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Medical exposure to ionising radiation and the risk of brain tumours: Interphone study group, Germany

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ABSTRACT

Background: The role of exposure to low doses of ionising radiation in the aetiology of brain tumours has yet to be clarified. The objective of this study was to investigate the association between medically or occupationally related exposure to ionising radiation and brain tumours.

Methods: We used self-reported medical and occupational data collected during the German part of a multinational case–control study on mobile phone use and the risk of brain tumours (Interphone study) for the analyses.

Results: For any exposure to medical ionising radiation we found odds ratios (ORs) of 0.63 (95% confidence interval (CI) = 0.48–0.83), 1.08 (95% CI = 0.80–1.45) and 0.97 (95% CI = 0.54–1.75) for glioma, meningioma and acoustic neuroma, respectively. Elevated ORs were found for meningioma (OR 2.32, 95% CI: 0.90–5.96) and acoustic neuroma (OR 6.45, 95% CI: 0.62–67.16) for radiotherapy to the head and neck regions.

Conclusion: We did not find any significant increased risk of brain tumours for exposure to medical ionising radiation.

1. Introduction

The association between brain cancer risk and exposure to ionising radiation, especially high exposures at high dose rates, has been well researched. Most of the evidence is based on studies on Hiroshima and Nagasaki atomic-bomb-survivors and on individuals treated with radiotherapy for tinea capitis as children.

Preston and colleagues found a significant dose-related excess of nervous system tumours in the atomic-bomb survivors, with the highest risk coefficient being for schwannoma.[1] They also found non-significant increases for meningioma, glioma, other nervous system tumours and pituitary gland tumours. There were some differences between males and females, and persons exposed during childhood had higher risks than those exposed during adulthood.

Epidemiological studies of persons who received radiation treatment to the scalp during childhood found an increased risk of malignant and benign intra-cranial tumours.[2–7] The excess risk for malignant tumours decreased with increasing age at irradiation.[4–6] Ron and colleagues found a strong dose–response relationship for the number of radiation treatments

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and level of exposure.[4] Persons having more than one treatment or exposures above 2.0 Gy (Gray) had a 20-fold increased risk for all head and neck tumours. The excess risk for exposed persons was highest for nerve sheathes tumours, intermediate for meningioma and lowest for glioma. Furthermore, in a pooled analysis of 2 Swedish cohorts of infants irradiated for skin haemangioma, a dose–response relationship between absorbed dose in the brain and the risk of developing intracranial brain tumours was found.[8] The risk was highest among infants exposed before the age of 5 months.

The role of low doses of ionising radiation in the aetiology of brain tumours is less clear. Medical ionising radiation is the largest man-made source of radiation exposure for populations.[9] Low doses of ionising radiation are used for diagnosis (X-rays, scans, scintigraphy) as well as for treatment. For example, the effective dose for the head region is estimated to be 0.03–0.20 mSv from a skull X-ray and 2.0–2.6 mSv from a skull computed tomography (CT).[10]

A possible association between dental radiological examinations, especially full-mouth X-ray examinations, and the risk of intra-cranial tumours has been suggested. Preston-Martin and colleagues found an increased risk of meningioma in women who had at least one full-mouth X-ray examination before 1945 (odds ratio (OR) = 4.0, $p < 0.01$), or before the age of 20 years (OR = 2.1, $p = 0.03$).[11] The authors observed similar results in a later study on men who had radiation treatment to the head before the age of 20 years (OR = 7.0, $p = 0.04$).[12] In another population based case–control study of incident brain tumours in adults, Ryan and colleagues found a possible increased risk for meningioma in males exposed to dental X-rays, but not in women.[13] Furthermore, they found a decreased risk for glioma associated with diagnostic X-rays (OR = 0.42). Rodvall and colleagues confirmed the results of an association between diagnostic dental X-rays and meningioma (OR = 2.1); however, their results were based on small numbers.[14] Longstreth and colleagues observed an association between dental X-rays and increased risk for intra-cranial meningioma for participants with 6 or more full-mouth series (OR = 2.06).[15] No statistically significant increased risk was observed for posterior bitewing examinations, panoramic or lateral cephalometric views.

Occupational exposure to ionising radiation has been studied in many settings such as nuclear power workers or radiologists. The results for brain tumours are, however, not very consistent, mainly as low numbers of cases are observed in each of the single studies.[16–18] None of the studies report an increased risk for brain tumours.

Recently, Philips and colleagues assessed the association between meningioma and ionising radiation in occupational and medical settings in a population-based case–control study and found no significant associations for diagnostic or occupational exposures.[19]

While a pathogenetic mechanism for ionising radiation is established as a tumour initiator by DNA damaging, no mechanism is known for biological effects from exposure to non-ionising radiation at levels lower than the protection guidelines.[20] However, one can theoretically speculate about a promoting effect of radio frequency/electromagnetic fields (RF-EMF) following a tumour initiation by exposure to ionising radiation. Studies investigating such synergistic effects of previous ionising radiation followed by RF-EMF are scarce. In an animal study with CBA/S mice, Heikkinen and colleagues did not find an increase of the incidence of any neoplastic lesions using different exposure models.[21] Several laboratory studies using low-frequency EMF or magnetic field exposure after ionising radiation also did not show conclusive effects.[21–23] In a military cohort study, Grayson observed no evidence that extremely low frequency EMF acts as a brain tumour promoter following ionising radiation exposure.[24]

In this paper, we report results from the German part of an international case–control-study on brain tumours (the so-called Interphone study) of the association between exposure to medical or occupational ionising radiation and risk of brain tumours. Additionally, we investigate the interaction between exposure to ionising radiation and radio frequency electromagnetic fields as emitted from mobile phones, in order to examine a possible joint effect.

2. Materials and methods

The Interphone study is a multi-national population based case–control study that was conducted using an international core protocol.[25] The study in Germany was conducted in the urban and rural areas surrounding the cities of Bielefeld, Mainz, Heidelberg and Mannheim, covering approximately 6.6 million inhabitants. The study was approved by the ethical commissions of the states to which these four cities belong.

2.1. *Study population*

The study population selection process for the German Interphone Study has been described elsewhere.[26,27] Briefly, patients diagnosed with incident glioma, meningioma or acoustic neuroma and admitted to one of the four neurosurgical clinics in the above-mentioned cities between October 15, 2000 and October 31, 2003 were eligible. According to the international study protocol, patients had to be 30–59 years of age on the date of diagnosis. However, in Germany, from October 1, 2001, as additional funding was obtained, patients aged 60–69 years were also included. Only patients with histological confirmation of their diagnoses, with sufficient knowledge of the German language to perform the interview and with main residency within the study region were eligible. The following types of brain tumours (*International classification of diseases for oncology*, third edition) were included: for glioma topography codes C71.0–C71.9 and morphology codes 9380–9383, 9390–9393, 9400–9401, 9410–9411, 9420–9421, 9424, 9440–9442 and 9450–9451; for meningioma topography code C70.0 and morphology codes 9530–9539; and for acoustic neuroma topography codes C72.4/D33.3 and morphology code 9560/0.

Controls were randomly selected from the compulsory population registries in the study area. They were drawn according to the gender, age and regional distribution of the eligible cases. Persons were excluded if their main residence was not within the study region, or if they did not have sufficient knowledge of the German language.

The participation rates were above 80% for all case groups and above 60% for controls. Post hoc individual 1:2 matching

by gender and age group (±2 years) was performed prior to the data-analyses to ensure that cases and their matched controls had the same exposure windows. As a result, 49 controls had no individual matching partner and were excluded.

2.2. Data collection

Cases and controls were personally interviewed by trained interviewers using the computer assisted personal interview system (CAPI) developed for the International study. Most cases were interviewed during their hospital stay whilst most controls were interviewed at home. Proxy interviews were conducted where a case or control was too ill to be interviewed or had died. A total of 52 proxy interviews were conducted; 40 for glioma cases, 5 for meningioma cases, 1 for acoustic neuroma case and 6 for controls (Table 1). The following information was collected: demographic characteristics, cellular phone use habits (make and model of phone, as well as frequency and duration of use), use of transmitters and ham radios, smoking habits, medical histories including diagnostic X-ray examinations and radiotherapy treatments as well as occupational activities, especially those related to EMF and ionising radiation.

2.3. Medical and occupational ionising radiation exposure assessment

During the interviews, we collected information on diagnostic X-ray examinations (including panorama/full mouth series) and radiotherapy treatments of the head and neck regions. The CAPI included questions on plain X-rays of the head and the teeth, CT scans, scintigrams and angiographies. Efforts were made to establish detailed information of lifetime exposure. Each examination was thus characterised by the year it was performed, the anatomical region concerned, the reason as to why the examination was performed and the frequency of examinations or treatment sessions. To check for plausibility, each reported examination was compared with the reason given for the procedure(s). In a few cases the reported information was corrected. Individuals who had had X-rays of individual teeth only were classified as not exposed.

Only exposures that had occurred two years before the date of diagnosis (cases) or reference date (date of diagnosis for matched case: controls) were taken into account.

The participants were grouped into three exposure categories according to the following criteria (If they fell into more than one category, the highest one was chosen):

- at least one plain X-ray of the head (including panorama/full mouth series, but not X-rays of single teeth) and neck;
- at least one CT, scintigram or angiography of the head and neck;
- at least one radiotherapy session.

They were furthermore grouped according to their age at first exposure to medical ionising radiation ($\leqslant$25 years or >25 years).

Occupational exposure to ionising radiation was also assessed in the interview. More than 2/3 of the 91 occupationally exposed participants were in the medical field (physicians, nurses, radiographers). Amongst the exposed professions were also engineers and soldiers. Only occupational exposures of a minimum of one year's duration which had occurred at least a minimum of two years before the reference date were considered.

2.4. Radio frequency electromagnetic radiation exposure assessment

Information on self-reported cellular phone use and on occupational histories was used as a basis for the assessment of exposure to RF-EMF. Participants who reported a mobile phone use of at least one call per week for 6 months or more were defined as regular users (see Schüz and colleagues[26]). Self-reported job activities of the participants were categorised by experts as sources of exposure to RF-EMF (see Berg and colleagues[27]). For the analysis here, only basic information on RF-EMF exposure was used to examine the possible interaction between ionising radiation and RF-EMF exposure.

Table 1 – Participation rates for the German part of the Interphone case–control study on cellular phone use and risks of brain tumours, 2000–2003

	Eligible	Participants	Participation rate (%)	Included in analysis[a]	
				Self-reported	Proxies
Cases					
Glioma	460	366	79.6	326	40
Meningioma	431	381	88.4	376	5
Controls					
Glioma and meningioma	2499	1535	62.7	1488	6
Acoustic neuroma					
Cases	109	97	89.0	96	1
Controls	368	202	54.5	194	0

a Post hoc 1–2 matching was done after data collection. As a result 49 controls, for which no partner could be found, were excluded from the analysis.

2.5. Statistical analysis

The data were analysed using SAS software, version 9.1 (SAS Institute, Inc., Cary, North Carolina). Initially, the study population was described according to the following demographic characteristics: gender, age, study centre, socio-economic status and urban/rural resident and smoking status. All analyses were performed separately for each tumour type (glioma, meningioma and acoustic neuroma). Multiple conditional logistic regression analysis was used to estimate odds ratios and their 95% confidence intervals. Medical exposure was analysed as a categorical variable (see above) while occupational exposure was coded as a binary variable (ever/never). For glioma and meningioma, the analyses were stratified by gender and study centre and adjusted for age at reference date (linear), socio-economic status (in three categories) and area of residence (urban/rural). For acoustic neuroma, the analyses were adjusted for centre and not stratified, as numbers in each centre were small. The adjustment was otherwise identical to that for the glioma and meningioma analyses.

For the investigation of a possible interaction between exposure to medical ionising radiation and RF-EMF at work or through the use of mobile phones, both ionising radiation and RF-EMF were each considered as binary variables and an interaction term was used in the logistic model. In sensitivity analyses, odds ratios for individually matched data as well as unadjusted odds ratios were estimated. The results showed minor differences from those of the main approach, so only the latter one is reported.

3. Results

The distribution of cases and controls according to age at reference date, study centre or area of residence did not show large variations (Table 2). For all three tumour types a higher proportion of cases than of controls reported a low socio-economic status. The risk estimation according to exposure to medical ionising radiation is shown in Table 3. Of the 2532 participants, 1868 were reported to have had at least one radiological examination of the head/neck region (600 cases and 1268 controls). Among exposed controls, 30.9% reported first exposure before or at the age of 25, and 69.1% after the age of 25 years. For any exposure to medical ionising radiation, including proxies, odds ratios (ORs) of 0.62 (95% CI = 0.47–0.82), 1.07 (95% CI = 0.80–1.44) and 0.94 (95% CI = 0.53–1.67) were found for glioma, meningioma and acoustic neuroma, respectively. The results did not change when age at first exposure was used as a further subdivision. Results also did not differ when proxy interviews were excluded from the analysis (data not shown).

A total of 917 participants had at least one plain X-ray of the head/neck region, including panoramic views; 916 had at least one CT scan of the head and neck, angiography of the head/neck blood vessels or a thyroid scintigram; and 35 had at least one radiotherapy session of the head/neck region (Table 4). No increased ORs were found with respect to all brain tumour types for participants who reported plain X-rays of the head/neck. For gliomas and acoustic neuromas, no increased ORs were observed for those who reported at least one CT scan, angiography or scintigraphy. A slightly increased risk was, however, seen with respect to meningioma. ORs for meningioma and acoustic neuroma were increased for at least one radiotherapy session, but risk estimates were based on small numbers.

A total of 91 participants reported occupational exposure to ionising radiation, mostly due to employment in medical occupations. For glioma and meningioma the proportion of cases and controls was very similar, whilst for acoustic neuroma the proportion of cases occupationally exposed was larger. No increased risk after occupational exposure to ionising radiation was observed for glioma and meningioma. An increased risk was observed for acoustic neuroma: OR = 2.49 (95% CI: 0.74–8.38). The confidence interval was, however, very wide and the estimate did not significantly differ from unity.

No statistically significantly increased interaction between exposure to medical and occupational ionising radiation and exposure to RF-EMF at work or through mobile phone use was seen (Table 5).

4. Discussion

Data from a large population-based case–control study were used to evaluate the association between low dose exposure to ionising radiation due to medical exposures of the head and neck regions as well as occupational exposure.

We found no clear association between diagnostic medical or occupational exposure to ionising radiation and meningioma or acoustic neuroma risk. For glioma, an unexplained statistically significant decreased risk following medical exposure to diagnostic ionising radiation was found. Following radiotherapy to the head and neck region, elevated odds ratios were observed for meningioma and acoustic neuroma, but not for glioma. These results are based on small numbers and should be interpreted with care. Further classifying participants according to the number of X-ray examinations did not reveal any trend (data not shown). We also found no interaction between exposure to medical or occupational exposure to ionising radiation and RF-EMF exposure at work and through mobile phone use, for brain tumour risk.

There are some major limitations in evaluating the effects of low dose radiation exposure in a case–control study. Our assessment of exposure to medical ionising radiation was based on self-reported information. Participants were asked about details such as reasons and dates of specific procedures. Some plausibility checks could be made, but information bias as well as recall bias could have influenced the results. Furthermore, proxies certainly had only limited knowledge on the exposure accrued by the study subjects. Excluding proxy information may have lead to selection bias as this affects only very ill persons and basically only glioma cases. However, analyses with and without proxies yielded very similar results. In consequence, we based our analyses on the ever/never statements of the participants only, and not on the reported numbers of images. It also has to be noted that radiation doses may vary substantially even for the same procedure, and has certainly decreased over the last years. The use of better technology such as digital

Table 2 – Participants' demographic characteristics and reported ionising radiation exposure (%)

	Glioma		Meningioma		Acoustic neuroma	
	Cases (n = 366) %	Controls (n = 732) %	Cases (n = 381) %	Controls (n = 762) %	Cases (n = 97) %	Controls (n = 194) %
Gender						
Male	59.0	59.0	27.0	27.0	52.6	52.6
Female	41.0	41.0	73.0	73.0	47.4	47.4
Age group (years)						
⩽39	16.4	16.7	10.2	10.1	22.7	21.1
40–49	22.7	23.6	20.5	21.8	23.7	24.2
50–59	30.9	28.6	34.9	34.0	25.8	24.7
⩾60	30.1	31.1	34.4	34.1	27.8	29.9
Study centre						
Bielefeld	27.3	27.7	26.0	26.8	14.4	13.9
Heidelberg/Mannheim	48.9	47.7	50.7	48.4	33.0	32.5
Mainz	23.8	24.6	23.4	24.8	52.6	53.6
Radiation exposure[a]						
Medical						
Never[b]	36.1	26.4	22.8	23.8	25.8	23.7
Ever	63.9	73.6	77.2	76.2	74.2	76.3
Occupational[c]						
None	95.6	95.1	97.6	97.6	93.8	96.9
Yes	4.4	4.9	2.4	2.4	6.2	3.1
SES[d]						
Low	7.1	4.8	9.7	7.1	6.2	4.1
Average	59.3	59.2	62.5	59.4	66.0	55.2
High	33.6	36.1	27.8	33.5	27.8	40.7
City resident[e]						
No	74.9	77.6	73.5	77.4	75.3	73.2
Yes	25.1	22.4	26.5	22.6	24.7	26.8
Smoking status						
Never smoker	46.2	41.1	50.4	48.7	59.8	41.8
Ex-smoker[f]	26.2	28.7	25.5	26.5	27.8	30.4
Current smoker	27.6	30.2	24.2	24.8	12.4	27.8

Interphone study, Germany, 2000–2003.
a Only participants with exposure at least two years before brain tumour diagnosis.
b Participants who reported individual dental X-ray examinations only were classified as never exposed.
c At least 1 year's exposure.
d Socio-economic status based on the highest school qualification and the highest level of occupational or academic training (see Schüz et al.[26]).
e City defined as having ⩾100 000 inhabitants.
f Defined as not having smoked at least two years before reference date.

machines, fast speed radiographic films and better techniques have contributed substantially to dose reduction.[28,29] Therefore the number of diagnostic procedures is a crude measurement for actual radiation exposure. Poppe and colleagues carried out a survey of 50 panoramic and 60 intraoral X-ray units and found large difference between doses of different X-ray units for the same examination. For maxillary molar examinations for example, they measured dose area products (DAP) ranging from 3.8 to 134.8 mGy cm.[2] For non-digital systems, the lowest dose measured was 17.4 mGy and the maximum was 134.8 mGy.[30,31] In the 1940s and 1950s, radiation exposure to the skin from a full mouth series was estimated to be 1000–3000 mGy and by 1993 it decreased to about 40 mGy. The reduction in radiation dose is due to improvements in technology and practice. For dental radiography the use of rectangular instead of circular collimation also serves to reduce skin radiation exposure.[28–30] We therefore did not calculate the exposure in mSv based on the self-reported data.

Our study, like most case–control studies, was liable to recall bias. The questionnaire used was quite long and extensive. Participants were not only asked about their medical histories, they also had to answer questions on past and current mobile phone use as well as on occupational history. The section on medical and occupational history made up the last part of the comprehensive questionnaire. Mainly glioma patients may have had problems in answering these extensive questions.

Another limitation common in case–control studies is selection bias. The response rates for cases and controls differed considerably (84.4% and 60.6%, respectively). We performed a non-responder analysis (see Schüz et al.[26]) and

Table 3 – Distribution of exposure to medical and occupational ionising radiation[a] (categorised according to age at first exposure and occupational exposure) and risks of brain tumours (Interphone study, Germany, 2000–2003)

	Glioma				Meningioma				Acoustic neuroma			
	Cases (n = 366)	Controls (n = 732)	OR[b]	95% CI	Cases (n = 381)	Controls (n = 762)	OR[b]	95% CI	Cases (n = 97)	Controls (n = 194)	OR[b]	95% CI
Medical exposure												
Never[c]	132	193	1.00		87	181	1.00		25	46	1.00	
Ever[d]	234	539	0.62	0.47–0.82	294	581	1.07	0.80–1.44	72	148	0.94	0.53–1.67
First exposure at age ⩽ 25 years	69	190	0.50	0.35–0.74	86	159	1.19	0.81–1.75	23	43	1.05	0.49–2.23
First exposure at age > 25 years	165	349	0.67	0.50–0.91	208	422	1.04	0.76–1.41	49	105	0.84	0.45–1.57
Occupational exposure[e]												
No	350	696	1.00		372	744	1.00		91	188	1.00	
Yes	16	36	0.99	0.54–1.84	9	18	1.05	0.46–2.42	6	6	2.49	0.74–8.38

a Only participants with exposure at least two years before brain tumour diagnosis.
b Odds ratios from conditional logistic analysis for frequency-matched data sets, stratified by gender and study centre and adjusted for age, SES and living in an urban area. For acoustic neuroma, stratification was done for gender but not for study centre.
c Participants who reported individual dental X-ray examinations only were classified as never exposed.
d Ever exposed participants were those who reported at least one plain X-ray, CT scan, angiography or one radiotherapy session of the head and neck region (including panoramic view of the mandible/maxilla), or thyroid scintigraphy at least two years before brain tumour diagnoses.
e At least 1 year's exposure.

Table 4 – Distribution for specific medical exposure to ionising radiation[a] and risks of brain tumours

	Glioma				Meningioma				Acoustic neuroma			
	Cases (n = 366)	Controls (n = 732)	OR[b]	95% CI	Cases (n = 381)	Controls (n = 762)	OR[b]	95% CI	Cases (n = 97)	Controls (n = 194)	OR[b]	95% CI
Medical exposure												
Never[c]	132	193	1.00		87	181	1.00		25	46	1.00	
Ever[d]	234	539	0.62	0.47–0.82	294	581	1.07	0.80–1.44	72	148	0.94	0.53–1.67
At least one plain X-ray examination (including panoramic view)[e]	122	298	0.58	0.42–0.80	112	269	0.87	0.62–1.23	36	80	0.84	0.44–1.60
At least one CT scan, angiography or scintigraphy[f]	109	232	0.67	0.48–0.93	172	303	1.22	0.88–1.68	33	67	0.90	0.46–1.76
At least one radiotherapy session	3	9	0.45	0.12–1.70	10	9	2.32	0.90–5.96	3	1	6.45	0.62–67.16

Interphone study, Germany, 2000–2003.
a Only participants with exposure at least two years before brain tumour diagnosis.
b Odds ratios from conditional logistic analysis for frequency-matched data sets, stratified by gender and study centre and adjusted for age, SES, living in an urban area and occupational exposure for ionising radiation. For acoustic neuroma, stratification was done for gender but not for study centre.
c Participants who reported individual dental X-ray examinations only were classified as never exposed.
d Ever exposed participants were those who reported at least one plain X-ray, CT scan, angiography or one radiotherapy session of the head and neck region (including panoramic view of the teeth), or thyroid scintigraphy at least two years before brain tumour diagnoses.
e Excluding CT, Angiography, Scintigraphy or Radiotherapy.
f Excluding radiotherapy and plain X-ray.

Table 5 – Interaction of radio frequency exposure through occupation or mobile phone use, medical and occupational exposure to ionising radiation[a] and risks of brain tumours

	Glioma				Meningioma				Acoustic neuroma			
	Cases (n = 366)	Controls (n = 732)	OR[b]	95% CI	Cases (n = 381)	Controls (n = 762)	OR[b]	95% CI	Cases (n = 97)	Controls (n = 194)	OR[b]	95% CI
(Reference group) no exposure to RF radiation/no exposure to medical ionising radiation	85	122	1.00		59	127	1.00		18	29	1.00	
No exposure to RF radiation/exposure to medical ionising radiation at:												
⩽25 years	34	89	0.52	0.32–0.86	50	89	1.28	0.79–2.07	11	15	1.19	0.43–3.25
>25 years	99	203	0.69	0.47–1.00	155	288	1.19	0.82–1.71	31	67	0.76	0.36–1.59
RF radiation exposure/no exposure to medical ionising radiation	47	71	0.96	0.60–1.54	28	54	1.14	0.65–2.02	7	17	0.65	0.21–2.02
RF radiation exposure/exposure to medical ionising radiation at:												
⩽25 years	35	101	0.47	0.29–0.79	36	70	1.15	0.67–1.98	12	28	0.73	0.28–1.92
>25 years	66	146	0.64	0.42–0.96	53	134	0.87	0.55–1.37	18	38	0.73	0.31–1.74
Occupational exposure[c]	16	36	1.01	0.55–1.88	9	18	1.07	0.47–2.44	6	6	2.53	0.76–8.37

Interphone study, Germany, 2000–2003.

a Only participants with exposure at least two years before brain tumour diagnosis.

b Odds ratios from conditional logistic analysis for frequency-matched data sets, stratified by gender and study centre and adjusted for age, socio-economic status and living in an urban area (see Section 2). For acoustic neuroma, stratification was done for gender but not for study centre.

c Multiple assessment possible.

discovered some differences between cases and controls regarding mobile phone use. Whether and in which direction this may also influence the exposure to ionising radiation remains unclear.

Although several studies have found an increased risk for brain tumours, especially in meningioma, after high exposure during childhood as a treatment for tinea capitis,[4–7] results after exposure to lower doses are not consistent. The majority of studies in which subjects were exposed to similar radiation dose levels as in our study are primarily on diagnostic dental radiology. Increased risks of brain tumours following medical exposure to diagnostic ionising radiation have been found in some studies,[11–15] but we could not confirm these observations. We did find a (even significantly) decreased risk for glioma after exposure to diagnostic procedures which is not consistent with most other studies. Chance or recall bias may explain these results. However, it should also be taken into consideration that the exposure to ionising radiation is very small and effects may be produced by unknown confounding variables.

Regarding radiotherapy of the head and neck region, our results for meningioma are comparable to those found by Hardell and colleagues[32] and Phillips and colleagues.[19] It should, however, be noted that the numbers of subjects in all these three studies are small. Finally, we did not find an association between the interaction of RF-EMF and ionising radiation exposure and brain tumour risk. However, it has to be taken into account that both exposures are low and their assessment may be prone to error. Additionally, the statistical power to estimate interaction is small and further subdivisions seem not to be adequate. A planned pooled analysis of the medical and professional ionising radiation data collected by all Interphone study partners will circumvent the problem of small numbers of participants.

In summary, we did not find an increased risk of any brain tumour type with exposure to ionising radiation during medical diagnostic procedures. With regard to high doses of ionising radiation during therapeutic procedures, there was a statistically non-significant increased risk for meningioma and acoustic neuroma. Due to the large uncertainty of the risk estimates, this has to be confirmed by future studies.

Conflict of interest statement

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