

## Use of cellular telephones and the risk for brain tumours: A case-control study

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**Abstract.** The use of cellular telephones has increased dramatically during the 1990's in the world. In the 1980's the analogue NMT system was used whereas the digital GSM system was introduced in early 1990's and is now the preferred system. Case reports of brain tumours in users initiated this case-control study on brain tumours and use of cellular telephones. Also other exposures were assessed. All cases, both males and females, with histopathologically verified brain tumour living in Uppsala-Örebro region (1994-96) and Stockholm region (1995-96) aged 20-80 at the time of diagnosis and alive at start of the study were included, 233 in total. Two controls to each case were selected from the Swedish Population Register matched for sex, age and study region. Exposure was assessed by questionnaires supplemented over the phone. The analyses were based on answers from 209 (90%) cases and 425 (91%) controls. Use of cellular telephone gave odds ratio (OR) = 0.98 with 95% confidence interval (CI) = 0.69-1.41. For the digital GSM system OR = 0.97, CI = 0.61-1.56 and for the analogue NMT system OR = 0.94, CI = 0.62-1.44 were calculated. Dose-response analysis and using different tumour induction periods gave similar results. Non-significantly increased risk was found for tumour in the temporal or occipital lobe on the same side as a cellular phone had been used, right side OR = 2.45, CI = 0.78-7.76, left side OR = 2.40, CI = 0.52-10.9. Increased risk was found only for use of the NMT system. For GSM use the observation time is still too short for definite conclusions. An increased risk for brain tumour in the anatomical area close to the use of a cellular telephone should be especially studied in the future.

### Introduction

Approximately one in every three people in Sweden has a cellular telephone and the use has increased markedly during the 1990's (1). In the 1980's only the analogue system operating at either 450 (NMT 450) or 900 (NMT 900) MHz was used. The digital system (GSM) was introduced in early 1990's and is now the system preferred by users.

For cellular phones the absorption of microwaves is highest close to the antenna and it declines rapidly with distance (2). Thus, exposure is highest in the anatomical area close to the ear used for a handheld cellular telephones, i.e., temporal and occipital lobe. In contrast, using a handsfree device or a fixed antenna connected by a wire to the cellular telephone minimises brain exposure.

We have previously evaluated the risk for brain tumours associated with exposure to extremely low frequency electromagnetic fields (3). Our conclusion was that there is no consistent pattern of an increased risk. However, there are no reports of the long-term health effects on humans by the use of cellular telephones. Case reports of brain tumour among cellular telephone users have initiated studies in this area (4). The aim of this study was to investigate exposure to radio frequency (RF) radiation as risk factor for brain tumours.

### Materials and methods

**Cases.** All cases with a histopathological diagnosis of brain tumour were identified from records at the Oncological Centre in Uppsala-Örebro region during 1994-96 and Stockholm region during 1995-96. Both sexes in the age group 20-80 years at the time of diagnosis and alive at the start of the study were included. In total 270 cases were identified. The responsible physicians of the cases were contacted for permission to include the patients. For medical reasons, e.g., too ill for participation, 37 patients were excluded. Thus, the study encompassed 233 cases.

**Controls.** Two controls to each case matched on sex, age (born the same year as the case) and study region were identified from the Swedish Population Register.

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*Assessment of exposure.* The investigation was approved by the institutional ethics committees. Information on exposures was assessed by a postal questionnaire. Thereby a complete working history was asked for as well as information on chemical exposures.

An especially trained interviewer, a nurse, supplemented the answers over the phone if data were unclear using written instructions in that connection. All subjects who stated use of a cellular telephone were contacted by the interviewer to confirm such exposure and if necessary to qualify the answers. In order to check if the digital GSM system or the analogue NMT system had been used the first digits in the phone number were asked for, i.e., 070 or 010, respectively. Interviews and coding of the answers were recorded without the knowledge whether it referred to a case or a control.

Detailed information on exposure to cellular telephones was assessed such as use during leisure time and in occupations, average minutes of exposure per day, years for exposure, type of cellular phone, use of hands-free devices and use in a car with fixed antenna on the car. Use of handheld cellular phones was separated from bag and car phones. Time for use of hands-free devices or in a car with fixed antenna was not included as exposure.

All exposures within one year prior to diagnosis were disregarded. The same year as for the case was used for the matched controls. Cumulative exposure in hours was calculated. A minimum cumulative time for exposure of 8 h was used for both cases and controls.

After informed consent copies of X-rays and histopathological reports were requested for the cases in order to obtain information whether the tumour was recurrent, histopathological type, and tumour localisation in the brain.

*Statistical methods.* Conditional logistic regression analysis for matched studies was used to calculate odds ratios (OR) and 95% confidence intervals (CI), (SAS Institute, Cary, NC). Analysis was also performed with a minimum tumour induction time of 5 or 10 years. In dose-response calculations the material was divided in two groups based on median number of hours for exposure among controls.

## Results

The questionnaire was answered by 217 cases and 439 controls. When scrutinising medical reports it turned out that 8 of the cases had a recurrent brain tumour. These cases were excluded from further analysis together with their 14 matched controls that had answered the questionnaire. Thus the final study encompassed 209 (90%) cases and 425 (91%) controls. X-ray reports were not obtained for 11 patients and histopathology for 12 patients who did not permit us to request such copies.

The mean age for both cases and controls was 50 years. Of the cases 106 were men and 103 women compared to 213 men and 212 women of the controls. The histopathological distribution of the diagnosis is shown in Table I and anatomical tumour localisation in Table II.

*Cellular telephones.* Use of cellular phone was reported by 78 cases (37.3%) and 161 controls (37.9%). The mean number of

Table I. Histopathological distribution of brain tumours, 197 patients in total. One case had both ependymoma and acoustic neurinoma.

| Histopathology     | No. of cases |
|--------------------|--------------|
| Malignant          | 136          |
| Glioblastoma       | 48           |
| Astrocytoma        | 46           |
| Oligodendroglioma  | 19           |
| Ependymoma         | 3            |
| Mixed glioma       | 16           |
| Malignant, NUD     | 4            |
| Benign             | 62           |
| Meningioma         | 46           |
| Acoustic neurinoma | 13           |
| Other benign       | 3            |

Table II. Anatomical tumour localisation, 198 patients in total. For tumours with borderline anatomical localisation both lobes are given.

| Tumour localisation                            | No. of cases |
|------------------------------------------------|--------------|
| Right brain                                    | 99           |
| Left brain                                     | 78           |
| Not applicable side<br>(e.g., central tumours) | 21           |
| Lobe                                           |              |
| Frontal                                        | 63           |
| Parietal                                       | 19           |
| Temporal                                       | 48           |
| Occipital                                      | 7            |
| Frontoparietal                                 | 20           |
| Temporoparietal                                | 8            |
| Parietooccipital                               | 5            |
| Cerebellum                                     | 5            |
| Not applicable lobe                            | 23           |

hours for use was for cases 511 (median 136, range 8-9000) and for controls 428 (median 136, range 8-6304).

Overall no increased risk for brain tumour was found, OR = 0.98, CI = 0.69-1.41, see Table III. No change of the results and no dose-response effect could be seen when different tumour induction periods were used. Separate analysis on use of GSM or NMT telephones yielded similar

Table III. Odds ratio (OR) and 95% confidence interval (CI) for exposure to cellular telephone. Number of exposed cases and controls is given. Dose-response calculations were based on median number of hours for exposure among controls.

|                          | Cases/controls | OR   | CI        |
|--------------------------|----------------|------|-----------|
| Latency period >1 year   |                |      |           |
| Total                    | 78/161         | 0.98 | 0.69-1.41 |
| <136 h                   | 38/76          | 1.01 | 0.64-1.58 |
| >136 h                   | 40/85          | 0.96 | 0.61-1.52 |
| -GSM                     | 44/92          | 0.97 | 0.61-1.56 |
| <88 h                    | 20/45          | 0.93 | 0.49-1.79 |
| >88 h                    | 24/47          | 1.00 | 0.56-1.80 |
| -NMT                     | 52/106         | 0.94 | 0.62-1.44 |
| <224 h                   | 28/51          | 1.05 | 0.62-1.77 |
| >224 h                   | 24/54          | 0.83 | 0.47-1.47 |
| Latency period >5 years  |                |      |           |
| Total                    | 34/69          | 0.83 | 0.49-1.42 |
| <424 h                   | 16/34          | 0.87 | 0.42-1.77 |
| >424 h                   | 18/35          | 0.80 | 0.40-1.61 |
| GSM                      | 4/12           | 0.26 | 0.03-2.10 |
| <292 h                   | 0/6            | -    | -         |
| >292 h                   | 4/6            | 0.67 | 0.07-6.41 |
| -NMT                     | 31/66          | 0.81 | 0.47-1.39 |
| <380 h                   | 17/33          | 0.93 | 0.47-1.86 |
| >380 h                   | 14/33          | 0.68 | 0.31-1.46 |
| Latency period >10 years |                |      |           |
| Total (NMT)              | 16/26          | 1.20 | 0.56-2.59 |
| <968 h                   | 9/13           | 1.32 | 0.47-3.70 |
| >968 h                   | 7/13           | 1.06 | 0.33-3.40 |

results. Exposure was also divided in quartiles without any dose-response effect (data not shown).

The same calculations as in Table III were performed for subjects who had used only GSM or only NMT phone, and for subjects who had used both systems. No increased risk was found. Also use during leisure time or in occupations was analysed. The results were not changed thereby (data not shown).

In Table IV results are presented for different tumour types and localisations of the tumours. No increased risk was found for malignant or benign tumours. For temporal or occipital localisation of the tumour on the same side as exposure to microwaves (ipsilateral tumours), a somewhat increased risk was seen, however only for use of the NMT system. Of the cases 28% had used left ear, 57% right ear and 15% both left and right ear during calls with a cellular

Table IV. Odds ratio (OR) and 95% confidence interval (CI) for exposure to cellular phone according to histopathological type of brain tumour and tumour localisation in relation to ear (side) used for cellular phone. Latency period >1 year.

|                           | Cases | OR   | CI        |
|---------------------------|-------|------|-----------|
| Right brain               | 37    | 1.08 | 0.65-1.82 |
| Right ear                 | 25    | 1.28 | 0.68-2.38 |
| Left brain                | 27    | 0.76 | 0.42-1.38 |
| Left ear                  | 9     | 0.74 | 0.28-1.91 |
| Temporal localisation     | 23    | 1.55 | 0.79-3.04 |
| Right side + right ear    | 8     | 3.03 | 0.88-10.4 |
| Left side + left ear      | 3     | 1.55 | 0.21-11.3 |
| Temporal or occipital*    | 25    | 1.47 | 0.78-2.77 |
| Right side + right ear    | 8     | 2.45 | 0.78-7.76 |
| NMT (ever)                | 7     | 2.56 | 0.72-9.12 |
| GSM (ever)                | 3     | 1.23 | 0.26-5.75 |
| Left side + left ear      | 5     | 2.40 | 0.52-10.9 |
| NMT (ever)                | 5     | 2.10 | 0.46-9.57 |
| GSM (ever)                | 1     | 0.78 | 0.07-8.88 |
| All malignant             | 53    | 0.98 | 0.63-1.50 |
| Right side + right ear    | 21    | 1.43 | 0.70-2.90 |
| Left side + left ear      | 6     | 0.58 | 0.17-1.92 |
| Astrocytoma, glioblastoma | 36    | 1.09 | 0.64-1.84 |
| Right side + right ear    | 13    | 1.30 | 0.54-3.13 |
| Left side + left ear      | 3     | 0.35 | 0.07-1.81 |
| All benign                | 22    | 1.00 | 0.50-2.01 |
| Right side + right ear    | 4     | 0.78 | 0.18-3.31 |
| Left side + left ear      | 3     | 1.33 | 0.27-6.56 |
| Meningioma                | 16    | 1.05 | 0.49-2.27 |
| Right side + right ear    | 3     | 0.92 | 0.20-4.16 |
| Left side + left ear      | 3     | 1.45 | 0.26-8.10 |

\*Temporoparietal tumour localisation included.

telephone. The corresponding frequencies for the controls were 30%, 61% and 9%.

In the study 13 cases were diagnosed with acoustic neurinoma. Exposure to cellular phones yielded OR = 0.78, CI = 0.14-4.20; 5 exposed cases. Of these only one case had the tumour on the same side as exposure to microwaves.

In Table V the cases with brain tumour in the temporal or occipital lobe and exposure to cellular phone on the same

Table V. Presentation of cases with brain tumour in temporal or occipital lobe (temporoparietal localisation included) and exposure to mobile phone on the same side. Tumour induction time for exposure is given.

| Age | Sex    | Histopathology    | Exposure<br>hours | Induction<br>time<br>(years) |
|-----|--------|-------------------|-------------------|------------------------------|
| 24  | Female | Meningioma        | NMT, 48           | 2-1                          |
| 31  | Female | Mixed glioma      | NMT, 112          | 8-4                          |
| 32  | Female | Astrocytoma       | NMT, 80           | 3-1                          |
| 37  | Female | Meningioma        | NMT, 568          | 11-3                         |
|     |        |                   | GSM, 136          | 3-1                          |
| 39  | Male   | Mixed glioma      | NMT, 80           | 2-1                          |
| 41  | Male   | Glioblastoma      | NMT, 16           | 4-1                          |
| 49  | Female | Glioblastoma      | NMT, 24           | 2-1                          |
| 52  | Female | Mixed glioma      | NMT, 408          | 3-1                          |
| 52  | Male   | Oligodendroglioma | NMT, 1064         | 14-1                         |
|     |        |                   | GSM, 240          | 4-1                          |
| 54  | Male   | Malignant, NUD    | NMT, 240          | 5-1                          |
| 55  | Female | Glioblastoma      | NMT, 120          | 4-1                          |
| 58  | Female | Oligodendroglioma | GSM, 136          | 3-1                          |
| 60  | Male   | Meningioma        | NMT, 104          | 14-10                        |
|     |        |                   | GSM, 88           | 2-1                          |

side are presented. Of the 13 tumours 10 were malignant. One case was exposed to GSM only. However, some of the cases had only few hours of exposure in total and short tumour induction time.

### Discussion

Recall bias may always influence the results in a case-control study with assessment of exposure by the use of questionnaires. However, the finding of increased risk only for NMT cellular telephones and tumour localisation in the anatomical area with highest exposure strongly indicates that recall bias had no major influence on the results in this study. Furthermore, ionising radiation is an established risk factor for brain tumours and was also found in this study to increase the risk (Hardell *et al.*, unpublished data).

Validation of exposure to cellular phones from telephone companies would have been desirable. However, it turned out to be impossible to get such data. Exposure was assessed by questionnaires in which also information on occupations and exposures to different agents were asked for. Thus the purpose of the investigation was blurred for the study subjects. All phone interviews and coding of the data were made blinded in order to minimise observational bias. Only living cases that were judged to be able to answer the questionnaire were included so as to get as high data quality as possible.

In this study we did not find an overall increased risk for brain tumours associated with exposure to cellular phones. The results were similar both for the analogue and digital system. No dose-response effect could be seen or any effect of tumour induction time.

A non-significantly increased risk for brain tumours located in the temporal or occipital lobe was found for persons who had used a cellular phone on the same side of the head, i.e., a tumour in the area with highest exposure. Increased risk was found both for right and left sided brain tumours with such exposure. The results were based on low numbers and must be interpreted with caution. It would have been desirable to combine left and right sided tumours in the analysis. However, exposure for the controls can not be grouped in that way since tumour localisation is an outcome, not an exposure and thus present only for the cases. Most of these cases were exposed to the NMT system and increased risk was found only for such use. However, few subjects had used the GSM system and the tumour induction period is still short since the digital system was introduced in the early 1990's. It should be noted that analogue telephones have at least three times higher output power than digital phones.

Acoustic neurinoma develops in an anatomical area with comparatively high exposure to microwave radiation from a mobile phone. However, we did not find any association in this study.

We analysed also different occupations and exposure to various agents as risk factors for brain tumours. These findings will be presented separately. The present results were not confounded by such other exposures.

Certainly further research should aim at investigations of the risk, if any, for brain tumours in the anatomical area closest to the ear used for a cellular phone.

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