Abstract. Quickly changing technologies and intensive uses of radiofrequency electromagnetic field (RF-EMF)-emitting phones pose a challenge to public health. Mobile phone users and uses and exposures to other wireless transmitting devices (WTDs) have increased in the past few years. We consider that CERENAT, a French national study, provides an important addition to the literature evaluating the use of mobile phones and risk of brain tumors. The CERENAT finding of increased risk of glioma is consistent with studies that evaluated use of mobile phones for a decade or longer and corroborate those that have shown a risk of meningioma from mobile phone use. In CERENAT, exposure to RF-EMF from digitally enhanced cordless telephones (DECTs), used by over half the population of France during the period of this study, was not evaluated. If exposures to DECT phones could have been taken into account, the risks of glioma from mobile phone use in CERENAT are likely to be higher than published. We conclude that radiofrequency fields should be classified as a Group 2A ‘probable’ human carcinogen under the criteria used by the International Agency for Research on Cancer (Lyon, France). Additional data should be gathered on exposures to mobile and cordless phones, other WTDs, mobile phone base stations and Wi-Fi routers to evaluate their impact on public health. We advise that the as low as reasonable achievable (ALARA) principle be adopted for uses of this technology, while a major cross-disciplinary effort is generated to train researchers in bioelectromagnetics and provide monitoring of potential health impacts of RF-EMF.
the Swedish study for >2,300 h of cumulative use (8). In three
studies, increased risks for meningioma were also found at
the highest cumulative hours of use (5,6,9).

At the highest years of use there were significant risks for
glioma (5,10), brain cancer (8) and acoustic neurana (11,12).
For studies with greater years of use, acoustic neurana tumor
volume increased compared to less years of use (7,12).

2. The CERENAT study

This French case-control study of cases ≥16 years of age diag-
nosed between June 2004 and May 2006 included 253 glioma
and 194 meningioma cases with two age- and gender-matched
controls per case selected between 2005 and 2008 (6).

Potential confounders considered were the level of
education, smoking, alcohol consumption, and occupational
exposures to pesticides, extremely low frequency electro-
magnetic fields (ELF-EMF), radiofrequency electromagnetic fields
(RF-EMF), and ionizing radiation. In spite of listing RF-EMF
as a potential confounder, separate analyses of exposures to
digitally enhanced cordless telephones (DECTs) were not
included, because questions about DECT use were not asked
in the questionnaire.

During the period when cases were selected, the prevalence
of French mobile phone use in 2004, 2005, and 2006 was 73,
78, and 84% respectively, while the use of cordless phones is
likely to have mirrored similar patterns of increasing use (13).

Risks of glioma were reported for ‘heavy mobile phone
use’ (≥896 cumulative hours of use) (Fig. 1). When ‘heavy
mobile phone use’ was examined by years since first use,
glioma risk increased from >1 year since first use, to >2 years,
and to >5 years, OR 2.89, [95% confidence interval (CI)
1.41-5.93], OR 3.03, (95% CI 1.47-6.26), and OR 5.30, (95% CI
2.12-13.23), respectively (6).

Risks were also reported by anatomical region. There was a
borderline significant risk for glioma in the temporal lobe, OR
3.94 (95% CI 0.81-19.08), which when combined with at least
5 years of use increased to a significantly elevated 5.3-fold risk;
for frontal lobe tumors there was a non-significant increased
risk, OR 1.87 (95% CI 0.62-5.64), and for other regions a signif-
icant increased risk, OR 3.61 (95% CI 1.00-12.96). Of the total
mobile phone radiation absorbed by the brain, the temporal
lobe absorbs 50-60% and the frontal lobe absorbs 14-18% (14).

The highest risk reported was among heavy mobile phone
users from environments known to have multiple sources of
WTDs at work and home in urban areas, OR 8.20 (95% CI
1.37-49.07).

Higher risks were found from reported ipsilateral use, OR
2.11 (95% CI 0.73-6.08) compared to contralateral use, OR
0.66 (95% CI 0.23-1.89).

The OR for analogue mobile phone use was 3.75 (95% CI
0.97-14.43), that for digital mobile phone use was 2.71 (95%
CI 1.03-7.10). This is consistent with mobile phone use constit-
tuting a risk factor for glioma, because analogue mobile phones
always radiated maximum power while the digital mobile
phone’s adaptive power control circuitry reduces the radiated
power consistent with an acceptable signal to noise ratio.

For several exposure categories there was an increased risk
with increased number of hours or calls per day of exposure:
‘average calling time per month (hours)’, p=0.02; ‘average
callings per month (hours)’, p=0.04; ‘cumulative duration of call
(hours)’, p=0.02.

Consistent with what is expected if there is a causal
association between risks of glioma from different estimated
exposure intensities, overall for ≥896 cumulative hours of use
(‘heavy mobile phone use’), there was a significant 2.9-fold
increased risk.

3. Underestimation of risk of glioma in CERENAT and
INTERPHONE

There are two principal reasons why the CERENAT find-
ings as well as those of INTERPHONE are likely to have
underestimated the risks of glioma from mobile phone use.
First, exposures to RF-EMF radiation from conventional
DECT can be substantial (15). Neither in INTERPHONE
nor in CERENAT were these exposures evaluated. However
Hardell et al (8,12) reported risks of brain tumors from these
devices similar to those from mobile phones. While in the
CERENAT study RF-EMF exposures from other sources
were listed as a potential confounder, questions were not asked
about DECT use. Thus, the reference category ‘no regular use’
included subjects who used a DECT. This misclassification of
exposure biases the findings towards the null.

Industry records reveal that the estimated prevalence of
DECT use in France (introduced into France in 1992) was well
above 50% between 2004 and 2006.

A second factor that could contribute to an underestima-
tion of risk is that the participation rate in CERENAT was
relatively low: 66% for cases and 45% for controls (6). The
13-country INTERPHONE study’s average participation rate
was 70% for glioma, 79% for meningioma, 56% for controls (5).
The authors of the INTERPHONE study acknowledged the
possible selection bias from low participation rates and calcu-
lated that these resulted in a 10% underestimation of risk and
the overall underestimation of glioma and meningioma risk
was per ‘the observed reductions below the null in the ORs in
ever regular mobile phone users for meningioma (21%, 95% CI
32-9) and glioma (19%, 95% CI 30-6)’ (5).

Hardell and Carlberg (16) suggested that the CERENAT
method for analyzing laterality of risk was incorrect. In reply
the CERENAT authors provided corrected calculations,
showing that ‘heavy’ users incurred greater ipsilateral risks
(≥896 cumulative hours of use) (17) (Table II). By using the
correction the OR for the highest cumulative hours of use for
glioma doubled.
For glioma, all ipsilateral ORs were greater than contralateral ORs. With two exceptions, this was also true for meningioma. Because ipsilateral use results in higher exposure than contralateral, this is consistent what is expected if mobile phone use is a risk for glioma and meningioma.

4. Meningioma elevated risk in CERENAT

'Heavy mobile phone' use was associated with increased risks of meningioma (but somewhat weaker than the risks for glioma): for >1 year, OR 2.57 (95% CI 1.02-6.44); for >2 years, OR 2.40 (95% CI 0.96-6.05), and for >5 years (5 cases), OR 1.44 (95% CI 0.43-4.80).

Risks were non-significantly elevated for temporal lobe (2 cases), OR 7.89 (95% CI 0.48-130.14) and for frontal lobe (5 cases), OR 4.82 (95% CI 0.78-29.63).

There was one significant and one borderline significant risk with increasing exposure: 'average calling time per month (hours)', p=0.04; and 'cumulative duration of calls (hours)', p=0.06 (6).
5. Evidence that electromagnetic radiation can act both as an initiator and a promoter of tumors

For an agent that initiates a tumor, a long time to detection is expected. Thus, brain tumors generally are believed to have a latency of a decade or more, ranging up to five decades in some studied populations. The average time (a statistical distribution) to diagnosis (latency) falls within an expected range of average times. In contrast, for an agent that acts at the later stages of carcinogenesis, an earlier diagnosis of already initiated tumors occurs (promotion).

With an average 2.9 years of mobile phone use Muscat et al (4) reported a borderline significant result for a rare brain cancer, OR 2.1 (95% CI 0.9-4.7). Auvinen et al (1) reported a significant increased risk of glioma with >2 years of mobile phone use, or 2.0, (95% CI 1.0-4.1), with a dose-response increase in OR of 1.2/year (95% CI 1.1-1.5).

The INTERPHONE Study Group (5) also found indications of promoting effects; the OR for glioma and meningioma with 1-4 years of use and for >1,640 cumulative hours of use was 3.77 (95% CI 1.25-11.4) and 4.80 (95% CI 1.49-15.4), respectively (Table I).

Hardell et al (18) also reported elevated risks with short-term use. For example, the OR for meningioma and acoustic neuroma with <1-5 years of digital mobile phone use for >64 h was 1.8 (95% CI 1.1-3.0) and 1.9 (95% CI 0.7-4.7), respectively. Hardell and Carlberg (15) wrote ‘...ipsilateral exposure indicated an early effect in glioma development, which is an increased risk with long latency. However, we also found an increased risk with short latency, indicating a late effect in tumor development...these results could be compatible with both tumor initiation and promotion’. This is illustrated in Fig. 2.

6. Discussion

In reviewing the epidemiological evidence on mobile phone use and brain tumors, The IARC Monograph Working Group (19) noted the limited data available from epidemiological studies at that time though noting that Hardell et al have conducted the most detailed and largest number of studies on the risks for glioma from wireless phone (mobile and/or cordless phone).

Morgan et al (20) suggested that the magnitude of the under-estimation of risk was 25% in the INTERPHONE study. This is consistent with the INTERPHONE Study Group (5) conclusion that their under-estimation was at least 19% based on ‘regular’ mobile phone use. Nevertheless, when minimal use was defined as the reference level, risks in the INTERPHONE study were significant: for 10+ years since first use compared to 1-1.9 years since first use, OR 2.18 (95% CI 1.43-3.31), for >1,640 cumulative hours of use compared to <5 h of use, OR 1.82 (95% CI 1.15-2.80).

The IARC Monograph Working Group concluded that radiofrequency fields were possible human carcinogens,

<table>
<thead>
<tr>
<th>Exposures</th>
<th>Glioma Ipsilateral(^a) OR (95% CI)</th>
<th>Glioma Contralateral(^b) OR (95% CI)</th>
<th>Meningioma Ipsilateral(^a) OR (95% CI)</th>
<th>Meningioma Contralateral(^b) OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not regular use</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>&lt;43</td>
<td>0.43 (0.21-0.88)</td>
<td>0.24 (0.10-0.57)</td>
<td>0.39 (0.16-0.96)</td>
<td>0.53 (0.23-1.19)</td>
</tr>
<tr>
<td>43-112</td>
<td>0.39 (0.18-0.84)</td>
<td>0.23 (0.08-0.63)</td>
<td>0.34 (0.13-0.85)</td>
<td>0.26 (0.10-0.68)</td>
</tr>
<tr>
<td>113-338</td>
<td>0.87 (0.43-1.75)</td>
<td>0.13 (0.04-0.44)</td>
<td>0.03 (0.01-0.25)</td>
<td>0.39 (0.17-0.92)</td>
</tr>
<tr>
<td>339-895</td>
<td>0.86 (0.39-1.93)</td>
<td>0.51 (0.21-1.28)</td>
<td>0.30 (0.08-1.15)</td>
<td>No data</td>
</tr>
<tr>
<td>≥896</td>
<td>2.11 (0.73-6.08)</td>
<td>0.66 (0.23-1.89)</td>
<td>2.29 (0.58-8.97)</td>
<td>1.18 (0.34-4.12)</td>
</tr>
<tr>
<td>Cumulative hours of use corrected</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not regular use</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>&lt;43</td>
<td>0.29 (0.11-0.80)</td>
<td>0.25 (0.07-0.95)</td>
<td>0.64 (0.15-2.73)</td>
<td>0.99 (0.34-2.90)</td>
</tr>
<tr>
<td>43-112</td>
<td>0.44 (0.16-1.23)</td>
<td>0.33 (0.10-1.08)</td>
<td>0.37 (0.10-1.39)</td>
<td>0.13 (0.02-1.07)</td>
</tr>
<tr>
<td>113-338</td>
<td>0.78 (0.27-2.24)</td>
<td>0.25 (0.06-1.02)</td>
<td>No data</td>
<td>0.65 (0.23-1.80)</td>
</tr>
<tr>
<td>339-895</td>
<td>1.69 (0.52-5.49)</td>
<td>0.23 (0.05-1.11)</td>
<td>0.14 (0.02-1.24)</td>
<td>No data</td>
</tr>
<tr>
<td>≥896</td>
<td>4.21 (0.70-25.52)</td>
<td>1.61 (0.36-7.14)</td>
<td>2.27 (0.42-12.39)</td>
<td>1.24 (0.21-7.48)</td>
</tr>
</tbody>
</table>

\(^a\)Side of use was considered as ipsilateral if the phone was used on the same side as the tumor or on both sides. \(^b\)Defined as contralateral if the phone was used on the opposite side of the tumor. No laterality was assigned for median tumor. CI, confidence interval.
Group 2B (19). Since then, a number of studies have been published of experimental results showing that radiofrequency fields affect cellular repair and increase biomarkers associated with cancer risk. In our view these results and several epidemiology studies (8,21) are consistent with what is expected if radiofrequency fields from mobile phone use are a cause of brain cancer: the higher the cumulative hours of use, the higher the risk; the longer the time since first use, the higher the risk; the higher the radiated power, the higher the risk; ipsilateral risk is higher than contralateral risk.

Thus, evidence published since the IARC review provides additional support, based on IARC criteria, for concluding that radiofrequency fields are probable human carcinogens; radiofrequency fields should now be classified Group 2A.

At the time of the IARC review it was known that when mobile phone use began as a teenager, the risks were higher than when use began as an adult (22,23). Since then, additional evidence has accrued of an increased risk to children. In the CEFALO study, using operator reported data, an OR of 2.15 (95% CI 1.06-4.29) was reported for children of median age 13 with >2.8 years since time from first subscription, combined with an increasing risk with increase in years since first use, P-trend=0.001 (24). In addition, the CEFALO authors reported an ipsilateral risk with >4 years of cumulative duration of subscriptions, OR 3.74 (95% CI 1.19-11.77) in combination of an increasing risk with increasing years of use, P-trend=0.02.

As the young adult brain is not fully myelinated, and wireless radiation has been shown to induce demyelination experimentally, it is plausible that wireless radiation could have a stronger impact on the developing brain than on older adults.

It has been suggested that if mobile phone use was causing brain cancer, with so many people using mobile phones there should be an increase in brain cancer, but there has been none (25,26). This is not correct.

Recently a significant annual percent change (APC) in age-adjusted rates of brain cancer between 1992 and 2006 was reported from the United States using data from three cancer registries: Los Angeles County (LAC), California Cancer Registry (CCR), and the SEER 12 cancer registry (27).

Table III shows this increase in brain cancer for the three anatomical regions that absorb the greatest proportion of the absorbed mobile phone radiation in the brain (81% at 900 MHz and 86% at 1,800 MHz) (14).

Table III. APC of GBM by brain increased glioma in three major cancer registries, 1992-2006 [adapted from Table III of Deltour et al (25)].

<table>
<thead>
<tr>
<th>Brain region</th>
<th>LAC</th>
<th>CCR</th>
<th>SEER 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal</td>
<td>+3.0</td>
<td>+2.4</td>
<td>+2.5</td>
</tr>
<tr>
<td>Temporal</td>
<td>+2.0</td>
<td>+1.9</td>
<td>+1.3</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>N/A</td>
<td>+11.9</td>
<td>+1.6</td>
</tr>
</tbody>
</table>

APC, annual percent change; GBM, glioblastoma multiforme; LAC, Los Angeles County; CCR, California Cancer Registry; N/A, not available; NS, not significant.
A retrospective cohort study of ~400,000 cell phone users in Denmark has been reported evaluating brain cancer risk in persons who began using cell phones in 1992-1994 compared to those who began to use cell phones later (30). The authors excluded business users from the exposed contingent they were unable to know if a phone registered to a business user was solely used by that person, including these same business users in the unexposed category. This misclassification of exposure impairs the ability of the study to detect an increase in risk, while it lacks statistical power, as it involves a small cohort for which exposure information has not been updated for 20 years.

7. Conclusions

The CERENAT study corroborates the significant risks of glioma associated with exposure to radiofrequency fields reported by the Swedish team and by the 13-country INTERPHONE study, and adds weight to the epidemiological evidence that radiofrequency fields, classified by the International Agency for Research on Cancer as a Group 2B (possible) carcinogen in 2011 should be reclassified as a Group 2A (probable) carcinogen.

In the CERENAT study, a significant increased risk of brain cancer was found from mobile phone use overall with an 8-fold increased risk for higher urban exposures. Three out of every four persons today live in mega-cities with populations of >10 million, many in the rapidly developing world where exposures to RF-EMF may be poorly controlled and access to medical treatment problematic. CERENAT also corroborates those few studies that have shown a risk of meningioma from mobile phone use.

The growth of mobile phone use worldwide has reached the level that in many nations there are more phones than adults. Exposures today can occur simultaneously from a number of WTDs such as mobile phones, mobile phone base stations (as known as masts or cell towers), and tablets, with the latter often being held quite close to the bodies of users (ignoring that the exposure limit is measured at 20 cm distance from tablets, laptop computer, and similar WTDs).

Until further evidence is available, it is prudent for policies about the use and development of WTDs rely on reducing exposures to the ALARA standard used in pediatric radiology. The ALARA approach would require hardware and software designers to create proximity sensors and embed flash notices regarding simple advisories about safer use within devices. In the meantime, we urge that serious national programs of training and research be established to train experts in evaluating this technology and establish appropriate monitoring and surveillance systems such as those in place for pharmaceuticals and other agents. This program could be funded by a fee of 2 cents/month to be paid equally from consumers, manufacturers, and providers into an independently operated research and training program.

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References