the observed gene-environment interactions are really causal. Further limitations of

[1] Luo J, Deziel NC, Huang H, Chen Y, Ni X, Ma S, Udelsman R, Zhang Y (2019): **Cell phone use and risk of thyroid cancer: a population-based case-control study in Connecticut.** Ann Epidemiol. 2019 Jan;29:39-45. https://www.ncbi.nlm.nih.gov/pubmed/30446214

the study are the retrospectively collected data on self-reported mobile phone use, and the random digit dialing procedure for selecting the control persons, which might have led to bias regarding participation rates of mobile phone versus fixed line network users. Further research on this topic is needed. Firstly, the antenna of newer mobile phones is located in the lower part of the device, and thus close to the thyroid gland when making calls. Secondly, the incidence of thyroid tumors has been increasing steadily in recent years and it is not clear whether this increase is exclusively due to improved diagnostics[2].

4) Dosimetric studies

Optimisation of 5G networks with regard to exposure (Matalatala et al. *2019)*

In view of the expected increase in wireless communication, it appears reasonable to optimise mobile network infrastructures with regard to energy consumption and radiation exposure. The study of Matalatala *et al. (2019)* used methods to optimise the design of 5G networks with adaptive antennas ("massive MIMO") with respect to location and configuration, combining minimal energy consumption, minimal downlink[3] and uplink[4] exposure, and maximum coverage. A suburban area of Ghent in Belgium was considered as an example. For this purpose, a so-called multi-cell network was configured, with each cell containing a base station antenna with several antenna elements. Realistic communication scenarios were simulated for the operation of the network. A dose was calculated by multiplying the exposure duration with the whole body SAR at maximum operation of all antenna elements. The study showed that when using a higher number of antenna elements per base station, the number of base stations required for a network with adaptive antennas decreases. This leads to a decrease in downlink exposure (-12% for electric field strength and -32% for the downlink dose) and an increase in the uplink dose (+70%), with both uplink and downlink dose increasing with the number of simultaneous users. For the area studied, the optimal 'massive MIMO' network consisted of 37 base stations with 64 antenna elements each. Moreover, this design resulted in a downlink exposure that was five times lower compared to the 4G reference scenario.

This simulation study presents a method for planning networks with adaptive antennas in a way that fewer base stations are needed, and exposure of the population is reduced. These simulations should be verified with measurements.

Specification of limit values for millimeter waves (Neufeld et al. *2020)*

In their letter in *Bioelectromagnetics*, Neufeld *et al.* (2020) point out possible violations of current RF-EMF guidelines if the main antenna beam has very short pulses (1ms and less) or is very narrow (1 mm). The authors argue that in this case a tenfold temperature increase can occur compared to the situation with a plane wave with the same averaged power density. They further argue that in the case of pulsed narrow beams, even more extreme temperature increases can occur according to the proposed new guidelines. In their conclusions, the authors request that the limit values should depend on the pulse duration in order to protect users of mobile phones operating in the frequency range from 6 to 30 GHz from temperature increases greater than those permitted by the guidelines.

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[2] Li M, Dal Maso L, Vaccarella S (2020): **Global trends in thyroid cancer incidence and the impact of overdiagnosis.** Lancet Oncology. https://doi.org/10.1016/S2213-8587(20)30115-7

[3] Communication from the mobile phone base station

[4] Communication from the mobile phone

The statements are based on simulation data, which, in addition to electromagnetic fields, also include a model for skin thermoregulation. This means that some basic assumptions about physiological reactions are also included in the models. It should be noted that the statements apply to sources in the frequency range from 6 to 30 GHz, which are operated close to the body. The described exposure scenarios are only conceivable in these specific situations. However, the extent to which they are practically relevant for future devices remains to be shown. It is evident that the currently existing guidelines do not account for all theoretically possible exposure scenarios. This should be taken into account in the next revision of the guidelines, or regulated by an additional clause in case such exposure situations will be introduced in the future.

References

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

List of abbreviations (pdf)