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Published on: 20 Dec 2000 - JAMA (American Medical Association)

Topics: Cancer

Handheld Cellular Telephone Use and Risk of Brain Cancer

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Context A relative paucity of data exist on the possible health effects of using cellular telephones.

Objective To test the hypothesis that using handheld cellular telephones is related to the risk of primary brain cancer.

Design and Setting Case-control study conducted in 5 US academic medical centers between 1994 and 1998 using a structured questionnaire.

Patients A total of 469 men and women aged 18 to 80 years with primary brain cancer and 422 matched controls without brain cancer.

Main Outcome Measure Risk of brain cancer compared by use of handheld cellular telephones, in hours per month and years of use.

Results The median monthly hours of use were 2.5 for cases and 2.2 for controls. Compared with patients who never used handheld cellular telephones, the multivariate odds ratio (OR) associated with regular past or current use was 0.85 (95% confidence interval [CI], 0.6-1.2). The OR for infrequent users (<0.72 h/mo) was 1.0 (95% CI, 0.5-2.0) and for frequent users (>10.1 h/mo) was 0.7 (95% CI, 0.3-1.4). The mean duration of use was 2.8 years for cases and 2.7 years for controls; no association with brain cancer was observed according to duration of use ($P=.54$). In cases, cerebral tumors occurred more frequently on the same side of the head where cellular telephones had been used (26 vs 15 cases; $P=.06$), but in the cases with temporal lobe cancer a greater proportion of tumors occurred in the contralateral than ipsilateral side (9 vs 5 cases; $P=.33$). The OR was less than 1.0 for all histologic categories of brain cancer except for uncommon neuroepitheliomatous cancers (OR, 2.1; 95% CI, 0.9-4.7).

Conclusions Our data suggest that use of handheld cellular telephones is not associated with risk of brain cancer, but further studies are needed to account for longer induction periods, especially for slow-growing tumors with neuronal features.

JAMA. 2000;284:3001-3007 www.jama.com

SINCE THE INTRODUCTION OF CELlular telephone service in the United States in 1984,[1] the number of subscribers has increased substantially every year. By the end of 1999, there were more than 86 million cellular telephone users.[2] Cellular telephones, which include handheld or mobile telephones, car telephones, and portable or bag telephones, operate on radiofrequency (RF) signals in the 800- to 900-MHz range.

Concerns have been raised about possible adverse health effects due to exposure to these signals. In particular, allegations that the use of handheld cellular telephones causes brain cancer[3] are based on the close proximity of the antenna, which is incorporated into the telephone receiver, to the head of the user.[4,5] These claims cannot be strongly supported or refuted because of the relative paucity of scientific data on this topic. The most highly exposed cranial areas from handheld cellular telephones are the ipsilateral ear and cheek regions. The absorption of RF energy in the brain decreases with distance from the ipsilateral ear.[6] There is less concern over intracranial RF exposure from a car-mounted telephone because the antenna is mounted on the roof and the vehicle acts as a shield. Portable cellular telephones, which are relatively uncommon, are another source of RF emissions, but because the antenna is contained in a carrying case, the exposure is not localized to the head.

The use of cellular telephones is one of several suspected risk factors for brain cancer, although the causes of this disease remain poorly understood. Predisposing genetic disorders and prior cranial radiotherapy account for a small percentage of cases. There is little evidence that the risk depends on cigarette smoking and alcohol consumption, and inconsistent findings have been reported for various environmental, occupational, and dietary exposures.[7,8] The health effects due to using cellular telephones are currently being studied in a number of populations. In preliminary reports of a case-control study conducted in Sweden, the risk of brain cancer was unrelated to using a handheld

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cellular telephone.[9,10] The hypothesis that handheld cellular telephone use is associated with primary brain cancer was tested in the current hospital-based study.

METHODS

Patients between the ages of 18 and 80 years were interviewed using a structured questionnaire between 1994 and early 1998 in New York, NY (Memorial Sloan-Kettering Cancer Center, New York University Medical Center, Columbia University Presbyterian Hospital), Providence, RI (Rhode Island Hospital), and Boston, Mass (Massachusetts General Hospital). A description of each type of cellular telephone (handheld, bag, car) was provided, and patients were asked if they had ever used a handheld cellular telephone on a regular basis (*regular* defined as having had a subscription to cellular telephone service). Information was obtained on the number of years of use, minutes/hours used per month, year of first use, manufacturer, and reported average monthly bill. Data on which hand was used to hold the cellular telephone was collected from 700 (78.6%) of the 891 patients. Requests were made to obtain billing records from the cellular telephone carrier in New York, in collaboration with Epidemiology Resources Inc (Newton, Mass). These efforts were unsuccessful and subsequently the patient was asked to estimate the average monthly cellular telephone bill (102 [71.8%] of the 142 handheld cellular telephone users). Other questionnaire items included demographics, smoking history, alcohol consumption, exposure to power frequency fields, occupation, and medical history. The interview was designed to last for about a half hour to ensure a high response rate and avoid patient fatigue. A dietary assessment was not conducted.

Collaboration was sought with oncologists, neurosurgeons, nursing, and other staff. The research interviewers were health professionals or health professionals in training. They were actively involved in the identification of eligible patients and consequently were knowledgeable about patients' medical conditions. The interviewers consulted with the hospital staff to determine the most appropriate time to approach patients. Eligible case patients (cases) were those diagnosed as having primary brain cancer within the past year (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]* codes 191.0-191.9 [70% interviewed in the same month or within 2 months of diagnosis]) and spoke English. The histologic type and the anatomic location of the tumor were obtained from pathology and magnetic resonance imaging reports.

Eligible control patients (controls) were inpatients from the same hospitals as the cases and identified from daily admission rosters. Controls were admitted for benign conditions, except at 2 study centers, which included predominately cancer patients (Memorial Sloan-Kettering Cancer Center and Massachusetts General Hospital). Patients diagnosed as having lymphoma or leukemia were not eligible for inclusion because these conditions are possibly linked to exposure from RF fields. In addition to matching by hospital, controls were frequency matched on a 1:1 ratio by age (± 5 years), sex, race, and month of admission. The list of the previous day's hospital admissions was obtained from the admissions office each morning. The admission list was reviewed sequentially and the first patient who met the eligibility criteria and was an appropriate match to a case was approached. An unmatched case remained in the study. To further confirm the patient's eligibility, the medical record was reviewed. All patients signed a consent form approved by the institutional review board of Memorial Sloan-Kettering Cancer Center (New York, NY). In the first year of the study, 43 of the case interviews and 6 of the control interviews were conducted with proxies. In subsequent years, all interviews were done with the patients.

Statistical Analysis

The Spearman correlation coefficient was calculated to measure the relationship between the monthly hours of handheld cellular telephone use and the reported monthly bill. For 17 patients whose employer paid the bill, the monthly bill was adjusted by the estimated percentage of use. The relationship between the frequency and the duration of telephone use was measured by the Pearson correlation coefficient. The relative risk of brain cancer associated with regular use of a handheld cellular telephone was estimated by the odds ratio (OR) and 95% confidence interval (CI). To determine if this association varied by study center, the crude OR was compared with the Mantel-Haenszel pooled summary OR. A stratified analysis was conducted by examining several suspected risk factors to identify potential confounders.

Three exposure measures were used for OR calculations: hours per month, years of use, and lifetime cumulative hours (hours of cellular telephone use per month multiplied by the number of years of use). These measures were grouped into 4 categories (3 categories for years of use) based on the distribution within the controls. Unconditional logistic regression analysis was conducted to derive the OR associated with each exposure level relative to the reference group of nonusers, while simultaneously adjusting for the matching factors, type of respondent (subject vs proxy), and other possible confounders. The interview date (month and year) was included in the model as a single continuous term. A test for trend was conducted by using the median quantile value as the exposure score in the logistic regression model. The reported *P* values for the trend tests are 2-sided. Nonparametric regression analyses were also conducted as an alternative method for assessing a dose-response relationship. This technique has become increasingly popular in retrospective studies since the categorization of the exposure variable into quantiles is an arbitrary method that could potentially

mask possible exposure affects within a category.[11] Restricted cubic splines with 3 prespecified knots positioned on the quartile boundary points were fitted using SAS/IML software[12] for each measure of cellular telephone use, controlling for the same covariates in the logistic regression models.[13]

Exploratory subset analyses were conducted by histologic groups based on *ICD-9-CM* codes and International Agency for Research on Cancer groupings,[14] and by the anatomic location of the brain lesion. The entire control set was used as the comparison group for both histologic and anatomic-specific subset analyses. In an analysis that was limited to just the cases who used cellular telephones, the χ^2 test was conducted to determine whether the proportion of all cerebral tumors that were left-sided vs right-sided differed by cellular telephone handedness (right vs left hand).

RESULTS

Of 571 eligible cases who were approached, 469 (82%) were successfully interviewed. There were 2 deaths, 25 refusals, and 75 who consented but were too ill to participate or were uncommunicative. In addition, 55 cases were not approached because of illness and 42 were excluded because English was not their spoken language. The response rate in the controls was 90%; half of the nonrespondents were refusals and half were unsuccessful interviews. A matched control was not found for all cases, especially those younger than 30 years. The matching requirement by the month of admission precluded adding additional controls at the end of the study, which could have biased the findings. The average date of interview occurred 5 months earlier for cases than controls.

The ages, years of education, and types of occupations were similar for the 469 cases and 422 controls (TABLE 1). Sixty-six cases (14%) and 76 controls (18%) reported using handheld cellular telephones (Table 1). In all subjects, cellular telephones were used more frequently by men than women, subjects aged 30 to 59 years, and salespersons. In most age, sex, race, and occupational groups, handheld cellular telephones were used about the same or slightly more frequently in both groups. In patients with less than 12 years of education, cellular telephones were used more often by controls than cases (17.7% vs 2.6%).

In the controls, there was little difference in the use of handheld cellular telephones by disease category except for cancer patients (TABLE 2). The lower user rate in cancer controls reflects their older mean age. For the age group of 60 years and older, cancer controls and other controls used cellular telephones at about the same rate (4.1% vs 5.6%). Of the 50 cancer controls who were younger than 60 years, 4 (8%) used cellular telephones, including 1 (8.3%) of 12 patients with gastrointestinal tract cancers, 1 (14.3%) of 7 with lung cancer, 1 (16.7%) of 6 with female reproductive cancers, and 1 (20%) of 5 with melanoma.

Three patients reported first using a handheld cellular telephone between 1980 and 1983; this date was recoded to 1984. Four cases and 1 control did not provide information on the frequency of use. All patients who used cellular telephones were current users, except for 4 patients who quit a year or more ago. The

Table 1. Characteristics of Case and Control Patients, 1994-1998

Characteristic*	No. (%) of Case Patients		No. (%) of Control Patients	
	Overall	Cellular Telephone Use	Overall	Cellular Telephone Use
Total	469	66 (14.1)	422	76 (18.0)
Sex				
Men	304 (64.8)	44 (14.5)	271 (64.2)	57 (21.0)
Women	165 (35.2)	22 (13.3)	151 (35.8)	19 (12.6)
Age, y				
<30	56 (11.9)	9 (16.1)	48 (11.4)	7 (14.6)
30-39	86 (18.3)	16 (18.6)	74 (17.6)	21 (28.4)
40-49	103 (22.0)	20 (19.4)	100 (23.7)	21 (21.0)
50-59	99 (21.1)	16 (16.1)	79 (18.7)	21 (26.6)
≥60	125 (26.7)	5 (4.0)	121 (28.7)	6 (5.0)
Total education, y				
<12	39 (8.3)	1 (2.6)	34 (8.0)	6 (17.7)
12	101 (21.5)	12 (11.9)	76 (18.1)	9 (11.8)
13-15	95 (20.3)	22 (23.2)	86 (20.4)	16 (18.6)
≥16	234 (49.9)	31 (13.3)	226 (53.6)	45 (19.9)
Race				
White	460 (98.1)	64 (13.9)	412 (97.6)	74 (18.0)
Other	9 (1.9)	2 (22.2)	10 (2.4)	2 (20.0)
Occupation				
Professional	144 (30.7)	18 (12.5)	139 (32.9)	20 (14.4)
Managerial	71 (15.1)	12 (16.9)	75 (17.8)	22 (29.3)
Sales	46 (9.8)	8 (17.4)	38 (9.0)	12 (31.6)
Clerical	65 (13.9)	11 (16.9)	49 (11.6)	7 (14.2)
Skilled	68 (14.5)	10 (14.7)	59 (14.0)	9 (15.3)
Semiskilled/ laborer/service worker	50 (10.7)	4 (8.0)	36 (8.5)	6 (16.7)
Household	25 (5.3)	3 (12.0)	26 (6.2)	0 (0)

*Hospital distribution of patients (cases/controls): New York University (216/225); Memorial Sloan-Kettering Cancer Center (99/65); New York Presbyterian (66/67); Massachusetts General (55/41); and Rhode Island Hospital (33/24).

Table 2. Handheld Cellular Telephone Use in Controls by Diagnostic Category

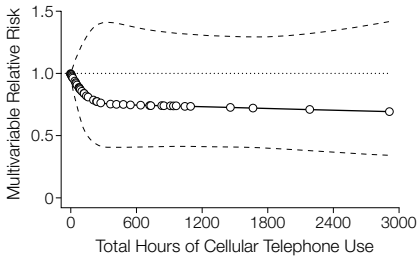
Diagnostic Category	No. (%) of Controls Who Ever Used a Cellular Telephone
Malignant neoplasm	99 (6.1)
Musculoskeletal disorder	71 (23.7)
Skin condition	19 (15.8)
Systemic disease	149 (20.8)
Other (V-codes, injury/signs)	84 (22.6)

Table 3. Odds Ratios for Brain Cancer by Amount and Duration of Handheld Cellular Telephone Use

Cellular Telephone Use	No. (%) of Cases (n = 469)	No. (%) of Controls (n = 422)	Multivariable Odds Ratio (95% Confidence Interval)*	*P* for Trend
No. of years				
0	403 (85.9)	346 (82.0)	1.0	
1†	21 (4.5)	30 (7.1)	0.7 (0.4-1.3)	.54
2-3	28 (6.0)	24 (5.7)	1.1 (0.6-2.0)	
≥4	17 (3.6)	22 (5.2)	0.7 (0.4-1.4)	
No. of hours/month				
0	403 (86.7)	346 (82.2)	1.0	
>0-≤0.72	19 (4.1)	20 (4.8)	1.0 (0.5-2.0)	
>0.72-≤2.1	10 (2.2)	17 (4.0)	0.5 (0.2-1.2)	.27
>2.1-≤10.1	20 (4.3)	18 (4.3)	0.9 (0.5-1.9)	
>10.1	13 (2.8)	20 (4.8)	0.7 (0.3-1.4)	
No. of cumulative hours‡				
0	403 (86.7)	346 (82.2)	1.0	
>0-≤8.7	17 (3.7)	18 (4.3)	1.0 (0.5-2.0)	
>8.7-≤60	12 (2.6)	19 (4.5)	0.6 (0.3-1.3)	.30
>60-≤480	19 (4.1)	19 (4.5)	0.9 (0.5-1.8)	
>480	14 (3.0)	19 (4.5)	0.7 (0.3-1.4)	

*Adjusted for age, years of education, sex, race, study center, proxy subject, and month and year of interview.
†Four cases used a cellular telephone for half a year.
‡Four cases and 1 control had missing data on frequency of use.

Figure. Nonparametric Regression Curve, 95% Confidence Interval, and Risk of Brain Cancer



correlation between the amount of cellular telephone use and the associated monthly bill was 0.58 ($P<.01$). For the 18 patients who had switched from 1 brand of handheld cellular telephone to the current brand, the correlation between the first handheld cellular telephone that was used and its corresponding monthly bill was 0.36 ($P=.15$).

The crude OR for brain cancer and regular handheld cellular telephone use was 0.74 (95% CI, 0.50-1.10) relative to nonusers. There was little heterogeneity in the hospital-specific ORs; the Mantel-Haenszel OR was 0.79 (95% CI, 0.60-1.10). In stratified analysis, the risk was calculated according to cigarette smoking status, alcohol consumption, and several proxy measures of electromagnetic field exposure (residence near a power station or high-voltage transformer; use of household electrical equipment, such as electric hair dryer, electric razor). There were few differences in the stratum-specific estimates. Few patients were ham radio operators or were occupationally exposed to RF fields due to sources other than cellular telephones (<1%).

The mean duration of handheld cellular telephone use was 2.8 years for cases and 2.7 years for controls. The multivariate OR associated with ever use of a handheld cellular telephone was 0.8 (95% CI, 0.6-1.2). When examined by duration of use, the OR was 0.7 (95% CI, 0.4-1.3) for 1 year of use and 0.7 (95% CI, 0.4-1.4) for 4 or more years of use (TABLE 3). The median monthly hours of use were 2.5 for cases and 2.2 for controls. There were little differences in the risk according to the frequency of cellular telephone use. The OR was 1.00 (95% CI, 0.50-2.00) associated with infrequent use (<three fourths per hour per month) and 0.70 (95% CI, 0.30-1.40) for frequent use (>10.1 hours of a month). The correlation between the number of hours and the number of years of cellular telephone use was 0.34 ($P<.01$). Using the cumulative exposure measure, the risk of brain cancer was also below 1 for all 4 exposure categories (Table 3). The estimated coefficients for the slope of the 3 exposure measures were negative, but the trend test values were not statistically significant.

The dose-response assessment using cubic splines gave results similar to that obtained from logistic regression analysis. The FIGURE shows the nonparametric regression curve for the relationship between lifetime hours of handheld cellular telephone use and brain cancer with knot positions at 8.7, 60, and 480 hours. The risk is estimated to be below 1 for nearly the entire range of observed exposure values but the corresponding 95% CIs for the risk values include 1.0. Changing the number of knots or knot position did not substantially alter the results. The cubic splines plotted for current frequency and duration of use were also similar to the results obtained by logistic regression in Table 3 (data not shown).

In handheld cellular telephone users, 86% of cases and 85% of controls reported usually extending the antenna during telephone calls. Of the 31 patients who switched from one brand of handheld cellular telephone to another, 8 (88.9%) of 9 cases and 12 (63.2%) of 19 controls reported usually extending the antenna when using the previous cellular telephone (3 missing observations; $P=.16$). Eighty-eight percent of all handheld cellular telephones were analog telephones. There were no case-control differences in the percentage who used digital telephones. There were also little case-control differences in the brand (manufacturer) of cellular telephone used. More than 50% of both cases and controls who used cellular telephones reported using 1 specific brand.

In case patients, the most common tumor site was the frontal lobe, followed by the temporal and parietal lobes. The risk of brain cancer in association with cellular telephone use was 1.1 or less for all brain sites (TABLE 4).

Information on cellular telephone handedness was obtained for 56 of the 66 cases who used handheld cellular

telephones. Five of the 56 cases reported no hand preference, and tumor laterality was not specified in an additional 9 cases. One case had a brainstem tumor. Of the remaining 41 cases, 26 usually used the cellular telephone on the same side of the head where the tumor occurred, compared with 15 who used the telephone on the contralateral side ($P=.06$). Of 14 cases with temporal lobe cancer that used cellular telephones, 5 were on the ipsilateral side and 9 were on the contralateral side ($P=.33$).

The histologic-specific risk estimates associated with handheld cellular telephone use are shown in TABLE 5. Gliomas, which are composed of neoplastic glial cells, include astrocytic tumors, oligodendrogliomas, and other types that can be classified by pathologic distinction and location. Neuroepitheliomatous (neuronal) cancers are rare tumors composed of ganglion cells, usually in combination with neoplastic glial cells. The OR for astrocytic tumors was 0.8 (95% CI, 0.5-1.2). The OR for neuroepitheliomatous cancers was 2.1 (95% CI, 0.9-4.7). Of the 35 cases with neuroepitheliomatous cancers, 10 were located in the temporal lobe and 4 of these 10 used cellular telephones. For both the glioma and neuronal histological types, a significant trend in the OR was not found with increased cumulative exposure.

Table 4. Odds Ratios for Brain Cancer and Handheld Cellular Telephone Use by Anatomic Location*

Brain Cancer Site	No. (%) Who Ever Used a Cellular Telephone	Multivariable Odds Ratio (95% Confidence Interval)†
Cerebrum		
Frontal lobe	126 (19.8)	1.1 (0.7-2.0)
Parietal lobe	60 (10.0)	0.8 (0.3-2.0)
Occipital lobe	21 (9.5)	0.8 (0.2-4.0)
Temporal lobe	108 (16.7)	0.9 (0.5-1.7)
Cerebrum (not lobes)	36 (7.4)	0.3 (0.1-1.1)
Cerebellum	8 (12.5)	0.9 (0.1-8.1)
Brainstem/ventricular/other	25 (16.0)	0.9 (0.3-2.8)
Unspecified	85 (9.4)	0.9 (0.4-2.2)

*Based on the *International Classification of Diseases, Ninth Revision, Clinical Modification*.
†Adjusted for age, years of education, sex, race, study center, proxy subject, and month and year of interview. Odds ratio calculations were determined by comparing each case subgroup with all controls.

Table 5. Odds Ratios for Brain Cancer and Handheld Cellular Telephone Use by Histologic Type of Tumor

Category (*ICD-9-CM* Code)*	No. (%) Cases (n = 469)	No. (%) Cellular Telephone Use	Multivariable Odds Ratio (95% Confidence Interval)†
Astrocytic	354 (75.5)	41 (11.6)	0.8 (0.5-1.2)
Glioblastoma (M9440)	244 (52.0)	29 (11.9)	NA
Astrocytoma (M9400-9421)	82 (17.5)	7 (8.5)	NA
Other glioma (M9380)	28 (6.0)	5 (17.9)	NA
Oligodendroglioma/mixed glioma (M9450-9451, 9382)	55 (11.7)	9 (16.4)	0.9 (0.4-2.1)
Ependymal (M9391-9394)	8 (1.7)	0 (0)	NA
Choroid plexus (M9390)	1 (0.2)	0 (0)	NA
Other (M9362, 9064, 9161)	6 (1.3)	1 (16.7)	NA
Not specified	10 (2.1)	1 (10.0)	NA
Neuroepitheliomatous (M9490-9523)‡	35 (7.5)	14 (40.0)	2.1 (0.9-4.7)

**ICD-9-CM* indicates *International Classification of Diseases, Ninth Revision, Clinical Modification*.
†Adjusted for age, years of education, sex, race, study center, proxy subject, and month and year of interview. Odds ratio calculations were determined by comparing each case subgroup with all controls. NA indicates not applicable.
‡Includes 18 gangliogliomas, 11 gangliogliomas, 4 neurocytomas, and 2 neuroepitheliomas.

COMMENT

The use of handheld cellular telephones was unrelated to the risk of brain cancer in the current study. The overall OR was less than 1.0, but the lack of a trend in the data does not support the interpretation of a protective effect. In other studies of cellular telephone use and brain cancer, the risk of various malignant and benign brain tumors was 0.98 (95% CI, 0.69-1.41) in a population-based study of 233 cases in Swedish.[9,10] A nonsignificant 2-fold risk was reported for ipsilateral temporal lobe tumors, however this association cannot be calculated independently from the published tables in the Sweden articles. In a cohort of 255 868 car, handheld, and other cellular telephone users, the standardized mortality rate for brain cancer was 3.7 in persons who used handheld cellular telephones for less than 2 minutes per day, compared with 2.0 for car telephone users after 1 year of follow-up (CIs not calculated) based on 2 and 4 deaths, respectively.[15] There were no deaths due to brain cancer in persons who used handheld cellular telephones for longer durations. A multinational case-control study of brain cancer has begun in 8 countries,[16] and in Denmark cellular telephone subscription information is being linked to a national death index.[17] In the United States, another hospital-based study of brain cancer was recently completed.[18]

It has been speculated that the increasing age-adjusted incidence of brain cancer (in Australia) since 1982 is due to analog cellular telephone use,[19] although there is sharp disagreement that these are related events.[20] Using data from the Surveillance, Epidemiology and End Results database and from Medicare imaging and biopsy records, Legler et al[21] reported that US brain cancer rates between 1975 and 1995 increased only in persons aged 70 years and older, and that this trend was likely due to improvements in diagnosis. This study and other surveys[22] found that cellular telephone use is relatively uncommon in the elderly.

Epidemiologic methods use surrogate measures of exposure to characterize cellular telephone RF exposure. Individual exposure levels due to cellular telephone emissions vary by cellular size,

amount of cellular telephone traffic, quality of the transmission, antenna extension, handset dimensions, and other factors. The deposition of cellular telephone RF energy in the head, however, depends on complex interactions of RF fields with biological tissue.[6,23] The RF energy that is absorbed in biological tissue is not highly correlated with radiated energy.[24,25] Consequently, the rate of total electromagnetic energy absorption in tissue is measured by the specific absorption rate using probes in phantom head models. In simulation studies involving cellular telephones placed to the ear, intracranial absorption of RF energy dissipates rapidly with distance from the cellular telephone antenna.[26] The specific absorption rate on the contralateral side is a small fraction of the exposure on the ipsilateral side, with the highest intracranial exposure in brain tissue behind the ipsilateral ear.[27] In humans, this region corresponds to the temporal lobe. In the current study, tumors were more likely to occur on the ipsilateral side of the head, but tumors in the temporal lobe were somewhat more likely to occur on the contralateral side. The laterality of the tumor in relationship with cellular telephone handedness was not statistically significant in either case.

Several biases were considered when interpreting the current findings. The use of cellular telephones in nonrespondents and in the 57 cases who were not approached might have differed from participating cases. In general, the severity of illness was greater in case than control patients, and consequently the recent use of cellular telephones in cases might have been overstated if disease symptoms resulted in a decline in the number of recent cellular telephone calls. The data also showed that the cellular telephone user rate was substantially lower in the 39 case patients who had not completed high school compared with controls with the same level of education. This could reflect a recall bias in case patients with fewer years of education or reflect a selection bias. However, nearly all cellular telephone users in this study were current users and it seems unlikely that recall bias could have been substantial. There was a moderate correlation between the estimated average monthly bill and the amount of cellular telephone use, which provides some assurance that cellular telephone usage patterns were described with reasonable accuracy. In a population-based survey, the correlation between reported cellular telephone use and actual 3-month billing records was 0.74.[28]

The choice of hospital controls, rather than a probability sample of the general population, could have introduced bias if the patient's medical condition was associated with using a handheld cellular telephone. For instance, control patients younger than 60 years with specific cancers used cellular telephones less frequently than other controls in this age group. Different referral patterns between cases and controls could have also introduced bias. Although 93% of cases and 92% of controls treated at the New York study centers lived in New York or New Jersey, there might have been differences in local referral patterns. However the percentage of all controls who used cellular telephones (18%) during the study period of 1994 to 1998 seems consistent with commercial subscription data (about 25% of total US population in 1998). None of the controls were admitted for injuries resulting from motor vehicle crashes or events associated with cellular telephone ownership.[15,29,30] The age and sex distribution of controls who used cellular telephones in this study (Table 2) was similar to a demographic study of 256 284 cellular telephone users in 4 large American cities.[22] In both studies, men were twice as likely to use cellular telephones as women. More than 9% of handheld cellular telephone users in this study reported no telephone hand preference, compared with 10% of users who reported switching hands in a survey of 3157 cellular telephones users.[28]

The validity of the case-control findings also depends on the exposure preceding the disease, but the onset for some brain tumors might have predated clinical diagnosis by several months or possibly by years. Most gliomas exhibit rapid tumor growth, although growth rates vary. Low-grade diffuse astrocytomas and gangliogliomas are characterized by slow-growth rates and are well differentiated. Evidence for a long latency for some brain tumors comes from findings of asymptomatic brain cancer detected in healthy individuals serving as controls for studies involving magnetic resonance imaging screening.[31]

The positive association between handheld cellular telephone use and neuroepitheliomatous cancers requires careful interpretation given recent changes in the morphologic criteria for brain cancer.[32] There is little diagnostic distinction between some gangliogliomas, the most common form of neuroepitheliomatous cancers in this study, and gliomas with entrapped neurons.[33] A common clinical feature of ganglioglioma is chronic epilepsy,[34] yet only 1 case patient with this histologic type reported a (12-year) history of epilepsy. Information was obtained on the follow-up care of 2 surgical case patients with ganglioglioma. Both received postoperative care at a different institution and were diagnosed as having glioma by a second neuropathologist. There were no diagnoses of neuroepitheliomatous cancers at some of the study centers, which could reflect hospital referral patterns. The ongoing case-control study of brain cancer in Sweden is population-based; however, there were no case patients with neuronal tumors. Histologic-specific risks according to cellular telephone use should be tested in other study populations.

Recent health risk assessments of RF fields emitted from mobile telephones are based on epidemiology, experimental findings, and studies of RF field interactions with biological tissue.[35,36] Based on a review of the literature, others concluded that there are few studies of well-characterized RF energy exposure and cancer in humans, although the evidence suggests a weak or a lack of association.[37,38] Reviews of in-vitro studies concluded that a genotoxic potential of RF fields has not been dem-

onstrated,[39,40] and it was recently argued that the energy levels from cellular telephone emissions are too low to initiate or promote cancer.[41] However, some experimental data do demonstrate biological events occurring after exposure to RF fields. Microwave radiation was reported to increase single-strand DNA breaks in rat brain cells,[42] although this finding was not confirmed elsewhere.[43] The incidence of lymphoma was increased following whole-body RF irradiation in a transgenic animal model,[44] but other animal studies involving RF exposure to the head found no increase[45] or decrease[46] in brain tumors. If RF energy from cellular telephones is tumorigenic, it might act as a promoter or in the progression phase of cancer.[16] The current study shows no effect with short-term exposure to cellular telephones that operate on (primarily) analog signals. Further studies are needed to account for longer induction periods, especially for slow-growing tumors. The RF fields emitted from digital cellular telephones might have different effects on biological tissue than analog telephones,[47] and studies are under way in several European countries that use primarily digital telecommunication networks.

Funding/Support: This project was supported by a contract from Wireless Technology Research LLC and Public Health Service grants NCI32617, NCI68384, and NCI17613.
Previous Presentation: Portions of this work were presented at the Second State of the Science Colloquium on the Public Health Impact of Wireless Technology, June 20, 1999, Long Beach, Calif; the International Workshop on Mobile Phone and Tumors of Brain, Head and Neck, November 13, 1999, Heidelberg, Germany; and the Colloque International de Communication Mobile-Effets Biologiques, April 19, 2000, Paris, France.
Acknowledgment: We are grateful to Anna Mondora, MS, for supervising the field staff, Vicki Liang, MS, and Preciosa Ong, BA, for computer systems administration, Brian Pittman, MS, for graphics, and the comments from anonymous reviewers.

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difference in results. The panel made 2 suggestions concerning the analysis of our 5.5-year test scores: (1) the use of raw test scores instead of standardized scores and the inclusion of the child's age at testing as an additional covariate in the analysis would provide better control for the age of the child at testing; and (2) adjustment for which of the 3 staff members administered the test battery would improve the precision of the analysis.

Methods. In the original study, all children were tested at a mean (SD) age of 66 (6) months and standardized test scores afforded inherent control for age, and intertester reliability among the 3 testers was consistently high. We reanalyzed the data from the 6 primary end points at 66 months, using the same statistical procedures reported earlier, except that raw test scores were used, and age at testing and tester were included as additional covariates in the regression analyses.

Results. The reanalyses confirmed our previous findings. The TABLE summarizes the results in the same format as our earlier report.[1] The significance and direction of the parameter estimates for prenatal and postnatal exposure are nearly identical to those reported earlier. We did find significant effects of both age at testing (to be expected since scores were no longer scaled) and tester (not unlikely since testers did not have 100% agreement). There continues to be an association among both prenatal and postnatal exposure and the Preschool Language Scale Total Score, as well as an association in males only among postnatal exposure and scores on the Woodcock-Johnson Applied Problems and the Bender Gestalt drawing and copying errors.

Comment. These associations continue to suggest beneficial effects with increasing mercury levels that may reflect dietary benefits of fish consumption. In a population exposed to MeHg from consumption of ocean fish, we continue to find no evidence of adverse effects.

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CORRECTION

Incorrect Hospital Name, Incorrect Numbers, and Rounding Errors: In the Original Contribution entitled "Handheld Cellular Telephone Use and Risk of Brain Cancer" published in the December 20, 2000, issue of THE JOURNAL (2000;284:3001-3007), a hospital was identified incorrectly, incorrect statistics appeared in the "Methods" section, and rounding errors appeared in 2 of the tables. On page 3001, Dr Neugut's affiliation should have read "Department of Medicine, Mailman School of Public Health, Columbia University, New York, NY." On page 3002, the first sentence in the "Methods" section should have read "New York Presbyterian Hospital" not "Columbia University Presbyterian Hospital." Also on page 3002, the second to last sentence in the second column should have been "In the first 2 years of the study, 100 of the case interviews (21%) and 22 of the control interviews (5%) were conducted with proxies." Also on page 3003, in Table 2, the corresponding values for "Musculoskeletal disorder" should have been "71 (23.9)." On page 3005, in Table 4, the corresponding values for "No. (%) Who Ever Used a Cellular Telephone" for "Cerebrum (not lobes)" should have been "36 (5.6)."