

## RESEARCH ARTICLE

# Changes in Brain Glioma Incidence and Laterality Correlates with Use of Mobile Phones – a Nationwide Population Based Study in Israel

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### Abstract

**Introduction:** Mobile phones are in extensive use worldwide and concerns regarding their role in tumor formation were raised. Over the years multiple studies were published in order to investigate this issue using several approaches. The current study looks at secular trends of brain gliomas (low and high grade) incidence and changes in tumor's laterality over 30 years in a population extensively using this technology with a possible correlation to the spread of use of mobile phones. **Materials and Methods:** All brain gliomas that were diagnosed from 1980-2009 were included and subdivided into two groups - low and high grade. Secular and periodic time trend analyses of incidence rates and changes in laterality were performed. Preferred side of head using mobile phones was assessed with a questionnaire in a sample of adult individuals. **Results:** A decrease in incidence of low grade gliomas (LGG) that correlated with introduction of mobile technology was found from 2.57, 2.34 and 2.79 for every 100,000 in the period 1980 to the end of 1994 to 1.72, 1.82 and 1.57, respectively, over the last three 5-years periods (1995-2009). High-grade glioma incidences increased significantly from 1980-2009 but in the period after mobile phones were introduced (1994-2009) a lower, non significant, rate of increase was observed in males and a lower one (significant) in females. A shift towards left sided tumor location for all adult gliomas combined and separately for LGG and HGG was noted from 1995 onward. The shift was more marked for those who were diagnosed in ages 20-49 ( $p=0.03$ ). **Conclusions:** We found a statistically significant decrease in LGG's over 30-years period that correlates with introducing of mobile phones technology and a shift in laterality towards left-sided tumors, the latter occurred in both low and high-grade gliomas.

**Keywords:** Brain tumors - glioma - grade - secular trend - incidence -laterality - mobile phones - Israel

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### Introduction

Mobile phones emitting low intensity radio frequency (RF) radiations are in extensive use worldwide with a steep increase over the last 15-20 years, with current estimate users of close to 5 billion. Concerns regarding the possibility of RF radiation associated health hazards; specifically tumor formation were raised soon after mobile phones use became prevalent. Over the years multiple studies were published in order to resolve this issue using several approaches: evaluating the ability of RF exposure lead to genetic and epigenetic alterations which may promote transformation of a normal cell into a malignant (or benign) tumor (Aalto et al., 2006; Khiat, 2006; Vecchio et al., 2007; Kaprana et al., 2008; Curcio et al., 2009; Gerner et al., 2010; Salama, 2010) Animal experiments to test the notion of a tumor promoting effects of RF radiation (Heimans et al., 1990; Special report to the Knesset on CT and MRI scanners, 2008; Luxemburg et al., 2010)

and human (case control or population-based) studies employing a retrospective approach trying to assess tumor rates and odds ratios (Primarily CNS tumors) by length of mobile phone use and tumor laterality (Lonn et al., 2005; Moulder et al., 2005; Milham, 2006; Takebayashi et al., 2006; Lahkola et al., 2007; Ahlbom et al., 2009; Myung et al., 2009; Saracci and Samet, 2010; The Interphone Study Group. Brain tumour risk, 2010). None of these studies could confirm a change in human cells than can be satisfactorily associated with malignant transformation, but some changes in neuronal activity of unknown clinical significance or biological implication were demonstrated (Aalto et al., 2006; Vecchio et al., 2007; Gerner et al., 2010; Lee et al., 2010). The case control human studies, some of which were flawed by to methodological issues (Han et al., 2009; Schüz, 2009; Vrijheid et al., 2009a: 2009b; Kundi, 2010; Aydin et al., 2011; Cardis, 2011) were for the most part inconclusive with some showing even a reduced risk for tumor formation in cell phone

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users (or “protective effect” in epidemiological terms) rather than an elevated risk (Ahlbom et al., 2009; Saracci and Samet, 2010; The Interphone Study Group Brain tumour risk, 2010; Frei et al., 2011). Moreover, those studies did not give a satisfactory level of evidence for the causal association needed between RF radiation and tumor formation or risk, as suggested by Sir Bradford Hill, (Hill, 1965) regarding biological plausibility, strength of association, consistency or biological gradient (dose response relationships).

The current study uses a different approach, looking at secular trends of brain gliomas (focusing on low grade gliomas) incidence and changes in tumor’s laterality over 30 years in Israeli population, that is one of the top user of mobile phones in terms of ownership and minutes of talks.

## Materials and Methods

We use the data of the Israeli National Cancer Registry (INCR) for the main analysis. All Brain Gliomas (ICD-O Ver.3 codes M938-948 and site code C71.0-C71.9) that were diagnosed in Israeli citizens from 1980-2009 were included. A detailed description of the INCR has been published elsewhere (Barchana, 2004) In brief, the INCR is a population-based central tumor registry established in 1960 and since 1982 reporting to the registry is mandatory (Statistical Abstract of Israel 2007, Number 58, 2008) The last audit of data completeness of malignant brain tumors concluded that registration was above 95% (Fishler et al., 2003). The INCR registers all data available on cancers using the International Classification of Diseases, Oncology (ICD-O) version-3 codes (SEER Program Self-Instructional Manual for Cancer Registrars, 1999).

At the INCR, upon a request of the late Prof. Baruch Modan (who first reported the association between scalp irradiation for Tinea Capitis treatment in the 1950’ of the last century and brain tumors - primarily meningioma (Werner, 1968; Modan, 1977a; 1977b; Ron, 1980; Ronet et al., 1988) laterality was a mandatory item for more than 30 years. Since not all Tinea Capitis irradiated individuals were identified to date, and previous exposure to that type of ionizing radiation could not be adequately excluded we did not include meningiomas in the current analysis. In the laterality analysis we included cases diagnosed from 1980-2008. Information regarding laterality is based on rich medical documentation, including hospital discharge forms, which are available for the registry during periodic updates several years after the incidence year. This is the basis of our decision to analyze laterality up to 2008 and explains differences in completeness of laterality data over the periods. Incidence rates of brain tumors (both benign and malignant) in Israel shows little variability between the Jewish sub-populations (based on place of birth, (Barchana, 2011)) and therefore we did not analyze changes by those categories.

Gliomas were subdivided according to their grade into two groups - low and high grade. Subdivision was made according the “The 2007 WHO Classification of Tumors of the Central Nervous System” (Louis et al., 2007) Histological grading is a means of predicting the biological

behavior of a neoplasm. The WHO classification includes a grading scheme that is a ‘malignancy scale’ ranging across a wide variety of neoplasms rather than a strict histological grading system (Kleihues and Cavenee, 2000).

Grade I and II applies to lesions with low proliferative potential or infiltrative tumors with a low-level proliferative activity. Due to the very limited number of cases in Grade I this group (several dozen in 30 years) was omitted from analysis and we actually used Grade II cases to represent the Low Grade Glioma’s (LGG) group. High-grade gliomas (grade III and IV by the WHO classification), is best represented by Glioblastoma Multiform that accounts for more than 40% of all gliomas.

We also looked at secular time trends in incidence and laterality for separate histological groups of Gliomas including Astrocytomas (ICD-O codes 9400/3-9384/1), Ependymomas (9393/1-9393/3), Medulloblastomas (9470/3-9506/1) and Gliomas (9380/3-9442/3). All codes are not continuous but define the morphology codes ranges.

We have also carried out a convenience sample survey among over 1,000 randomly selected Israeli adults (age 18 and above) regarding the side of head against which mobile phone was used. A voluntary based questionnaire was distributed in several work places and travelers’ clinics in all parts of the country. Responders were all adult subjects. The questionnaire included age, gender and a scale to describe the preferred side of use ranging from right, mostly right, both sides, mostly left or mobile phone use only in the left head side. Information on mobile phone use in the country was obtained from the ministry of communications (Cohen, 2010).

### Statistical analysis

Age-standardized incidence rates were computed per 100,000 of the population, standardized to the ‘World Standard Population’. The rates were computed for each grade, gender as well as for Israeli Jews and Arabs separately for each year of diagnosis and for six 5-years interval (1980-4, 1985-9, 1990-4, 1995-9, 2000-4, 2005-2009). This subdivision serves for detecting changes over the entire period and represents two periods prior to the massive penetration of mobile technology (1980-1994), and two others (2000-2009) when penetration rates were 100% and over. The Israeli population data, by age group and gender were retrieved from the Central Bureau of Statistics (Statistical Abstract of Israel 1980-2009, 2011). Trend analysis was computed by using linear regression. Tests of significance used confidence intervals of 95% and a significant result was obtained when the P value was less than 0.05.

We checked changes in laterality trends (excluding ICD-O codes C71.5 and C71.6 that are gliomas in the central part of the brain and thus can not be assessed for laterality) by calculating rate ratio using the number of events occurring in the right side of the brain against those in the left side by year of diagnosis and periods. Calculation was made for two 10-years periods and one 9-years period from 1980-2009 (1980-89, 1990-99 and 2000-2008) and significance of changes were tested.

Similar tests were applied for the 5-years periods. These calculations were performed for all gliomas, low and high-grade gliomas. The same statistical tests were applied here.

## Results

### *Incidence Trends*

For low grade gliomas (LGG) 5-years interval adjusted incidence rates in Jewish males were 2.57, 2.34 and 2.79 for every 100,000 from 1980 to the end of 1994 and decreased over the last three 5-years periods (1995-2009) to 1.72, 1.82 and 1.57 respectively. The same magnitude of decrease in incidence was observed for Jewish females (from adjusted incidence of 1.93, 1.72 and 1.78-1.38, 1.17 and 1.04 respectively of the 5-years periods spanning 1980-2009). The decrease in males was on average 30% and in females 35% between the 1980-1994 period compared with the 1995-2009 period. The numbers of cases among Israeli Arabs were low (2-23 cases in each 5 years period) and therefore were omitted from the analysis. It seems that gliomas in Arabs did not present the same changes in trends.

Analysis of the entire period from (1980-2009) showed that there was a significantly decreased incidence in LGG both for men (estimate parameter: -0.22, p-value=0.05) and women (estimate parameter: -0.19, p-value<0.001). For the period 1994-2009, an even sharper decrease was noted (-0.35, p-value=0.07 for men and -0.25, p-value=0.03 for women).

For high-grade gliomas (HGG), a constant increase in incidence rates was noted for the entire observation period. In males the ASR increased from 2.58/100,000 to 3.92, 4.12, 5.5, and 6.2 with a slight decrease to 5.7 in the last period (2004-2009). In females, high-grade glioma rates rose from 1.8 to 2.5, 3.3, 3.5, 3.8 to reach 4 new cases each 100,000 in 2005-2009. These changes reflect an increase of 65% in males and 50% in female.

In the longer period (from 1980-2009) there was a significant increase in incidence both for men (estimate parameter: 0.48, p-value=0.07) and women (estimate parameter 0.25, p=0.05). Changes in incidence for high-grade gliomas in the period after mobile phones were introduced (1994-2009) demonstrate a lower, non-significant rate of increase in males 0.007 and 0.13 (p=0.01) in females.

Analysis of all gliomas combined (5,263 cases) reveals an increased incidence from the 1980-1994 period to the 1995-2009 period by 25% in males and 12.5% in females, reflecting changes in HGG that constitutes 72% of all gliomas.

Analyzing specific brain gliomas incidence rates by morphology types from 1980-2009 (5-years periods) reveals the same pattern in Astrocytomas as for LGG where incidence trends sharply decreased from the period 1995-1999 compared to prior periods and remained at the low level in the two following periods. Astrocytoma's rates for Jewish males were 2.15, 2.1 and 2.35/100,000 in the first three periods respectively and dramatically decreased to 1.71, 1.59 and 1.46 from 1995-2009. The same pattern in incidence rates for Astrocytomas was observed for Jewish females (1.65, 1.58, 1.68 and than 1.21, 1.25 and

0.89 new cases for every 100,000 in 2005-2009). Only few Medulloblastoma and Ependymoma are located in the brain hemispheres. Incidence rates along the 30-years period were stable for Ependymoma (0.7, 0.1, 0.24, 0.14, 0.18 and 0.16/100,000, Male Jews) and increased for Medulloblastoma (0.01, 0.05, 0.1, 0.19, 0.16 and 0.17 new cases per 100,000 Jewish males).

### *Laterality*

All gliomas combined: A shift towards left sided tumor location noted for all adult gliomas combined from 1995 onward. Rate Ratios for right: left sidedness resulted in 1.08 from 1980-1989, 1.02 in the next 10-years period and 0.92 in the last periods (p value <0.01). Examining the 5-years periods, the average rate ratio was 1.07 from 1980-1994 (i.e. 7% more right-sided gliomas compared with left sided) and in the period encompassing 1995-2008 rate ratio changed to 0.94 (namely 6% more tumors were diagnosed in the left side). P-value was close to statistical significance (0.06). A further analysis of all-gliomas combined by age at time of diagnosis shows that there was a statistically significant shift from Right side to Left for those who were diagnosed in ages 20-49 (RR between the three ten years periods=0.89, p=0.03) and a slighter change in those 50 years and more at time of diagnosis (RR=0.95, non significant).

### *Low grade gliomas*

A similar pattern was observed for the low grade gliomas (LGG) where in the first 10-years period (1980-1989) right-sided tumors prevailed (RR=1.07) and in the second and third 10 and 9 years periods there was a significant change towards left (RR=0.92 and 0.93 respectively, p=0.04). Examining the 5-years period reveals a left sided tumors predominance at the beginning of the period (1990-1994) where rate ratios (right Vs. left) were 1.04 and 1.10 (denoting 4 and 10% more cases in the right hemisphere) and a shift towards left-sided tumors in each of the following periods (respective RR of 0.92, 0.92 and 0.93 in 2000-2004). This shift partially corresponds to the period when low-grade gliomas adjusted incidence rates dropped by 30%.

Overall there were 18.5% of cases where laterality was not registered, including bi-lateral cases (8% of them). Completeness of data was less in 2009 and therefore was not entered in analysis.

### *High grade gliomas*

A similar pattern of changes in laterality was observed for HGG as well. In the first 10-years period there were 8% more right-sided HGG, and similar results were in the following period (7%, 1990-1999). The last period in analysis (2000-2008) showed a shift versus left where an excess of 8% was noted in the left head side (p<0.01).

### *Laterality of using mobile phones*

The survey included 1,000 adult Israelis of which 52% males and 48% females. The majority, of the participants reported right hand dominance. 45% reported they use to talk using a mobile phone only on the right side of the head and 25% said they mostly the right side. 13%

**Table 1. Age Standardized Rates (ASR, World Standard Population) of gliomas by grade and 5-years incidence periods, Israeli Jews, 1980-2009**

Period of Incidence		Males		Females	
		No. of Cases	ASR/100,000	No. of Cases	AS/100,000
Low grade glioma (Grade II)	1980-1984	128	2.57	99	1.93
	1985-1989	120	2.34	98	1.72
	1990-1994	170	2.79	123	1.78
	1995-1999	126	1.72	116	1.38
	2000-2004	150	1.82	104	1.17
	2004=2009	149	1.57	101	1.04
Totals:		843		641	
High Grade gliomas (Grade III-IV)	1980-1984	130	2.58	98	1.77
	1985-1989	208	3.91	152	2.49
	1990-1994	260	4.08	234	3.29
	1995-1999	412	5.56	299	3.46
	2000-2004	536	6.21	400	3.81
	2004=2009	573	5.64	477	4.06
Totals:		2119		1660	
All Gliomas Combined	1980-1984	258	5.15	197	3.71
	1985-1989	328	6.26	250	4.2
	1990-1994	430	6.86	357	5.07
	1995-1999	538	7.28	415	4.45
	2000-2004	686	8.02	504	4.98
	2004-2009	722	7.21	578	5.1
Totals:		2962		2301	5263*

**Table 2. Laterality of Gliomas by grade and period of diagnosis, Adult Jewish population in Israel' 1980-2008**

Period	Right	Left	Not Paired	Unknown	Total cases	RR (Rt Vs. Lt)
LGG P=0.04						
1980-1989	186 45%	174 42%	11 3%	39 10%	410	1.07
1990-1999	169 34%	184 37%	5 1%	145 29%	503	0.92
2000-2008	152 35%	164 38%	7 2%	110 25%	433	0.93
Totals:	507	522	23	294 18.5%	1346	
HGG P<0.01						
1980-1989	235 41%	217 38%	11 2%	101 18%	564	1.08
1990-1999	386 33%	362 31%	32 3%	400 34%	1180	1.07
2000-2008	550 31%	599 34%	8 0%	609 34%	1766	0.92
Totals	1171	1178	51	1110 31%	3510	
All Gliomas P<0.01						
1980-1989	421 43%	391 40%	22 2%	150 15%	984	1.08
1990-1999	555 33%	546 32%	37 2%	545 32%	1683	1.02
2000-2008	702 32%	763 35%	15 1%	719 33%	2199	0.92
Totals:	1678	1700	74	1404 35%	4856	

\*LGG=Low Grade Gliomas, HGG=High Grade Gliomas, RR=Rate Ratio

stated alternating between both sides and the remaining 17% stated they used the phone on the left side (7.5%) or mostly on left (9.5%). Younger participants (ages 18-29) tended to use mobile phone on both sides more than the elder population (17% as opposed to 9% in the older users) but the overall use rate was predominantly on the right side of the head (68%).

*Mobile phone penetration*

Official data on mobile phone penetration (number of mobile phones per total population) are available since 1994, when all four providers serving the country were fully operating. In 1994, 2% of the population had a mobile

phone, within three years the penetration rate was 29% and 67% by year 2000 (corresponding to 4.2 million users). In 2003 penetration rates reached 100% and by the end of 2009, 9.6 millions phones were used by the countries' 7.5 million inhabitants yielding a penetration rate of 128%.

The actual penetration rates are probably higher than stated here. Of 7.5 Million citizens in Israel (Central bureau of statistics, 2008 Average) 2.1 millions (28%) are of ages 0 to 14 and did not own or regularly used mobile phones, at least during the first period of introduction of mobile technologies. Therefore corrected penetration rates (CrPR - number of mobile phones in the population age 15 and more) should be 3.5% in 1994, 36% in 1997, 57% in 1999 and 110% in 2001.

**Discussion**

In the current study a steep decline in the rate of low-grade gliomas over a 30-year period was demonstrated. Incidence of high-grade gliomas, that continuously increased from the 80's seems to slow down since the start of massive use of mobile phones and, though still increasing in incidence, the pace of increase diminished markedly and was not significant in men in the last period examined. Moreover, there was a shift in the anatomical location of brain tumors from predominantly right to more left sided located tumors, both for high and low grade tumors. These changes coincided with a sharp increase of mobile phone use in Israel and within 6 years from its introduction about 100% of adult population regularly use this technology. These observation addresses an important, large-scale health-related event with potential consequences in terms of cancer incidence and population behavior patterns.

While rates of brain cancer in general are rising in many modern societies over the past three or more decades, rates of Astrocytomas tend to decrease significantly (Wrensch et al., 2002; Hess, 2004) and in particular the low grade Astrocytomas (Houben et al., 2006). Most of the Low Grade Gliomas (LGG) are Astrocytomas, which explains the similarity of our finding to previous studies, but as an entity of Low-grade Gliomas, this group is of low proliferative potential and thus low penetrability was not generally explored. Moreover, laterality of tumors was assessed only in case-control based studies that are prone for biases due to misclassifications, selection or recall biases (Han et al., 2009; Schüz, 2009; Vrijheid et al., 2009a; 2009b; Kundi, 2010; Aydin et al., 2011; Cardis, 2011). Indeed, laterality is a key requirement in order to establish a causal association between exposure (RF radiation in this case) and outcome (CNS tumors). Results from the largest multi center multinational study published to date show a reduced OR in all categories of use for gliomas; and even the OR for ≥10 years since start of use was 0.98 (95%CI 0.76-1.26). As for laterality, the OR for temporal lobe tumors with regular use was 0.86 (95%CI 0.66-1.13) and only for the highest decile of cumulative call time was the OR for temporal lobe tumors appreciably elevated (1.87, 95%CI 1.09-3.22) and no dose-response effect preceded this observation (The Interphone Study Group. Brain tumour risk, 2010) Changes in diagnostic

techniques over time (CT scans and MRI) can play a role in the changing incidence of gliomas in general in both senses. A more accurate diagnosis can shift cases from being categorized as brain tumor to one of the glioma types and vice-versa (Heimans et al., 1990). Laterality is less prone to be influenced by those changes because it is calculated as the proportion of all gliomas detected and not as a part of entire brain tumors. Moreover, for assessment of laterality even a less advance imaging machines can be sufficient. Number of CT Scanning machines and MRI's in Israel is low and stands on 7.18 and 1.5 per million inhabitants respectively (the OECD countries average rates are 20.6 and 9.8) (Special report to the Knesset on CT and MRI, 2008) but since 1995 (earliest available data) there was a doubling in number of scans performed (from 60/1,000 inhabitants to 120/1000 in 2009 for CT scans and from 6 to 16/1,000 for MRI) (Luxemburg et al., 2010). These changes could possibly lead to a more accurate diagnosis but are not likely to cause a decrease in LGG or to change the incidence trends of HGG, both diagnosis that are based not only on imaging techniques.

To date, studies that have focused on assessing the cellular effects of RF radiation could not provide any consistent and clear evidence for cellular effects that may lead to neoplastic transformation, a basic requirement for showing biological plausibility of a cancer related effects. Similarly animal studies failed also to provide any consistent evidence for the cancer promoting effects of RF radiation (Gurbuz et al., 2010; Kowalczyk et al., 2010; Lee et al., 2010). Epidemiological studies also failed to clearly and consistently prove an excess cancer or tumor risk (in terms of odds ratios) for cell phone users. Such failures were attributed by some authors to structural biases in the study design itself (Schüz, 2009; Kundi, 2010; Saracci, 2010; Barchana, 2011). Moreover, most of the individual-based research reported a "protecting effect" of this low-intensity radiation on users: users had less brain tumors than non-users (or controls) and tumors prevailed on the contralateral side rather than ipsilateral. Some authors concluded that the lack of a demonstrable carcinogenic effect in epidemiological studies is related to the relatively, short time of exposure to RF radiation. Other researchers have been using the sole finding of an excess risk in a small group of "heavy users" that was not related to a true dose-response effect.

Exposure to RF from phones is localized and therefore, if a risk exists it is likely to be greatest for tumors in regions with greatest energy absorption (Cardis et al., 2008) A recently published study (Volkow et al., 2011) demonstrated that while using a mobile phone, brain metabolism was increased in the orbito-frontal cortex and the temporal pole areas of the brain, areas that are close to where phone's antenna meets the head. Authors concluded, "This finding is of unknown clinical significance". Notably the finding in that study, an increase in intracellular metabolism of glucose should be viewed in light of the fact that a decrease in the brain glucose metabolism is associated with the development of Alzheimer disease (Daulatzai, 2010; Herholz, 2010). Other studies have shown other, non-carcinogens effects on the brain such as local increase in oxygen consumption (Curcio et al.,

2009) and an effect on regional cerebral blood flow (Alto et al., 2006) Interpretation of those results and their clinical relevance and implication is not clear; as is the debate weather they represent a deleterious effect or a protective effect.

Reports demonstrating that RF radiation cause a biological effect on brain tissue combined with the changes described above that have a temporal correlation with massive exposure to those radiations, can be interpreted in the following way: RF radiation does cause metabolic changes in the adjacent tissue in sense of increasing blood flow and metabolism, that are part of the regular way the human body reacts in front of threads. LGG that initiated in parts of the brain influenced by the radiation face an "over-reaction" by the immune system stimulated by the radiation and cannot thrive. This speculation derives from the observation that LGG, that are of low penetrability potential, and therefore are more easily manageable, are those that are influenced for the most (and therefore in the parts of the head influenced by the radiation tend to decrease, and this decrease leads to an overall decrease in number of tumors) while HGG are less susceptible to the repair mechanisms due to their biological aggressive nature.

Several published works showed that brain tumors are related to Socio-Economical Status (SES) and people of higher SES are at a higher risk for developing brain tumors (Demers, 1991; Navas-Acién et al., 2002; Chakrabarti et al., 2005). Mobile phones penetration in the Israeli society was very rapid and reached 100% of the adult population in 6 years since its introduction to the general public. Noteworthy during the first years of marketing (from 1989-1995) only high SES individuals could afford this technology. This fact can supports the results of this study, since the high-SES individuals that were (before the full penetration of the technology) may be at a higher risk for brain tumors were also the first ones to use it and still there was an impressive decline in LGG rates.

There are two key points emerging from the data presented herein, and both relate to the core evidence required for proving a causal association: temporality - a steep decrease in incidence of LGG in correlation with and in parallel to massive use of mobile phones (together with discontinuation of the increase in HGG) and the shift in laterality of both LGG's and high-grade gliomas. This shift in tumor location in the brain from right to left is not due to changes of public behavior reporting the prevailing right side use of mobile phones, nor is it affected from reporting or other biases since the data used is a national population-based cancer registry of a high completeness and accuracy levels. The observation is based on large sample size (more than 5,200 gliomas including 1,400 LGG's) collected in 30 years. Laterality data completeness rates are reasonable also in the last periods checked (75% for LGG and more than 80% in the entire 30-years period), and, due to our familiarity with national cancer registry's operations, there is no reason to believe a unidirectional misclassification bias existed. The fact that changes in laterality are more marked in the younger population (ages 20-49), gives strength to the possible linkage to mobile phone use both in sense of temporality and given

the fact that younger people are making more use with this technology.

In conclusions, Brain tumors are increasing in most modern populations over the last decades but there is no clear explanation to this ascent. In this work we focused on secular trends of Gliomas in a manner that was not explored before and in the context of mobile phones use. We found a statistically significant decrease in LGG's over 30-years period that correlates with introducing of mobile phones technology and a shift in laterality towards left-sided tumors, the latter occurred in both Low and High-grade gliomas. The approach we used, though based on semi ecological data, is in-line with other observations and does not support the assumption that mobile phone use is a causative factor for brain gliomas.

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