Abstract: The study objective was to investigate patterns of reported non-malignant brain and CNS tumor incidence over a time period encompassing 1997-2008 during which time the Benign Brain Tumor Cancer Registries Amendment Act (PL 107-260) was passed and implemented. Analyses of 75,350 incident non-malignant brain and CNS tumors from eleven population-based central registries revealed that there were statistically significant increases in the age-adjusted incidence rate for non-malignant tumors for those diagnosed prior to 2002 and over the time period from 2002 until 2005. However, no significant change in the age-adjusted incidence rate for non-malignant tumors was observed over the time period 2005 to 2008 indicating that the incidence from this time period may quantify the “true” incidence of non-malignant brain and CNS tumors in the United States.

Key words: brain, non-malignant, central nervous system, incidence, patterns

Introduction

Brain and central nervous system (CNS) tumors are often devastating both in terms of morbidity and mortality and the importance of requiring the reporting of all primary brain tumors regardless of tumor behavior (malignant or non-malignant) has been recognized.\(^1,2\) The Central Brain Tumor Registry of the United States (CBTRUS), in collaboration with participating state cancer registries, demonstrated in 1992 the feasibility of collecting data on all primary brain and CNS tumors in the United States\(^3\) and has since promoted the collection of these data globally.\(^4\) Passed in 2002, the Benign Brain Tumor Cancer Registries Amendment Act (Public Law 107-260; ftp.resource.org/gpo.gov/laws/107/publ260.107.pdf; accessed February 3, 2012) required central cancer registries supported by the National Program of Cancer Registries (NPCR) to expand data collection on primary brain and CNS cancer incidence to include tumors of non-malignant (benign and uncertain) behavior in addition to malignant behavior beginning with diagnosis year 2004. In keeping with the spirit which advocated for enactment of this law, other standard setters in surveillance and reporting of non-malignant tumors has not been consistent. These factors, along with implementation of Public Law 107-260, have undoubtedly influenced non-malignant primary brain and CNS tumor incidence patterns. Thus, the primary objective of this study was to evaluate patterns of reported incidence rates of non-malignant brain tumors diagnosed over a time period which spans the introduction and implementation of Public Law 107-260.

Methods

The Central Brain Tumor Registry of the United States (CBTRUS) has compiled population-based incidence data on all primary brain and CNS tumors, regardless of biologic behavior, since 1992. Data from 11 population-based state
cancer registries (Arizona, Colorado, Delaware, Idaho, Maine, Massachusetts, Minnesota, Montana, North Carolina, New York, and Virginia) that collaborated with the CBTRUS and collected both malignant and non-malignant primary brain tumors diagnosed from 1997-2008 were analyzed. Representing close to 22% of the population in the United States, almost all of these central registries currently have achieved gold standard certification from NAACCR. Use of these data was approved by the University of Illinois at Chicago Institutional Review Board. Primary brain and CNS tumors were defined using the International Classification of Diseases for Oncology (ICD-O-3)\textsuperscript{22} site codes of C70.0-C72.9, C75.1-C75.3 and C30.0 (histology codes 9522-9523). Non-malignant tumors were defined as those with ICD-O-3 behavior codes of “0” (benign) or “1” (uncertain).

Age-adjusted incidence rates and confidence intervals at the 95% level were calculated using SEER*Stat 7.0.9.\textsuperscript{24} Population data available from the US Census Bureau were obtained from the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program Web site (seer.cancer.gov/pophdata/) to calculate incidence rates. Incidence rates per 100,000 were analyzed for each respective diagnosis year and were age-adjusted to the 2000 US Standard Population. To further investigate the potential for sharp changes in age-adjusted incidence rates over time, Joinpoint 3.5.2 (piece-wise regression) software was utilized.\textsuperscript{25} Join points correspond to a point in time of a change in the trend where 2 different sloped lines come to a juncture, and the software fits the simplest join-point model that the trend data will allow. Using the grid search method, the permutation test model (model: \(\ln[y]=xb\)) assessed changes in age-adjusted incidence rates with a minimum number of 3 observations from a join point to either end of the data and a minimum of 3 observations between 2 join points. The annual percent change (APC) with corresponding 2-sided 95% confidence intervals (CI) for each trend segment was calculated with Joinpoint 3.5.2 software using weighted least squares regression.

**Results**

A total of 75,350 incident non-malignant brain and CNS tumors diagnosed from 1997-2008 were included in these analyses. A join-point analysis of the non-malignant brain and CNS tumor incidence over time revealed 2 junctures where the slope of the age-adjusted incidence rate trend line changed (Figure 1). Overall, a statistically significant increase in the age-adjusted incidence rate for non-malignant tumors diagnosed prior to 2002 was found (APC=7.0). During that time period, the age-adjusted incidence rate increased from 6.7 in 1997 to 9.3 per 100,000 person-years in 2002. A shift in the slope of the age-adjusted incidence rate trend was observed over the time period from 2002-2005, with a statistically significant increase in the non-malignant age-adjusted incidence rate (APC=12.2). The age-adjusted incidence rate during this time period increased more rapidly, from 9.3 in 2002 to 12.8 per 100,000 person-years in 2005. This shift in rates was primarily driven by the “jump” in age-adjusted incidence rates from diagnosis year 2003 (9.9 per 100,000 person-years) to diagnosis year 2004 (12.1...
per 100,000 person-years). As previously noted, diagnosis year 2004 was the first year mandated for implementation of the law. Conversely, no significant changes for non-malignant age-adjusted incidence rates were observed over the time period 2005-2008 (APC=0.0), with the rates slightly increasing from 12.8 in 2005 to 13.0 per 100,000 person-years in 2008.

A similar pattern was found in both males and females when analyzed separately (Figure 2). Males demonstrated changes in the slope of the age-adjusted incidence rate trend in 2001 and 2005, with a significant increase from 1997-2001 (APC=5.1), a larger increasing incidence from 2001-2005 (APC=10.8), and a flattening out of the incidence from 2005-2008 (APC=0.7). From 1997-2001, the age-adjusted incidence rate increased from 5.4 to 6.6 per 100,000 person-years, while from 2005-2008, the age-adjusted incidence rate for non-malignant brain tumors slightly increased in males from 9.9 to 10.2 per 100,000 person-years. The slope of the age-adjusted incidence rate trend in females significantly increased from 1997-2002 (APC=7.4), increased at a faster rate from 2002-2005 (APC=12.4), and showed no change in the age-adjusted incidence rate from 2005-2008 (APC=0.2). From 1997-2002, the age-adjusted incidence rate increased from 7.8 to 11.0 per 100,000 person-years, while from 2005-2008, the age-adjusted incidence rate changed very little (15.4 to 15.5 per 100,000 person-years, respectively).

**Discussion**

The Benign Brain Tumor Cancer Registries Amendment Act (Public Law 107-260) has had a profound impact on non-malignant brain and CNS tumor incidence patterns in the United States. The study findings indicated substantial changes in non-malignant-specific reporting across the time period 1997-2008, particularly for the time period surrounding implementation of the law in diagnosis year 2004. A significant increase in the age-adjusted incidence of all primary and malignant brain and CNS tumors in the United States before the early 2000s has been noted by others. Studies which have included data after this time period have reported flat or downward trends in the age-adjusted incidence of malignant brain tumors. Many of these previous studies only included data on malignant brain tumors and those studies that did include non-malignant tumors reported data prior to diagnosis year 2004 and, therefore, do not reflect the impact of Public Law 107-260. Much of the large increasing trend in incidence of non-malignant brain tumors prior to 2004 was likely attributable to factors associated with refinement of standards, variable reporting requirements, and legislative inconsistencies that influenced case ascertainment. As mentioned previously, coding and classification changes for brain and CNS tumors were implemented during this time. Alternatively, some of the increase in incidence may be related to environmental exposures, diet, or other factors that could not be assessed in this data analysis.

The increasing trend in brain and CNS tumor age-adjusted incidence between 2002-2005 seen in this study is reminiscent of the increase in brain tumor incidence reported after the introduction of CT scans and MRIs. This increasing trend in reporting of non-malignant brain tumor incidence most likely reflects many dynamic factors and an enormous amount of activity in the cancer registry community preparing for and adapting to the new legislation targeted for implementation in diagnosis year 2004.

Although the collection of non-malignant brain and CNS tumors was voluntary prior to 2004, among all CBTRUS collaborating state cancer registries, some actively collected data on non-malignant tumors, while others passively collected data on these tumors. At least 1 state cancer registry collected data on non-malignant brain tumors but did not collect data on non-malignant spinal cord tumors. In addition, tumors that were not histologically confirmed may not have been required to be reported to the state cancer registry. As a large percentage of non-malignant brain and CNS tumors are not histologically confirmed, but rather diagnosed by radiography or other non-invasive means, this resulted in an underreporting of non-malignant tumors. It is apparent that data collected prior to 2004 significantly underestimated the true incidence of non-malignant brain tumors. It is likely that some continued under-reporting in the years directly following enactment of the law (eg, diagnosis year 2004) occurred as the state cancer registries worked to ensure reporting from all sources.

Looking at its data from 2004-2007, the NAACCR Data Use and Research Committee Data Assessment Work Group involving benign/borderline brain and ONS tumors reported at the NAACCR Annual Meeting in 2011 that incomplete data for non-malignant brain tumors are likely to be found in NAACCR central registries especially for states with low rate ratios and low rates for non-malignant brain tumors. The possible underreporting of cases detected radiographically without microscopic examination has also been noted in a study of intracranial meningiomas in Denmark, Finland, Norway, and Sweden diagnosed between 1968-1997. More recently, an 18% increase in reporting of non-malignant brain tumors through the use of electronic capture of radiology reports was reported by a single institution.

The relatively constant non-malignant brain and CNS tumor incidence rates during 2005-2008 suggest stabilization in reporting under the Act’s governance. Current collection of non-malignant brain and CNS tumors in the United States as reflected in diagnosis years 2004-2008 has been guided by Uniform Data Standards and under 1 federal law. State cancer registries are now required to actively collect data on all brain and CNS tumors (ICD-O-3 codes C70.0-72.9 and C75.1-75.3) regardless of behavior and method of diagnostic confirmation. Quality control measures to ensure complete ascertainment of brain and CNS tumors, especially non-malignant tumors, will continue to be essential.

In summary, under mandatory collection with standardized reporting requirements, it is believed that the reported age-adjusted incidence of non-malignant brain and CNS tumors in the United States is more closely reflecting the “true” incidence. Given the findings of the study, it should also be emphasized that any evaluation of trends in non-malignant or total brain and CNS tumors must be made cautiously, and only if a registry can satisfy the high-quality
standards for diagnosis years prior to implementation of the law in 2004. Trends in malignant brain and CNS tumors may be evaluated from earlier years depending upon the completeness of case ascertainment of the respective data set.

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