

Exposure to high frequency electromagnetic fields, biological effects
and health consequences (100 kHz-300 GHz)

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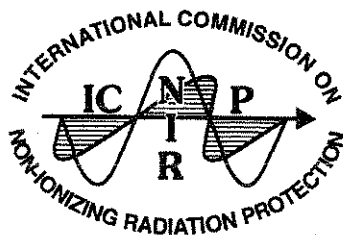
Review of

the scientific evidence on dosimetry, biological effects, epidemiological observations, and health consequences concerning exposure to high frequency electromagnetic fields (100 kHz to 300 GHz)

Editors:

Paolo Vecchia, Rüdiger Matthes, Gunde Ziegelberger

James Lin, Richard Saunders, Anthony Swerdlow



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laboratory animal studies is rather consistent and suggests that mobile phone type RF exposure has no effect on auditory function. It is also clear that, like humans, animals can hear the pulsed RF characteristic of radar above given thresholds through a thermoelastic expansion mechanism. Studies of the effects of high peak power RF pulses and ultrawide band (UWB) RF has been somewhat diverse and sporadic. Acute exposure to either does not appear to elicit any cardiovascular changes in anesthetized rats.

Overall, the results of recent animal carcinogenicity studies are rather consistent and indicate that such effects on rodents are not likely at SAR levels up to 4 W kg^{-1} . *In vivo* and *in vitro* genotoxicity studies also generally indicate a lack of effect. With regard to *in vitro* studies of non-genotoxic effects such as cell signaling, gene and protein expression, the results are more equivocal. The evidence from studies using measurements of calcium ion concentration, does not support the earlier positive reports of modulated RF effects on calcium ion efflux. There is insufficient research regarding RF effects on nitric oxide signaling, gap junctions and receptor clustering to be conclusive. Recent studies suggest that the RF exposure has no or very little effect on the expression of cancer-related genes (proto-oncogenes and tumor suppressor genes). However, the results of studies of RF exposure on stress protein expression, particularly on hsp, have so far been inconsistent, with both positive and negative outcomes. Heating remains a potential confounder and may account for some of the positive effects reported. More recently, studies using powerful, high-throughput screening techniques, capable of examining changes in the expression very large numbers of genes and proteins, have often shown a limited number of alterations where some genes were up-regulated and others down-regulated, and the expression and phosphorylation of some proteins were changed. However, the magnitude of reported changes was very small and may be of limited functional consequence. In terms of effects on cell behavior, the results of studies on cell proliferation and differentiation, apoptosis and cell transformation are mostly negative.

Thermally significant RF exposure can impair male fertility and cause increased embryo and fetal losses and increase the incidence of fetal malformations and anomalies. Such effects have not been consistently shown at exposure levels that do not induce temperature elevation of 1°C or more. The studies that have addressed postnatal developmental indices or behavior after prenatal exposure to low level RF radiation have generally reported lack of effects. Effects resulting from long-term exposure during the development of juvenile animals have been addressed in only a few studies, and the data are insufficient for conclusions.

Cataract in the eyes of anesthetized rabbits remains a well-established thermal effect of RF exposure. However, primates appear less susceptible to cataract induction than rabbits, and opacities have not been observed in primates following either acute or prolonged exposures.

II.6.2. Conclusions

Overall, it is concluded that:

- The mechanisms by which RF exposure heats biological tissue are well understood and the most marked and consistent effect of RF exposure is that of heating, resulting in a number of heat-related physiological and pathological responses in human subjects and laboratory animals. Heating also remains a potential confounder in *in vitro* studies and may account for some of the positive effects reported.
- Recent concern has been more with exposure to the lower level RF radiation characteristic of mobile phone use. Whilst it is in principle impossible to disprove the possible existence of non-thermal interactions, the plausibility of various non-thermal mechanisms that have been proposed is very low.
- Concerning cancer-related effects, the recent *in vitro* and animal genotoxicity and carcinogenicity studies are rather consistent overall and indicate that such effects are unlikely at SAR levels up to 4 W kg^{-1} . With regard to *in vitro* studies of RF effects on non-genotoxic end-points such as cell signaling and gene/protein expression, the results are more equivocal, but the magnitudes of the reported RF radiation induced changes are very small and of

III.A. EPIDEMIOLOGY OF HEALTH EFFECTS OF RADIOFREQUENCY EXPOSURE*

ABSTRACT

We have undertaken a broad review of epidemiological knowledge about the effects of RF on human health in order to summarize the current state of knowledge, to explain the methodological issues that are involved, and to aid in the planning of future studies. We have looked at epidemiological studies on chronic disease causation; for completeness we have also included epidemiological studies on symptoms although such studies are usually better conducted by laboratory volunteer experiments. For the purpose of this review we have divided the literature into studies of RF exposure from occupational sources, from transmitters, and from mobile phones.

Results of epidemiological studies to date give no consistent or convincing evidence of a causal relation between RF exposure and any adverse health effect. On the other hand, these studies have too many deficiencies to rule out an association. A key concern across all studies is the quality of assessment of RF exposure. Despite the rapid growth of new technologies using RF, little is known about population exposure from RF sources and even less about the relative importance of different sources. An important element in improving future studies would be the use of a meter to monitor individual exposure. The need for better exposure assessment is particularly strong in relation to transmitter studies, because the relation between distance and exposure is very weak. Although the likelihood is low fields emanating from base stations would create a health hazard, because of their weakness, this possibility is nevertheless a concern for many people. Another general concern in mobile phone studies is that the lag periods that have been examined to date are necessarily short. The implication is that if a longer period is required for a health effect to occur, the effect could not be detected in these studies. The majority of research has focused on brain and head and neck tumors but studies on other health effects may be equally justified. Another gap in research is children. Children are increasingly heavy users of mobile phones, they may be particularly susceptible to harmful effects, and they are likely to accumulate many years of exposure.

* This review was first published in Environmental Perspectives 112 (17): 1741-1754; Dec. 2004 and is reproduced here with updates drafted in 2009.

Acoustic neuroma can cause unilateral deafness, which could lead to cessation of phone use (and hence spuriously reduced risks). Alternatively, the deafness could lead to the diagnosis of an otherwise unrecognized tumor and hence lead to spuriously increased risks. Hearing loss associated with acoustic neuromas may influence the side of phone use as the tumor progresses, resulting in preferred contralateral phone use relative to the tumor. This is not predictable, however, since hearing can be preserved in the presence of large vestibular schwannomas and, conversely, hearing loss can frequently occur as the result of radiologically static, small tumors (Rutherford et al 2005). Potential effects on the side of mobile phone use or earlier detection of tumors should, however, affect all available studies similarly; this cannot explain the discrepancies in the results.

Unlike the situation for gliomas and meningiomas, laterality virtually defines the anatomical position of acoustic neuromas, and all ipsilateral acoustic neuromas arise close to the mobile phone handset position. Therefore if reliable unbiased information on side of exposure could be obtained, it would be possible to conduct a powerful unbiased analysis of the effect of mobile phone exposure on acoustic neuroma risk. This analysis, however, is hampered by inconsistency in side of phone use, reporting bias resulting from the tumor diagnosis, and the symptom-based changes in use noted above. The results indicating an increased risk associated with ipsilateral phone use but no overall raised risk again raise questions about the contribution of reporting bias. Thus, the elevated ipsilateral risk beyond 10 years in the large Nordic-UK analysis seems more likely to represent reporting bias than a causal effect, because the latter should lead to a raised risk (although diluted) for users overall beyond 10 years - a finding that was not seen in the overall Nordic-UK data.

As was the case for meningioma, acoustic neuromas are often present for years before diagnosis. Thus, the only data about phone use that are of any potential relevance to acoustic neuroma etiology may be the exposure occurring many years before diagnosis. The available data make it unlikely that there is any substantial raised risk of acoustic neuroma in relation to mobile phone use in the ten years preceding the diagnosis of the tumor. The results leave uncertainty as to whether there are raised risks beyond 10 years from initial use.

III.B.6. SALIVARY GLAND TUMORS: RESULTS AND INTERPRETATION

There is no consistent evidence of an increased risk of salivary gland tumors among mobile phone users (Table III.B.5, Fig. III.B.4) based on four case-control studies (Auvinen et al 2002; Hardell et al 2004; Sadezki et al 2008; Lonn et al 2006) and one cohort study (Schuz 2006b). One study (Auvinen et al 2002) showed an increase in risk for ever-use compared with never-use and for greater cumulative years of exposure, but the results were based on few cases and had very wide confidence intervals. There was no indication of a raised risk in any of the other studies including that of Hardell. Pooling the results from all studies gave risk estimates slightly below unity in all exposure categories (Table III.B.5). Both publications from the Interphone study reported higher risk estimates associated with ipsilateral phone use at least 10 years prior to diagnosis, with an OR of 2.6 (0.9-7.9) in the Lonn study (2006), and 1.6 (0.7-3.7) in the study by Sadezki et al (2008). Corresponding ORs for contralateral use were, however, considerably reduced in both studies: 0.3 (0.0-2.3) and 0.6 (0.2-2.3), respectively. Thus, reporting bias seems likely to explain these findings.

Single studies of tumors at other sites (pituitary adenoma (Takebayashi et al 2008), non-Hodgkin's lymphoma (Hardell et al 2005b), testicular cancer (Hardell et al 2007), uveal melanoma (Stang et al 2001) are not discussed here. The main results for these cancer sites are shown in eTable 2.

III.B.7. CONCLUSIONS

In the last few years the epidemiologic evidence on mobile phone use and risk of brain and other tumors of the head has grown considerably. In our opinion, overall the studies published to date do not demonstrate a raised risk within approximately ten years of use for any tumor of the brain or any other

head tumor. However, some key methodologic problems remain - for example, selective non-response and exposure misclassification. Despite these methodologic shortcomings and the still limited data on long latency and long-term use, the available data do not suggest a causal association between mobile phone use and fast-growing tumors such as malignant glioma in adults, at least those tumors with short induction periods. For slow-growing tumors such as meningioma and acoustic neuroma, as well as for glioma among long-term users, the absence of associations reported thus far is less conclusive because the current observation period is still too short. Currently data are completely lacking on the potential carcinogenic effect of exposures in childhood and adolescence.