

# Radio-Frequency Fields and Cancer

## Technical Update - EMF Health Studies

Exposure to radio-frequency (RF) electromagnetic fields (EMF) has become commonplace in countries throughout the world. The advent during the last two decades of a spate of new technologies using RF energy has resulted in numerous new sources of exposure to low-level fields in public and residential

ly, the often highly visible base station antennas that receive and transmit mobile phone signals. Base station antennas are installed on freestanding towers (masts), in public places such as airports and shopping centers, inside buildings, and on buildings (Figure 1). An extensive network of antennas is located

are now part of the everyday work environment. In addition, electric fields close to AM radio broadcast towers can induce voltages in nearby transmission towers, construction cranes, and guy wires that may pose an RF burn hazard and produce reradiated RF fields that may contribute to exposure.



Figure 1. Mobile phone base station antennas on a building.

environments, with higher field levels occurring in occupational settings. The continued introduction of new sources of exposure has triggered concern about the possibility that RF fields could affect health.

Public concern has focused on RF exposure from cellular mobile telephones and, especial-

ly, the often highly visible base station antennas that receive and transmit mobile phone signals. Base station antennas are installed on freestanding towers (masts), in public places such as airports and shopping centers, inside buildings, and on buildings (Figure 1). An extensive network of antennas is located on electric power system infrastructure; RF fields close to these antennas (shown in Figure 2) can exceed exposure guideline limits. Electric power company workers may be exposed to these fields and to RF energy from mobile telephones, paging, point-to-point microwave, two-way radio, walkie-talkies, and other RF and wireless technologies that

Epidemiologists have studied populations in both occupational and residential environments to investigate possible health effects from exposure to RF fields. A number of occupational studies conducted during the latter part of the last half-century have investigated cancer, cardiovascular disease, adverse reproductive outcomes, cataracts, and other health outcomes. Residential studies conducted more recently have mainly examined RF exposure from radio and television transmitters and from mobile telephony, particularly in relation to leukemia and brain cancer. Currently, the International Agency for Research on Cancer (IARC) is coordinating a multinational series of case-control studies of mobile phone use, acoustic neuroma, and brain and parotid gland tumors. The studies from this series—collectively known as the INTERPHONE Study—that have been published to date are included in this summary, which focuses on cancer studies.

### RF Exposure

RF energy is nonionizing radiation occupying the frequency range between about 10 kHz and 300 GHz on the electromagnetic spectrum. Within this range lie the frequencies



Figure 2. Mobile telecommunications antennas mounted on an electric power transmission tower.

used for mobile telecommunications systems and other technologies that produce RF fields (Figure 3). In addition to mobile phones and base stations, broadcast television and radio antennas can be sources of low-level public exposure, depending on factors such as station power, antenna radiation pattern, and distance from the antenna.

Occupational RF exposures occur during a number of industrial processes. One of the most important sources of occupational exposure is RF dielectric heating, used for heating, sealing, drying, curing, embossing, or melting vinyl and other materials that are poor electrical conductors. In medical settings, exposures can occur from sources such as magnetic resonance imaging (MRI) equipment, diathermy equipment for heating to relieve pain and inflammation, and electrosurgical units. Exposure to relatively high RF fields can occur in some situations from radar systems used for air traffic control and for military applications. Workers in the ra-

dio and television broadcasting and telecommunications industries, as well as the electric power industry, can also be exposed to high RF field levels close to transmitting antennas; fields very close to television and FM radio antennas can be extremely high.

The amount of exposure a person receives from an RF field depends on many factors, including the person's grounding state, body size, posture, and time in the field, as well as the frequency, nonuniformity, polarization, and intensity of the field. At more than about a wavelength from the source, in the far field, field intensity is generally expressed as power density in  $\text{mW}/\text{cm}^2$  or  $\mu\text{W}/\text{cm}^2$ . In the near field, the region close to the source with respect to wavelength, fields are measured as uncoupled electric fields and magnetic fields in  $\text{V}/\text{m}$  and  $\text{A}/\text{m}$ , respectively. Field intensity in this region depends primarily on the power input to an antenna and the size of the antenna.

Both public and occupational RF exposure is limited by safety guidelines. In the United States, the guidelines most often used are the 1996 Federal Communications Commission (FCC) guidelines, the only guidelines with regulatory enforcement. Other guidelines include the 1999 and 2005 editions of the Institute of Electrical and Electronics Engineers (IEEE) standard. In other countries, the 1998 guidelines issued by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) are those most widely used (revision of these guidelines is currently under way). Guidelines set basic restrictions limiting internal body dose from RF exposure and set reference levels designed to ensure that the basic restrictions will not be exceeded. Basic restrictions are based on the specific absorption rate (SAR), the power absorbed per kg of body tissue. The SAR is measured in  $\text{W}/\text{kg}$ . Most guidelines specify a basic restriction of  $0.4 \text{ W}/\text{kg}$  (whole-body average) for occupational exposure and  $0.08 \text{ W}/\text{kg}$  for public exposure; the basic restriction for occupational exposure incorporates a safety factor of 10, and the basic restriction for public exposure incorporates a safety factor of 50. The FCC RF guidelines allow spatial and temporal averaging of exposure and permit higher SAR limits for small areas of tissue and for extremities. For exposure from mobile phones, the FCC limit is an SAR of  $1.6 \text{ W}/\text{kg}$ , measured over any 1 g of tissue.

A comprehensive review of RF exposure standards is available in a 2004 EPRI technical report, and a 2002 EPRI resource paper provides an overview of RF exposure fundamentals.

### Biological Effects of RF Exposure

Exposure to high levels of RF fields is known to cause adverse health effects through heating

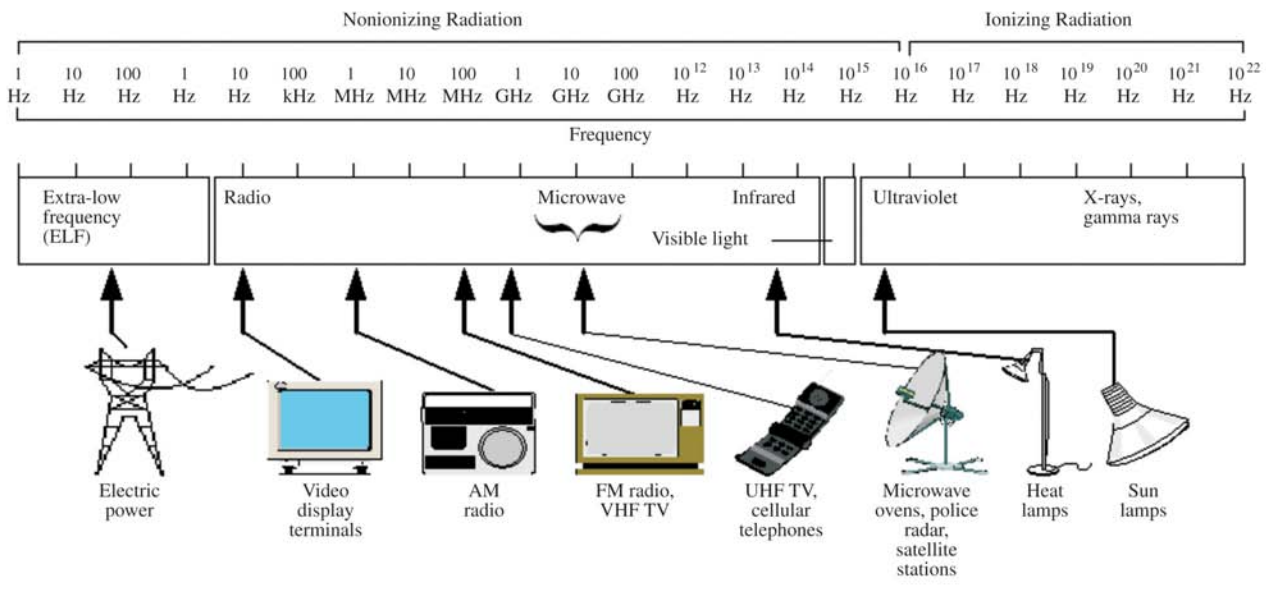


Figure 3. The electromagnetic spectrum. Radio frequencies range from about 10 kHz to 300 GHz.

of body tissue. Laboratory studies have shown that adverse effects can occur if tissue or body temperature rises by more than 1°C; an SAR of at least 4 W/kg is required to produce this amount of heating (basic restrictions in exposure guidelines are based on this threshold, with an added safety margin). Adverse effects might be caused either by elevated body temperature or by extra strain on the body as it attempts to dissipate heat. Tissues and cells in the central nervous system, the testes, and the lenses of the eyes are particularly sensitive to damage from either whole-body or localized heating, but other tissues, such as liver, kidney, and muscle, can also be affected. Non-cancer health outcomes that have been associated with whole-body heating include cardiovascular mortality, birth defects, and impaired ability to perform complex tasks. In addition, deep burns can result from direct contact with active transmitting antennas or with ungrounded conductive cables or guy wires carrying induced RF voltages. Regarding the carcinogenic potential of RF fields

high enough to cause tissue heating, Moulder et al. (2005) have noted that although animal studies do not provide evidence that RF energy can act as a primary carcinogen, there is some evidence that whole-body heating can promote cancer development.

Many laboratory studies have investigated possible nonthermal effects of exposure to low-intensity RF fields. Recent studies with human volunteers have reported some effects on sleep, inconsistent changes in cardiovascular function, and some evidence of headaches and other subjective symptoms, but too little to permit conclusions. Volunteer studies have also found subtle, transient neurobehavioral effects such as lack of concentration, although there is some evidence of somewhat sharpened attention and decreased reaction times with acute exposure. Neurobehavioral effects have also been reported in some high-quality animal studies. Some cell studies have reported field-dependent changes in heat-shock proteins, which are synthesized in increased amounts to protect cells against dam-

age when they are subjected to unusually high temperatures and other stresses. Cell studies provide no consistent evidence that RF fields can cause genotoxic effects, such as genetic mutations or DNA-strand breaks, that might lead to initiation of cancer. This evidence supports well-conducted animal studies indicating that long-term RF exposure does not promote cancer development.

### Epidemiologic Studies

Epidemiologic studies investigating RF exposure and cancer can be grouped into three categories: occupational and military studies, transmitter studies, and mobile phone studies. As pointed out in reviews by the ICNIRP Standing Committee on Epidemiology (Ahlbom et al. 2004) and others, many of these studies have methodologic limitations and inadequate exposure assessment. Among methodologic limitations are low participation rates, small numbers of study subjects, the use of random-digit dialing for control selection in case-control studies, the use of death certificates for information on jobs and



Figure 4. Radio-frequency antennas of various types.

causes of death, confounding from exposures present along with RF fields, and testing for multiple exposures (in multiple comparisons, some associations are likely to arise from chance). Exposure assessment has been particularly problematic. Most studies have relied on proxies such as job title, mobile phone use, or distance from a transmitting antenna (Figure 4) rather than actual measurements or, for occupational studies, job-exposure matrices that are based on measurements. Moreover, the relevant aspect of exposure that might lead to health effects has not yet been identified. In addition to external field intensity, possibilities include cumulative exposure, average exposure during a specified period of time, and peak exposure; however, determination of the SAR is necessary to estimate the actual dose to specific body tissues. In mobile phone studies, additional difficulties present themselves: mobile phones have come into use too recently for studies to detect effects that might occur a long time after exposure, and rapidly changing mobile phone

technology complicates exposure assessment. However, improved exposure assessment is being attempted in new studies.

### Occupational and Military Studies

**Cohort Studies.** One of the earlier investigations of RF exposure and cancer was a 1980 cohort study of U.S. Navy men (Robinette et al.). In this study, cancer mortality during a 20-year follow-up period was compared between about 20,000 men whose jobs in 1950–1954 were judged to have high radar exposures and about 20,000 men with low-exposure jobs. Among men with high-exposure jobs, deaths from respiratory tract cancers, but not other cancers, were significantly increased. Quite different results were reported in a 2002 update of this study with 40 years of follow-up (Groves et al.): deaths from respiratory tract cancers, as well as total deaths and total cancer deaths, were significantly reduced in the high-exposure group, whereas nonlymphocytic leukemia deaths

were significantly increased for aviation electronics technicians, one of three high-exposure jobs (standardized mortality ratio [SMR] = 2.2, 95% confidence interval [CI] 1.3–3.7). However, actual radar exposures were unknown and could have been high in both groups of men; also, confounding from other exposures, including 60-Hz fields and solvents, is possible. Another military study (Garland et al. 1990) used medical records to investigate leukemia among active-duty U.S. Navy personnel in occupations with potential EMF exposure during 1974–1984. Based on 102 cases, the study found no increase in incidence rates compared to rates for the general population. A cohort study of military personnel in Poland examined cancer incidence from 1971–1985 (Szmigielski 1996), with exposure assessed as likely or unlikely based on military records. Although the study reported a doubling of total cancers as well as considerable excesses of several types of cancer among those likely to be exposed, these findings are inconsistent with those of other studies and, because more sources of exposure information were used for subjects who developed cancer than for those who did not, may well result from bias.

In a 1988 study of 67,829 male amateur radio operators in the United States that can be classified along with the occupational studies, Milham used death certificates to identify the causes of 2485 deaths that occurred in 1979–1984. Mortality was statistically significantly increased for some lymphatic cancers, such as non-Hodgkin's lymphoma (SMR = 162), and for acute myeloid leukemia (AML) but not other types of leukemia (SMR = 176). However, confounding from other exposures such as electric shock and soldering fumes is possible. In a 1996 study, Tynes et al. used cancer registry information to identify new

cancer cases among a cohort of 2619 female Norwegian radio and telegraph operators. The authors reported an increased risk of breast cancer (relative risk, RR = 1.5, 95% CI 1.1–2.0) and uterine cancer (RR = 1.9, 95% CI 1.0–3.2) among these women compared with the Norwegian female population, but exposure to light at night, ELF fields, and other potential confounding factors could have affected the results.

In 1997 Lagorio et al. conducted a cohort study of cancer mortality among female plastics workers in Italy. The analyses, which included 481 women followed from 1962–1992, showed a nonsignificant excess in mortality from all cancers based on six cases among women using RF dielectric heat sealers. The study was very small, and confounding from solvent and chemical exposures is possible.

A 2000 study (Morgan et al.) examined cancer mortality among a cohort of 195,775 employees of a U.S. wireless communication products company who were followed for 20 years. Based on a qualitative job-exposure matrix, RF exposure was classified as background, low, moderate, or high. For highly exposed employees compared to either the general population or to cohort members with low or background exposure, no excess risk was found for brain cancer, leukemias, or lymphomas.

**Case-Control Studies.** Several occupational studies used a case-control design. Two were nested case-control studies within occupational or military cohorts. The first (Armstrong et al. 1994) examined cancer incidence among electric utility workers in Canada and France in relation to pulsed EMF. For 2679 incident cancer cases and for controls, exposure was assessed using a job-exposure matrix based on electric field measurements made with meters

that recorded both RF and extremely low frequency (ELF) fields. Adjustment was made for other relevant exposures. A significantly increased risk of lung cancer was found with cumulative pulsed EMF exposure, with an odds ratio (OR) of 3.1 (95% CI 1.6–6.0) in the highest exposure group of 84 cases, but it is not clear whether this increase was associated with RF fields, and overall lung cancer risk was not elevated in comparison with the general population. The second nested case-control study (Grayson 1996) investigated brain cancer among U.S. Air Force personnel in relation to EMF exposure estimated using a job-exposure matrix developed by an expert group. The 230 cases identified from service records had a small, statistically significant excess risk with RF EMF exposure compared to 920 controls (OR = 1.4, 95% CI 1.0–1.9).

A 1987 case-control study (Thomas et al.) included 435 male cases who died of brain cancer, as recorded on death certificates, and 386 controls who died of other causes. Information on occupation was obtained from relatives. An increased risk was found for men who had ever held an electrical or electronics job likely to involve RF radiation, but the risk was also increased for men in such jobs who did not have RF exposure and for men in jobs involving solvents and other exposures. In a 1990 case-control study, Hayes et al. identified 271 testicular cancer cases and 259 controls with other cancers at three medical centers. The results were inconsistent: an increased risk was observed for self-reported RF exposure but not for exposure based on job title.

Male breast cancer was investigated in a 1991 population-based study of occupational EMF exposure (Demers et al.). The study included 227 incident cases identified from U.S. cancer registries and 300 controls selected through

random-digit dialing and from Medicare eligibility lists. For radio and communications workers who had ever been employed in a job classified as involving potential exposure to EMF, breast cancer risk was nonsignificantly increased; this result was based on only seven cases. In a 1995 U.S. study of female breast cancer, Cantor et al. included 33,000 cases who had died from breast cancer in 1984–1989 and 117,000 matched controls. Job information was collected from death certificates, and a job-exposure matrix was used to estimate exposure to 31 different agents. The authors found no trend in breast cancer risk with either likelihood or level of RF EMF exposure.

Ocular melanoma was examined in a 1996 study of 221 male cases and 447 controls (Holly et al.) that reported a significantly increased risk with exposure to microwaves or radar (OR = 2.1, 95% CI 1.1–4.0). However, this study assessed a large number of different exposures that were self-reported and identified controls through random-digit dialing. In a 2001 study, Stang et al. found an increased risk of ocular melanoma with self-reported occupational exposure for several hours a day to radio sets (OR = 3.3, 95% CI 1.2–9.2) based on nine cases, but there was no increase in risk with exposure to radar. The authors acknowledged that the study had several methodologic limitations.

## Transmitter Studies

Several studies have investigated cancer risk (mostly leukemia) among populations residing near radio or television transmitting antennas. Some have investigated reports of cancer clusters near antennas; however, since cancer clusters can arise purely by chance, random chance is a likely explanation for most.



Figure 5. FM radio broadcast antennas. Photo reprinted with permission from Richard Tell Associates, Inc.

Cancer patterns were found to be essentially random with respect to distance from a large San Francisco television antenna in a 1992 study by Selvin et al. The study examined distributions of incident cases of childhood leukemia (51 cases), brain cancer (35 cases), and lymphatic cancer (37 cases). A 1994 case-control study of a cluster of 12 acute childhood leukemia cases in Hawaii (Maskarinec et al.) examined distance from radio towers in addition to other risk factors. The authors concluded that chance could have been responsible for the results, which showed a non-significant excess of leukemia among children who had lived within 2.6 miles of the towers before diagnosis.

In Australia, Hocking et al. (1996) compared cancer incidence in three municipalities surrounding three Sydney television transmitters with incidence in six farther municipalities. Power densities at various distances from the transmitters were calculated from information on frequency, power, and period

of broadcasting. For children and adults combined, the RR for total leukemia incidence was 1.2 (95% CI 1.1–1.4); for children, the RR for leukemia incidence was 1.6 (95% CI 1.1–2.3). Brain cancer risk was not elevated in either children or adults. There was little control for confounding from other exposures in this study. A 1998 study by McKenzie et al. that reexamined the Hocking et al. results found that acute lymphoblastic leukemia (ALL) incidence was increased in only one local government area close to the transmitters and not in another with similar RF exposure; these results suggest that some other factor is responsible for the excess risk.

A 1997 study in the UK by Dolk et al. investigated a reported cluster of leukemias and lymphomas in adults living near a television and FM radio transmitter (Figure 5) at Sutton Coldfield. Using a national database of postcoded cancer registrations for 1974–1986 along with census population and socioeconomic data, the authors assessed the incidence of 11 types of cancer based on comparison of observed and expected numbers of cases. They found an excess risk for adult leukemia within 2 km of the transmitter (RR=1.8, 95% CI 1.2–2.7), with a statistically significant decline in risk with increasing distance from the transmitter out to 10 km. For childhood leukemia, there were two cases compared with 1.1 expected within 2 km of the transmitter. In a second 1997 study that included areas around 20 other radio/television transmitters in the UK, Dolk et al. found no increased risk of adult leukemia near the transmitters and a decrease in risk with increasing distance that was of borderline significance; for childhood leukemia there was neither a significant increase in risk near the transmitters nor a significant decline in risk with increasing distance. A 2001 follow-up study by Cooper et al. that used cancer in-

cidence data for 1987–1994 found no significant risk increases for adult or childhood leukemia close to transmitters and no significant decline in risk for adults with distance. There was a marginally significant decline in risk for children (boys only) with increasing distance, based on small numbers.

In 2002 publication of a study of leukemia in children and adults living near the high-power Vatican radio station created a stir in Italy (Michelozzi et al.). The authors reported a statistically significant increase in leukemia risk for children living up to 6 km from transmitters (standardized incidence ratio, SIR = 2.2, 95% CI 1.0–4.1) as well as significant decreases with increasing distance in both childhood leukemia incidence and male adult leukemia mortality. The study was based on small numbers of cases and, like other transmitter studies, used distance as a surrogate for exposure.

### Mobile Phone Studies

Most recent studies of RF exposure and cancer have investigated mobile phone use. Exposure from mobile phones varies with geographic location, the strength of base station signals, the position in which the phone is held, the size of the head, and the average number and duration of calls, as well as the type of phone. Older analogue phones introduced in the early 1980s operate at higher power levels than the newer, “second-generation” digital phones of the 1990s, such as Global System for Mobile Communications (GSM) phones. Some studies have investigated RF exposure from cordless as well as cellular phones; older cordless phones were analogue phones with higher exposure levels than the newer Digital Enhanced Cordless Telecommunications (DECT) phones. Cordless phone handsets communicate with base stations located at telephone outlets in homes or offices.



Figure 6. A mobile phone base station with an antenna array on a freestanding tower.

Many mobile phone studies have relied on billing records from mobile phone companies to determine use and estimate exposure, although this method of exposure assessment may be affected by limited access to billing records and by people sharing phones, using more than one phone, and switching carriers. The more recent studies have estimated exposure according to total minutes of phone use per month or other time period and duration of use over a period of years, as reported by study participants. This method is often subject to recall bias, and it does not take exposure variation due to phone model and position into account, nor does it consider geographic location with respect to base stations (Figure 6) or base station signal strength. However, the use of phones that record power output and call duration by some INTERPHONE Study participants, along with assessment in the study of factors affecting power output, may lead to improved exposure assessment.

**Cohort Studies.** Phone company billing records were used to identify a cohort of over 255,000 mobile phone users and determine their phone use in a 1996 U.S. study by Rothman et al. Information on mortality during the year 1994 was obtained through record linkage. The authors found no increase in overall mortality among users of mobile phones with built-in antennas compared to users of portable phones without antennas in the handsets. In a further analysis, Dreyer et al. (1999) found no increased risk of brain tumors or leukemia with increased use of mobile phones. In another cohort study in Denmark, Johansen et al. (2001) identified 420,095 individual mobile phone subscribers from phone company records and ascertained cancer incidence for 1982–1995 through linkage to the Danish Cancer Registry. Users of analogue phones were followed for an average of 3.5 years, and users of GSM digital phones were followed for an average of 1.9 years. No risk increases for brain cancer, salivary gland

cancer, or leukemia were found among users of either type of phone compared to risk in the Danish population.

**Case-Control Studies.** Hardell et al. conducted several case-control studies of mobile telephone use and cancer in Sweden. The first study, published in 1999, included 209 cases with malignant or benign brain tumors diagnosed in 1994–1996 who were alive at the time of the study and 425 matched controls selected from the Swedish Population Register. Exposure was assessed through questionnaires and phone interviews. Cumulative duration of use and latency periods of up to 10 or more years were examined. No significant associations were found with either analogue or GSM digital phone use. However, later analyses (2000, 2001) found that phone use on the same side of the head as tumors (ipsilateral use) occurring in the temporal, temporoparietal, and occipital areas of the brain increased the risk for these tumors (OR = 2.6, 95% CI 1.0–6.7). In a larger follow-up study in 2002, brain tumor risk increased with use of analogue phones, but not digital or cordless phones, more than a year before diagnosis; the risk increased with longer latency periods. Ipsilateral analogue phone use was associated with an increased risk of temporal tumors. For all three phone types, brain tumor risk decreased with contralateral use (use on the side of the head opposite to the side where the tumor is located); this finding, along with increased risk with ipsilateral use, suggests that the results might have arisen from recall bias, with cases systematically overreporting phone use on the same side of the head as their tumors. Further analyses published in 2003 reported similar findings to the 2002 study. In a 2005 study of benign brain tumors, meningioma risk increased with use of analogue phones, par-

ticularly with a latency period greater than 10 years. Risk of malignant tumors was similarly increased in a 2006 study, but in this study risk was also elevated for digital and cordless phones (despite the very low power output of cordless phones). A 2006 pooled analysis of data from two of the previous studies on malignant brain tumors also found that analogue, digital, or cordless phone use increased risk, with higher risks for latency periods of over 10 years and for ipsilateral exposure. In a similar 2006 pooled analysis of data on benign brain tumors, meningioma risk was increased with analogue phone use for more than 10 years.

Hardell et al. investigated salivary gland cancer in a 2004 study, reporting no associations with analogue, digital, or cordless phone use, although few subjects reported use for more than 10 years. A 2005 study of non-Hodgkin's lymphoma found an increased risk of the T-cell type with digital and cordless phone use, but the results were based on low numbers. In the 2002 brain tumor study and the 2005 study of benign brain tumors, risk of acoustic neuroma (a benign cranial nerve tumor) was also investigated. Risk was elevated with analogue phone use in the 2002 study and with analogue phone use, especially with long latency periods, as well as with digital phone use in the 2005 study. In the 2006 pooled analysis of benign brain tumor studies, acoustic neuroma risk was significantly increased for both digital and cordless phone use, but risk for analogue phone use was highest, especially with a latency period of more than 15 years (OR=3.8, 95% CI=1.4–10). Several methodological issues, including recall bias, may have affected results from the Hardell et al. studies.

A 2000 U.S. hospital-based study of 469 malignant brain tumor cases and 422 matched

controls (Muscat et al.) found no associations with frequency or duration of handheld mobile phone use, as reported in interviews. The mean duration of use in this study was less than 3 years for cases. In a similar 2002 study with 90 acoustic neuroma cases and 86 controls, Muscat et al. reported no associations with level or laterality of phone use. A 2001 U.S. hospital-based study (Inskip et al.) of 782 cases with malignant or benign brain tumors and 799 controls also found no significant risk increases with frequency of mobile phone use or duration of use up to 5 or more years, and no association with laterality or tumor location. In a 2002 registry-based study in Finland that determined phone use from mobile phone company records for an average subscription length of 2–3 years, Auvinen et al. found no association with overall incidence of either brain tumors or salivary gland cancers. However, there was an association between analogue phone use and glioma, a type of brain tumor (OR = 2.1, 95% CI 1.3–3.4). The study included 398 brain tumor and 34 salivary gland cancer cases, with five controls per case. This study had no information about the frequency or duration of calls. A 2006 meta-analysis of studies of mobile phone use and intracranial tumors by Lakhola et al. included 2780 cases from 12 studies, including three 2005 INTERPHONE studies (Lönn et al., Christensen et al., and Schoemaker et al.) that will be discussed later. The results indicated that mobile phone use was not associated with risk for all intracranial tumors or for glioma or meningioma, but was nonsignificantly associated with risk for acoustic neuroma.

Stang et al.'s 2001 ocular melanoma study (described in the occupational studies section) examined occupational exposure to mobile phones as well as radio sets. For sub-



*Figure 7. Reporting of cellular telephone use by epidemiologic study participants may not match the number of calls made or the duration of calls as recorded in phone company records.*

jects reporting probable or certain exposure to mobile phones, ocular melanoma risk was elevated (OR = 4.2, 95% CI 1.2–14.5).

**INTERPHONE Study.** The INTERPHONE Study comprises a multinational series of separate population-based case-control studies investigating mobile phone use and other potential risk factors (including occupational exposure to EMF across the frequency range) that may be related to brain tumors (both benign and malignant meningiomas and gliomas), acoustic neuroma, and parotid gland tumors. The studies are expected to include, in total, about 6000 glioma and meningioma cases, 1000 acoustic neuroma cases, and 600 parotid gland tumor cases and their respective controls. According to IARC, these numbers, along with a focus on relatively young people (ages 30–59) with a high past prevalence of mobile phone use and on regions with high, long-term phone use, are sufficient to detect a 1.5-fold risk increase with a 5–10-year latency period. The 13 participating countries are Australia, Canada, Denmark, Finland,

France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, and the UK. Studies in each of these countries follow the same core protocol. Exposure is assessed using a computer-assisted questionnaire administered during in-person interviews, with validation through comparison of interview information to information from both phone company records and software-modified phones. An exposure index developed by a committee of experts includes information on mobile phone networks and phone types.

The first INTERPHONE Study results for brain tumors were published in 2005 by Lönn et al., who identified 371 glioma cases and 273 meningioma cases diagnosed in Sweden during 2000–2002, with 674 controls randomly selected from the study base population and stratified on residential area, age, and gender. For both glioma and meningioma, no increased risk was observed with regular mobile phone use (use once a week on average for at least 6 months), long-term use (use for 10 years or more), cumulative hours of use, cumulative number of calls made, type of phone used (analogue or digital), tumor location, or laterality of phone use.

The second brain tumor study (Christensen et al. 2005) included 252 glioma cases and 175 meningioma cases diagnosed in Denmark during 2000–2002 and 822 matched controls randomly chosen from the Danish population register. As in the Swedish study, cellular telephone use (Figure 7) was not associated with an increased risk of either glioma or meningioma. In this study, the investigators compared information from questionnaires to information from phone company records for a small number of cases and controls; they found some agreement for the number of calls made and no agreement for the duration of the calls. This finding highlights the

potential for exposure misclassification when exposure assessment relies on questionnaire-based, self-reported phone use.

A study of cellular and cordless phones and risk of glioma and meningioma in Germany was published in 2006 (Schüz et al. 2006a). The study included 366 glioma cases and 381 meningioma cases diagnosed during 2000–2003, with 1494 matched controls randomly chosen from population registries. No associations were found for overall use of cellular phones, but a nonsignificantly increased risk of glioma was found with 10 or more years of use, based on 12 cases. Cordless phone use was not related to risk of either glioma or meningioma; these results were supported by a further analysis of the study data (Schüz et al. 2006b) using location of DECT cordless phone base stations near subjects' beds as a proxy for continuous, low-level, nighttime RF exposure.

Another German study (Berg et al. 2006) examined brain tumor risk in relation to occupational RF exposure, using interview information collected in the Schüz et al. study. Subjects were persons who had worked in occupations associated with exposure to RF radiation. Occupations were classified as having no exposure, improbable exposure, probable exposure, or high exposure (defined as exposure that may exceed ICNIRP limits for the general public). The duration of exposure was calculated for each subject who had worked in an exposed job. No significant associations were found for either glioma or meningioma.

A UK study of glioma risk and mobile phone use included 966 cases diagnosed during 2000–2004 and 1716 controls randomly chosen from general practitioner lists (Hepworth et al. 2006). No associations were found,

except that risk was significantly increased with ipsilateral phone use (OR = 1.2, 95% CI 1.0–1.5). However, a significant risk reduction with contralateral use suggests that the increase might be due to recall bias.

In a 2006 study in Denmark and Sweden, Lönn et al. included 60 cases of malignant tumors of the parotid gland (the largest of the salivary glands) and 112 cases of pleomorphic adenoma (a benign type of salivary gland tumor) diagnosed during 2000–2002, with 681 controls. No risk increases were found for either type of tumor.

Four studies of acoustic neuroma have been published to date. The first study (Lönn et al. 2004) included 148 Swedish cases diagnosed during 1999–2002 and 604 controls. Risk was not increased with short-term mobile phone use after a short latency period, but was increased with ipsilateral use for 10 years or more (RR = 3.9, 95% CI 1.6–9.5). In contrast, a 2004 Danish study (Christensen et al.) with 106 cases diagnosed in 2000–2002 and 212 controls found no risk increase. Data from these two studies were pooled with data from four other case-control studies of acoustic neuroma in the Nordic countries and the UK in a 2005 study by Schoemaker et al. Results for 678 cases and 3553 controls indicated an elevated risk for ipsilateral phone use for 10 years or longer (OR = 1.8, 95% CI 1.1–1.3). In the latest study of acoustic neuroma risk, Takebayashi et al. (2006) included 101 cases recruited in Japan in 2000–2004 and 339 controls. The study found no significant risk increases.

Among the strengths of the INTERPHONE studies is use of population-based, random control-selection methods. The main limitation of the studies is that exposure assessment is based on mobile telephone use reported

by subjects in response to a questionnaire. Questionnaire-based information may not be adequate to assess all of the factors relevant to exposure, such as telephone antenna geometry, the isolation of the antenna from the phone, the distance of the antenna from the head, and the power level of the phone—all of which may significantly influence exposure. Another concern is the potential for recall bias. Nevertheless, the studies are of good quality and the pooled results will provide a much larger data set than was previously available.

### Overall Evaluation

In a 2004 review of the epidemiology of health effects from RF exposure, the ICNIRP Standing Committee on Epidemiology concluded that the results of the epidemiologic studies reviewed “give no consistent or convincing evidence of a causal relation between RF exposure and any adverse health effect.” However, the Committee added, “these studies have too many deficiencies to rule out an association.” The UK’s National Radiological Protection Board (NRPB; now the Radiation Protection Division of the Health Protection Agency) agreed, stating in a 2004 review that “the overall evidence from the more methodologically sound studies, including those conducted recently of mobile phone users, does not indicate that RF exposures increase the risk of cancer. However, the evidence is not conclusive.” Both ICNIRP and the NRPB pointed out the need for continuing research, especially since little information is available on cumulative exposures from mobile phone use over many years.

IARC has now received data from all of the countries participating in the INTERPHONE Study and expects to complete an analysis of the pooled results before the end of 2006. The final INTERPHONE Study

results and a subsequent IARC review of the evidence for the carcinogenicity of RF EMF, possibly in mid-2008, may provide sufficient data to draw firmer conclusions.

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### Electric Power Research Institute

3420 Hillview Avenue, Palo Alto, California 94304 • PO Box 10412, Palo Alto, California 94303 USA  
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