

Incidence trends of adult malignant brain tumors in Finland, 1990–2016

Tuomas Natukka^a , Jani Raitanen^{b,c}, Hannu Haapasalo^{a,d} and Anssi Auvinen^b 

^aFaculty of Medicine and Life Sciences, University of Tampere, Tampere, Finland; ^bFaculty of Social Sciences, University of Tampere, Tampere, Finland; ^cUKK Institute for Health Promotion Research, Tampere, Finland; ^dDepartment of Pathology, FIMLAB Laboratories, Tampere University Hospital, Tampere, Finland

ABSTRACT

Background: Several studies have reported increased incidence trends of malignant gliomas in the late 1900s with a plateau in the 2000s, but also some recent increases have been reported. The purpose of our study was to analyze incidence trends of malignant gliomas in Finland by morphology and tumor location.

Material and methods: Data on 4730 malignant glioma patients were obtained from case notifications to the nationwide, population-based Finnish Cancer Registry (FCR), and less detailed data on 3590 patients up to 2016. Age-standardized incidence rates (ASR) and average annual percent changes (APCs) in the incidence rates were calculated by histological subtype and tumor location.

Results: The incidence rate of gliomas was 7.7/100,000 in 1990–2006 and 7.3 in 2007–2016. The incidence of all gliomas combined was stable during both study periods, with no departure from linearity. In an analysis by age group, increasing incidence was found only for ages 80 years and older (1990–2006). During both study periods, incidence rates were increasing in glioblastoma and decreasing in unspecified brain tumors. In 1990–2006, rates were also increasing for anaplastic oligodendroglioma, oligoastrocytoma and unspecified malignant glioma, while decreasing for astrocytoma. As for tumor location, incidence in 1990–2006 was increasing for frontal lobe and brainstem tumors, as well as those with an unspecified location, but decreasing for the parietal lobes, cerebrum and ventricles.

Conclusions: No increasing incidence trend was observed for malignant gliomas overall. An increasing incidence trend of malignant gliomas was found in the oldest age group during 1990–2006.

ARTICLE HISTORY

Received 13 January 2019
Accepted 29 March 2019

Introduction

Gliomas comprise a heterogeneous group of brain tumors originating from glial cells. They are the most common malignant central nervous system (CNS) tumors (80%) [1]. However, age-standardized incidence rate (ASR) (age-standardized to the world standard population) of malignant CNS tumors in Europe is 5.6/100,000 (2018 estimate), making them only the 17th most common cancer type [2]. In Finland, the incidence rates were 5.5/100,000 for males and 4.3/100,000 for females (2003–2007) (world standard population) [3]. Despite their rarity, malignant gliomas contribute disproportionately to cancer mortality because of their poor prognosis [4]. Although the prognosis of malignant glioma has improved during the recent decades, mortality is still very high [5,6].

Several studies have reported increasing incidence of gliomas, especially among the elderly, until the early 1990s, when the increasing trend has leveled off [7–12]. The increasing incidence rates can be partly explained by the introduction of CT and MRI during the 1970s and 1980s, resulting in detection of cases that would have remained

undiagnosed earlier [13]. Even though several recent studies have shown stable incidence [7–9,12,14–20], the findings have not been entirely consistent [5,21–23].

Our aim is to analyze incidence trends of malignant gliomas by histological type and anatomic location using data from a well-established, high-quality cancer registry with nationwide coverage.

Material and methods

Data sources

The data for the study were obtained from the Finnish Cancer Registry (FCR) on all primary malignant brain tumors (ICD-O-3 morphology codes 9380–9451) and unspecified malignant brain tumors (ICD-O-3 morphology code 8000) diagnosed during 1990–2006. The cancer registry data covered date of diagnosis, primary site, histological type, malignancy and any previous cancers. Sex and age of the patient were reported, but no personal identifiers (or date of birth) were obtained. Data on population size by age, gender and

calendar year for calculation of incidence rates were obtained from Statistics Finland [24].

The histological (morphology) classification of brain tumors used at FCR prior to 2008 was very crude and did not comply with ICD-O. Therefore, detailed histological type, grading and location of the tumor were abstracted from the text fields in the cancer notifications (altogether 9389 clinical notifications and 13,217 laboratory notifications on 5638 unique cancer patients during 1990–2006, including subsequently excluded cases). In Finland, unique personal identification codes have been widely used since the late 1960s. They allow unequivocal identification (barring errors) and are used for elimination of duplicate records and for deterministic record linkage.

Based on the detailed diagnostic information in the text fields of the cancer registry notifications, tumor histological type and anatomic site were systematically reclassified according to ICD-O-3 [25]. Clinical notifications were primarily used to define tumor location and laboratory notifications for morphology. If multiple histological types were mentioned in synchronous cancer notifications for the same patient, the more specific and more malignant type was used. If the subsequent notification was issued at least one week later, the earliest notification was used in order to avoid classifying cases into more malignant phenotype due to progression after the initial diagnosis. However, if a pathologist had corrected the diagnosis within a week, the later notification was used (assuming that e.g., the initial diagnosis was based on a perioperative of fresh tissue and the latter on additional staining and more comprehensive evaluation). Multiple primaries were identified based on the code assigned by the cancer registry.

In addition, we obtained the most recent data on primary malignant brain tumors from the FCR diagnosed during 2007–2016. This data were not as detailed as that abstracted from the notifications, but consisted only of frequencies of cases by year, sex, age group and histological type, and, therefore, we could not perform as detailed analyses as from the data coded by ourselves. We also obtained frequencies of cases diagnosed based on death certificate only from the FCR during 1990–2016. The proportion of microscopically verified cases in the earlier study period was estimated by assuming that the case was microscopically verified if the patient had at least one laboratory notification.

Classification and exclusion criteria

We focused on adult primary malignant gliomas in the brain (ICD-O-3 topography code C71). Patients younger than 20 years were excluded because brain tumors in children and adolescents are biologically different from adults [1,26] and we wanted to focus on a homogenous tumor entity. Benign (grade I) brain tumors according to the 2007 WHO classification of CNS tumors [27] were also excluded. If the initial histological type was subsequently reclassified as other than malignant glioma, the tumor was excluded. Table 1 shows subtypes of malignant glioma included in our study. Unspecified brain tumors (ICD-O-3 morphology code 8000

Table 1. Brain tumor subtypes classified as malignant glioma in our study.

Glioma subtype	Morphology code
Astrocytic tumors	
Astrocytoma	9400, 9411, 9420
Anaplastic astrocytoma	9401
Glioblastoma	9440–9442
Oligodendroglial tumors	
Oligodendroglioma	9450
Anaplastic oligodendroglioma	9451
Oligoastrocytic tumors	
Oligoastrocytoma grade II and III	9382
Ependymal tumors	
Ependymoma	9391, 9393
Anaplastic ependymoma	9392
Unspecified malignant glioma	9380
Other malignant tumors	
Other specified tumors of the brain	9381, 9390, 9424, 9430, 9470, 9471, 9473, 9505
Unspecified tumors of the brain	8000

with topography code C71) were included as a separate category.

Primary site of origin was defined based on ICD-O-3 topography classification. Cases with two locations (e.g., frontotemporal) were classified as reported for the most common combinations (subsites that comprised over 1% of all tumors). If three or more locations were reported, the location was classified as overlapping. Uncommon site combinations (subsites with two locations comprising less than one percent of all tumors) were combined as ‘other specified locations’.

Statistical analyses

We calculated ASR with 95% confidence intervals (CI) for all tumors combined, by gender, calendar year, histological type and anatomic location using the 2013 European standard population [28]. Age-specific incidence rates were calculated for 10-year age groups. Crude incidence rates from the most recent data (2007–2016) were calculated and used for incidence trend analyses. We also obtained ASR for all tumors combined and by gender and histological type for 2007–2016, but not detailed enough data for analyses of incidence trend by age group or gender.

Age- and gender-adjusted incidence trends for each histological subtype and location were analyzed using Poisson regression, with number of cases as the outcome and population size as the offset term to estimate the average annual percent change (APC) in incidence rate. Mutually adjusted gender- and age group-specific incidence trends were also analyzed for 1990–2006. For incidence trend analyses, we used the classification principles presented above, with the exception that we assigned cases with two locations by dividing a half case to both locations. Thereby, only ICD-O-3 codes C71.0–C71.9 were used for incidence trend analyses. In addition, we calculated the proportion of microscopically verified cases and death certificate only cases during the study period and conducted trend analyses to evaluate any change over time.

We investigated whether the incidence trend deviated from linearity by adding calendar year of diagnosis as a categorical variable to the Poisson regression model containing a linear term for year, with a significant categorical term

Table 2. Incidence and APC in age- and gender-adjusted incidence trends of adult malignant brain tumors by gender, age, year period and histological type in Finland 1990–2006.

	Frequency		Age-standardized incidence rate (/100,000)		Annual percent change	
	<i>n</i>	%	Rate	95% CI	APC	95% CI
Total	4730	100.0	7.7	7.5–7.9	+0.1	–0.5, +0.7
Gender						
Male	2542	53.7	9.3	8.9–9.6	–0.2	–1.0, +0.6
Female	2188	46.3	6.5	6.3–6.8	+0.5	–0.4, +1.4
Age ^a						
20–29	268	5.7	2.4	2.1–2.7	–1.0	–3.3, +1.5
30–39	513	10.8	4.1	3.8–4.5	0.0	–1.8, +1.8
40–49	705	14.9	5.2	4.9–5.6	–1.1	–2.6, +0.4
50–59	932	19.7	8.1	7.6–8.7	+0.3	–1.0, +1.6
60–69	1026	21.7	12.2	11.5–13.0	–0.5	–1.7, +0.7
70–79	909	19.2	15.2	14.2–16.2	+0.2	–1.2, +1.5
80+	377	8.0	12.6	11.3–13.9	+4.8	+2.6, +7.0
Year period						
1990–1993	1042	22.03	7.6	7.2–8.1		
1994–1997	1064	22.49	7.5	7.1–8.0		
1998–2001	1107	23.40	7.6	7.1–8.0		
2002–2006	1517	32.07	7.9	7.5–8.4		
Histology						
Astrocytic tumors						
Astrocytoma	574	12.1	0.8	0.8–0.9	–2.8	–4.4, –1.1
Anaplastic astrocytoma	481	10.2	0.7	0.7–0.8	–0.4	–2.2, +1.4
Glioblastoma ^b	2284	48.3	3.8	3.7–4.0	+0.8	–0.0, +1.7
Oligodendroglial tumors						
Oligodendroglioma	215	4.5	0.3	0.3–0.3	–0.2	–2.9, +2.6
Anaplastic oligodendroglioma	135	2.9	0.2	0.2–0.2	+6.0	+2.3, +9.8
Oligoastrocytic tumors						
Oligoastrocytoma grade II and III	238	5.0	0.3	0.3–0.4	+6.6	+3.8, +9.5
Ependymal tumors						
Ependymoma	45	1.0	0.1	0.0–0.1	+4.2	–1.9, +10.8
Anaplastic ependymoma	16	0.3	0.0	0.0–0.0	–1.2	–10.6, +9.2
Unspecified malignant glioma	111	2.3	0.2	0.2–0.2	+6.7	+2.6, +11.0
Other malignant tumors						
Other specified tumors of the brain	41	0.9	0.1	0.0–0.1	+3.0	–3.3, +9.7
Unspecified tumors of the brain	590	12.5	1.1	1.0–1.2	–4.5	–6.0, –2.9

^aAge-specific rates^b*p* = .053Statistically significant APC are in bold (*p* < .05).

indicating a departure from linearity. In addition, we further investigated the possible deviation from linearity by adding squared year term as a continuous variable to the Poisson regression model. We also analyzed whether the incidence trends differed significantly between subgroups defined by gender, age group, histological type or anatomic location by adding an interaction term (the product of year and gender and in a separate analysis of year and age group, year and histological type or year and anatomic location) to the Poisson regression model for the years 1990–2006, and used the likelihood ratio test to compare the goodness of fit of the two nested models. In a sensitivity analysis, we evaluated whether distributing unspecified malignant gliomas and unspecified tumors of the brain to the specific histological subtypes by the percentage of each subtype (assuming the information was missing at random) affected the incidence trends. Statistical analyses were performed using Stata version 15.1 (StataCorp, College Station, TX) and Microsoft Excel version 16.0 (Microsoft, Redmond, WA, USA).

Results

Between 1990 and 2006, 4730 malignant glioma cases in adults were reported to the FCR and 3590 cases in 2007–2016.

The ASR of all gliomas combined was 7.7/100,000 (95% CI: 7.5–7.9/100,000) in 1990–2006 (Table 2) and 7.3/100,000 in 2007–2016 (Table 3). Of the diagnoses during 1990–2006, 77.7% were microscopically verified. During 1990–2016, 12.4% of the diagnoses were based on death certificate only. The proportion of cases diagnosed based on death certificate only did not change markedly over time (APC: –0.7%; 95% CI: –1.6, +0.0). However, the proportion of microscopically verified cases decreased slightly (APC: –0.9%; 95% CI: –1.6, –0.3).

Gliomas were more common in men (4506 cases, 54.2%), with an ASR of 9.3/100,000 (95% CI: 8.9–9.6/100,000) in 1990–2006 and 8.6/100,000 in 2007–2016. In women, the ASR was 6.5/100,000 (95% CI: 6.3–6.8/100,000) in 1990–2006 and 6.1/100,000 in 2007–2016. During the earlier study period, most malignant gliomas were diagnosed in the age group 60–69 years (1026 cases, 21.7%), but the highest age-specific incidence rate was in the ages 70–79 years (15.2/100,000; 95% CI: 14.2–16.2/100,000). Incidence increased with age at an average rate of 37.6% (95% CI: +35.4, +39.9) increment per each decade of age.

Astrocytic tumors comprised 67.5% of all gliomas and glioblastoma was the most common histological subtype (4060 cases, 48.8%), ASR being 3.8/100,000 (95% CI: 3.7–4.0/100,000) in 1990–2006 and 3.5/100,000 in 2007–2016 (Tables

Table 3. Incidence and APC in incidence trends of adult malignant brain tumors in Finland 2007–2016.

	Frequency		Age-standardized incidence rate (/100,000)	Annual percent change	
	<i>n</i>	%		APC	95% CI
Total	3590	100.00	7.3	-0.5	-1.7, +0.7
Total (only specific types)	2872	80.00	6.2	+0.9	-0.4, +2.2
Gender					
Men	1964	54.71	8.6		
Women	1626	45.29	6.1		
Histology					
Astrocytic tumors					
Astrocytoma	297	8.27	0.7	-2.9	-6.7, +1.0
Anaplastic astrocytoma	202	5.63	0.5	+7.3	+2.2, +12.7
Glioblastoma	1776	49.47	3.5	+1.9	+0.2, +3.5
Oligodendroglial tumors					
Oligodendroglioma grade II and III	273	7.60	0.7	-3.7	-7.6, +0.4
Oligoastrocytic tumors					
Oligoastrocytoma grade II and III	216	6.02	0.6	-1.5	-6.5, +3.7
Unspecified malignant glioma	108	3.01	0.2	+6.2	-1.5, +14.4
Other malignant tumors					
Other specified tumors of the brain	126	3.51	0.3	-3.6	-9.3, +2.4
Unspecified tumors of the brain	592	16.49	0.9	-6.0	-8.6, -3.3

Statistically significant APC are in bold ($p < .05$).

Table 4. Incidence and APC in age- and gender-adjusted incidence trends of adult malignant brain tumors by location in Finland 1990–2006.

	Frequency		Age-standardized incidence rate (/100,000)		Annual percent change	
	<i>n</i>	%	Rate	95% CI	APC	95% CI
Total	4730	100.00	7.7	7.5–7.9	+0.1	-0.5, +0.7
Location						
Frontal	1108	23.4	1.7	1.6–1.8	+1.7	+0.6, +2.8
Frontotemporal	272	5.8	0.4	0.4–0.5		
Frontoparietal	146	3.1	0.2	0.2–0.3		
Temporal	969	20.5	1.6	1.5–1.7	-0.6	-1.8, +0.5
Temporoparietal	231	4.9	0.4	0.3–0.4		
Temporo-occipital	85	1.8	0.1	0.1–0.2		
Parietal	395	8.4	0.6	0.6–0.7	-2.4	-4.0, -0.9
Parieto-occipital	111	2.3	0.2	0.1–0.2		
Occipital	152	3.2	0.3	0.2–0.3	-0.1	-2.6, +2.5
Cerebrum	178	3.8	0.3	0.3–0.3	-3.5	-6.2, -0.7
Ventricles	63	1.3	0.1	0.1–0.1	-6.0	-10.4, -1.4
Cerebellum	74	1.6	0.1	0.1–0.2	-3.8	-8.0, +0.5
Brainstem	97	2.1	0.2	0.1–0.2	+5.8	+1.7, 10.0
Overlapping	238	5.0	0.4	0.4–0.5	+2.1	-0.6, +4.8
Other specified	82	1.7	0.1	0.1–0.2		
Unspecified location	529	11.2	0.9	0.8–1.0	+2.3	+0.5, +4.1

Statistically significant APC are in bold ($p < .05$).

2 and 3). Unspecified tumors of the brain comprised 12.5% of all tumors (590 cases) in 1990–2006 and 16.5% in 2007–2016 (592 cases).

Most malignant gliomas diagnosed in 1990–2006 were located in the cerebral lobes (73.4%) (Table 4). Frontal lobe was the most common location with 1108 cases (23.4%), ASR being 1.7/100,000 (95% CI: 1.6–1.8/100,000). Temporal lobe was almost as common with 969 cases (20.5%) and an ASR of 1.6/100,000 (95% CI: 1.5–1.7/100,000). Tumors with an unspecified location comprised 11.2% of all gliomas.

Overall, the ASR of gliomas was stable during 1990–2006 (Figure 1). The APC in the incidence rate of all gliomas was close to zero (APC: +0.1%; 95% CI: -0.5, +0.7) (Table 2). In addition, there was no indication of deviation from linearity, i.e., no evidence of change in the overall incidence trend during the study period (likelihood ratio test with year as a categorical variable $p = .19$; likelihood ratio test with squared year term as a continuous variable $p = .61$). No clear trend was observed in incidence rates of gliomas

during 2007–2016 either (APC: -0.5%; 95% CI: -1.7, +0.7; Supplementary Figure 1).

Graphical presentation of the annual incidence rates by gender showed no difference in incidence trends between genders in 1990–2006 (Figure 2), which was also confirmed using an interaction term in Poisson regression analysis (likelihood ratio test $p = .33$). A difference in incidence trends between the age groups was observed, when tested using an interaction term in Poisson regression analysis (likelihood ratio test $p = .001$). However, the only significant increase in incidence rates was in the oldest age group (80+ years), with an APC of +4.8% (95% CI: +2.6, +7.0) (Table 2).

A difference in incidence trends between histological types during 1990–2006 was evident (likelihood ratio test $p < .001$). The incidence trend of glioblastoma was slightly increasing (APC: +0.8%; 95% CI: -0.0, +1.7 for 1990–2006 and +1.9%; 95% CI: +0.2, +3.5 for 2007–2016; Tables 2 and 3). A decreasing ASR was found for unspecified tumors of the brain (APC: -4.5%; 95% CI: -6.0, -2.9 for 1990–2006

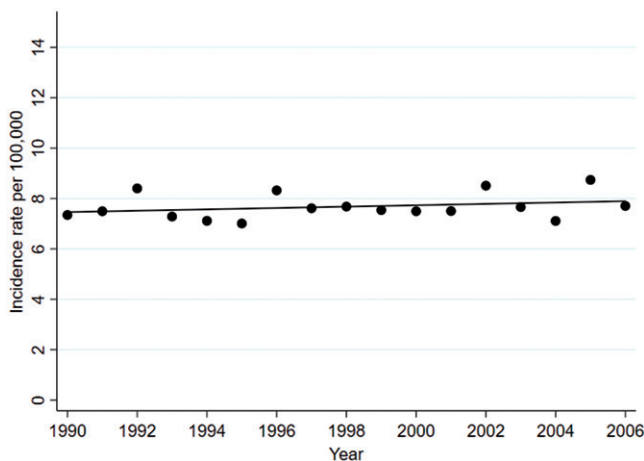


Figure 1. Incidence trend of malignant gliomas in Finland 1990–2006.

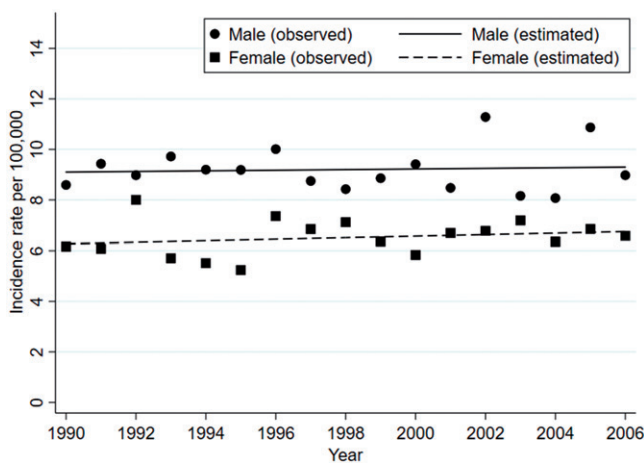


Figure 2. Incidence trends of malignant gliomas by gender in Finland 1990–2006.

and -6.0% ; 95% CI: $-8.6, -3.3$ for 2007–2016), whereas incidence of unspecified malignant glioma increased by $+6.7\%$ per year (95% CI: $+2.6, +11.0$) in 1990–2006 and at a nearly identical rate in 2007–2016. Incidence of oligoastrocytoma increased in 1990–2006 (APC: $+6.6\%$; 95% CI: $+3.8, +9.5$), but not any more during the later period. During the earlier study period, significant increase in ASRs was also observed for anaplastic oligodendroglioma (APC: $+6.0\%$; 95% CI: $+2.3, +9.8$), while incidence trend of astrocytoma showed a decrease of -2.8% per year (95% CI: $-4.4, -1.1$). Incidence of anaplastic astrocytoma increased in 2007–2016 (APC: $+7.3\%$; 95% CI: $+2.2, +12.7$). In addition, imputing specific histologic types (in similar proportion to those with known cell type) to unspecified tumors had no substantial effect on the incidence trends in 1990–2006 (Supplementary Table 1).

We also found a difference in incidence trends between anatomic locations during 1990–2006 (likelihood ratio test $p < .001$). Incidence trends were increasing for the frontal lobe (APC: $+1.7\%$; 95% CI: $+0.6, +2.8$), brainstem (APC: $+5.8\%$; 95% CI: $+1.7, +10.0$) and unspecified locations (APC: $+2.3\%$; 95% CI: $+0.5, +4.1$) (Table 4). Trends were decreasing for the parietal lobes (APC: -2.4% ; 95% CI: $-4.0, -0.9$),

cerebrum (APC: -3.5% ; 95% CI: $-6.2, -0.7$) and ventricles (APC: -6.0% ; 95% CI: $-10.4, -1.4$).

Discussion

In analyses of the incidence trends of adult malignant gliomas in Finland during 1990–2016, we found no increase for gliomas overall. Also, there was no difference in incidence trends between the genders. Incidence rates in the oldest age group (80+ years) increased throughout the earlier study period (1990–2006), while younger age groups showed no such increase. Incidence of glioblastoma increased slightly throughout the study period, while unspecified tumors of the brain showed a decreasing incidence trend. During 1990–2006, significant increases were observed for anaplastic oligodendroglioma, oligoastrocytoma and unspecified malignant glioma, whereas incidence of astrocytoma decreased. In addition, incidence of anaplastic astrocytoma increased in 2007–2016. Incidence rates for tumors in the frontal lobe, brainstem and unspecified location increased throughout the earlier study period. In contrast, tumor incidence decreased in the parietal lobes, cerebrum and ventricles.

Our results are consistent with the most recent studies [7–9,12,14–20,29]. Some studies have reported increasing trends in young adults in their 20s [7,19], but increasing trends have been more commonly found in the oldest age groups [7,9,11,12,14,20–23,29,30] similar to our results. We also found a slightly increasing incidence trend for the most common histological subtype, glioblastoma, which is consistent with several other studies [1,5,7–9,11,17,18]. A study from United States showed an increasing incidence trend for gliomas in the frontal lobe and decreasing trends for the cerebrum, ventricles and overlapping subtypes [17]. Our findings were comparable otherwise, but we also found a decreasing trend for tumors in the parietal lobes and an increasing trend for brainstem tumors.

The overall ASR of all gliomas in our study was 7.7/100,000 in 1990–2006 and 7.3/100,000 in 2007–2016, which is relatively high compared to other studies. A Finnish study reported incidence rate of 4.7/100,000 for all gliomas, but it was based on only 331 cases, and analyses were mainly focused on anatomic locations of brain tumors [31]. Cancer Incidence in Five Continents (CI5) Volume X reports incidence rates for brain and CNS tumors of 7.7/100,000 (adjusted to the world standard population) for Finnish men aged 20+ and 5.9/100,000 for females (2003–2007) [3]. Incidence rates of malignant gliomas comparable to ours were reported from Northwestern England (7.2/100,000; adjusted to the European standard population) [16]. A Danish study also reported quite similar incidence of gliomas (7.3/100,000; including grade I tumors, which comprised only 2.1% of all tumors) [32]. However, their rates for glioblastoma were higher than in our study (5.1/100,000 vs. 3.8/100,000). Several studies have reported lower incidence rates [8,15], which may be partly attributable to inclusion of children or non-Caucasian ethnic groups, or incomplete case ascertainment. A number of studies have also reported similar or higher incidence rates, but they have covered either

all CNS tumors or benign brain tumors, and are therefore not comparable [5,7,14,22].

One possible explanation for the increasing incidence in the oldest age group is improvement in diagnostics. Availability of MRI and CT scans has increased the use of these diagnostic methods. Besides increasing the overall incidence, more frequent use of MRI imaging may have affected particularly the diagnosis of brain stem tumors, which are better visualized with MRI than with CT. More active treatment of brain tumors in elderly patients has probably improved the detection and diagnostic accuracy of cases in age groups older than 60–70 years, as it has likely increased both biopsies and resections, and hence specific diagnoses.

Unspecified brain tumors decreased during the study period and, therefore, some of the specific histological subtypes must have increased simply owing to more accurate diagnostics including modern immunohistochemistry, i.e., cases earlier assigned as unspecified were classified more accurately in more recent years. An increase in unspecified malignant gliomas simultaneously with a decrease in unspecified tumors of unknown malignancy could be explained by increased diagnosis based on imaging only. The increase in unspecified malignant gliomas was of similar magnitude in relative terms, but corresponds to smaller numbers of cases due to smaller frequencies. In contrast, tumors with unspecified location increased, which slightly decreased incidence rates in some specific locations. There was no clear change in proportions of microscopically confirmed cases or death certificate only cases during the study period.

Very few countries have a comprehensive, well-established nationwide population-based cancer registry with multiple sources of information and documented completeness of coverage. In Finland, cancer incidence data have been collected by the FCR since 1953 and notification of cancer cases to the registry has been mandatory since 1961. Case notifications are received from hospitals, health care professionals, pathology laboratories and Statistics Finland's cause of death data [33]. The data received from different sources are then compared and double-checked to verify the accuracy of every diagnosis. Furthermore, the unique personal identification number allows elimination of duplicate records. Therefore, our data based on the FCR are very comprehensive and reliable. In addition, we abstracted information from every report for each case and reclassified histological type and anatomic site of presentation according to ICD-O-3 to improve the accuracy and comparability of the classification.

Finland has centralized the treatment of malignant brain tumors into five university hospitals, which makes diagnoses very standardized and consistent, thus improving also the reliability of the data at the FCR. Also, there were no major changes in brain tumor classification during our study period, ensuring consistency of data throughout the study period.

Our study had also some limitations. Re-evaluation of the tumor slides by an experienced neuropathologist would have further improved the accuracy and reliability of the

diagnoses, but this is not feasible in a large population-based study. Therefore, we could not retrospectively apply the recent 2016 WHO classification of CNS tumors. Our systematic reclassification and detailed analyses did not cover the most recent years but focused on the time period with insufficient detail of tumor classification at the cancer registry. The tabular data for the later period did not allow detailed analyses of trend in 2007–2016. Also, the number of cases in several subgroups was fairly small, limiting the precision of the estimates. We did not conduct join-point analyses, as the incidence rates were very flat.

There are also some limitations concerning the systematic reclassification process. Some patients had discrepancies in diagnoses between cancer notifications, making it difficult to define the correct diagnosis. Also, incomplete information in cancer notifications may have affected the results by inducing misclassification.

The stable incidence rates of malignant gliomas suggest no major increase in public exposure to major risk factors. Although usage of mobile phones increased dramatically during our study period, overall incidence rates of malignant gliomas did not increase at all. Furthermore, we observed no increasing incidence rates in the temporal lobes, which are the most exposed part of the brain from the radiofrequency electromagnetic fields emitted by mobile phones.

The recently updated 2016 WHO classification of tumors of the CNS is the first to use molecular and genetic parameters besides histological features to define several CNS tumor entities including malignant gliomas. In this study, the increase in oligodendroglial tumor incidence and the decrease of astrocytoma incidence might be due to the introduction of the chromosome 1p/19q-analysis in the diagnosis of oligodendrogliomas in the early 2000s [34].

Further studies are necessary to evaluate the impact of the new WHO classification system and to determine the most recent incidence rates. Also, if the latency between radiofrequency field exposure and tumor development is very long, future studies with more recent data assessing longer exposure and latency periods will be needed.

In conclusion, no increase in adult malignant gliomas overall was found for Finland in 1990–2016. However, an increase in the oldest age group during 1990–2006 was observed, comparable to several other populations. An increase in glioblastoma was accompanied by a decrease in unspecified tumors, complicating the interpretation of trends in specific tumor types.

Acknowledgments

We thank Ms. Katja Kuukka for her instrumental contribution in abstracting the data from the cancer registry notifications, Heini Huhtala, MSc, for her contribution to data analysis, Joonas Haapasalo, MD, PhD, for clinical advice and Aapeli Nevala, BSc, from the Finnish Cancer Registry for assistance with the data.

Ethics statement

Our study follows the principles of the Declaration of Helsinki.

Disclosure of interest

No potential conflict of interest was reported by the authors.

Funding

This study was financially supported by the Competitive State Research Financing of the Expert Responsibility area of Tampere University Hospital [#9U001].

ORCID

Tuomas Natukka  <http://orcid.org/0000-0002-3804-6536>

Anssi Auvinen  <http://orcid.org/0000-0003-1125-4818>

References

- [1] Ostrom QT, Gittleman H, Liao P, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2010–2014. *Neuro Oncol.* 2017;19:v1–v88.
- [2] Ferlay J, Ervik M, Lam F, et al. Global cancer observatory: cancer today. Lyon, France: International Agency for Research on Cancer; 2018. Available from: <https://gco.iarc.fr/today> accessed 2019 Mar 15.
- [3] Forman D, Bray F, Brewster DH, et al. Cancer incidence in five continents, Vol. X (electronic version). Lyon: International Agency for Research on Cancer; 2013. Available from: <http://ci5.iarc.fr> accessed 2019 Mar 15.
- [4] Rouse C, Gittleman H, Ostrom QT, et al. Years of potential life lost for brain and CNS tumors relative to other cancers in adults in the United States, 2010. *Neuro Oncol.* 2016;18:70.
- [5] Ho VKY, Reijneveld JC, Enting RH, et al. Changing incidence and improved survival of gliomas. *Eur J Cancer.* 2014;50:2309–2318.
- [6] Visser O, Ardanaz E, Botta L, et al. Survival of adults with primary malignant brain tumours in Europe; results of the EURO CARE-5 study. *Eur J Cancer.* 2015;51:2231–2241.
- [7] Arora RS, Alston RD, Eden TOB, et al. Are reported increases in incidence of primary CNS tumours real? An analysis of longitudinal trends in England, 1979–2003. *Eur J Cancer.* 2010;46:1607–1616.
- [8] Deorah S, Lynch CF, Sibenaller ZA, et al. Trends in brain cancer incidence and survival in the United States: surveillance, epidemiology, and end results program, 1973 to 2001. *Neurosurg Focus.* 2006;20:E1.
- [9] Hess KR, Broglio KR, Bondy ML. Adult glioma incidence trends in the United States, 1977–2000. *Cancer.* 2004;101:2293–2299.
- [10] Deltour I, Johansen C, Auvinen A, et al. Time trends in brain tumor incidence rates in Denmark, Finland, Norway, and Sweden, 1974–2003. *J Natl Cancer Inst.* 2009;101:1721–1724.
- [11] Lönn S, Klæboe L, Hall P, et al. Incidence trends of adult primary intracerebral tumors in four Nordic countries. *Int J Cancer.* 2004;108:450–455.
- [12] Nomura E, Ioka A, Tsukuma H. Trends in the incidence of primary intracranial tumors in Osaka, Japan. *Jpn J Clin Oncol.* 2011;41:291–294.
- [13] Helseth A. The incidence of primary central nervous system neoplasms before and after computerized tomography availability. *J Neurosurg.* 1995;83:999–1003.
- [14] Kim SJ, Ioannides SJ, Elwood JM. Trends in incidence of primary brain cancer in New Zealand, 1995 to 2010. *Aust N Z J Public Health.* 2015;39:148–152.
- [15] Lin Y, Chiu H, Chiou M, et al. Trends in the incidence of primary malignant brain tumors in Taiwan and correlation with comorbidities: a population-based study. *Clin Neurol Neurosurg.* 2017;159:72–82.
- [16] Sehmer EAJ, Hall GJ, Greenberg DC, et al. Incidence of glioma in a northwestern region of England, 2006–2010. *Neuro Oncol.* 2014;16:971–974.
- [17] Zada G, Bond AE, Wang YP, et al. Incidence trends in the anatomic location of primary malignant brain tumors in the United States: 1992–2006. *World Neurosurg.* 2012;77:518–524.
- [18] Dubrow R, Darefsky AS. Demographic variation in incidence of adult glioma by subtype, United States, 1992–2007. *BMC Cancer.* 2011;11:325.
- [19] Inskip PD, Hoover RN, Devesa SS. Brain cancer incidence trends in relation to cellular telephone use in the United States. *Neuro Oncol.* 2010;12:1147–1151.
- [20] Crocetti E, Trama A, Stiller C, et al. Epidemiology of glial and non-glial brain tumours in Europe. *Eur J Cancer.* 2012;48:1532–1542.
- [21] Dobes M, Shadbolt B, Khurana VG, et al. A multicenter study of primary brain tumor incidence in Australia (2000–2008). *Neuro Oncol.* 2011;13:783–790.
- [22] Etxeberria J, Román ES, Burgui R, et al. Brain and central nervous system cancer incidence in Navarre (Spain), 1973–2008 and projections for 2014. *J Cancer.* 2015;6:177–183.
- [23] Pouchieu C, Gruber A, Berteaud E, et al. Increasing incidence of central nervous system (CNS) tumors (2000–2012): findings from a population based registry in Gironde (France). *BMC Cancer.* 2018;18:653.
- [24] Statistics Finland. 2018. Available from: https://www.stat.fi/index_en.html (accessed 2018 Jul 17).
- [25] World Health Organization: International Classification of Diseases for Oncology: ICD-O. 2018. Available from: <http://codes.iarc.fr/> (accessed 2018 Jul 2).
- [26] Broniscer A, Baker SJ, West AN, et al. Clinical and molecular characteristics of malignant transformation of low-grade glioma in children. *J Clin Oncol.* 2007;25:682–689.
- [27] Louis DN, Ohgaki H, Wiestler OD, et al. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol.* 2007;114:97–109.
- [28] Eurostat. 2018. Available from: <http://ec.europa.eu/eurostat/web/main/home> (accessed 2018 Jul 17).
- [29] Nilsson J, Järås J, Henriksson R, et al. No evidence for increased brain tumour incidence in the Swedish national cancer register between years 1980–2012. *Anticancer Res.* 2019;39:791–796.
- [30] Fuentes-Raspall R, Solans M, Roca-Barceló A, et al. Descriptive epidemiology of primary malignant and non-malignant central nervous tumors in Spain: results from the Girona cancer registry (1994–2013). *Cancer Epidemiol.* 2017;50:1–8.
- [31] Larjavaara S, Mäntylä R, Salminen T, et al. Incidence of gliomas by anatomic location. *Neuro Oncol.* 2007;9:319.
- [32] Rasmussen BK, Hansen S, Laursen RJ, et al. Epidemiology of glioma: clinical characteristics, symptoms, and predictors of glioma patients grade I-IV in the Danish neuro-oncology registry. *J Neurooncol.* 2017;135:571–579.
- [33] Leinonen MK, Miettinen J, Heikkinen S, et al. Quality measures of the population-based Finnish cancer registry indicate sound data quality for solid malignant tumours. *Eur J Cancer.* 2017;77:31–39.
- [34] Jenkins RB, Curran W, Scott CB, et al. Pilot evaluation of 1p and 19q deletions in anaplastic oligodendrogliomas collected by a national cooperative cancer treatment group. *Am J Clin Oncol.* 2001;24:506–508.