Simulation of the Incidence of Malignant Brain Tumors in Birth Cohorts That Started Using Mobile Phones When They First Became Popular in Japan

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Over 20 years have passed since the initial spread of mobile phones in Japan. Epidemiological studies of mobile phone use are currently being conducted around the world, but scientific evidence is inconclusive. The present study aimed to simulate the incidence of malignant brain tumors in cohorts that began using mobile phones when they first became popular in Japan. Mobile phone ownership data were collected through an Internet-based questionnaire survey of subjects born between 1960 and 1989. The proportion of mobile phone ownership between 1990 and 2012 was calculated by birth cohort (1960s, 1970s, and 1980s). Subsequently, using the ownership proportion, the incidence of malignant brain tumors was calculated under simulated risk conditions. When the relative risk was set to 1.4 for 1,640 h or more of cumulative mobile phone use and the mean daily call duration was 15 min, the incidence of malignant brain tumors in 2020 was 5.48 per 100,000 population for the 1960s birth cohort, 3.16 for the 1970s birth cohort, and 2.29 for the 1980s birth cohort. Under the modeled scenarios, an increase in the incidence of malignant brain tumors was shown to be observed around 2020.

Keywords: brain cancer; cell phone; exposure; risk estimation; epidemiology

INTRODUCTION

The history of mobile phones in Japan began in 1979 with the release of the automobile telephone service [NTT Docomo, 2017]. In 1991, the first compact mobile phone (weighing approximately 250 g) was released. In 1993, mobile phone service using digital transmission began. In 1994, the initial cost and usage fees for mobile phones were significantly reduced, resulting in the spread of mobile phones throughout Japan. By the end of June 2017, the number of mobile phone subscribers in Japan had reached 163 million [Telecommunications Carriers Association, 2017].

More than 20 years have passed since the initial spread of mobile phones in Japan. Epidemiological studies of mobile phone use are currently being conducted around the world [INTERPHONE Study Group, 2010, 2011], including several studies in Japan [Takebayashi et al., 2006, 2008; Sato et al., 2011]. In 2011, the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) published a carcinogenicity evaluation of mobile phone use [Baan et al., 2011; IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2013]. IARC classified radiofrequency electromagnetic fields as "possibly carcinogenic to humans" (Group 2B).

The evidence for an association between mobile phone use and the risk of malignant brain tumors has been continuously evaluated [Scientific Committee on Emerging and Newly Identified Health Risks, 2015]. However, shortcomings in exposure assessment and participation in studies based on individual data have been pointed out [Deltour and Schüz, 2014]. If there is a substantial risk of malignant brain tumors

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associated with mobile phone use, elevated incidence should be observable in the population. The WHO assigned a high priority to the "monitoring of brain tumors incidence trends through well-established population-based cancer registries, if possible combined with population exposure data" [WHO, 2010].

The present study aimed to simulate the incidence of malignant brain tumors in the birth cohorts that started using mobile phones when they first became popular in Japan. We believe that such a study can provide basic data that will be useful for epidemiological studies of mobile phone use in Japan.

MATERIALS AND METHODS

Data regarding mobile phone ownership were collected through a questionnaire survey. Survey subjects were people who were born before 2005 (6 years old or over in 2012). Subjects were recruited by distributing color, double-sided, letter-sized flyers describing the survey at elementary schools, junior high schools, high schools, and colleges in Japan. The target schools were randomly extracted using the nationwide school database [National School Data Institute, 2007]. About 700,000 flyers were distributed to schools by post. We asked the schools to distribute flyers to all students at their school. The target subjects of the survey were students and their parents/guardians. The subjects were asked to complete the survey online through the survey website, which was accessible from personal computers and mobile devices. Parents/guardians responded to the survey on behalf of elementary and junior high school students. The survey was conducted continuously between 2008 and 2012. Data on mobile phone ownership were collected retrospectively in the survey.

In total, 7,550 subjects completed the survey, accounting for about 1% of the number of leaflets distributed. The survey contained items on mobile phone ownership, year of first mobile phone ownership, average duration of calls, average number of calls per day, percentage of using the left and right ear when talking on a mobile phone, use of hands-free devices, birth year, sex, and dominant hand. Details of the survey are also described in previous reports [Sato et al., 2016, 2017]. In the present study, we used data on the year of first mobile phone ownership, average duration of calls, average number of calls per day, birth year, and sex. The study protocol was approved by the institutional review board at Tokyo Women's Medical University. Informed consent to participate was obtained from all subjects before completing the survey.

The proportion of mobile phone ownership was calculated using data for the end of 2012. The subjects of the analysis were those born between 1960 and 1989 (22 years old to 51 years old in 2012, $n = 1{,}322$). The proportion of mobile phone ownership was calculated using the number of observed persons in each year and the number of mobile phone owners in each year (from 1990 to 2012, 1960s birth cohort $n = 543$, 1970s birth cohort $n = 544$, and 1980s birth cohort $n = 235$). Sex was adjusted by equalizing the weight of male and female subjects in each year (from 1990 to 2012) and in each birth cohort (1960s, 1970s, and 1980s). The incidence of malignant brain tumors was estimated based on the baseline incidence (I_0), relative risk (RR), proportion of the non-exposed group in the population (P_0), and proportion of the exposed group in the population (P_1) as follows:

$$\text{Estimated Incidence} = I_0 \times P_0 + RR \times I_0 \times P_1$$

The incidence of malignant brain tumors reported by the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10: C70-C72) in 1990 was used as the baseline risk [Katanoda et al., 2016], since mobile phone use before 1990 was not common in the general public. In the present study, the total male and female incidence was used. The relative risk of glioma was set to 1.2, 1.3, and 1.4 for a length of mobile phone use of 10 years or more. The proportion of glioma was set to 30% of total malignant brain tumors [The Committee of the Brain Tumor Registry of Japan, 2014, 2017]. In addition, when the relative risk of glioma was 1.4 for 1,640 h or more of cumulative mobile phone use, the incidence of malignant brain tumors was calculated when the mean daily call durations were 10, 15, and 20 min. For example, when daily call duration was 15 min, the relative risk was 1.4 for 18 years of mobile phone use (1,640 h/15 min/365.25 days = 18.0 years). In all birth cohorts, the average call duration per day was about 15 min. In the simulation, calculations were also made for call durations of 10 min and 20 min to clarify how much the incidence of malignant brain tumors changed when the average call duration changed. We assumed that the proportion of mobile phone ownership from 2013 to 2020 would be the same as that in 2012. The calculation was performed by birth cohort (1960s, 1970s, and 1980s). Statistical analyses were performed using the epiDisplay Package of R Statistical Software (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Table 1 shows the age and sex distributions of the study subjects. The number of subjects was 1,322.

TABLE 1. Age and Sex Distributions of Study Subjects

	Male		Female		Total	
Birth cohort	*n*	%	*n*	%	*n*	%
1960s	241	44.4	302	55.6	543	100.0
1970s	240	44.1	304	55.9	544	100.0
1980s	119	50.6	116	49.4	235	100.0
Total	600	45.4	722	54.6	1,322	100.0

The number of female subjects ($n = 722$) somewhat exceeded the number of male subjects ($n = 600$). The 1980s cohort had the smallest number of subjects ($n = 235$).

Table 2 and Figure 1 show the change in the proportion of mobile phone ownership by birth cohort. Ownership of mobile phones began in the early 1990s. In the 1970s birth cohort, 90% of subjects owned a mobile phone by 2001. In the 1960s and 1980s birth cohorts, 90% of subjects owned a mobile phone by 2005. Penetration of mobile phone ownership was the fastest in the 1970s birth cohort, followed by the 1960s and 1980s birth cohorts. The mean daily call duration was 14.8 min (standard deviation (SD) = 44.8) in the 1960s birth cohort, 16.4 min (SD = 36.6) in the 1970s birth cohort, and 15.4 min (SD = 30.3) in the 1980s birth cohort (data not shown).

Table 3 shows the results of a simulation of the incidence of malignant brain tumors by birth cohort. When the relative risk was set to 1.3 for a length of mobile phone use of 10 years or more, the incidence of malignant brain tumors in 2020 was 5.41 per 100,000 population for the 1960s birth cohort, 3.09 for the 1970s birth cohort, and 2.29 for the 1980s birth cohort. When the relative risk was set to 1.4 for 1,640 h or more of cumulative mobile phone use and the mean daily call duration was 15 min, the incidence of malignant brain tumors in 2020 was 5.48 per 100,000 population for the 1960s birth cohort, 3.16 for the 1970s birth cohort, and 2.29 for the 1980s birth cohort.

DISCUSSION

The present study revealed the change in the incidence of malignant brain tumors under simulated conditions. The incidence of malignant brain tumors was calculated by setting the incidence in 1990 as the baseline risk. Comparing baseline risk and simulation results, the simulated incidence began to increase around 2015 and clearly increased in 2020.

Previous meta-analyses [Bortkiewicz, 2017; Bortkiewicz et al., 2017; Prasad et al., 2017] reported

TABLE 2. Change in the Proportion of Mobile Phone Ownership by Birth Cohort

	Year																							
Birth cohort	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
1960s	2.6	3.7	6.4	8.3	11.0	17.9	28.1	35.4	45.2	52.7	66.7	73.5	80.3	84.4	88.4	91.2	93.2	93.8	94.6	94.8	95.6	95.8	96.5
1970s	1.2	1.5	2.1	5.1	11.0	21.7	36.8	54.0	71.3	78.9	88.8	91.7	93.7	95.1	96.4	97.0	97.3	97.5	97.5	97.8	97.8	98.2	99.3
1980s	0.3	0.3	0.3	0.3	0.9	1.9	2.6	4.8	14.1	28.9	46.8	57.9	71.4	76.8	82.4	93.7	96.8	97.5	98.1	98.1	98.1	98.4	99.2

Values represent percentage (%). The proportion was adjusted for sex by equalizing the weight of male and female subjects. 1960s birth cohort $n = 543$, 1970s birth cohort $n = 544$, and 1980s birth cohort $n = 235$.

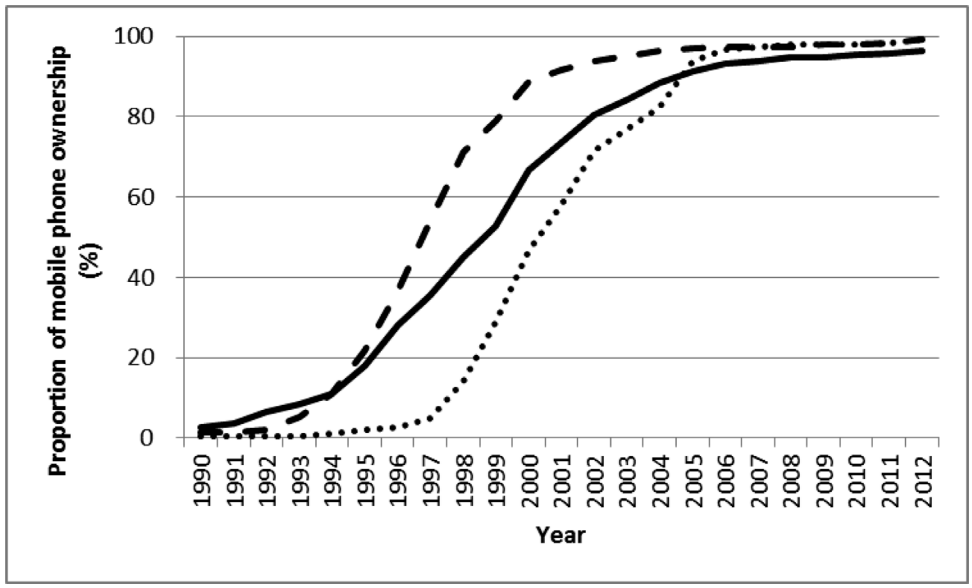

Fig. 1. Change in the proportion of mobile phone ownership by birth year. The proportion was adjusted for sex by equalizing the weight of male and female subjects. Solid line: birth years 1960–69. Dashed line: birth years 1970–79. Dotted line: birth years 1980–89.

TABLE 3. Simulation of the Incidence of Malignant Brain Tumors by Birth Cohort

			Year				
	Mean daily call duration	Birth cohort	2000	2005	2010	2015	2020
Baseline incidence							
		1960s	2.10	2.35	2.84	4.03	4.98
		1970s	1.33	1.64	2.10	2.35	2.84
		1980s	1.73	1.35	1.33	1.64	2.10
Relative risk							
1.2 for length of		1960s	2.10	2.38	2.95	4.25	5.27
mobile phone use of		1970s	1.33	1.66	2.21	2.49	3.01
10 years or more		1980s	1.73	1.35	1.37	1.73	2.22
1.3 for length of		1960s	2.10	2.39	3.01	4.36	5.41
mobile phone use of		1970s	1.33	1.67	2.27	2.56	3.09
10 years or more		1980s	1.73	1.35	1.39	1.78	2.29
1.4 for length of		1960s	2.11	2.40	3.07	4.47	5.55
mobile phone use of		1970s	1.33	1.68	2.32	2.62	3.17
10 years or more		1980s	1.73	1.35	1.40	1.82	2.35
1.4 for 1,640 h or	10 min	1960s	2.10	2.35	2.84	4.03	5.05
more of cumulative		1970s	1.33	1.64	2.10	2.35	2.88
mobile phone use		1980s	1.73	1.35	1.33	1.64	2.10
	15 min	1960s	2.10	2.35	2.87	4.25	5.48
		1970s	1.33	1.64	2.11	2.55	3.16
		1980s	1.73	1.35	1.33	1.67	2.29
	20 min	1960s	2.10	2.37	2.96	4.42	5.54
		1970s	1.33	1.64	2.24	2.61	3.17
		1980s	1.73	1.35	1.34	1.78	2.35

Values are the incidence of malignant brain tumors per 100,000 population.

that the relative risk was 1.33 or 1.46 for a length of mobile phone use of 10 years or more. Therefore, in the present study, we conducted a simulation on mobile phone use of 10 years or more. However, previous meta-analysis studies seem to have a weak point in the selection of studies and analysis method used. The INTERPHONE study reported that the relative risk of glioma was 1.4 for 1,640 h or more of cumulative mobile phone use [INTERPHONE Study Group, 2010]. The present study showed an increase in the incidence of malignant brain tumors in the population to be observed around 2020, assuming that there is a risk, as indicated in the previous studies.

The incidence of malignant brain tumors in Japan was estimated using the regional cancer registry [Hori et al., 2015; National Cancer Center Japan, 2017]. Malignant brain tumors are rare cancers, affecting 2.4 patients per 100,000 population in Japan, and the incidence of glioma is about 30% of this [The Committee of the Brain Tumor Registry of Japan, 2014, 2017]. By conducting a consistency check study until 2020 for all three birth cohorts (1960s, 1970s, and 1980s), we can verify the consistency between the estimated increase in the incidence and real time trend, similar to what has been done in Nordic countries [Deltour et al., 2012], the United States [Little et al., 2012], and Australia [Chapman et al., 2016]. According to a report from the Regional Cancer Registry in Japan [Hori et al., 2015; National Cancer Center Japan, 2017], the incidence of malignant brain tumors was 1.65 per 100,000 population in 2000, 1.83 in 2005 and 2.30 in 2010 for the 1960s birth cohort, and 0.94 in 2000, 1.39 in 2005, and 1.91 in 2010 for the 1970s birth cohort. These observed incidences were lower than the simulated incidence, and also lower than the baseline incidence. For the 1980s birth cohort, the incidence of malignant brain tumors was 1.24 in 2000, 1.56 in 2005, and 1.50 in 2010. The observed incidences in 2005 and 2010 were larger than the simulated incidences. The 1980s birth cohort was in their 20s in 2010 and the incidence of malignant brain tumors was very low. Therefore, there is a possibility that accidental error was included in the observed incidences. In the future, we need to closely observe how the incidence of malignant brain tumors in these birth cohorts (1960s, 1970s, and 1980s) changes.

A decreasing trend in the incidence of malignant brain tumors was reported in both males and females between 1993 and 2007 in Japan [Miranda-Filho et al., 2017]. In that analysis, the age-adjusted incidence of subjects aged 15 years old and over was shown. On the other hand, another study reported that the annual incidence of malignant brain tumors tended to increase between 1990 and 2010 in subjects in their 20s and 30s [Sato et al., 2016]. These previous studies analyzed time series changes in the incidence of malignant brain tumors in the Japanese population. In the present study, we focused on the birth cohorts that started using mobile phones when they first became popular in Japan. It is necessary to pay attention to the period of time when analyzing the incidence of malignant brain tumors in the Japanese population. The 1990s overlap with the time during which computed tomography (CT) and magnetic resonance imaging (MRI) became popular in Japan [The Organisation for Economic Co-operation and Development, 2018]. The spread of CT and MRI likely increased the number of diagnoses. Therefore, in the analysis of malignant brain tumor incidence, researchers must ensure that these effects are excluded when considering increased incidence.

The present study focused on the birth cohorts that started using mobile phones when they first became popular in Japan. The penetration of mobile phones was the fastest in the 1970s birth cohort. The reason for this is thought to be that the members of the 1970s birth cohort were in their 20s in the late 1990s to early 2000s when mobile phones spread rapidly in Japan. During that period, the members of the 1960s birth cohort were in their 30s and members of the 1980s birth cohort were in their teens. Because the 1970s birth cohort has been using mobile phones since their introduction, the cumulative time of mobile phone use is considered to be the largest among the three cohorts. If mobile phone use is associated with risk of malignant brain tumors, an increase in the incidence of malignant brain tumors may be confirmed first in the 1970s birth cohort. Meanwhile, the situation of mobile phone usage may change due to changes in mobile phone user habits, mobile phone technology, and other factors. With the spread of smartphones in recent years, social media has become popular and there is a possibility that the average call duration of mobile phone users has changed. If the call duration of smartphone users is lower, the increase in the incidence of malignant brain tumors may be observed later.

The 1980s birth cohort in the present study had slightly fewer subjects ($n = 235$) than the 1960s ($n = 543$) and 1970s ($n = 544$) birth cohorts. Therefore, the penetration curve of mobile phones was somewhat irregular compared to the other two birth cohorts. However, this was not considered to have a large influence on the results of the present study. In terms of sex, slightly more females participated in this study. Therefore, sex adjustment was carried out when calculating the proportion of mobile phone ownership.

The recruitment of participants in the present survey was low, accounting for about 1% of the number of leaflets distributed. Several factors are thought to have affected recruitment. Subjects for the survey were recruited by distributing flyers, and the subjects needed to access the survey website to complete the questionnaire. Therefore, it is possible that the obtained sample was affected by selection bias. We compared the proportion of mobile phone ownership in our study participants with the proportion of ownership reported in another survey of the general population. According to the Communication Usage Trend Survey conducted by the Japanese Ministry of Internal Affairs and Communication [2017], ownership of mobile phones in 2010 ($n = 14{,}549$) was 97.3% for those in their 20s, 95.0% for those in their 30s, and 94.2% for those in their 40s. In the present study, the ownership of mobile phones in 2010 was 98.1% for those in their 20s (birth years: 1980–89), 97.8% for those in their 30s (birth years: 1970–79), and 95.6% for those in their 40s (birth years: 1960–69). Therefore, the proportion of mobile phone ownership did not differ significantly. The Communication Usage Trend Survey reported household mobile phone ownership rates of 10.6% in 1995, 75.4% in 2000, and 89.6% in 2005. A rapid increase in the proportion of mobile phone ownership from 1995 to 2005 was also observed in the present study. In addition, there is a possibility that the mean daily call duration was biased, and its direction (i.e., underestimated or overestimated) is unknown. Therefore, in the simulation, in addition to the average call duration of 15 min, 10 min (short call duration) and 20 min (long call duration) were used in the calculations.

The present survey retrospectively investigated the year of first ownership of a mobile phone. Although many subjects used a mobile phone for 10 to 15 years since they first owned a mobile phone, we believe that the recall bias is not large since one's first mobile phone is a major life event and the recall of this event is relatively reliable [Pettersson et al., 2015].

The incidence of malignant brain tumors varies with age and sex [Hori et al., 2015; National Cancer Center Japan, 2017]. In the present study, the effect of age was reflected in the baseline incidence. As for sex, the simulation was carried out using the total male and female incidence. In the present study, it was difficult to calculate the proportion of mobile phone ownership by sex because the sample size was low.

CONCLUSION

Epidemiological studies on mobile phone use have mainly focused on malignant brain tumors as a health outcome. The present study revealed that under the modeled scenarios, an increase in the incidence of malignant brain tumors was shown to be observed around 2020. In future epidemiological studies on mobile phone use, we believe that it will be necessary to investigate whether or not the incidence of malignant brain tumors is actually increased in 1960s, 1970s, and 1980s birth cohorts.

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