

## Carcinogenicity of radiofrequency electromagnetic fields



In May, 2011, 30 scientists from 14 countries met at the International Agency for Research on Cancer (IARC) in Lyon, France, to assess the carcinogenicity of radiofrequency electromagnetic fields (RF-EMF). These assessments will be published as Volume 102 of the IARC Monographs.<sup>1</sup>

Human exposures to RF-EMF (frequency range 30 kHz–300 GHz) can occur from use of personal devices (eg, mobile telephones, cordless phones, Bluetooth, and amateur radios), from occupational sources (eg, high-frequency dielectric and induction heaters, and high-powered pulsed radars), and from environmental sources such as mobile-phone base stations, broadcast antennas, and medical applications. For workers, most exposure to RF-EMF comes from near-field sources, whereas the general population receives the highest exposure from transmitters close to the body, such as handheld devices like mobile telephones. Exposure to high-power sources at work might involve higher cumulative RF energy deposited into the body than exposure to mobile phones, but the local energy deposited in the brain is generally less. Typical exposures to the brain from rooftop or tower-mounted mobile-phone base stations and from TV and radio stations are several orders of magnitude lower than those from global system for mobile communications (GSM) handsets. The average exposure from use of digital enhanced cordless telecommunications (DECT) phones is around five times lower than that measured for GSM phones, and third-generation (3G) phones emit, on average, about 100 times less RF energy than GSM phones, when signals are strong. Similarly, the average output power of Bluetooth wireless hands-free kits is estimated to be around 100 times lower than that of mobile phones.

EMFs generated by RF sources couple with the body, resulting in

induced electric and magnetic fields and associated currents inside tissues. The most important factors that determine the induced fields are the distance of the source from the body and the output power level. Additionally, the efficiency of coupling and resulting field distribution inside the body strongly depend on the frequency, polarisation, and direction of wave incidence on the body, and anatomical features of the exposed person, including height, body-mass index, posture, and dielectric properties of the tissues. Induced fields within the body are highly non-uniform, varying over several orders of magnitude, with local hotspots.

Holding a mobile phone to the ear to make a voice call can result in high specific RF energy absorption-rate (SAR) values in the brain, depending on the design and position of the phone and its antenna in relation to the head, how the phone is held, the anatomy of the head, and the quality of the link between the base station and phone. When used by children, the average RF energy deposition is two times higher in the brain and up to ten times higher in the bone marrow of the skull, compared with mobile phone use by adults.<sup>2</sup> Use of hands-free kits lowers exposure to the brain to below 10% of the exposure from use at the ear, but it might increase exposure to other parts of the body.<sup>3</sup>

Epidemiological evidence for an association between RF-EMF and cancer comes from cohort, case-control, and time-trend studies. The populations in these studies were exposed to RF-EMF in occupational settings, from sources in the general environment, and from use of wireless (mobile and cordless) telephones, which is the most extensively studied exposure source. One cohort study<sup>4</sup> and five case-control studies<sup>5–9</sup> were judged by the Working Group to offer potentially useful information

regarding associations between use of wireless phones and glioma.

The cohort study<sup>4</sup> included 257 cases of glioma among 420 095 subscribers to two Danish mobile phone companies between 1982 and 1995. Glioma incidence was near the national average for the subscribers. In this study, reliance on subscription to a mobile phone provider, as a surrogate for mobile phone use, could have resulted in considerable misclassification in exposure assessment. Three early case-control studies<sup>5–7</sup> encompassed a period when mobile phone use was low, users typically had low cumulative exposures, time since first use of a mobile phone was short, and effect estimates were generally imprecise; the Working Group considered these studies less informative. Time-trend analyses did not show an increased rate of brain tumours after the increase in mobile phone use. However, these studies have substantial limitations because most of the analyses examined trends until the early 2000s only. Such analyses are uninformative if excess risk only manifests more than a decade after phone use begins, or if phone use only affects a small proportion of cases—eg, the most heavily exposed, or a subset of brain tumours.

The INTERPHONE study,<sup>8</sup> a multicentre case-control study, is the largest investigation so far of mobile phone use and brain tumours, including glioma, acoustic neuroma, and meningioma. The pooled analysis included 2708 glioma cases and 2972 controls (participation rates 64% and 53%, respectively). Comparing those who ever used mobile phones with those who never did yielded an odds ratio (OR) of 0.81 (95% CI 0.70–0.94). In terms of cumulative call time, ORs were uniformly below or close to unity for all deciles of exposure except the highest decile (>1640 h of use), for which the OR for glioma was 1.40 (95% CI 1.03–1.89). There was suggestion of an increased risk for ipsilateral exposure (on the same



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### Upcoming meetings

Oct 11–18, 2011

Bitumen and bitumen fumes, and some heterocyclic polycyclic aromatic hydrocarbons

Feb 7–14, 2012

Polymaviruses (SV40, BK, JC, and Merkel cell viruses) and malaria

June 5–12, 2012

Diesel and gasoline engine exhausts and some nitroarenes

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## Conflicts of interest

MS's spouse owns shares (worth €1350) in Telstra, a telecommunications company in Australia. BA has received travel and accommodation expenses for presentations on mobile phone use and brain tumours, from various Australian organisations and government groups. EC has received travel and accommodation expenses for presentations organised by France Telecom. RdS has received research support from Fondation Santé et Radiofréquences, and was a paid advisor (<€1000) for the plaintiff's lawyer on a lawsuit involving radiofrequency exposure. NK is director and board member of the non-profit IT'IS foundation that performs exposure assessments for industry and governments, and is president of the board and shareholder of Near-Field Technology AG, which controls two companies that develop near-field measurement instruments, simulation software, and medical test equipment. All other Working Group members, specialists, representatives, and secretariat declared no conflicts of interest.

side of the head as the tumour) and for tumours in the temporal lobe, where RF exposure is highest. Associations between glioma and cumulative specific energy absorbed at the tumour location were examined in a subset of 553 cases that had estimated RF doses.<sup>10</sup> The OR for glioma increased with increasing RF dose for exposures 7 years or more before diagnosis, whereas there was no association with estimated dose for exposures less than 7 years before diagnosis.

A Swedish research group did a pooled analysis of two very similar studies of associations between mobile and cordless phone use and glioma, acoustic neuroma, and meningioma.<sup>9</sup> The analysis included 1148 glioma cases (ascertained 1997–2003) and 2438 controls, obtained through cancer and population registries, respectively. Self-administered mailed questionnaires were followed by telephone interviews to obtain information on the exposures and covariates of interest, including use of mobile and cordless phones (response rates 85% and 84%, respectively). Participants who had used a mobile phone for more than 1 year had an OR for glioma of 1.3 (95% CI 1.1–1.6). The OR increased with increasing time since first use and with total call time, reaching 3.2 (2.0–5.1) for more than 2000 h of use. Ipsilateral use of the mobile phone was associated with higher risk. Similar findings were reported for use of cordless phones.

Although both the INTERPHONE study and the Swedish pooled analysis are susceptible to bias—due to recall error and selection for participation—the Working Group concluded that the findings could not be dismissed as reflecting bias alone, and that a causal interpretation between mobile phone RF-EMF exposure and glioma is possible. A similar conclusion was drawn from these two studies for acoustic neuroma, although the case numbers were substantially smaller than for glioma. Additionally, a study from Japan<sup>11</sup> found some evidence of an increased risk for acoustic neuroma

associated with ipsilateral mobile phone use.

For meningioma, parotid-gland tumours, leukaemia, lymphoma, and other tumour types, the Working Group found the available evidence insufficient to reach a conclusion on the potential association with mobile phone use. Epidemiological studies of individuals with potential occupational exposure to RF-EMF have investigated brain tumours, leukaemia, lymphoma, and other types of malignancy including uveal melanoma, and cancers of the testis, breast, lung, and skin. The Working Group noted that the studies had methodological limitations and the results were inconsistent. In reviewing studies that addressed the possible association between environmental exposure to RF-EMF and cancer, the Working Group found the available evidence insufficient for any conclusion.

The Working Group concluded that there is “limited evidence in humans” for the carcinogenicity of RF-EMF, based on positive associations between glioma and acoustic neuroma and exposure to RF-EMF from wireless phones. A few members of the Working Group considered the current evidence in humans “inadequate”. In their opinion there was inconsistency between the two case-control studies and a lack of an exposure-response relationship in the INTERPHONE study results; no increase in rates of glioma or acoustic neuroma was seen in the Danish cohort study,<sup>4</sup> and up to now, reported time trends in incidence rates of glioma have not shown a parallel to temporal trends in mobile phone use.

The Working Group reviewed more than 40 studies that assessed the carcinogenicity of RF-EMF in rodents, including seven 2-year cancer bioassays. Exposures included 2450 MHz RF-EMF and various RF-EMF that simulated emissions from mobile phones. None of the chronic bioassays showed an increased incidence of any tumour type in tissues or organs of animals exposed to RF-EMF for 2 years. An increased

total number of malignant tumours was found in RF-EMF-exposed animals in one of the seven chronic bioassays. Increased cancer incidence in exposed animals was noted in two of 12 studies with tumour-prone animals<sup>12,13</sup> and in one of 18 studies using initiation-promotion protocols.<sup>14</sup> Four of six co-carcinogenesis studies showed increased cancer incidence after exposure to RF-EMF in combination with a known carcinogen; however, the predictive value of this type of study for human cancer is unknown. Overall, the Working Group concluded that there is “limited evidence” in experimental animals for the carcinogenicity of RF-EMF.

The Working Group also reviewed many studies with endpoints relevant to mechanisms of carcinogenesis, including genotoxicity, effects on immune function, gene and protein expression, cell signalling, oxidative stress, and apoptosis. Studies of the possible effects of RF-EMF on the blood-brain barrier and on a variety of effects in the brain were also considered. Although there was evidence of an effect of RF-EMF on some of these endpoints, the Working Group reached the overall conclusion that these results provided only weak mechanistic evidence relevant to RF-EMF-induced cancer in humans.

In view of the limited evidence in humans and in experimental animals, the Working Group classified RF-EMF as “possibly carcinogenic to humans” (Group 2B). This evaluation was supported by a large majority of Working Group members.

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We declare that we have no conflicts of interest.

- 1 IARC. IARC monographs on the evaluation of carcinogenic risks to humans, vol 102. Non-ionizing radiation, part II: radiofrequency electromagnetic fields. Lyon: International Agency for Research on Cancer (in press).
- 2 Christ A, Gosselin MC, Christopoulou M, Kühn S, Kuster N. Age-dependent tissue-specific exposure of cell phone users. *Phys Med Biol* 2010; **55**: 1767–83.
- 3 Kühn S, Cabot E, Christ A, Capstick M, Kuster N. Assessment of the radio-frequency electromagnetic fields induced in the human body from mobile phones used with hands-free kits. *Phys Med Biol* 2009; **54**: 5493–508.
- 4 Schüz J, Jacobsen R, Olsen JH, Boice JD Jr, McLaughlin JK, Johansen C. Cellular telephone use and cancer risk: update of a nationwide Danish cohort. *J Natl Cancer Inst* 2006; **98**: 1707–13.
- 5 Muscat JE, Malkin MG, Thompson S, et al. Handheld cellular telephone use and risk of brain cancer. *JAMA* 2000; **284**: 3001–07.
- 6 Inskip PD, Tarone RE, Hatch EE, et al. Cellular-telephone use and brain tumors. *N Engl J Med* 2001; **344**: 79–86.
- 7 Auvinen A, Hietanen M, Luukkonen R, Koskela RS. Brain tumors and salivary gland cancers among cellular telephone users. *Epidemiology* 2002; **13**: 356–59.
- 8 INTERPHONE Study Group. Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case-control study. *Int J Epidemiol* 2010; **39**: 675–94.
- 9 Hardell L, Carlberg M, Hansson Mild K. Pooled analysis of case-control studies on malignant brain tumours and the use of mobile and cordless phones including living and deceased subjects. *Int J Oncol* 2011; **38**: 1465–74.
- 10 Cardis E, Armstrong BK, Bowman JD, et al. Risk of brain tumours in relation to estimated RF dose from mobile phones—results from five Interphone countries. *Occup Env Med* 2011; published online June 9. DOI:10.1136/oemed-2011-100155.
- 11 Sato Y, Akiba S, Kubo O, Yamaguchi N. A case-case study of mobile phone use and acoustic neuroma risk in Japan. *Bioelectromagnetics* 2011; **32**: 85–93.
- 12 Repacholi MH, Basten A, GebSKI V, Noonan D, Finnie J, Harris AW. Lymphomas in E mu-Pim1 transgenic mice exposed to pulsed 900 MHz electromagnetic fields. *Radiat Res* 1997; **147**: 631–40.
- 13 Szmigielski S, Szudzinski A, Pietraszek A, Bielec M, Janiak M, Wrembel JK. Accelerated development of spontaneous and benzopyrene-induced skin cancer in mice exposed to 2450-MHz microwave radiation. *Bioelectromagnetics* 1982; **3**: 179–91.
- 14 Hruby R, Neubauer G, Kuster N, Frauscher M. Study on potential effects of "902-MHz GSM-type Wireless Communication Signals" on DMBA-induced mammary tumours in Sprague-Dawley rats. *Mutat Res* 2008; **649**: 34–44.