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On the association between glioma, wireless phones, heredity and ionising radiation

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Abstract

We performed two case–control studies on brain tumours diagnosed during 1 January 1997 to 30 June 2000 and 1 July 2000 to 31 December 2003, respectively. Living cases and controls aged 20–80 years were included. An additional study was performed on deceased cases with a malignant brain tumour using deceased controls. Pooled results for glioma yielded for ipsilateral use of mobile phone odds ratio (OR) = 2.9, 95% confidence interval (CI) = 1.8–4.7 in the >10 years latency group. The corresponding result for cordless phone was OR = 3.8, 95% CI = 1.8–8.1. OR increased statistically significant for cumulative use of wireless phones per 100 h and per year of latency. For high-grade glioma ipsilateral use of mobile phone gave OR = 3.9, 95% CI = 2.3–6.6 and cordless phone OR = 5.5, 95% CI = 2.3–13 in the >10 years latency group. Heredity for brain tumour gave OR = 3.4, 95% CI = 2.1–5.5 for glioma. There was no interaction with use of wireless phones. X-ray investigation of the head gave overall OR = 1.3, 95% CI = 1.1–1.7 for glioma without interaction with use of wireless phones or heredity. In conclusion use of mobile and cordless phone increased the risk for glioma with highest OR for ipsilateral use, latency >10 years and third tertile of cumulative use in hours. In total, the risk was highest in the age group <20 years for first use of a wireless phone.

Keywords: Brain tumours; Glioma; Mobile phone; Cordless phone; Risk factors; Interaction

1. Introduction

The use of mobile phones has increased rapidly especially during the last decade. Worldwide, an estimate of 5.9 billion mobile phone subscriptions has been reported at the end of 2011 by the International Telecommunication Union (ITU; http://www.itu.int/ITU-D/ict/facts/2011/material/ICTFactsFigures2011.pdf).

In Sweden analogue mobile phones (NMT; Nordic Mobile Telephone System) were introduced in the early 1980s and closed down in 2007. The digital phones (GSM; Global System for Mobile Communication) started in the early 1990s. Nowadays mobile phones are used more than landline phones in Sweden (http://www.pts.se/upload/Rapporter/Tele/2011/sv-telemarknad-halvar-2011-pts-er-2011–21.pdf). Another type of wireless phone is cordless desktop phones, e.g., Digital Enhanced Cordless Telecommunication (DECT), used instead of fixed landline phones.

During use of wireless phones radiofrequency electromagnetic fields (RF-EMF) are emitted. The brain is the major target organ for near-field exposure during handheld use. Thus, fear of an increased risk for brain tumours from RF fields emitted from mobile phones has dominated the debate during the last decade.

More than a decade ago we published results from our first case–control study on brain tumours diagnosed during 1994–1996 and use of mobile phones [1]. Overall we did not find an association, but there was some indication of increased risk in the most exposed part of the brain [2]. The results were based on rather low numbers of exposed subjects and different types of brain tumours. However, these findings stimulated us to continue this research area with a larger number of cases diagnosed during 1997–2003 including cases with both benign and malignant brain tumour.

Several reviews on this research area have been published since before [3–7]. Furthermore, International Agency for Research on Cancer (IARC) concluded on May 31, 2011 that

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exposure to RF-EMF emissions is a possible human carcinogen, Group 2B [8]. This decision was in large part based on the Hardell group studies and the IARC Interphone study [9,10], but also on occupational studies. The full text with a comprehensive review will be published as a Monograph [11].

The aim of this article is to give an overview of our results regarding glioma for the study period 1997–2003 with some further analyses of other risk factors. The studies were approved by the ethical committees.

2. Materials and methods

First, cases diagnosed during 1 January 1997 to 30 June 2000 were included. These results were published separately [12,13]. This was followed by the next study period, 1 July 2000 to 31 December 2003 [14]. The methods were the same including the same inclusion criteria and an identical questionnaire in both studies. However, the geographical area differed somewhat during these two study periods, see the publications for further details.

All cases were reported to a cancer registry and had histopathological verification of tumour diagnosis. Both men and women aged 20–80 years at the time of diagnosis were included and all were alive at the time of inclusion in the study. Matched controls were identified from the Swedish Population Registry. The study included use of wireless phones (mobile and cordless phones), as well as asking questions on e.g., occupational exposures. Use of wireless phones was carefully assessed by a self-administered questionnaire. The information was supplemented over the phone. The ear that had mostly been used during calls with mobile phone and/or cordless phone was assessed by separate questions; >50% of the time for one side, or equally for both sides. This information was checked during the supplementary phone calls. Moreover every person that had used a mobile phone received after that a letter asking them again to specify the ear that had been used during phone calls and to what extent that side of the head was mostly used. There was a very good agreement for the result using these three methods to assess these data.

Tumour localisation for the cases was defined by using medical records including computer tomography (CT) and/or magnetic resonance imaging (MRI). The matched control was assigned the same side as the tumour of the respective case. Use of the wireless phone was defined as ipsilateral (≥50% of the time), or contralateral (<50% of the time) in relation to tumour side. In the calculation of cumulative hours of use over the years we used information on time period (years of use) and average number of minutes per day during that period. Use in a car with external antenna was disregarded as well as use of a handsfree device. We adopted a minimum latency period of one year, i.e. exposure ≤1 year before diagnosis was disregarded (corresponding time for the matched control). Hence, we could define latency period and cumulative use for the different phone types.

The questionnaire contained also a number of other questions on e.g., occupations, exposure to different agents, smoking habits, medical history including hereditary risk factors, and exposure to ionising radiation. Also these questions were supplemented over the phone by the interviewer at the same time as regarding use of wireless phones. A structured protocol was used also for these questions.

In a review commissioned by the former Swedish Radiation Protection Agency (now called the Swedish Radiation Safety Authority) it was suggested that the exclusion of deceased cases was a source of bias in our studies [15]. The scientific reason for this suggestion was not given.

As a response to that critique we performed a study on the cases with a malignant brain tumour who had died before inclusion in the case–control studies 1997–2003. These cases represented patients with a poor prognosis, mostly with astrocytoma grade IV tumour. Controls were selected from the Death Registry in Sweden.

Two groups of controls were included, one group consisted of controls that had died from other types of malignant diseases than brain tumour and one group of controls that had died from other diseases than cancer. Relatives to both cases and controls were identified through the Swedish Population Registry at the Swedish Tax Agency. The study encompassed 464 cases and 464 controls that had died from a malignant disease and 463 controls with other causes of death. Exposure was assessed by a questionnaire sent to the next of kin to each deceased case and control. The questionnaire was similar as in previous studies.

This investigation confirmed the previous results of an association between mobile phones and malignant brain tumours [16]. It was concluded that the critique made by Boice and McLaughlin [15] was scientifically unfounded.

Use of wireless phones is widespread among children and adolescents [17,18]. This has given concern of an especially high risk for brain tumours in young users. Children's brain absorbs higher radiation from RF-EMF emissions than adults [19,20]. This is due to the smaller head, thinner skull bone and higher conductivity of the brain tissue. The developing brain is more sensitive to toxins [21] and it has been shown that the brain is developing until the age of about 20 years [22]. Previously, we found that the brain tumour risk was highest in the youngest age group at diagnosis, 20–29 years [23], which warrants further analyses.

In the following we give an overview of the results regarding use of wireless phones for the study period 1997–2003 [16,24,25], but also results on X-ray investigations, heredity and potential interaction with use of wireless phones. We give also results based on age at first use of a mobile or a cordless phone.

2.1. Statistical methods

All analyses were done using StataSE 10.1 (Stata/SE 10.1 for Windows; StataCorp., College Station TX). Odds ratios (OR) and 95% confidence interval (CI) were calculated using

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Table 1
Odds ratio (OR) and 95% confidence interval (CI) for glioma and use of wireless phones [16,24,26]. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	>1–5 year latency		>5–10 year latency		>10 year latency		Total, >1 year latency	
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI
Glioma ($n = 1148$)								
Wireless phone								
Study 1997–2000 (living)	159/441	1.0, 0.8–1.3	107/221	1.3, 0.98–1.7	33/51	1.6, 0.97–2.5	299/713	1.1, 0.9–1.4
Study 2000–2003 (living)	73/214	1.4, 0.9–2.1	92/163	2.0, 1.4–3.1	74/82	2.9, 1.9–4.7	239/459	1.9, 1.3–2.7
Study 1997–2003 (deceased)	39/42	1.0, 0.6–1.6	50/37	1.4, 0.8–2.3	43/16	2.7, 1.4–5.3	132/95	1.4, 0.95–2.0
Studies 1997–2003 (all)	271/697	1.0, 0.9–1.3	249/421	1.4, 1.2–1.8	150/149	2.1, 1.6–2.8	670/1267	1.3, 1.1–1.5
Mobile phone								
Study 1997–2000 (living)	148/358	1.1, 0.9–1.5	58/142	1.1, 0.8–1.5	31/44	1.7, 1.04–2.8	237/544	1.2, 0.9–1.5
Study 2000–2003 (living)	70/183	1.4, 0.9–2.2	68/118	1.9, 1.2–3.0	57/55	3.2, 1.9–5.3	195/356	1.9, 1.3–2.7
Study 1997–2003 (deceased)	32/30	1.1, 0.6–1.9	30/26	1.2, 0.6–2.2	35/7	5.2, 2.1–13	97/63	1.5, 0.97–2.3
Studies 1997–2003 (all)	250/571	1.1, 0.9–1.4	156/286	1.3, 0.99–1.6	123/106	2.5, 1.8–3.3	529/963	1.3, 1.1–1.6
Ipsilateral (living)	141/205	1.7, 1.3–2.2	81/124	1.6, 1.1–2.3	57/45	2.9, 1.8–4.7	279/374	1.8, 1.4–2.3
Contralateral (living)	63/192	0.8, 0.6–1.2	40/87	1.1, 0.7–1.6	29/29	2.4, 1.4–4.4	132/308	1.0, 0.8–1.3
Cordless phone								
Study 1997–2000 (living)	97/267	1.0, 0.7–1.3	64/119	1.5, 1.03–2.1	3/10	0.7, 0.2–2.6	164/396	1.1, 0.9–1.5
Study 2000–2003 (living)	80/170	1.9, 1.2–2.9	52/100	2.0, 1.2–3.2	29/35	2.9, 1.6–5.3	161/305	2.0, 1.4–3.0
Study 1997–2003 (deceased)	28/26	1.1, 0.6–2.1	36/25	1.5, 0.8–2.7	13/10	1.2, 0.5–2.9	77/61	1.3, 0.8–2.0
Studies 1997–2003 (all)	205/463	1.2, 0.9–1.5	152/244	1.5, 1.2–1.9	45/55	1.7, 1.1–2.6	402/762	1.3, 1.1–1.6
Ipsilateral (living)	106/188	1.4, 1.1–1.9	74/106	1.8, 1.3–2.6	20/15	3.8, 1.8–8.1	200/309	1.6, 1.2–2.1
Contralateral (living)	61/142	1.0, 0.7–1.5	37/73	1.3, 0.9–2.1	11/20	1.5, 0.7–3.3	109/235	1.2, 0.9–1.6

unconditional logistic regression analysis. The unexposed category consisted of subjects that reported no use of mobile or cordless phones, or latency period ≤ 1 year. Adjustment was made for vital status, sex, age (as a continuous variable), socio-economic index (SEI) and year of diagnosis. The same year as for the case was used for the corresponding control. Note, that laterality of the tumour was not available for all cases, e.g., midline tumours or tumours in both hemispheres. Laterality analysis was not made for the group of wireless phone use since it could differ for mobile phone and cordless phone for the same person. Only living cases and controls were included in these analyses since laterality use of wireless phones was not assessed in the study on deceased cases and controls [16]. Other results than use of wireless phones were based on questionnaire data for living cases and controls.

3. Results

The results on use of wireless phones were based on 1251 cases with malignant brain tumour (response rate 85%) and 2438 controls (response rate 84%). The corresponding response rates for only living subjects were 90% and 89%, respectively.

3.1. Glioma

Most cases had glioma ($n = 1148$) so we present in the following results for that type of tumour. Results for other malignant brain tumours can be found in another publication [26]. Latency was divided in three categories, >1–5 years, >5–10 years, and >10 years from first use of a wireless phone until diagnosis of glioma. Both use of mobile and cordless phone gave an increased risk overall, highest in the latency group >10 years, increasing further for ipsilateral use; mobile phone OR = 2.9, 95% CI = 1.8–4.7 and cordless phone OR = 3.8, 95% CI = 1.8–8.1. Highest ORs were found in the >10 year latency group for total wireless phone use as well (see Table 1).

OR increased statistically significant for cumulative use of wireless phones per 100 h and latency time (see Table 2). Cumulative use of wireless phones yielded highest risk in the third tertile (>426 h) with OR 1.5, 95% CI 1.2–1.9. Similar results were found for mobile phone and cordless phone use.

It is common that both mobile and cordless phones are used by the same person. In Table 3 results are shown for subjects with use of both phone types, mobile phone only, and cordless phone only. No statistically significant risk was found in the shortest latency period. For only use of mobile phone OR increased with latency yielding for >10 year latency OR = 2.6, 95% CI = 1.7–4.1. For only cordless phone use highest risk was obtained in the >5–10 year latency time; OR = 1.9, 95% CI = 1.3–2.9. However, the calculations in the longest latency period were based on few subjects regarding cordless phone.

3.2. Age-dependent risk

We used three age groups for first use of a wireless phone; <20 years, 20–49 years and 50–80 years. For glioma first use of a wireless phone <20 years of age gave OR = 2.3, 95% CI = 1.3–4.3 (Table 4). A similar pattern of increased risk in

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Table 2
Odds ratio (OR) and 95% confidence interval (CI) for glioma and cumulative lifetime use in hours (tertiles), per 100 h cumulative use and per year of latency of mobile and cordless phones [26]. Numbers of exposed cases (Ca) and controls (Co) are given in tertiles. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	First tertile (h)		Second tertile (h)		Third tertile (h)		Per 100 h cumulative use	Per year of latency
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	OR, CI	OR, CI
Glioma ($n = 1148$)								
Wireless phone	183/426	1.2, 0.9–1.4	202/425	1.2, 0.97–1.5	285/416	1.5, 1.2–1.9	1.014, 1.008–1.019	1.056, 1.037–1.075
Mobile phone	152/322	1.3, 1.05–1.7	156/333	1.2, 0.9–1.5	221/308	1.5, 1.2–1.9	1.023, 1.013–1.034	1.060, 1.039–1.082
Cordless phone	116/271	1.1, 0.9–1.5	111/241	1.2, 0.9–1.6	175/250	1.6, 1.3–2.1	1.012, 1.004–1.019	1.049, 1.023–1.075

Wireless phone: first tertile 1–91 h; second tertile 92–426 h; third tertile >426 h.
Mobile phone: first tertile 1–36 h; second tertile 37–183 h; third tertile >183 h.
Cordless phone: first tertile 1–122 h; second tertile 123–456 h; third tertile >456 h.

Table 3
Odds ratio (OR) and 95% confidence interval (CI) for glioma and use of different combinations of wireless phones [26]. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	>1–5 year latency		>5–10 year latency		>10 year latency		Total, >1 year latency	
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI
Glioma ($n = 1148$)								
Both mobile and cordless phone	52/153	0.9, 0.6–1.3	118/213	1.4, 1.05–1.8	91/92	2.2, 1.6–3.1	261/458	1.4, 1.1–1.7
Mobile phone only	142/328	1.2, 0.9–1.5	76/135	1.4, 0.98–1.9	50/42	2.6, 1.7–4.1	268/505	1.3, 1.1–1.6
Cordless phone only	77/216	1.0, 0.8–1.4	55/73	1.9, 1.3–2.9	9/15	1.2, 0.5–2.9	141/304	1.3, 0.99–1.6

the <20 years group was also found for mobile and cordless phone use.

3.3. Astrocytoma

Astrocytoma is the most common type of glioma. The severity of the disease is depending on grade; grades I–II are grouped as low-grade and grades III–IV as high-grade astrocytoma. Results for low-grade glioma are presented in Table 5. OR increased with latency, though the results for latency >10 years were based on low numbers. Overall ipsilateral use of mobile phone gave OR = 1.8, 95% CI = 1.02–3.1 and cordless phone OR = 1.7, 95% CI = 0.98–3.1.

Third tertile of cumulative use of wireless phones gave OR = 1.7 of borderline statistical significance (Table 6). Also the ORs per 100 h cumulative use and year of latency were of borderline statistical significance. In Table 7 results are presented for use of both mobile and cordless phones for the subject as well as mobile phone or cordless phone only. Increased ORs were found but based on low numbers.

The most common type of astrocytoma is the high-grade type. Clearly we found increased risk for use of both mobile and cordless phones increasing with latency period (Table 8). Also in the shortest latency group, >1–5 years, ipsilateral use of mobile phone yielded increased risk, OR = 1.8, 95% CI = 1.3–2.6 and cordless phone use OR = 1.6, 95% CI = 1.1–2.3. No increased risk was found for contralateral use in that latency group. Highest risk was found in the >10 years latency group for ipsilateral use; mobile phone OR = 3.9, 95% CI = 2.3–6.6 and cordless phone OR = 5.5, 95% CI = 2.3–13. Contralateral use in the latency groups >5–10 years and >10 years gave increased ORs, although with lower point estimates than for ipsilateral use.

ORs for use of both mobile and cordless phones increased with cumulative number of hours in tertiles with highest risk in the third tertile, OR = 1.8, 95% CI = 1.4–2.4 (Table 9). OR increased statistically significant per 100 h of cumulative use and year of latency for wireless phones and also mobile and cordless phones separately.

In Table 10 results are displayed for use of mobile or cordless phones only, and use of both phone types. Both phone

Table 4
Odds ratio (OR) and 95% confidence interval (CI) for glioma in different age groups for first use of the wireless phone [16,24,26]. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	Glioma ($n = 1148$)	
	Ca/Co	OR, CI
Wireless phone	670/1267	1.3, 1.1–1.5
<20 years old	25/27	2.3, 1.3–4.3
20–49 years old	377/746	1.3, 1.1–1.6
≥50 years old	268/494	1.3, 1.1–1.6
Mobile phone	529/963	1.3, 1.1–1.6
<20 years old	17/14	3.1, 1.4–6.7
20–49 years old	315/581	1.4, 1.1–1.7
≥50 years old	197/368	1.3, 1.01–1.6
Cordless phone	402/762	1.3, 1.1–1.6
<20 years old	16/16	2.6, 1.2–5.5
20–49 years old	206/437	1.2, 0.9–1.5
≥50 years old	180/309	1.4, 1.1–1.7

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Table 5
Odds ratio (OR) and 95% confidence interval (CI) for low-grade (I-II) astrocytoma and use of wireless phones [16,24,26]. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	>1–5 year latency		>5–10 year latency		>10 year latency		Total, >1 year latency	
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI
Astrocytoma, low-grade ($n = 132$)								
Wireless phone								
Study 1997–2000 (living)	27/441	1.2, 0.7–2.0	19/221	1.8, 0.96–3.4	5/51	1.9, 0.7–5.3	51/713	1.4, 0.8–2.3
Study 2000–2003 (living)	18/214	1.6, 0.6–4.3	13/163	1.4, 0.5–4.0	6/82	1.6, 0.5–5.4	37/459	1.5, 0.6–3.8
Study 1997–2003 (deceased)	0/42	–	3/37	3.0, 0.5–17	1/16	1.9, 0.1–24	4/95	1.5, 0.3–7.6
Studies 1997–2003 (all)	45/697	1.2, 0.8–2.0	35/421	1.6, 0.99–2.7	12/149	1.7, 0.8–3.4	92/1267	1.4, 0.9–2.1
Mobile phone								
Study 1997–2000 (living)	28/358	1.4, 0.8–2.5	8/142	1.2, 0.5–2.9	4/44	1.9, 0.6–5.9	40/544	1.4, 0.8–2.4
Study 2000–2003 (living)	14/183	1.4, 0.5–4.2	8/118	1.1, 0.3–3.9	3/55	1.4, 0.3–6.4	25/356	1.3, 0.5–3.7
Study 1997–2003 (deceased)	0/30	–	2/26	2.1, 0.3–15	1/7	3.1, 0.2–46	3/63	1.2, 0.2–6.7
Studies 1997–2003 (all)	42/571	1.4, 0.8–2.2	18/286	1.3, 0.7–2.4	8/106	1.7, 0.7–4.0	68/963	1.4, 0.9–2.2
Ipsilateral (living)	24/205	2.0, 1.1–3.6	12/124	1.6, 0.7–3.7	3/45	1.1, 0.3–4.1	39/374	1.8, 1.02–3.1
Contralateral (living)	11/192	1.0, 0.5–2.2	3/87	0.5, 0.1–1.8	4/29	2.1, 0.6–7.6	18/308	1.0, 0.5–1.9
Cordless phone								
Study 1997–2000 (living)	15/267	1.1, 0.5–2.1	12/119	2.0, 0.98–4.3	2/10	2.0, 0.3–11	29/396	1.4, 0.8–2.5
Study 2000–2003 (living)	16/170	1.5, 0.5–4.2	8/100	1.3, 0.4–4.1	3/35	1.3, 0.3–5.9	27/305	1.4, 0.5–3.7
Study 1997–2003 (deceased)	1/26	1.4, 0.1–15	1/25	1.0, 0.1–13	0/10	–	2/61	1.0, 0.1–6.9
Studies 1997–2003 (all)	32/463	1.2, 0.7–2.1	21/244	1.6, 0.9–2.8	5/55	1.4, 0.5–3.9	58/762	1.3, 0.8–2.1
Ipsilateral (living)	15/188	1.4, 0.7–2.8	15/106	2.4, 1.2–5.1	4/15	3.2, 0.7–13	34/309	1.7, 0.98–3.1
Contralateral (living)	14/142	1.2, 0.6–2.6	4/73	1.1, 0.3–3.3	0/20	–	18/235	1.1, 0.5–2.1

Table 6
Odds ratio (OR) and 95% confidence interval (CI) for low-grade (I-II) astrocytoma and cumulative lifetime use in hours (tertiles), per 100 h cumulative use and per year of latency of mobile and cordless phones [26]. Numbers of exposed cases (Ca) and controls (Co) are given in tertiles. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	First tertile (h)		Second tertile (h)		Third tertile (h)		Per 100 h cumulative use	Per year of latency
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	OR, CI	OR, CI
Astrocytoma, low-grade ($n = 132$)								
Wireless phone	26/426	1.4, 0.8–2.4	26/425	1.2, 0.7–2.0	40/416	1.7, 0.998–2.7	1.008, 0.997–1.019	1.040, 0.994–1.089
Mobile phone	23/322	1.6, 0.9–2.8	21/333	1.2, 0.7–2.2	24/308	1.3, 0.7–2.3	1.021, 1.001–1.042	1.035, 0.981–1.093
Cordless phone	15/271	1.1, 0.6–2.1	18/241	1.3, 0.7–2.4	25/250	1.7, 0.9–2.9	1.005, 0.989–1.022	1.038, 0.977–1.102

Wireless phone: first tertile 1–91 h; second tertile 92–426 h; third tertile >426 h.
Mobile phone: first tertile 1–36 h; second tertile 37–183 h; third tertile >183 h.
Cordless phone: first tertile 1–122 h; second tertile 123–456 h; third tertile >456 h.

types were risk factors for astrocytoma grades III–IV. Mobile phone only gave highest risk in the >10 year latency group with OR = 2.8, 95% CI = 1.7–4.6. Use of only cordless phone gave in the latency group >5–10 years OR = 2.4, 95% CI 1.6–3.7, whereas the numbers in the >10 year latency group were too low for meaningful interpretation.

3.4. Ionising radiation

X-ray investigations of the head and neck region yielded OR = 1.0, 95% CI = 0.8–1.2 ($n = 290$ cases, 792 controls), data not in table. No increased ORs were found for X-rays of the neck or sinus. Dental X-rays overall or cumulative

Table 7
Odds ratio (OR) and 95% confidence interval (CI) for low-grade (I-II) astrocytoma and use of different combinations of wireless phones [26]. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	>1–5 year latency		>5–10 year latency		>10 year latency		Total, >1 year latency	
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI
Astrocytoma, low-grade ($n = 132$)								
Both mobile and cordless phone	10/153	1.0, 0.4–2.1	17/213	1.5, 0.8–2.8	7/92	1.4, 0.6–3.5	34/458	1.3, 0.7–2.2
Mobile phone only	21/328	1.4, 0.8–2.4	9/135	1.5, 0.7–3.3	4/42	2.2, 0.7–6.8	34/505	1.4, 0.9–2.4
Cordless phone only	14/216	1.3, 0.7–2.6	9/73	2.4, 1.05–5.3	1/15	1.7, 0.2–16	24/304	1.6, 0.9–2.8

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Table 8
Odds ratio (OR) and 95% confidence interval (CI) for high-grade (III-IV) astrocytoma and use of wireless phones [16,24,26]. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	>1–5 year latency		>5–10 year latency		>10 year latency		Total, >1 year latency	
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI
Astrocytoma, high-grade ($n = 820$)								
Wireless phone								
Study 1997–2000 (living)	91/441	1.0, 0.7–1.4	67/221	1.4, 0.98–2.0	22/51	1.6, 0.9–2.8	180/713	1.2, 0.9–1.5
Study 2000–2003 (living)	37/214	1.2, 0.7–2.0	64/163	2.4, 1.5–3.9	60/82	3.8, 2.3–6.4	161/459	2.1, 1.4–3.2
Study 1997–2003 (deceased)	35/42	1.0, 0.6–1.7	46/37	1.5, 0.9–2.5	39/16	2.8, 1.4–5.6	120/95	1.4, 0.97–2.1
Studies 1997–2003 (all)	163/697	1.0, 0.8–1.3	177/421	1.6, 1.3–2.0	121/149	2.5, 1.8–3.4	461/1267	1.4, 1.1–1.7
Mobile phone								
Study 1997–2000 (living)	85/358	1.1, 0.8–1.6	38/142	1.2, 0.8–1.8	21/44	1.7, 0.98–3.1	144/544	1.2, 0.9–1.6
Study 2000–2003 (living)	38/183	1.3, 0.8–2.2	49/118	2.3, 1.4–3.9	50/55	4.3, 2.5–7.6	137/356	2.2, 1.4–3.3
Study 1997–2003 (deceased)	32/30	1.2, 0.7–2.2	27/26	1.2, 0.6–2.3	31/7	5.2, 2.1–13	90/63	1.6, 0.996–2.5
Studies 1997–2003 (all)	155/571	1.2, 0.9–1.5	114/286	1.5, 1.1–1.9	102/106	3.0, 2.1–4.2	371/963	1.5, 1.2–1.8
Ipsilateral (living)	85/205	1.8, 1.3–2.6	58/124	2.1, 1.4–3.1	47/45	3.9, 2.3–6.6	190/374	2.1, 1.6–2.7
Contralateral (living)	33/192	0.8, 0.5–1.2	25/87	1.3, 0.7–2.2	22/29	3.1, 1.6–5.9	80/308	1.1, 0.8–1.5
Cordless phone								
Study 1997–2000 (living)	56/267	1.0, 0.7–1.4	42/119	1.7, 1.1–2.6	1/10	0.4, 0.1–3.6	99/396	1.2, 0.9–1.6
Study 2000–2003 (living)	47/170	2.0, 1.2–3.4	37/100	2.4, 1.4–4.2	22/35	3.7, 1.8–7.2	106/305	2.4, 1.5–3.7
Study 1997–2003 (deceased)	22/26	1.0, 0.5–2.0	35/25	1.7, 0.9–3.0	13/10	1.4, 0.6–3.4	70/61	1.4, 0.9–2.1
Studies 1997–2003 (all)	125/463	1.2, 0.9–1.5	114/244	1.7, 1.3–2.3	36/55	2.0, 1.2–3.2	275/762	1.4, 1.2–1.8
Ipsilateral (living)	68/188	1.6, 1.1–2.3	50/106	2.2, 1.5–3.4	15/15	5.5, 2.3–13	133/309	1.8, 1.4–2.5
Contralateral (living)	30/142	1.0, 0.6–1.6	25/73	1.7, 1.02–2.9	8/20	1.9, 0.8–4.7	63/235	1.3, 0.9–1.8

Table 9
Odds ratio (OR) and 95% confidence interval (CI) for high-grade (III-IV) astrocytoma and cumulative lifetime use in hours (tertiles), per 100 h cumulative use and per year of latency of mobile and cordless phones [26]. Numbers of exposed cases (Ca) and controls (Co) are given in tertiles. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	First tertile (h)		Second tertile (h)		Third tertile (h)		Per 100 h cumulative use	Per year of latency
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	OR, CI	OR, CI
Astrocytoma, high-grade ($n = 820$)								
Wireless phone	113/426	1.1, 0.8–1.4	147/425	1.4, 1.1–1.8	201/416	1.7, 1.3–2.2	1.016, 1.010–1.022	1.072, 1.050–1.094
Mobile phone	93/322	1.3, 0.95–1.7	111/333	1.3, 1.01–1.7	167/308	1.8, 1.4–2.4	1.029, 1.017–1.041	1.076, 1.052–1.100
Cordless phone	79/271	1.2, 0.9–1.7	69/241	1.2, 0.9–1.7	127/250	1.8, 1.4–2.4	1.014, 1.006–1.023	1.067, 1.038–1.098

Wireless phone: first tertile 1–91 h; second tertile 92–426 h; third tertile >426 h.
Mobile phone: first tertile 1–36 h; second tertile 37–183 h; third tertile >183 h.
Cordless phone: first tertile 1–122 h; second tertile 123–456 h; third tertile >456 h.

life time numbers were not risk factors for glioma. In total, increased risk was found for X-ray of the head, OR = 1.3, 95% CI = 1.1–1.7 ($n = 149$ cases, 289 controls). Using a latency period of >1 year yielded in the group with more than one time X-rays of the head OR = 2.0, 95% CI = 1.3–3.0. The risk was highest in the >1–5 year latency and more than one time X-rays of the head, OR = 2.8, 95% CI = 1.3–6.1. For 9 cases and 8 controls no information was obtained for year of first X-ray of the head. There was no interaction with use of mobile or cordless phones (data not in table).

3.5. Heredity

First degree relative with cancer, excluding brain tumour, was not a risk factor for malignant brain tumours (see Table 11). Brain tumour in a first degree relative was reported

Table 10
Odds ratio (OR) and 95% confidence interval (CI) for high-grade (III-IV) astrocytoma and use of different combinations of wireless phones [26]. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for vital status, age, gender, SEI-code and year of diagnosis.

	>1–5 year latency		>5–10 year latency		>10 year latency		Total, >1 year latency	
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI
Astrocytoma, high-grade ($n = 820$)								
Both mobile and cordless phone	29/153	0.9, 0.6–1.4	78/213	1.5, 1.1–2.1	78/92	3.0, 2.0–4.4	185/458	1.6, 1.3–2.1
Mobile phone only	94/328	1.2, 0.9–1.6	55/135	1.5, 1.04–2.2	37/42	2.8, 1.7–4.6	186/505	1.4, 1.1–1.8
Cordless phone only	40/216	0.8, 0.6–1.2	44/73	2.4, 1.6–3.7	6/15	0.9, 0.3–2.6	90/304	1.2, 0.9–1.6

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Table 11
Odds ratio and 95% confidence interval (CI) for first degree relative with reported cancer (brain tumours excluded) or brain tumour. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for age, gender, SEI-code and year of diagnosis.

	Heredity, all cancer excluding brain tumour			Heredity, brain tumour		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI
All malignant	279/704	1.1	0.9–1.3	39/31	3.2	2.0–5.3
Glioma	263/704	1.1	0.9–1.3	38/31	3.4	2.1–5.5
Astrocytoma	220/704	1.1	0.9–1.4	33/31	3.6	2.2–6.0
Grades I–II	31/704	1.1	0.7–1.7	5/31	4.3	1.6–12
Grades III–IV	189/704	1.1	0.9–1.4	28/31	3.5	2.1–6.0
Other glioma[a]	43/704	0.9	0.6–1.3	5/31	2.3	0.9–6.0
Other malignant	16/704	0.8	0.4–1.4	1/31	1.0	0.1–8.0

[a] Oligodendroglioma and other/mixed glioma.

by 39 cases with malignant brain tumour and 31 controls. This yielded OR = 3.2, 95% CI 2.0–5.3. The results were similar for glioma and subtypes of astrocytoma. There was no statistically significant interaction between heredity and use of wireless phones (see Table 12).

4. Discussion

In the present analyses we included all cases, both living and deceased, with a malignant brain tumour in our previous studies giving higher statistical power for subgroup analysis. All controls for the study period 1997–2003 were included, both for cases with malignant and benign brain tumour as we have discussed in another publication [26]. Thus, in the unconditional logistic regression analysis we adjusted for vital status, age, gender, SEI-code and year of diagnosis (the same year for the matched control as for the corresponding case).

The main result of this study was an increased risk for glioma associated with use of both mobile and cordless phones, and they were independent risk factors. The risk increased with latency and cumulative use and OR was highest for ipsilateral use. It is noteworthy that increased OR was found for ipsilateral use also in the shortest latency group, >1–5 years. Similar results for glioma were found in the separate report of the French part of Interphone study [27] but also in Interphone in total [9]. Thus analyses restricted to ever regular users yielded for glioma in the 2–4 years group of time since start of use OR = 1.68, 95% CI = 1.16–2.41 increasing in the 10+ years group to OR = 2.18, 95% CI = 1.43–3.31 (see Appendix 2 in that publication [9]).

Also for low-grade astrocytoma highest OR was found in the >10 years latency group and for ipsilateral exposure in our study. Several calculations were based on low numbers and there was no consistent pattern of statistically significant increased ORs.

Regarding high-grade astrocytoma the calculations were based on larger numbers ($n = 820$) than for low-grade ($n = 132$). Clearly an increased risk was found for use of both mobile and cordless phones. The results are biologically relevant. Thus, OR increased with latency time, cumulative use and was highest for ipsilateral use. In the >10 years latency group ipsilateral use of mobile phone yielded OR = 3.9, 95% CI = 2.3–6.6, and cordless phone OR = 5.5, 95% CI = 2.3–13. Also contralateral use gave increased OR, although lower than for ipsilateral use. Obviously this group of cases had lower exposure in the tumour area than those with ipsilateral use. It should be noted that contralateral use was defined as less than 50% use on the same side of the brain as the tumour was located. Thus, some of these persons might in fact have had some use on the same side of the brain as the tumour developed, although less than 50% of the time.

Exposure to ionising radiation is an established risk factor for brain tumours (for overview see [28]). In a recent cohort study childhood CT scans were reported to increase the subsequent risk of both leukaemia and brain tumours [29]. In our first study on brain tumours we found that X-ray investigations of the head and neck region increased the risk yielding OR = 1.64, 95% CI = 1.04–2.58 [2]. In the present study

Table 12
Odds ratio (OR) and 95% confidence interval (CI) for glioma and use of wireless phones in relation to heredity (first degree relative) for brain tumours. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for age, gender, SEI-code and year of diagnosis.

	Analogue		Digital		Mobile phone		DECT		Wireless phone	
	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI	Ca/Co	OR, CI
No heredity, unexp phone	282/978	(1.0), –	282/978	(1.0), –	282/978	(1.0), –	282/978	(1.0), –	282/978	(1.0), –
Heredity, unexp phone	14/12	4.5, 2.0–9.9	14/12	4.5, 2.0–9.9	14/12	4.5, 2.0–10	14/12	4.5, 2.1–10	14/12	4.5, 2.0–10
No heredity, exp phone	151/293	1.4, 1.1–1.8	356/761	1.4, 1.1–1.7	412/883	1.3, 1.1–1.6	312/692	1.4, 1.1–1.7	514/1153	1.3, 1.1–1.6
Heredity, exp phone	11/4	7.9, 2.5–25	17/15	3.2, 1.6–6.7	20/17	3.3, 1.7–6.5	13/9	4.1, 1.7–9.8	24/19	3.6, 1.9–6.8
	p, interaction = 0.76		p, interaction = 0.25		p, interaction = 0.26		p, interaction = 0.50		p, interaction = 0.34	

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X-ray investigations of the head increased the risk for glioma. The highest risk was found in the group with a short latency and more than one X-ray investigation. No validation of exposure by using medical records was done. It can therefore not be excluded that some of the X-ray investigations of the head were related to diagnostic procedures. Nevertheless, using >1 year latency X-ray investigation of the head more than one time gave an increased risk overall. The statistical analyses showed that use of wireless phones and X-ray investigations of the head were independent risk factors for glioma.

First degree relative with a brain tumour was more frequent among the glioma cases than the controls. This is in agreement with reported familial aggregation of glioma. Thus in a large study there were 77% more glioma among family members than expected [30]. We found no association with other types of malignant tumours. Heredity and use of mobile and cordless phones were independent risk factors for glioma.

The higher risk for both mobile and cordless phone use at young age seen in our study may reflect potentially higher susceptibility to RF-EMF among children and adolescents [21] and higher exposure [20] than for adults. However, data on children are scarce besides our findings. The multicentre case–control study CEFALO, conducted in Denmark, Sweden, Norway, and Switzerland included children and adolescents aged 7–19 years diagnosed with a brain tumour between 2004 and 2008 [31]. It has been commented in detail by Söderqvist et al. [32] since serious methodological problems exist as exemplified below.

For example the data collection and analyses of use of cordless phones were not valid. Use of cordless phones was assessed only 'in the first 3 years' of use, a most peculiar definition for which the authors gave no explanation for or reference to. Furthermore, the study never considered wireless phone use, including both mobile and cordless phones, as the exposure category. IARC categorised wireless phone use as a relevant exposure group [8]. Instead, Aydin et al. [31] in the CEFALO study included use of cordless phones in the 'unexposed' category, so risk estimates for mobile phone use might therefore be underestimated. Similarly mobile phone use was included among the 'unexposed' when considering use of cordless phones and thereby potentially concealing an increased risk.

The CEFALO study yielded a statistically non-significant increased risk for brain tumours among regular users of mobile phones, OR = 1.36 (95% CI = 0.92–2.02). This OR increased somewhat with cumulative duration of subscriptions and duration of calls [31]. Further support of a true association was found in the results based on operator-recorded use for 62 cases and 101 controls, which for time since first subscription >2.8 years yielded a statistically significant OR of 2.15 (95% CI = 1.07–4.29) with a statistically significant trend ($p = 0.001$). In spite of the limitations in study design and analyses the data indicate a moderately increased risk that together with our results warrant precaution of exposure among children and adolescents.

The Interphone study on brain tumours was initiated by recommendations from several expert groups to study possible health effects of exposure to RF-fields [33,34]. It was performed at 16 research centres in 13 countries during varying time periods between 2000 and 2004 conducted under the guidance of IARC.

Subgroup analyses showed statistically significant increased risk for glioma in the highest exposure group, i.e. those who had used their mobile phone for ≥1640 h, yielding OR = 1.40, 95% CI = 1.03–1.89 [9]. The risk increased further for ipsilateral exposure to OR = 1.96, 95% CI = 1.22–3.16 and for tumours in the most exposed part of the brain, the temporal lobe, OR = 1.87, 95% CI = 1.09–3.22 in the highest exposure group for glioma. Analyses restricted to ever regular users clearly showed increasing risk for glioma based on time since start of regular use (years), cumulative call time (hours) and cumulative number of calls (see Appendix 2 in that publication [9]). In fact there is good agreement between our results and the Interphone findings if the same inclusion and exclusion criteria for cases and controls are used [35].

Estimated RF dose from mobile phone use in the tumour area was also associated with an increased risk for glioma in a publication from parts of the Interphone group [10]. The risk increased with increasing total cumulative dose of specific energy (J/kg) absorbed at the estimated tumour centre for more than 7 years before diagnosis with an OR of 1.91, 95% CI = 1.05–3.47 in the highest quintile of exposure. For the first time amount of radiation absorbed (rather than just its proxy which is years of exposure and cumulative hours of use) was linked to tumour induction, which is an important result.

The Nordic part of Interphone published a study relating brain tumour location to mobile phone radiation [36]. The results seemed to contradict the findings by Cardis et al. [10], but used a different, less clear method. Only 42 cases had used the mobile phone for 10 years or more and no analysis was made of the highest exposed group with longest duration of use. Thus, this study is much less informative and less sophisticated that the one by Cardis et al. [10].

In Denmark a cohort of mobile phone subscribers was designed and started in co-operation between The International Epidemiology Institute (IEI), Rockville, MD, USA, and the Danish Cancer Society. The cohort was established for the time period 1982–1995 by grants from two Danish telecom operation companies (TeleDenmark Mobil and Sonafon), by IEI, and by the Danish Cancer Society. A total of 723,421 subscribers were identified but the initial cohort consisted of only 58% of these subscribers. A thorough review of the study including the latest publication [37] has been made by us [38].

The IARC working group's main reason for not using the Danish study as evidence for its evaluation was that it "could have resulted in considerable misclassification in exposure assessment" [8]. The authors have themselves pointed out the main causes of such considerable exposure misclassification [37] such as mobile phone subscription holders not using the

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phone were classified as "exposed"; non-subscribers using the mobile phone were classified as "unexposed"; corporate subscribers of mobile phones (200,507 people), which are likely to have been heavy users, were classified as "unexposed"; persons with a mobile phone subscription later than 1995 were classified as "unexposed"; and use of cordless phones, which we have linked to excess risks of brain tumours, was not assessed, i.e. those who had used a cordless phone only were also classified as "unexposed".

Other limitations are the absence of analysis by laterality and of actual exposure data. These and other shortcomings in this cohort study have been discussed elsewhere in more detail [38]. It is clear from these limitations that the authors conclusion that "In this update of a large nationwide cohort study of mobile phone use, there were no increased risks of tumours of the central nervous system, providing little evidence for a causal association." is not soundly based [37].

There are by now several meta-analyses and reviews on this topic. We made a thorough review of the methods in our studies compared with the Interphone studies [39]. We concluded that several of the Interphone findings display differential misclassification of exposure due to observational and recall bias. There were low participation rates for both cases and controls, for example in some countries only 51% of the cases and 42% of the controls participated. This is to be compared with 90% response rate for cases with malignant brain tumours and 89% for controls in the Hardell-group studies on living subjects [24]. Furthermore, due to bed-side interviews in the Interphone studies it was known to the interviewer if it was a case or a control that was interviewed. Use of cordless phones was not properly assessed in the Interphone study, or at least not reported.

Myung et al. compared methods and results in studies on the use of mobile phones and the risk for brain tumours [6]. Our studies were judged to be of better quality compared with Interphone. However, one important issue was not covered in that review, namely as noted above that we also assessed use of cordless phones in contrast to the Interphone study group. RF-EMF emissions from a cordless phone are in the same magnitude as from a digital mobile phone, something that has been pointed out several times [14,40]. Moreover cordless phones are used for longer calls than mobile phones. Including such use in the 'unexposed' group as in the Interphone study would bias the OR towards unity.

We regard bedside interviews of cases, as in the Interphone study, to be a major disadvantage and ethically questionable. At that time the patient has not fully recovered from e.g., surgery, may not have been fully informed about the diagnosis, treatment and prognosis and may even be under sedation by drugs. In fact patients scored significantly lower than controls due to recalling of words (aphasia), problems with writing and drawing due to paralysis in the Danish part of Interphone [41]. Obviously observational bias could have been introduced thereby during the bedside interviews. On the contrary our cases received a postal questionnaire approximately 2 months after diagnosis and could give the answers in a relaxed manner, a situation similar to the controls. In principle all cases and controls were after that interviewed over the phone to verify and clarify different exposures. This was blinded as to case or control status.

We investigated the possibility of recall and observational bias in our second case–control study [12]. Use of wireless phone was similar among cases and controls regardless if they reported a previous cancer or if a relative helped to fill in the questionnaire. Potential observational bias during phone interviews was analysed by comparing change of exposure in cases and controls after these interviews. No statistically significant differences were found, showing that our results could not be explained by observational bias, for further details see discussion in that publication [12]. All interviews were performed by educated persons using structured instructions and protocol.

5. Conclusions

Certainly results from the Hardell-group as well from the Interphone group show an increased risk for glioma associated with long term mobile phone use. Also use of cordless phones increases the risk when properly assessed and analysed. The risk is highest for ipsilateral exposure to the brain of RF-EMF emissions. Adolescents seem to be at higher risk than adults. IARC concluded that RF-EMF emissions overall, e.g., occupational and from wireless phones, are 'possibly carcinogenic to humans', Group 2B [8].

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References

[1] L. Hardell, Å. Näsman, A. Påhlson, A. Hallquist, K. Hansson Mild, Use of cellular telephones and the risk for brain tumours: a case–control study, International Journal of Oncology 15 (1999) 113–116.
[2] L. Hardell, K. Hansson Mild, A. Påhlson, A. Hallquist, Ionizing radiation, cellular telephones and the risk for brain tumours, European Journal of Cancer Prevention 10 (2001) 523–529.
[3] L. Hardell, K. Hansson Mild, M. Carlberg, F. Söderqvist, Tumour risk associated with use of cellular telephones or cordless desktop telephones, World Journal of Surgical Oncology 4 (2006) 74.
[4] L. Hardell, M. Carlberg, K. Hansson Mild, Epidemiological evidence for an association between use of wireless phones and tumor diseases, Pathophysiology 16 (2009) 113–122.
[5] M. Kundi, The controversy about a possible relationship between mobile phone use and cancer, Environmental Health Perspectives 117 (2009) 316–324.
[6] S.K. Myung, W. Ju, D.D. McDonnell, Y.J. Lee, G. Kazinets, C.T. Cheng, et al., Mobile phone use and risk of tumors: a meta-analysis, Journal of Clinical Oncology 27 (2009) 5565–5572.

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[7] A.G. Levis, N. Minicuci, P. Ricci, V. Gennaro, S. Garbisa, Mobile phones and head tumours. The discrepancies in cause-effect relationships in the epidemiological studies – how do they arise? Environmental Health 10 (2011) 59.
[8] R. Baan, Y. Grosse, B. Lauby-Secretan, F. El Ghissassi, V. Bouvard, L. Benbrahim-Tallaa, et al., Carcinogenicity of radiofrequency electromagnetic fields, Lancet Oncology 12 (2011) 624–626.
[9] INTERPHONE Study Group, Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case–control study, International Journal of Epidemiology 39 (2010) 675–694.
[10] E. Cardis, B.K. Armstrong, J.D. Bowman, G.G. Giles, M. Hours, D. Krewski, et al., Risk of brain tumours in relation to estimated RF dose from mobile phones: results from five Interphone countries, Occupational and Environmental Medicine 68 (2011) 631–640.
[11] IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 102. Non-Ionizing radiation, Part II: Radiofrequency Electromagnetic Fields [includes mobile telephones], in press.
[12] L. Hardell, A. Hallquist, K. Hansson Mild, M. Carlberg, A. Påhlson, A. Lilja, Cellular and cordless telephones and the risk for brain tumours, European Journal of Cancer Prevention 11 (2002) 377–386.
[13] L. Hardell, K. Hansson Mild, M. Carlberg, Further aspects on cellular and cordless telephones and brain tumours, International Journal of Oncology 22 (2003) 399–407.
[14] L. Hardell, M. Carlberg, K. Hansson Mild, Case–control study of the association between the use of cellular and cordless telephones and malignant brain tumors diagnosed during 2000–2003, Environmental Research 100 (2006) 232–241.
[15] J.D. Boice, J.K. McLaughlin, Epidemiologic Studies of Cellular Telephones and Cancer Risk – A Review, SSI Publication, 2002, p. 16. Accessed at: http://www.stralsakerhetsmyndigheten.se/Publikationer/Rapport/Stralskydd/2002/200216/.
[16] L. Hardell, M. Carlberg, K. Hansson Mild, Mobile phone use and the risk for malignant brain tumors: a case–control study on deceased cases and controls, Neuroepidemiology 35 (2010) 109–114.
[17] F. Söderqvist, L. Hardell, M. Carlberg, K. Hansson Mild, Ownership and use of wireless telephones: a population-based study of Swedish children aged 7–14 years, BMC Public Health 7 (2007) 105.
[18] F. Söderqvist, M. Carlberg, L. Hardell, Use of wireless telephones and self-reported health symptoms: a population-based study among Swedish adolescents aged 15–19 years, Environmental Health 7 (2008) 18.
[19] E. Cardis, I. Deltour, S. Mann, M. Moissonnier, M. Taki, N. Varsier, et al., Distribution of RF energy emitted by mobile phones in anatomical structures of the brain, Physics in Medicine & Biology 53 (2008) 2771–2783.
[20] A. Christ, M.C. Gosselin, M. Christopoulou, S. Kühn, N. Kuster, Age-dependent tissue-specific exposure of cell phone users, Physics in Medicine & Biology 55 (2010) 1767–1783.
[21] L. Kheifets, M. Repacholi, R. Saunders, E. van Deventer, The sensitivity of children to electromagnetic fields, Pediatrics 116 (2005) e303–e313.
[22] N.U. Dosenbach, B. Nardos, A.L. Cohen, D.A. Fair, J.D. Power, J.A. Church, et al., Prediction of individual brain maturity using fMRI, Science 329 (2010) 1358–1361.
[23] L. Hardell, K. Hansson Mild, M. Carlberg, A. Hallquist, Cellular and cordless telephone use and the association with brain tumors in different age groups, Archives of Environmental Health 59 (2004) 132–137.
[24] L. Hardell, M. Carlberg, K. Hansson Mild, Pooled analysis of two case–control studies on use of cellular and cordless telephones and the risk for malignant brain tumours diagnosed in 1997–2003, International Archives of Occupational and Environmental Health 79 (2006) 630–639.
[25] L. Hardell, M. Carlberg, Mobile phones, cordless phones and the risk for brain tumours, International Journal of Oncology 35 (2009) 5–17.
[26] L. Hardell, M. Carlberg, K. Hansson Mild, Pooled analysis of case–control studies on malignant brain tumours and the use of mobile and cordless phones including living and deceased subjects, International Journal of Oncology 38 (2011) 1465–1474.
[27] M. Hours, M. Bernard, L. Montestrucq, M. Arslan, A. Bergeret, I. Deltour, et al., Téléphone mobile, risque de tumeurs cérébrales et du nerf vestibuloacoustique: l'étude cas-témoins INTERPHONE en France, Revue de'Epidemiologie et de Santé Publique 55 (2007) 321–332.
[28] S. Preston-Martin, R. Munir, I. Chakrabarti, Nervous system, in: D. Schottenfeld, J.F. Fraumeni Jr. (Eds.), Cancer Epidemiology and Prevention, Oxford University Press, 2006, pp. 1173–1195.
[29] M.S. Pearce, J.A. Salotti, M.P. Little, K. McHugh, C. Lee, K.P. Kim, et al., Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study, Lancet 380 (2012) 499–505.
[30] M.E. Scheurer, C.J. Etzel, M. Liu, J. Barnholtz-Sloan, F. Wilund, B. Tavelin, et al., Familial aggregation of glioma: a pooled analysis, American Journal of Epidemiology 172 (2010) 1099–1107.
[31] D. Aydin, M. Feychting, J. Schüz, T. Tynes, T.V. Andersen, L.S. Schmidt, et al., Mobile phone use and brain tumors in children and adolescents: a multicenter case–control study, Journal of the National Cancer Institute 103 (2011) 1264–1276.
[32] F. Söderqvist, M. Carlberg, K. Hansson Mild, L. Hardell, Childhood brain tumour risk and its association with wireless phones: a commentary, Environmental Health 10 (2011) 106.
[33] A. McKinlay, Possible health effects related to the use of radiotelephones: recommendations of a European Commission Expert Group, Radiology Protection Bulletin 187 (1997) 9–16.
[34] E. Cardis, L. Richardson, I. Deltour, B. Armstrong, M. Feychting, C. Johansen, et al., The INTERPHONE study: design, epidemiological methods, and description of the study population, European Journal of Epidemiology 22 (2007) 647–664.
[35] L. Hardell, M. Carlberg, K. Hansson Mild, Re-analysis of risk for glioma in relation to mobile telephone use: comparison with the results of the Interphone international case–control study, International Journal of Epidemiology 40 (2011) 1126–1128.
[36] S. Larjavaara, J. Schüz, A. Swerdlow, M. Feychting, C. Johansen, S. Lagorio, et al., Location of gliomas in relation to mobile telephone use: a case–case and case–specular analysis, American Journal of Epidemiology 174 (2011) 2–11.
[37] P. Frei, A.H. Poulsen, C. Johansen, J.H. Olsen, M. Steding-Jessen, J. Schüz, Use of mobile phones and risk of brain tumours: update of Danish cohort study, BMJ 343 (2011) d6387.
[38] F. Söderqvist, M. Carlberg, L. Hardell, Review of four publications on the Danish cohort study on mobile phone subscribers and risk of brain tumours, Reviews on Environmental Health 27 (2012) 51–58.
[39] L. Hardell, M. Carlberg, K. Hansson Mild, Methodological aspects of epidemiological studies on the use of mobile phones and their association with brain tumors, Open Environmental Sciences 2 (2008) 54–61.
[40] M. Redmayne, I. Inyang, C. Dimitriadis, G. Benke, M.J. Abramson, Cordless telephone use: implications for mobile phone research, Journal of Environmental Monitoring 12 (2010) 809–812.
[41] H.C. Christensen, J. Schüz, M. Kosteljanetz, H.S. Poulsen, J.D. Boice Jr., J.K. McLaughlin, et al., Cellular telephones and risk for brain tumors: a population-based, incident case–control study, Neurology 64 (2005) 1189–1195.

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