

**1. Hansson Mild K, Hardell L, Kundi M, Mattsson MO.  
Mobile telephones and cancer: Is there really no evidence of an association? (Review). Int J Mol Med.  
2003 Jul;12(1):67-72.**

**2. <http://www.bioelectromagnetics.org/newsletter/news169.pdf>**

Dear Editor,

In the last Bioelectromagnetics Newsletter the press release of the Swedish Radiation Protection Authority concerning a literature review on cellular telephones and cancer risk was published.

In this report it is concluded that there is no consistent evidence for an increased risk for any type of cancer. John D. Boice Jr. and Joseph K. McLaughlin from the International Epidemiology Institute, the authors of the review, came to this conclusion by the balance of evidence from epidemiological studies and to a lesser extent from long-term animal studies. They relied heavily on five in their view 'well-designed' studies, while studies that demonstrated an association, mainly the Swedish studies by Hardell et al. (1999, 2000, 2001, 2002a), were seen as methodologically deficient. This assessment is only too understandable since Boice or McLaughlin or both co-authored three of these 'well-designed' studies. Because of the importance of this issue for future research and projected reviews (e.g. ICNIRP scheduled a review of epidemiological studies for HF fields for 2003) it might be of value to consider the criteria for the assessment of epidemiological studies in this context. To start with I may confess that according to my evaluation the five 'well-designed' studies are inconclusive due to methodological deficits while the studies of Hardell et al. and Stang et al. (2001) despite some weaknesses are methodologically superior. Instead

of going into detail of the specific evaluation I may point out the decisive criteria for the assessment:

- Design and analysis of the study must conform to the hypothesized mechanism of action of the agent in question. This criterion has been more or less neglected by all studies. Most studies state in their discussion that it is unlikely emissions from mobile phones may initiate malign transformation (it should be noted, however, that this does not preclude an influence at initiation stage!) rather an influence on progression (e.g. tumor growth) is assumed. It is easy to show that for cohort studies the incidence ratio is always smaller than the effect of exposure on the transition rate from initiation to clinical manifestation. Hence assuming that an agent acts by increasing tumor growth rate must result in a different design and analysis (e.g. Poisson process modeling the cell division parameter). Also for case-control studies the odds ratio must be estimated based on a time-to-tumor model including time of first use, because modeling mere presence or absence of the agent (mobile phone use) results only in an estimate of the incidence ratio that is biased according to the above argument.
- The only necessary criterion of causation is that the exposure precedes the disease (this criterion of B.Hill has been forgotten in the well known papers by Repacholi & Cardis, 1997, Repacholi & Stolwijk, 1991 and Bernhard, 1999) that are the basic documents about the evaluation of evidence by ICNIRP). From this criterion it follows that reasonable latencies have to be considered. There is only scarce evidence concerning latencies for carcinoma, however, about five years seems to be the absolute minimum. Most of the studies addressed

by Boice and McLaughlin have insufficient latencies.

It might be argued that for the study of an effect on tumor growth rather than malign transformation latency is less important.

This argument, however, is mistaken: Not only that such a study must be designed and analyzed in a different way (see first point) there is a stage when the tumor starts growing autonomously that no external environmental influence can be assumed to alter this process significantly. Hence it is still necessary to adjust latency to the known developmental stages of the malign process. E.g. for high grade brain tumor no study on growth rate makes sense because it are typically only weeks between first clinical signs and diagnosis.

On the other extreme, some brain tumors are growing for decades until they manifest themselves clinically.

- For localized tumors and localized exposures a case is only constituted by a coincidence of localization of tumor and exposure site. For brain tumors and cellular telephone use only fronto-parietal, parietal, temporal and occipital locations (depending on the type of mobile phone) and cranial nerves along the exposed regions on the side of the head the telephone has been used can be considered. All other locations must not be included (because this would represent case misclassification).

This holds, however, not for all histological types, because e.g. tumors of microglial origin may grow on locations different from the location of transformation.

- Exposure assessment should be done by personnel blinded for case status in case-control studies. This aspect has only been considered by Hardell et al. and to some extent also by Stang et al.

- Exposure needs to be differentiated by type. To combine different types of phones that differ in essential features of exposure amounts to exposure misclassification (e.g. bag telephones and hand-held telephones). In the future, use of handsfree sets has to be considered as well. There is no agreement yet as to the correct exposure meter. Therefore, different surrogates should be explored. Note that measurements of energy absorption for different individuals demonstrated huge differences in the amount of absorbed energy, such that only very crude estimates can be given based on type and model of a mobile phone.

- In cohort studies care must be taken to avoid ‘contamination’ of reference or control cohorts. There is insufficient correlation between billing records, subscription files etc. and individual use of a mobile phone. Often the person paying the bill and holding the subscription is not identical with the person that is using the telephone. E.g. as a result standardized incidence ratios in Johansen’s et al. (2001) study are biased towards zero hypothesis. Also Auvinen et al. (2002) relied solely on subscription files (and not even from all providers).

- Recall bias has to be considered in case-control studies. Recall bias may result in spurious positive as well as negative results depending on the sign of the correlation between bias and case-status. Possibly the best way to avoid recall bias is to assess exposure by more than one source of information (e.g. interviews with subjects as well as proxies, interviews plus subscription records). Another method is not to focus on a specific exposure but to assess various conditions.

The above stated criteria are the most important in addition to

those that apply for all epidemiological investigations. It may be stressed that considering specific types of tumors and longterm use, there is still no study that has enough statistical power to detect moderately elevated risks from mobile phone use. The recent study by Hardell et al. (2002b) with an extended number of cases and controls approaches this power goal but is still not conclusive concerning specific types of tumors.

Considering the evidence accumulated up to now concerning a possible relationship between mobile phone use and cancer, the conclusion of Boice and McLaughlin is premature and the basis for their decision cannot be scientifically defended.

Best regards,

Michael Kundi, Professor

Institute of Environmental Health

Medical Faculty, University of Vienna, Austria

### *References*

Auvinen A, Hietanen M, Luukkonen R, Koskela RS. 2002. Brain tumors and salivary gland cancers among cellular telephone users.

Epidemiology 13:356–59.

Bernhard JH. 1999. ICNIRP initiatives. Rad Prot Dosimetry 83:5–7.

Hardell L, Näsman Å, Pålsson A, Hallquist A, Mild KH. 1999. Use of cellular telephones and the risk for brain tumours: A case-control study. Int J Oncol 15:113–16.

Hardell L, Nasman Å, Pålsson A, Hallquist A. 2000. Case-control study on radiology work, medical X-ray investigations, and use of cellular telephones as risk factors for brain tumors. MedGenMed.

May 4.

Hardell L, Mild KH, Pålsson A, Hallquist A. 2001. Ionizing radiation,

cellular telephones and the risk for brain tumours. *Eur J Cancer Prev* 10:523–29.

Hardell L, Hallquist A, Mild KH, Carlberg M, Pålsson A, Lilja A.

2002a. Cellular and cordless telephones and the risk for brain tumours. *Eur J Cancer Prev* 11:377–86.

Hardell L, Mild KH, Carlberg M. 2002b. Case-control study on the use of cellular and cordless phones and the risk for malignant brain tumours. *Int J Radiat Biol* 78:931–36.

Inskip PD, Tarone RE, Hatch EE, Wilcosky TC, Shapiro WR, Selker RG, Fine HA, Black PM, Loeffler JS, Linet MS. 2001. Cellular-telephone use and brain tumors. *N Engl J Med* 344:79–86.

Johansen C, Boice JD Jr, McLaughlin JK, Olsen JH. 2001. Cellular telephones and cancer – a nationwide cohort study in Denmark. *J Natl Cancer Inst* 93:203–207.

Johansen C, Boice JD Jr, McLaughlin JK, Christensen HC, Olsen JH. 2002. Mobile phones and malignant melanoma of the eye. *Br J Cancer* 86:348–49.

*Kundi's References, continued*

Muscat JE, Malkin MG, Thompson S, Shore RE, Stellman SD, McRee D, Meugot AI, Wynder EL. 2000. Handheld cellular telephone use and risk of brain cancer. *JAMA* 284:300–17.

Repacholi MH, Cardis E. 1997. Criteria for EMF health risk assessment. *Rad Prot Dosimetry* 72:305–12.

Repacholi MH, Stolwijk JA. 1991. Criteria for evaluating scientific literature and developing exposure limits. *Radiat Prot Aust* 9(3):79–84. *Cancer* 86:348–49.

Stang A, Anastassiou G, Ahrens W, Bromen K, Bornfeld N, Jöckel KH. 2001. The possible role of radiofrequency radiation in the development of uveal melanoma. *Epidemiology* 12:12.

### 3. Arbetsliv direkt, 01-02-12, Eva F Dahlgren, Artikel nr: 2316

Professor kritiserar mobiltelefonundersökning

Kan mobiltelefoner ge cancer? Nej, hävdade en dansk forskargrupp nyligen. Risken kan inte avfärdas, anser däremot Kjell Hansson Mild, professor vid Arbetslivsinstitutet och ledamot av Stewartkommissionen, den brittiska regeringens forskningsråd för mobiltelefoni.

Kjell Hansson Mild är kritisk till den danska studie som förra veckan slog fast att det inte är någon risk att drabbas av cancer om man talar i

mobiltelefon. I studien jämfördes 420 000 personer som hade mobiltelefonabonnemang i Danmark 1982-1995 med det danska cancerregistret. Mobiltelefonabonnenterna fick inte mer cancer än andra danskar.

- Inte ens om du skickat röntgenstrålning på den här gruppen människor hade du fått någon cancereffekt, säger Kjell Hansson Mild.

- Här blandas de som använder mobilen regelmässigt minst 60 minuter varje dag med dem som ringer mindre än två minuter i veckan. Det är omöjligt att säga något om hur strålningen påverkar högkonsumenter. Och det är exponeringstiden som har betydelse, säger han.

- Inte heller har man tittat på vilken typ av telefon de använder och hur

den används. Exponeringen från olika telefoner kan skilja med en faktor tio, säger Kjell Hansson Mild. Värst är en högstrålande telefon där en kort antenn stryker utmed huvudet. De som använder telefonen i bilen utsätts

däremot inte för någon strålning alls eftersom den passerar genom

ytterantennen.

- Om man blandar och spär ut en grupp på det här viset måste man exponera den för ett verkligt kraftfullt cancerogent ämne om det ska synas någon effekt, konstaterar Kjell Hansson Mild.

Den danska studien hade inte för avsikt att titta på om det finns något

samband mellan mobiltelefoni och hjärnsjukdomar som demens, Parkinson etc.

Hur ser forskningsläget ut när det gäller ett sådant eventuellt samband?

- Med EEG kan man påvisa klara förändringar i hjärnan. Det visar studier från Tyskland, England, Ryssland och Finland. Hjärnans elektriska aktivitet och funktioner som minne och reaktionsförmåga påverkas. Efter en halvtimmes

exponering kvarstår dessa förändringar i hjärnan 10-20 minuter. Om man

somnar strax efter samtalet kvarstår förändringen 30 minuter i sömnen, säger Kjell Hansson Mild.

- Men om detta ger hälsoeffekter vet man inte, tillägger han.