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Original Contribution

Location of Gliomas in Relation to Mobile Telephone Use: A Case-Case and Case-Specular Analysis

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The energy absorbed from the radio-frequency fields of mobile telephones depends strongly on distance from the source. The authors' objective in this study was to evaluate whether gliomas occur preferentially in the areas of the brain having the highest radio-frequency exposure. The authors used 2 approaches: In a case-case analysis, tumor locations were compared with varying exposure levels; in a case-specular analysis, a hypothetical reference location was assigned for each glioma, and the distances from the actual and specular locations to the handset were compared. The study included 888 gliomas from 7 European countries (2000–2004), with tumor midpoints defined on a 3-dimensional grid based on radiologic images. The case-case analyses were carried out using unconditional logistic regression, whereas in the case-specular analysis, conditional logistic regression was used. In the case-case analyses, tumors were located closest to the source of exposure among never-regular and contralateral users, but not statistically significantly. In the case-specular analysis, the mean distances between exposure source and location were similar for cases and speculars. These results do not suggest that gliomas in mobile phone users are preferentially located in the parts of the brain with the highest radio-frequency fields from mobile phones.

brain neoplasms; cellular phone; glioma; telephone

Use of mobile telephones has become common worldwide since the beginning of the 1990s (1). Mobile phones emit radio-frequency electromagnetic fields; these fields have not been shown to be tumorigenic (2), but research is still ongoing to investigate whether low-level radio-frequency fields have adverse health effects.

Several studies have been conducted on the association between mobile phone use and brain tumors, with unclear results. There is no clear evidence for increased risk of gliomas related to mobile phones, but the exposure and latency times analyzed have been limited (3–5). Recent reviews have concluded that, to date, there is no consistent support for a causal effect of mobile phone use on glioma risk even with use of 10 or more years' duration (2, 6).

Two previous studies have evaluated the location of glioma in relation to mobile phone use (7, 8), but with very small sample sizes (approximately 100 cases). Because the radio-frequency field emitted by mobile phones penetrates the brain in a highly localized fashion, occurrence of tumors in the part of the brain closest to the handset would be expected if there were an etiologic effect. The absorbed radio-frequency energy transmitted to the tissue from a mobile phone depends primarily on the distance from the source, decreasing to one-tenth in 5 cm (9).

The current analysis was based on data from 7 European study centers within the Interphone Study, an international collaborative case-control study with the main objective of assessing whether mobile phones increase the risk of brain tumors (10). Our aim in this analysis was to investigate whether gliomas among mobile phone users are located closer to the presumed position of the mobile phone handset (the source of the radio-frequency field) than gliomas among nonusers.

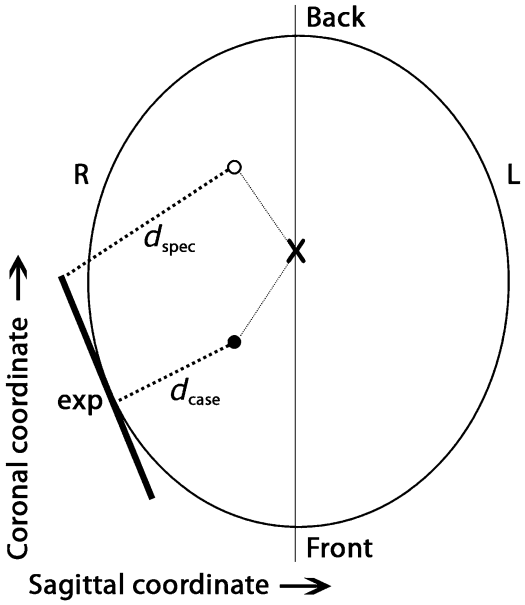

Figure 1. Schematic representation of assignment of the coronal coordinates for a specular analysis of mobile phone use and glioma risk. In the axial projection (*x*-axis, sagittal coordinate; *y*-axis, coronal coordinate), the midpoint for a case is indicated with a solid circle and the corresponding specular location is indicated with an open circle. The distance from the source of exposure (exp) is denoted by *d* separately for the case (d_{case}) and for the specular location (d_{spec}). Axial coordinates were obtained in a similar fashion using a coronal projection. R, right; L, left.

MATERIALS AND METHODS

Materials

Eligible cases were all patients with glioma diagnosed in one of the 7 Interphone countries (or areas within the country) (Denmark, Finland, Germany, Italy, Norway, Sweden, and Southeast England) between September 2000 and January 2004 (study periods varied between countries), with tumor midpoint(s) defined in 3 dimensions by neuroradiologists on the basis of computerized tomography or magnetic resonance imaging. A specific location (midpoint(s)) was assigned to 912 cases, that is, 63% of all glioma cases diagnosed during the study period that fulfilled the study inclusion criteria. The inclusion criteria were age at diagnosis 18–69 years (with some variation between countries), no prior diagnosis of brain tumor, and histologic confirmation ($n = 910$) or diagnostic imaging allowing unambiguous classification of the tumor type ($n = 2$). The case selection is described in further detail elsewhere (10).

All gliomas were assigned 1 or more midpoints by neuroradiologists, blind to the data on mobile phone use, in each center. The coordinates for the midpoint were recorded using a software program (GridMaster; Vompras GmbH, Düsseldorf, Germany) designed for the Interphone Study. In GridMaster, 3 projections (axial, sagittal, and coronal) form a 3-dimensional grid (1 cm × 1 cm × 1 cm). Cases with no clear single midpoint (i.e., irregularly shaped tumors; $n = 116$) were assigned several midpoints (thus also several sets of coordinates). Multifocal cases (with nonadjacent midpoints) were excluded from the study ($n = 24$). For each case with multiple midpoints, the mean of the tumor midpoints was defined (for calculating the distance to the exposure source).

All case patients were interviewed (83% personally, 17% via proxies) about their mobile phone use. Phone use during the 18 months prior to glioma diagnosis was excluded from the analyses, as was use of hands-free devices. Use of cordless (DECT (Digital Enhanced Cordless Telecommunications)) phones was not included. Regular use was defined as at least 1 call per week for a period of 6 months or more.

The study protocols were approved by local ethical review boards in each center.

Statistical methods

We used 2 types of analyses to evaluate the anatomic distribution of gliomas within the brain in relation to mobile phone use. A case-case analysis was based on comparing exposed and unexposed cases using dichotomous exposure indicators. A case-specular analysis contrasted the actual location of the case with a hypothetical (specular) location assigned for each case as a mirror image on the opposite side of the same hemisphere in terms of axial and coronal axes (Figure 1).

The main exposure indicator in the analyses was the shortest estimated distance from the midpoint of the glioma to the putative source of exposure, that is, the typical location of the phone. A line from the external orifice of the ear canal to the corner of the mouth was assigned to represent the position of the phone. The entire phone was regarded as the source of exposure, since most GSM (Global System for Mobile Communications) phones have an integrated antenna, with the whole body of the phone emitting a radio-frequency field.

The exposure line (approximately 6.7 cm) was divided into 100 segments of similar length. The distance from the midpoint of the glioma was calculated separately to each of the 101 points, and the shortest was used as the main exposure indicator.

To avoid potential recall bias, distance was calculated to the nearest source of exposure on the same side of the head as the glioma was located, irrespective of the patient's reported typical side of phone use.

In the case-specular analysis, 3-dimensional coordinates were defined for the specular cases, representing a hypothetical control location symmetrically reflecting the location of the actual case across the midpoint of the axial and coronal planes. In accordance with the rationale of the case-specular study design, the specular location represented the exposure that would have been incurred if the tumor had been located in another location (11). This counterfactual "control" was contrasted in the analysis with the actual case.

We constructed the specular locations (from which the distance was calculated similarly to the actual cases) using a geometric "mirror reflection" through a center point. This center point was defined as the point that resulted in a similar

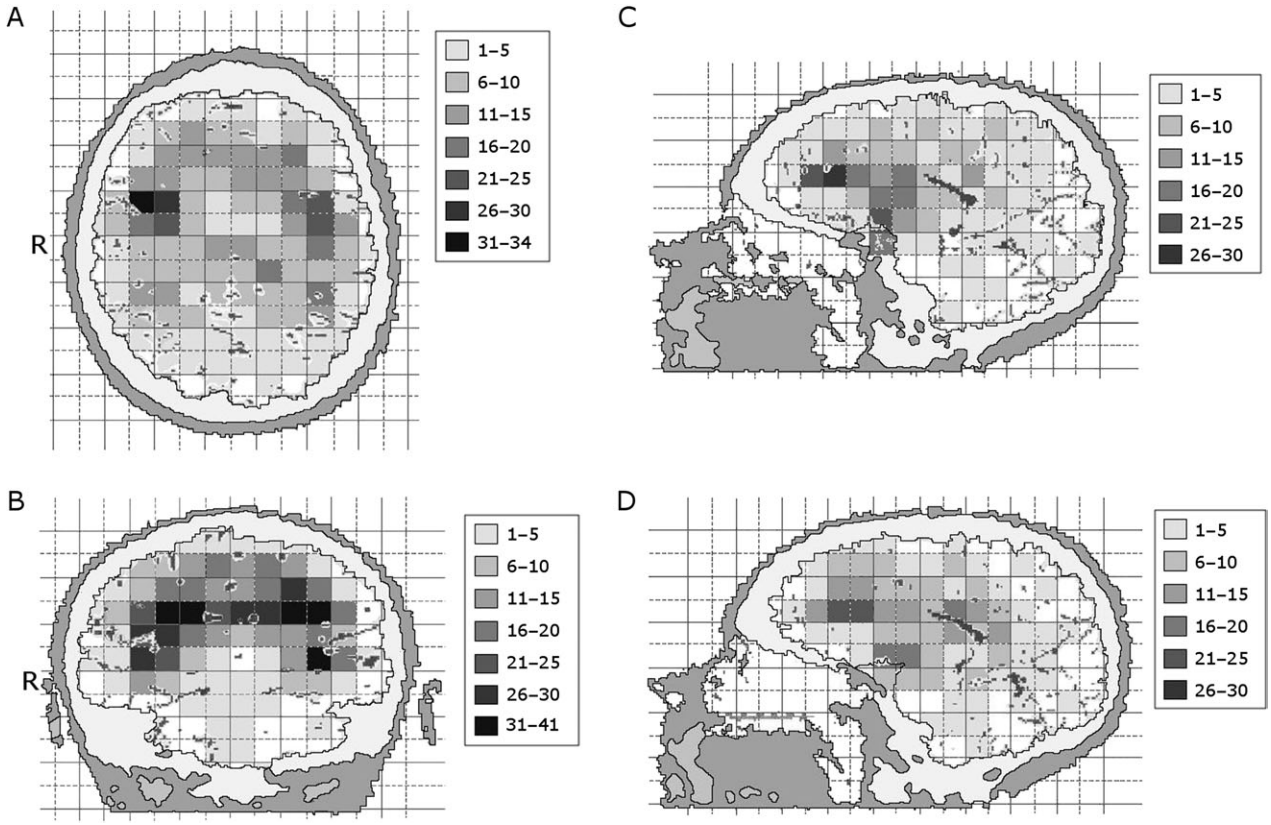

Figure 2. Anatomic distribution of gliomas in different projections of the brain. The shades of gray represent the number of gliomas in each 1-cm × 1-cm square, with smoothing based on adjacent squares. A) Axial projection (frontal part at top); B) coronal projection (facing the front); C) sagittal projection (right hemisphere); D) sagittal projection (left hemisphere). R, right.

distance from the exposure line for unexposed cases (i.e., never-regular users) and their specular controls. The anatomic center point of the brain could not be used, because gliomas are not symmetrically distributed within the brain and therefore using the zero point of the anatomic coordinate axes would have led to an asymmetrical distribution of the specular locations (and hence bias). Thus, the center point used was based on the mean coordinates of cases among never-regular users (the unexposed group). The procedure for the axial coordinate is illustrated in Figure 1. The same procedure was used for coronal projection. For the sagittal projection, an identical coordinate on the sagittal axis was used (i.e., the specular location had a distance to the falx cerebri identical to that of the actual case).

The specific locations of gliomas are presented in 4 projections to demonstrate the heterogeneous distribution of gliomas (which restricted the use of the anatomic midpoint of the brain as the origo). These figures are shown using an axial projection of the brain, a coronal projection, and right and left sagittal projections (Figure 2).

In the analyses of differences in distances of glioma from the exposure line, the statistical significances were evaluated using the Mann-Whitney test. When analyzing differences of glioma distribution by lobe and by increasing level of intensity or duration of mobile phone use, chi-squared tests were used.

In the case-case analysis, unconditional logistic regression was used, with distance between the midpoint of the glioma and the presumed source of exposure as a binary outcome ($\leq$5 cm, $>$5 cm). The cutpoint was chosen because the energy from radio-frequency fields is predominantly absorbed by the tissue within 5 cm of the phone (9). Exposure indicators analyzed included regular use, cumulative call time, laterality (preferred side of use), and duration of use (years). Never-regular use of a mobile phone was considered the unexposed reference category in all analyses. Phone users were divided into tertiles by cumulative call time (0.001–46, 47–339, or $>$339 hours, with a median of 133 hours and a maximum of 20,000 hours). Similarly, duration of use was categorized into 3 groups, with cutpoints chosen to correspond to those in previous studies (1.5–4, 5–9, or $\geq$10 years of use). All analyses were adjusted for country, sex, age group, and socioeconomic status.

Case-specular analyses were conducted using conditional logistic regression. The odds ratios were calculated with distance as the exposure variable and case/specular status as the outcome. The explanatory variables included regular phone use, cumulative call time, and duration of use in years.

Table 1. Location of Gliomas in the Hemispheres of the Brain in Relation to the Self-Reported Side of Mobile Telephone Use Among Glioma Patients From 7 European Countries, 2000–2004*[a]

Side of Glioma	Laterality of Phone Use		
	Right	Left	Total
Right	160	47	207
Left	123	86	209
Total	283	133	416

* P for heterogeneity < 0.001.
[a] Statistical significance for heterogeneity was evaluated on the basis of Fisher's exact test.

The statistical software Stata 8.2 (Stata Corporation, College Station, Texas) was used in all analyses.

RESULTS

A total of 912 cases fulfilled the inclusion criteria, with 1 or more midpoints of glioma recorded. Of these, 24 cases (3%) were excluded because they had several nonadjacent midpoints. Of the remaining 888 cases, 116 (13%) had 2 or more midpoints (range, 2–21; mean = 3.6; median, 2).

Altogether, 518 (58%) gliomas were in men and 370 (42%) in women. Information on mobile phone use was obtained from 873 cases (98%), with 57% ($n = 495$) being regular mobile phone users and 43% ($n = 378$) reporting no regular use. The median cumulative call time among regular users was 133 hours, while the mean call time was 917 hours.

Preferred laterality of use was known for 490 cases (99% of all regular users). Of these, 59% used the phone primarily on the right side, 28% on the left side, and 13% on both sides. The reported side of use and the brain hemisphere where the glioma was located are presented in Table 1.

Regular mobile phone use was most common in the youngest subjects, among men, and among subjects with the highest level of education (Table 2). There were no differences in phone use (regular vs. never-regular) between cases with only 1 glioma midpoint and those with several midpoints (14% of never-regular users had several midpoints vs. 12% of regular users; $P = 0.65$).

Tumors were located in the right hemisphere in 46% of cases, in the left hemisphere in 46% of cases, and in a central location in 7% of cases. Glioma cases included in the present study were most frequently located in the frontal lobe (40% of 733 gliomas with a cerebral lobe assigned), followed by the temporal lobe (30%). There were no major differences in the distribution of gliomas by cerebral lobe between regular phone users and never-regular users (Table 3). The distributions by lobe were also comparable between regular users and never-regular users when gliomas were subdivided into glioblastomas and other gliomas.

The mean distance between exposure source and tumor location did not vary substantially by the indicators of mobile phone use, being somewhat shorter among cases who had never used a mobile phone regularly or who reported a preferred side of use as contralateral to the tumor (in comparison with regular or ipsilateral users) (Table 4). The mean distance was slightly longer for cases with the highest cumulative call time and for those who had used a mobile phone for 10 years or more, but the differences were not significant. In addition, the mean distances were relatively similar between countries (range, 6.08–6.51 cm; $P = 0.29$).

In the case-case analysis, nonsignificantly decreased odds ratios for gliomas located within 5 cm of the presumed phone location were found among regular users as compared with never-regular users (Table 5). All of the odds ratios for the higher categories of intensity or duration of mobile phone use were below unity in these analyses, indicating no excess risk in the highly exposed parts among regular users versus never-regular users, although all of the upper confidence limits were above 1.

In the case-specular analysis, the average distances from the source of exposure were comparable for actual and specular glioma cases (6.25 cm vs. 6.24 cm ($P = 0.49$), with median values of 6.34 cm (standard deviation, 1.60; range, 2.42–10.7) and 6.26 cm (standard deviation, 1.38; range, 2.98–11.0), respectively). The distribution of the distances of the actual glioma cases showed more kurtosis ($P < 0.001$, with a peak at 6–7 cm) than that for the specular gliomas. The specular cases, on the other hand, showed some evidence of skewness ($P = 0.002$; 2 cases exceeded the expected range, i.e., $\mu + 3 \times б$) that was not observed among the actual cases.

In the case-specular analyses with distance as a categorical variable, a slightly larger proportion of glioma cases than speculars were within 5 cm of the presumed typical phone location (Table 6). However, the confidence intervals covered unity. In addition, no significantly increased odds ratio was found among regular users or those with the highest exposure; on the contrary, the highest odds ratios were observed among never-regular users and among regular users with the lowest call time. A 2-fold increased odds ratio was found in subjects who had used a mobile phone for 10 years or more, but the confidence interval included unity. With distance as a categorical variable, all odds ratios were above unity, also for the unexposed. In the analyses of distance as a linear variable, no increased odds ratios were observed.

Separate analyses of digital and analog phones did not show substantially different results from the main analyses, nor did analyses by histologic subgroup of gliomas (glioblastomas and other gliomas separately). In addition, the analyses were relatively similar even after the exclusion of cases with multiple (adjacent) midpoints or cases with only proxy respondents.

DISCUSSION

Our results do not support the hypothesis of gliomas among mobile phone users being preferentially located in the parts of the brain with the highest radio-frequency exposure. In the case-case analyses, gliomas among contralateral and never-regular users, representing lower radio-frequency exposures, had a shorter mean distance between the tumor midpoint and the presumed source of exposure

Table 2. Demographic Characteristics of Regular Users and Never-Regular Users of Mobile Telephones Among Glioma Patients From 7 European Countries, 2000–2004[a]

	Regular Users (n = 495)		Never-Regular Users (n = 378)		Total	P for Heterogeneity
	No.	Row %	No.	Row %		
Sex						
Male	329	65	180	35	509	
Female	166	46	198	54	364	<0.001
Age, years						
18–39	149	71	60	29	209	
40–49	145	64	82	36	227	
50–59	171	50	173	50	344	
60–69	30	32	63	68	93	<0.001
Education[b]						
Compulsory	77	46	91	54	168	
Secondary	161	56	129	44	290	
Upper secondary	135	61	86	39	221	
University	120	63	71	37	191	0.01
Country						
Denmark	53	37	89	63	142	
Finland	78	79	21	21	99	
Germany	52	40	77	60	129	
Italy	76	72	30	28	106	
Norway	100	62	62	38	162	
Sweden	97	56	77	44	174	
United Kingdom	39	64	22	36	61	<0.001

[a] Information on usage was missing for 15 cases (n = 873).
[b] Information on education was missing for 3 cases.

than ipsilateral and regular users. In the case-specular analysis, both exposed and unexposed glioma cases had tumors nonsignificantly located within 5 cm from the phone more frequently than the hypothetical locations assigned for speculars, but no such pattern was found in analyses by amount of phone use. In both models, glioma cases were closer to the exposure line in long-term users, but the differences remained nonsignificant.

We applied a novel approach for studying focal effects of radio-frequency fields emitted by mobile phones in the etiology of gliomas. Instead of concentrating on crude indicators of phone use, as in most previous studies, the method utilizing tumor location enabled us to focus on risk in relation to the postulated distribution of the radio-frequency field within the brain. This offered a biologically and physically more meaningful and more specific measure of radio-frequency exposure than phone usage pattern.

To our knowledge, the case-specular method has not been previously used in brain tumor studies, but it was developed for studies on residential (extremely low frequency) electromagnetic fields from power lines and childhood cancer (12, 13). In those analyses, the residential location was the exposure indicator, for which specular indices were obtained. In our case, hypothetical tumor locations were generated following the same principles. The analysis resembles a case-case study, but with the advantage of avoiding potential confounding.

The radio-frequency field decreases sharply in the brain tissue, with 90% of the energy to the head being absorbed

Table 3. Distribution of Gliomas in the Cerebral Lobes Among Regular Users and Never-Regular Users of Mobile Telephones From 7 European Countries, 2000–2004

	Total[a]		Regular Users		Never-Regular Users	
	No.	%[b]	No.	%[b]	No.	%[b]
Lobe*						
Frontal	293	40	175	43	115	37
Temporal	220	30	113	28	104	33
Parietal	169	23	91	22	75	24
Occipital	51	7	31	8	19	6
Total	733	100	410	100	313	100

* P for heterogeneity = 0.23.
[a] The numbers of regular and never-regular users do not add to the total, since information on mobile phone use was missing for some cases.
[b] Percentages are shown as the distribution in the cerebral lobes.

Table 4. Distance Between Glioma and Source of Mobile Telephone Exposure, in Relation to Exposure Variables, Among Glioma Patients From 7 European Countries, 2000–2004

	Mean Distance[a], cm	Distance From Exposure[a]				*P* for Heterogeneity
		≤5 cm		>5 cm		
		No.	%	No.	%	
Glioma cases	6.25	200	23	688	77	
Regularity of mobile phone use[b]						0.39
Regular use	6.29	107	22	388	78	
Never-regular use	6.19	91	24	287	76	
Cumulative call time, hours[c]						0.41
0.001–46	6.29	33	21	125	79	
47–339	6.27	38	25	114	75	
>339	6.36	30	19	129	81	
Duration of use, years[d]						0.82
1.5–4	6.31	65	21	239	79	
5–9	6.28	30	21	112	79	
≥10	6.38	10	24	32	76	
Laterality[e]						0.80
Ipsilateral	6.37	51	21	195	79	
Contralateral[f]	6.29	37	22	133	78	
Speculars	6.24	166	19	722	81	0.71
Ipsilateral speculars	6.26	47	19	199	81	
Contralateral specular[f]	6.36	30	18	140	82	

[a] Distance between the midpoint of the glioma and the presumed source of exposure.
[b] Information was missing on 15 cases.
[c] Cumulative call time <0.001 hour, never-regular use, or missing information for 419 cases.
[d] Regular use <1.5 years, never-regular use, or missing information for 400 cases.
[e] Use on both sides, glioma located centrally, or missing information on both sides for 472 cases.
[f] Distance was calculated to the closest (ipsilateral) exposure line despite the knowledge of contralaterality.

in the tissue within 5 cm of the handset. Nearly all (97%–99%) of the energy from a mobile phone is absorbed by the hemisphere on the side of the phone, with the highest exposure being to the temporal lobe (50%–60%) (9).

In our study, no excess of gliomas was found in the temporal lobe among regular users compared with never-regular users (28% vs. 33% of the locations in the cerebral lobes). Overall, the distribution of anatomic locations in our study was similar to previously reported findings (14–17), with a somewhat lower relative frequency of gliomas in the frontal lobe in our data (35% of all brain locations vs. 40%–53% previously reported) and a higher frequency in the occipital lobe (6% vs. 2%–3%).

Side of use was ignored in the case-specular analyses, and glioma cases overall, among both regular mobile phone users and never-regular users, were slightly closer to the exposure source than the hypothetical locations assigned for specular, but the differences were not significant and disappeared when exposure was analyzed in more detail. The only suggestion of an increased risk was related to long-term use in this analysis, but with a wide confidence interval. The odds ratios for different exposure indicators showed hardly any departure from unity when distance was considered as a continuous variable, and in analyses among users, the point estimates for the higher exposure groups never exceeded those for less mobile phone usage.

Our localization approach was based on the 3-dimensional midpoint(s) of the glioma, as defined by neuroradiologists, for its unequivocal nature compared with the theoretically relevant point of origin, which is no longer identifiable at the time of diagnosis. The midpoint is a crude but robust measure. It has limitations, particularly for large, irregularly shaped tumors close to the margin of the brain tissue. The size of gliomas was reported as being smaller among regular mobile phone users in 1 study (18), but that study had a relatively small number of glioma cases. However, in another study, vestibular schwannomas were reported to be larger among regular users than among never-regular users, though no association with amount of use was reported (19). If a similar (unknown) mechanism also influenced gliomas, they might be larger among mobile phone users. Larger gliomas may not grow symmetrically around their point of origin but towards the center of the brain, for example, resulting in the midpoint being further from the cortex and thus the exposure. Therefore, larger tumor sizes among mobile phone users could potentially cause a bias towards the null. In our study, gliomas with several midpoints were slightly further away from

Table 5. Odds Ratio for a Distance of ≤5 cm Between the Glioma Midpoint and the Typical Source of Mobile Telephone Exposure in All Regular Mobile Phone Users Compared With Never-Regular Users (Case-Case-Analysis) Among Glioma Patients From 7 European Countries, 2000–2004

Exposure Characteristic	Crude OR	95% CI	Adjusted OR[a]	95% CI
Frequency of use (regular use)	0.87	0.63, 1.20	0.80	0.56, 1.15
Cumulative call time, hours				
0.001–46	0.82	0.52, 1.29	0.82	0.51, 1.31
47–339	1.04	0.67, 1.60	0.97	0.60, 1.56
>339	0.72	0.46, 1.15	0.58	0.35, 0.96
Laterality of use				
Ipsilateral	0.82	0.56, 1.21	0.80	0.52, 1.22
Contralateral	0.87	0.56, 1.34	0.77	0.47, 1.24
Duration of use, years				
1.5–4	0.86	0.60, 1.23	0.85	0.57, 1.25
5–9	0.84	0.53, 1.35	0.71	0.43, 1.18
≥10	0.99	0.47, 2.08	0.85	0.39, 1.86

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Adjusted for age, education, sex, and country.

Table 6. Odds Ratio for the Distance Between the Glioma Midpoint and the Typical Position of the Mobile Telephone, Measured as Both a Categorical Variable (≤5 cm) and a Continuous Variable, in All Cases Compared With Speculars (Case-Specular Analysis) Among Glioma Patients From 7 European Countries, 2000–2004

Exposure Characteristic	Glioma Midpoint ≤5 cm (vs. >5 cm) From Mobile Phone		Increasing Distance From Exposure Point, per cm	
	OR	95% CI	OR	95% CI
Total (all cases vs. all speculars)	1.22	0.99, 1.51	1.00	0.95, 1.07
Never-regular users				
Regular use	1.19	0.89, 1.59	0.99	0.92, 1.08
Never-regular use	1.30	0.95, 1.80	1.01	0.92, 1.11
Cumulative call time, hours				
0.001–46	1.39	0.81, 2.38	1.00	0.87, 1.16
47–339	1.21	0.74, 1.97	0.99	0.86, 1.13
>339	1.00	0.59, 1.69	1.01	0.88, 1.16
Duration of use, years				
1.5–4	1.15	0.80, 1.66	0.98	0.89, 1.09
5–9	1.04	0.61, 1.76	1.02	0.89, 1.18
≥10	2.00	0.68, 5.85	1.08	0.82, 1.42

Abbreviations: CI, confidence interval; OR, odds ratio.

the exposure line than those with only 1 midpoint (6.44 cm vs. 6.22 cm; $P = 0.15$).

In the case-specular analysis, the hypothetical alternative location in the coronal and axial axes of the 3-dimensional brain model was assigned symmetrically across the midpoint of the plane to reflect the location of the case. The center points of the axes (in relation to which the specular coordinates were obtained) were chosen on the basis of the median values observed among never-regular users, in accordance with the null hypothesis. The number of such cases was substantial (more than 370), and the precision should have been adequate.

However, in the case-specular analyses, the odds ratios were slightly above unity for never-regular phone users as well (Table 6). This indicates that the reference point was not necessarily located on an exact basis, rendering the results of the case-specular analysis somewhat difficult to interpret.

Never-regular users were, on average, older and more commonly female, and if these factors affect the tumor location, bias could be introduced. Nevertheless, in our data, the average distances from the exposure line did not differ significantly between age groups (ranging from 6.14 cm in persons aged 50–59 years to 6.43 cm in persons aged 40–49 years; $P = 0.32$), whereas there was a borderline-significant difference between the sexes (6.16 cm in men vs. 6.37 cm in women; $P = 0.051$). This higher proportion of women among the unexposed may have driven the center point somewhat further from the exposure line (since gliomas among women are located further from the line), which may accentuate the differences in distances when comparing all cases and all speculars.

We addressed histologic subtypes of glioma in a very simplified fashion by dividing the gliomas into 2 subgroups (glioblastoma and other), and the results for the 2 groups were largely similar to those of the main analyses. However, both etiologic factors and preferential locations may vary by the molecularly defined subtype of the tumor, which we could not investigate further in this study.

Because of the short penetrance of the radio-frequency field into the head, exposure emitted by a mobile phone is virtually confined to the brain hemisphere on the side of the phone. However, most people do not use their phone exclusively on one side. Several earlier studies found an increased risk on the side of head where the user reported that the phone had predominantly been used (2). Frequently, however, this has been accompanied by a deficit on the contralateral side, giving rise to suspicion of recall bias (overestimation of use on the side of the tumor by the cases, with corresponding underreporting on the other side).

The only finding consistent with the study hypothesis was a statistically significant excess of gliomas on the self-reported side of mobile phone use (Table 1). However, the more detailed analyses failed to support this finding. The reported predominant side of use is prone to recall bias, and in our interpretation such bias is a likely explanation for this specific result.

Case-case analysis overcomes the discrepancy of information between cases and controls. The results of our

case-case analysis did not show differences by laterality of use in relation to tumor location.

Because only cases were included in our study, selection bias arising from lower participation among controls, particularly nonusers of mobile phones, was avoided (20, 21). Still, even if only cases were included, reported usage may have been inaccurate. Slight underestimation of the number of calls and substantial overestimation of call duration have been demonstrated in short-term recall (22). However, such overestimation would distort the current results only if it were related to the location of the tumor.

The main limitation of this study was the relatively short time since first exposure. While one-fifth of the cases ($n = 184$) had used mobile phones for at least 5 years, only 5% ($n = 42$) had used mobile phones for 10 or more years, which adds considerable uncertainty to our results on long-term exposure. No statistically significant difference was found for gliomas among cases with 5–9 years of use or $\geq$10 years of use in terms of mean distance to the typical phone location in our case-case or case-specular analyses. Even though, in the case-specular analysis, the odds ratio was increased 2-fold for cases with $\geq$10 years of use, the confidence intervals of the risk estimates for the increasing categories of duration of use remained wide.

To our knowledge, this is the largest study on detailed glioma localization published to date, with 888 glioma cases from 7 countries. Further research with similar methods but a larger number of long-term users is warranted.

In conclusion, the results do not indicate that gliomas are located in excess in the brain tissue presumably receiving the highest-intensity electromagnetic field among regular mobile phone users. Cumulative call time, duration of use, and laterality were not consistently associated with the location of the gliomas.

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