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Prevalence of brain neoplasms: the emerging role of advanced magnetic resonance imaging techniques in neuro-oncology diagnosis and treatment

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ABSTRACT

Less than 3% of glioblastoma patients are still alive at 5 years after diagnosis, elder age being the most important and reliable predictive index of poorer consequence. The incorporation of physiologic MR imaging, such as DWI, proton MRS, and PWI, as part of the mainstream clinical imaging protocol has empowered neuroradiologist to begin the course of combining radiology with biology in brain neoplasms to provide meaningful and clinically relevant end points and biomarkers for clinical trials and assessment of malignancy. Much work lies ahead, however, to validate and provide efficacy of these methods in improving diagnostic accuracy, affecting patient care, monitoring dynamic changes within brain neoplasm and normal brain throughout treatment, and forming them as the arbitrator of inventive therapy that may one day show management of brain neoplasm a reality.

KEY WORDS: brain neoplasm, magnetic resonance imaging, neuro-oncology.

1. INTRODUCTION

Brain Neoplasm Epidemiology: Less than 3% of glioblastoma patients live for at 5 years after identification, elder age being the most significant and reliable prognostic factor of poorer consequence(Ohgaki, 2009). Gliomas are constituents of numerous inherited neoplasm syndromes, but the occurrence of these syndromes is very low. Many ecological and life factors counting numerous jobs, environmental carcinogens, and diet have been described to be associated with an elevated glioma risk, but the only factor clearly related with an amplified risk is therapeutic X-irradiation. Especially, children treated with X-irradiation for acute lymphoblastic leukemia display a significantly raised risk of emerging gliomas and primitive neuroectodermal neoplasms, often within 10 years after therapy (Ohgaki, 2009). Primary brain cancers are a varied group of neoplasms arising from dissimilar cells of the central nervous system (CNS); althoughrare, there is evidence that the incidence of these neoplasms has been rising for as much as fifty years (Ostrom and Barnholtz-Sloan, 2011). The overall incidence of brain neoplasms for benign and malignant neoplasms combined is 18.71 per 100,000 person-years; 11.52 per 100,000 person-years for benign neoplasms and 7.19 per 100,000 person-years for malignant neoplasms; however, it should be kept in mind that occurrence, reaction to treatment, and continued existence after diagnosis vary greatly by age at diagnosis, histologic type of neoplasm, and degree of neurologic compromise (Ostrom and Barnholtz-Sloan, 2011). The only established environmental risk factor for brain neoplasms is ionizing radiation exposure; in addition, contact to radiofrequency electromagnetic fields via cellphone has been recognized as a possible risk factor for brain neoplasm development (Ostrom and Barnholtz-Sloan, 2011). Though, investigations have been erratic and indecisivebecause of systematic changes in study designs and difficulty of accurately measuring cell phone use. Recently studies of genetic risk factors for brain neoplasms have expanded to genome-wide association studies; moreover, genome-wide studies of somatic genetic changes in neoplasms show correlation with clinical outcomes (Ostrom and Barnholtz-Sloan, 2011). Brain neoplasms are among the scariest of health conditions; in fact, the Brain Neoplasm Epidemiology Consortium has called them an orphan disease because research funding is limited. They are relatively rare, developing in approximately 16.5 per 100,000 people in the United States each year. The most common types are gliomas and meningiomas. Gliomas are usually malignant (cancerous), while 90% of meningiomas are benign (non-cancerous). Glioblastoma multiforme (GBM) is the most deadly, with a 5-year survival rate of 3.3%. However, some malignant types have 5-year survival rates of more than 70%; benign neoplasms can also cause serious illness or death, depending on their size and location (Fugate, 2016). Although many risk factors have been examined over the past several decades, there are few consistent findings, possibly because of small sample sizes in individual studies and differences between studies in patients, neoplasm types and methods of classification (Bondy, 2008).

The consortium identified epidemiological factors associated with brain neoplasms as follows (Fugate, 2016):

Ionizing radiation: There is a strong association between brain neoplasms and exposure to radiation from occupational exposure, treatment for previous cancers, nuclear test fall-out, and in the survivors of the atomic bombs used on Hiroshima and Nagasaki. Ionizing radiation includes high-frequency sources such as x-rays, gamma rays, and particle beams. Non-ionizing radiation includes lower-frequency sources such as cell phones and power lines. There has been a great deal of concern about everyday radiation sources, but the authors of Reference 1 report that cell phones, power lines, and low-dose x-rays (such as dental x-rays) are possibly not risk factors for brain neoplasms.

- Genetic factors. There are several subtypes of brain neoplasms linked to specific genes, and family history is a risk factor.
- Gender. Men have more malignant brain neoplasms than women, while women have a higher rate of non-malignant brain neoplasms (mostly meningiomas) than men.
- Ethnicity. In the United States, whites have the highest rate of brain neoplasms. Developed countries have higher rates than less developed countries.
- Age. Brain neoplasms can occur at any age, but they are rare in children and more common with increasing age.
- Epilepsy, seizure, or convulsions. These can be early symptoms, although many patients with these symptoms do not have brain neoplasms.
- Occupational exposure to carcinogens and heavy metals.

The annual, global, age-standardized incidence of main malignant BTs is about 3.7 per 100,000 for men and 2.6 per 100,000 for women (Parkin, 2002). Rates appear to be higher in more advanced countries (men, 5.8 per 100,000; women, 4.1 per 100,000) than in less advanced states (men 3.0 per 100,000; women 2.1 per 100,000) (Parkin, 2002). The distribution of neoplasm types varies substantially by age group (Parkin, 2002). In Sweden, medulloblastoma (23.5%) and first stage glioma (31.7%) are the most common kinds of neoplasms in pediatric patients aged ≤15 years (Parkin, 2002)

Worldwide, age-standardized death for primary malignant BTs is ≈2.8 per 100,000 population for men and 2.0 per 100,000 population for women (GLOBOCAN). Like incidence rates, the estimated mortality is higher in more developed countries (men, 4.1 per 100,000; women, 2.7 per 100,000) than in less developed countries (men, 2.2 per 100,000; women, 1.6 per 100,000) (GLOBOCAN).

Progress in diagnostic technologies and ascertainment, chiefly for nonmalignant BTs, may account for much of the modest surge in incidence; in addition, changes in neoplasm classification and coding modalities are accountable for some of the upsurges in incidence for BTs histologies, such as oligodendroglioma and astrocytoma, and not otherwise specified (GLOBOCAN).

The presence and role of human cytomegalovirus infection in glioblastoma is still controversial (Cobbs, 2013). Epilepsy is common in patients with brain neoplasms and can considerablytouch daily life, even if the neoplasm is under control (van Breemen, 2007; Rasolabadi, 2015). Numerous factors affect the mechanism of seizures in brain neoplasms, including neoplasm type, neoplasm location and perineoplasmal and genetic changes (van Breemen, 2007). Prophylactic use of antiepileptic drugs is not suggested, and likelyexchangesamid antiepileptic and chemotherapeutic agents persuades against the use of enzyme-inducing antiepileptic drugs (van Breemen, 2007). The purpose of incident brain neoplasm cases is significantso as todefine disease patterns and to recognize the reasons of the disease, and it is vital for the management, evaluation and planning of healthcare services for disease control (Gigineishvili, 2014). Information about incidence rates of primary brain neoplasms in Georgia during last decades was only available from hospital-based pilot studies (Gigineishvili, 2014). In past decade, the situation changed radically. With some postponement, progressive neuroimaging machines have been extensively introduced in Georgia, and several state-of-art 1.5 tesla MRI units and multi-slice CT scanners are available both in clinical and ambulatory settings. Since imaging of the brain provides precise info about brain structures, today, a patient with a supposed brain neoplasm is regularly examined by an imaging diagnostic tool, which is a effortless, noninvasive and fast medical test; in these circumstances, a review of CT and MRI results is a necessary step for obtaining accurate information about brain neoplasm incidence (Gigineishvili, 2014). The crude incidence rate was 11.11 per 100,000 person-years, whereas the overall annual age-standardized incidence rate (ASR) per 100,000 person-years was 10.62, with similar rates in 2009 (10.25) and 2010 (10.99) (Gigineishvili, 2014). Among specified neoplasms (n = 444), benign and borderline tumours accounted for 65.5% (ASR = 3.15) and malignant brain tumours for the remaining 34.5% (ASR = 1.67) (Gigineishvili, 2014). The difference in ASRs among benign/borderline and malignant neoplasms was statistically significant (SRR = 1.88, 95% CI: 1.55; 2.29) (Gigineishvili, 2014). The change in the incidence rates may be because of several reasons. For instance, a lesser frequency rate in Georgia than in wealthy states may reflect the little care to subtle and sometimes obscure symptoms of brain neoplasms and as a concern low healthcare application, complicated by insufficient or lack of health insurance coverage amongst the population (Gigineishvili, 2014). Additionally, CT and MRI imaging systems are concentrated only in large cities and therefore

these diagnostic methods are too expensive and inaccessible for large parts of the rural population (Gigineishvili, 2014). In central nervous system (CNS) a heterogeneous group of glial and non-glial may cause rare cancers (Crocetti, 2012). A study was conducted to guess the load (incidence, prevalence, survival and proportion of cured) for the principal CNS cancers in Europe (EU27) and in European areasby means of population-based statistics from cancer registries contributing in the RARECARE project (Crocetti, 2012). Several 44,947 rare CNS cancers were diagnosed from 1995 to 2002 (with follow up at 31st December 2003): 86.0% astrocytic (24% low grade, 63% high grade and 13% glioma NOS), 6.4% oligodendroglial (74% low grade), 3.6% ependymal (85% low grade), 4.1% Embryonal neoplasms and 0.1% choroid plexus carcinoma; incidence rates differextensively across European regions particularly for astrocytic neoplasms ranging from 3/100,000 in Eastern Europe to 5/100,000 in United Kingdom and Ireland. Overall, about 27,700 new infrequent CNS cancers were estimated every year in EU27, for a yearly occurrence rate of 4.8 per 100,000 for astrocytic, 0.4 for oligodendroglial, 0.2 for ependymal and embryonal neoplasms and less than 0.1 for choroid plexus carcinoma (Crocetti, 2012). Five-year relative survival were 74.2% for ependymal (80.4% low grade and 36.6% high grade), 62.8% for choroid plexus carcinomas and 56.8% for embryonal neoplasms. Survival rates for astrocytic tumours were comparatively greater in Northern and Central Europe than in United Kingdom and other eastern areas of European states. The divergent accessibility of diagnostic imaging methods and/or radiation therapy tools across Europe may be the reason to clarify the described survival changes (Crocetti, 2012). In Europe, the uniform (World) frequency of primary CNS tumors ranges from 4.5 to 11.2 cases per 100,000 men and from 1.6 to 8.5 per 100,000 women, the two most common CNS tumor, high-grade glioma and brain metastasis occur more frequently during adulthood and especially among the elderly (Crocetti, 2012). The study showed that rare CNS cancers represent a huge range of neoplasms with different biological characteristics and unlike epidemiological features (Crocetti, 2012). As regards time trends, data from the present study show stable (or even decreasing) incidence trends in all the age-classes analyzed with the exception of the age-group 60+ years which shows an increasing trend (Crocetti, 2012). The increased use of technology imaging devices, such as computed tomography (CT) and MRI, may have contributed to the more precise diagnosis of such neoplasms. Trends for CNS with and without microscopic confirmation showed an increase in incidence for microscopic verified cases especially among the elderly. The improved ability to diagnose brain neoplasms by stereotactic and frameless biopsy procedures may have contributed to the increase in microscopically verified cases (Crocetti, 2012). The geographical differences in 1-year survival may be due to a variation in the timeliness of diagnosis and therapy which may exert its effect in the short term. Brain cancer 1-year survival in 23 European countries ranged between 34.2% and 48.3%, with high survival estimates in Switzerland, France, Sweden, Belgium and Italy and lower estimates in Poland, Czech Republic, Ireland, Denmark and United Kingdom–Northern Ireland (Crocetti, 2012). In the treatment of brain cancer, radiotherapy is widely used. Therefore, the access to radiotherapy might influence the treatment outcome and consequently survival of CNS neoplasms (Crocetti, 2012). However, the lower survival rates reported in this study for some EU regions could be explained by less accessibility to Magnetic Resonance Imaging (MRI) (Crocetti, 2012). Gliomas account for more than 70% of all brain neoplasms, and of these, glioblastoma is the most frequent and malignant histologic type; there is a tendency to a greater frequency of gliomas in very developed, developed states (Ohgaki, 2009). Also, less than 3% of glioblastoma patients are still thriving at 5 years after diagnosis, grownup age being the most significant and consistent prognostic factor of minorconcern. Gliomas are components of several inherited neoplasm syndromes, but the occurrence of these syndromes is very low. Many environmental and lifestyle factors counting numerous jobs, environmental carcinogens, and diet have been reported to be associated with an elevated glioma risk, but the only factor clearly associated with an increased risk is therapeutic X-irradiation. In particular, children treated with X-irradiation for severe lymphoblastic leukemia display a significantly raised risk of developing gliomas and primitive neuroectodermal neoplasms, often within 10 years after therapy (Ohgaki, 2009; Ahmadi, 2014). Gliomas comprise almost 80% of primary malignant brain neoplasms, and they result in more years of life lost than do any other neoplasms (Schwartzbaum, 2006). Glioblastoma, the most common type of glioma, is associated with very poor survival, so glioma epidemiology has focused on identifying factors that can be modified to prevent this disease. Merely two comparatively rare factors have so far been decisively revealed to cause glioma risk—contact to high doses of ionizing radiation, and inherited mutations of extremely penetrant genes associated with rare syndromes. Also, first sign shows a minor glioma risk among people with allergic conditions and high levels of serum IgE. New investigation has focused on recognizing germline polymorphisms related with risk of glioma, and using molecular markers to classify glial neoplasms into more-homogenous groups. Since gene products perhapsrelate with ecological factors or growing signals to produce gliomas, huge studies are needed to analyze associations between polymorphisms and glioma (Zandi, 2013; Zandi, 2014). Cohort studies of immune factors and glioma risk are being started to confirm the effects of case–control investigations. Studies of polymorphisms of genetic pathways with strong prior hypotheses are being intended, and whole-genome scans are being planned to investigate susceptible families and case–control series. The Brain Neoplasm Epidemiology Consortium has been formed to co-ordinate these studies (Schwartzbaum, 2006). The term

'glioma' includes all neoplasms that are thought to be of glial cell source. There is around a fourfold change in the occurrence of primary malignant brain neoplasms between countries with a high incidence (e.g. Australia, Canada, Denmark, Finland, New Zealand and the US) and regions with a low incidence (e.g. Rizal in the Philippines and Mumbai in India). Differences in diagnostic practices and completeness of reporting make all geographic comparisons difficult. In addition, higher incidence rates appear in countries—and perhaps in states within the US—with greater access to health care and better medical care. Some geographic variation is not easily attributable to this phenomenon; though, as malignant brain neoplasms are twice as common in Northern Europe as they are in Japan. Therefore, ecological factors might account for some of the observed geographic differences (Schwartzbaum, 2006). The prognosis for patients with glioma is often very poor (only ~2% of patients aged 65 years or older, and only 30% of those under the age of 45 years at GM diagnosis, survive for 2 years or more), and treatments to cure GM have yet to be devised. The only firmly established exogenous environmental cause of glioma is exposure to therapeutic or high-dose radiation, although high-dose chemotherapy for treatment of cancers at sites other than the brain has also been linked to this condition (Fathi, 2014). Genetic factors control the degree of risk from these contacts; Relling,[15] showed that among children preserved with cranial irradiation and intensive antimetabolite therapy for acute lymphocytic leukemia, those with germline polymorphisms leading to low or absent thiopurine methyltransferase action were significantly more probable than persons without such polymorphisms to subsequently develop brain cancer. Similar studies need to be conducted among adults. One focus of molecular genetic studies should be the interface between the recognized ecological risk factor, contact to therapeutic doses of ionizing radiation, and DNA repair polymorphisms. If the DNA repair pathway that is pertinent to ionizing radiation exposure and glioma risk could be documented, it might be used to investigate links between extra ecological factors and glioma risk. One of the most hopeful areas for future glioma research is the role of immune factors in neoplasm development. All observations from case–control studies based on molecular biomarkers (e.g. viral antibodies, IgE levels) that could probably be changed by the attendance of the neoplasm need to be long-established in cohort investigation where serum has been collected well in advance of neoplasm development (Rahmani Tanha, 2016). Main brain tumors have appealed high attention in current year's science, though the survival rate is not good, there are numerous reports suggesting an increasing trend in incidence rates (Deorah, 2006). The bulk of this increase is reportedly due to rising incidence rates among the elderly and children. Although the exact reasons behind this trend are debatable, one reason could be that our ability to diagnose intracranial neoplasms improved dramatically after the introduction of CT in the 1970 and MR imaging in the early 1980s. The use of stereotactic brain biopsy procedures and a more violent approach toward the diagnosis of elderly persons with neurological symptoms have similarly made their own offerings to the observed trend (Fatehi, 2016; Fatehi, 2016). It is not recognized whether these technological advances are completely accountable for the increasing trend or if environmental and lifestyle risk factors or the increase in life expectancy are driving the incidence rates. Recently, several epidemiological investigation trying to link the use of cellular phones with the rate of brain neoplasms have altered fear of brain cancer incidence. An evaluation of the tendency of amplified brain cancer cases has vital implications, both from clinical and community health viewpoints, because it may lead to the improvement of diagnostic methods or the identification of a potential new risk factor. Accurate presumptions of incidence rates support clinicians select an appropriate sample size for their clinical studies. Public health officials base their resource allocations and functions on such accurate estimates of disease burden in the community. Furthermore, histology-specific trends could suggest possible explanations for the rate of disease incidence, counting etiological risk factors (Deorah, 2006). The term "brain neoplasms" refers to a mixed group of neoplasms originating from intracranial tissues and the meninges with grades of malignancy ranging from benign to metastatic (McKinney, 2004). Each form of neoplasm has its individual biology, treatment, and prognosis and each is likely to be caused by different risk factors. Even "benign" neoplasms can be lethal due to their site in the brain, their ability to infiltrate locally, and their propensity to transform to malignancy. This makes the classification of brain neoplasms a difficult science and creates problems in describing the epidemiology of these conditions. Public perception generally fails to distinguish between different neoplasm subtypes and although treatments and prognosis may vary, the functional neurological consequences are frequently similar. This article will give an overview of the burden of brain neoplasms in the population, looking at the major subtypes where possible, in addition to giving a summary of current views on possible causes (McKinney, 2004). Malignant neoplasms of the brain are an infrequent occurrence accounting for approximately 2% of all cancers in adults. Approximately 4400 people are recently diagnosed with a brain neoplasm each year in the UK compared to over 40 000 women with breast cancer and approximately 25 000 men with prostate cancer. The greatest proportion of adult neoplasms is supratentorial, arising in the frontal, temporal and parietal lobes, and the majority (86%) are gliomas which include astrocytomas, glioblastomas, oligodendroblastomas, and unspecified gliomas. Threefold alteration in the incidence of brain neoplasms have been stated between countries universal and changes are also seen amid ethnic groups within the same state. Advanced states appear to have the peak rates of brain neoplasms but this may be a result of better registration systems which include benign neoplasms. However, the magnitude of the

variation is less compared to other cancers—for example, up to 10-fold differences is seen for breast cancer. Topographical difference has to be cautiously understood as, unlike other cancers, the criteria and registration of brain neoplasms is not always reliable. The occurrence of brain neoplasms rises with age. Figure 2 illustrates the age incidence curve showing a drop in incidence in those over 75 years. It is thought this may well be artefactual and occurring as a consequence of neoplasms of the brain being less likely to be investigated and detected in the elderly. Symptoms in older people may be explained by other co-morbid conditions such as strokes or physicians may be reluctant to undertake thorough investigations.

Inclinations over time can only be considered valid when based upon data collected according to the same definitions and reporting practice. Inconsistencies and changes over time may be the explanation for the observed rises which have been attributed to various factors. Improved differential diagnosis of brain neoplasms which might have previously been diagnosed as strokes or metastatic neoplasms are also a source of concern. Access to services will have improved, making it more likely that a patient with a neoplasm is registered. In addition, histopathological technology has increased the specificity of neoplasm diagnosis and thus an apparent increase in specific neoplasm types—for example, astrocytomas—may merely be a consequence of fewer non-specific diagnoses being registered. In Norway and the USA specific studies investigating whether time trends can be accounted by these factors suggest that the reported increase in brain neoplasms is likely to be an artefact of changing diagnostic and reporting practice. The levelling off of incidence in the 1990s in the USA supports this assertion. Steady rises in the rates of brain neoplasms in children under 14 years and the elderly over 70 years are most clearly documented. For children this may be explained by changes in the environment, but the increase over time in older patients is more likely attributed to changes in the delivery of care associated with a greater likelihood of full evaluation and intervention (McKinney, 2004). The length of survival following diagnosis of a brain neoplasm is dependent on both the age of the patient, histologic subtype and grade of the neoplasm, and presenting symptoms (McKinney, 2004). For patients diagnosed between 1981 and 1985 only 8% survived to 10 years. There are known to be geographical differences in the delivery of care to cancer patients within the UK and this may be reflected in long term survival. Recent comparisons of survival from adult brain neoplasms in eight former National Health Service (NHS) regions (in 1999) and Wales have shown differences between regions and over time within a region. Differences may be accounted for by temporal changes in registration practice, but one particular aspect which is difficult to explain is the observed variation in survival for men and women within a region. It seems unlikely that care and treatment would vary according to sex for patients living in the same area and these differences remain unexplained. Levels of social class measured in deprivation categories are seen to influence survival, with those living in more affluent areas generally having improved survival with the effect seen most prominently at one year post-diagnosis. Geographical differences in survival exist between countries. The five year survival of patients diagnosed with any type of brain neoplasm in England, Wales, and Scotland is approximately 13% in men and 16% in women. Across Europe equivalent figures are 17% and 20% in men and women, respectively, and generally the UK figures are 10% below the USA. The discrepancy is potentially explained by the fact that figures from the USA include neoplasms classified as benign which would not be registered in many of the UK cancer registration schemes. The overall poor survival for this group of neoplasms masks differences for subtypes. Meningiomas, both benign and malignant, for example, have a much better prognosis whereas GBM has the poorest survival in all age groups. Other factors associated with survival chances include age, with younger adults faring better, being female, which slightly improves survival, as well as the location of the neoplasm and the extent of neoplasm resection. More recent studies have shown that further characterization of neoplasms by molecular and genetic markers can provide useful prognostic indicators although there is little information in the literature as markers are not routinely recorded for the majority of patients. However, with improved and systematic recording of the molecular characteristics of neoplasms, the relation to progression and prognosis will be clarified (McKinney, 2004). Brain neoplasms are the second most common cancer in children, comprising 15–25% of all pediatric malignancies, and they are the most common solid neoplasm. Different proportions of histological subtypes are present in children compared to adults, with gliomas (approximately 40%) and medulloblastomas (approximately 25%) mainly arising infratentorially, with the remainder, germ cell neoplasms and craniopharyngiomas, occurring in the midline. There is a minor peak in occurrence in early childhood accounted for by medulloblastomas. Studies in the USA, Sweden, and the UK have reported what appear to be true rises in incidence over the last three decades which are mysterious by changes in diagnostic practice, treatment, or classification. The question of whether this is a real and continuing effect can only be answered by future surveillance using accurate and complete population based registers. Survival for children with brain neoplasms has improved by 16% since 1971 in England and Wales. The prognosis in children is superior to that of adults with an overall probability of surviving to five years of 59% in England and Wales for those diagnosed 1986–90 compared to 72% in the USA (McKinney, 2004). Current thinking suggests that brain neoplasms develop as a consequence of accumulated genetic alterations that permit cells to evade normal regulatory mechanisms and destruction by the immune system (McKinney, 2004). These alterations may be in part or wholly inherited but any agents—chemical,

physical or biological—that damage DNA is possible neurocarcinogens. Investigations of the causes of brain neoplasms should ideally address the concurrent influence of both genetic factors and ecological contacts. Genetic predisposition to developing brain neoplasms is associated with certain inherited syndromes such as tuberous sclerosis, neurofibromatosis types 1 and 2, nevoid basal cell carcinoma syndrome, and syndromes involving adenomatous polyps. These syndromes account for 1–2% of all neoplasms. Common differences in the structure of detailed genes are recognized to be related with basic cellular metabolic processes such as oxidation, detoxification, DNA stability and repair, and immune functioning. Such genetic polymorphisms may well be related with the expansion of brain neoplasms in the attendance or absence of environmental carcinogens. However, the limited findings available so far have failed to consistently identify any precise polymorphisms, but this remains a possibly productive line of investigation and future large sample studies are needed (McKinney, 2004). Ionizing radiation given in therapeutic doses is one of the few known risk factors for brain neoplasms. The now discontinued low dose radiation treatment of tinea capitis and skin disorders in children increased the risk of brain neoplasms well into adulthood as doe's radiotherapy for childhood tumors and leukemia. Survivors of the atomic bomb in Hiroshima have amplified risks of meningioma in proportion to their level of exposure. In utero exposure does not appear to affect the risk for the developing fetus. Diagnostic *x* rays do not appear to be linked to gliomas, but full mouth dental *x* rays have been associated with meningiomas in a small number of studies (McKinney, 2004).

Community anxiety over the possible harmful health effects of using mobile phones have resulted in a number of investigations of possible links with brain neoplasms (McKinney, 2004). When assessing the literature on this topic interpretation of a small number of early studies from the USA and Sweden must be cautious. However, with the exponential increase in the ownership and duration of use of these hand held devices it will be important to continue investigations with respect to digital phones, allowing for a latent period of several decades in the development of a neoplasm (McKinney, 2004). Power frequency extremely low frequency magnetic fields (ELF-MF) of 50–60 Hz are used in domestic and industrial electricity supplies presenting a virtually ubiquitous exposure to the population, although levels of exposure do vary. The possibility of adverse health effects has generated considerable public concern, despite scant epidemiological and biological support in the research literature. The biological basis for ELF-MF being involved in malignant transformation is not strong as there is no consistent research which shows this low energy exposure has any direct effects on disrupting cellular DNA or metabolic pathways. Studies of occupational exposure to high levels of ELF-MF and the risk of brain neoplasms have mixed findings. Variation in results can be explained by differing study methodologies and sample size, the latter affecting the power to detect increased risk. One substantial difference is the method used to assess ELF-MF exposure; this varies from the use of proxies such as wiring configuration codes, distance from distribution equipment, and historic load data to direct measures of exposure. The lack of consistency between independent research projects and the difficulties with measuring the exact exposure levels of the individuals at work makes interpretation problematic. For mothers exposed at work during their pregnancy there does not seem to be any enlarged risk of their child after developing a brain neoplasm (McKinney, 2004).

Atopic diseases such as asthma, eczema, and allergies can be markers of immune dysfunction. In a number of independent studies from different countries atopic conditions have been shown to be "protective", particularly in the development of gliomas. Patients with gliomas report fewer symptoms of atopy compared to control subjects. This relation is an interesting one and might indicate a role for immunologic factors in causation (McKinney, 2004). Attributing the cause of brain neoplasms to these compounds or other dietary factors such as vitamin supplements has received mixed support in the published literature. Dietary assessment is fraught with problems and it may be that the ingestion of potentially toxic compounds is offset by the ingestion of antioxidants which promote DNA repair. Nitrate levels in drinking water have also been investigated but no consistent associations found (McKinney, 2004).

The low calorie sweetener aspartame has been commonly used in a number of food products for over 15 years. It has been suggested to be involved in the etiology of some brain neoplasms based principally on the results of laboratory experiments. The biological basis for any influence which aspartame could have on the risk of developing a brain neoplasm is unclear (McKinney, 2004). Tobacco smoke is carcinogenic but many constituents do not pass the blood–brain barrier. Smoking does not appear to be strongly linked to brain neoplasms either in adults who smoke themselves or via maternal smoking in pregnancy (McKinney, 2004). In the working population many jobs in various industries involve exposure to carcinogenic or neurotoxic compounds counting organic solvents, polycyclic aromatic hydrocarbons, lubricating oils, and phenols and the question has been frequently asked as to whether such exposure is related to brain neoplasms. Despite numerous studies no consistent risks have been isolated for any chemical or group of workers apart from those in the petrochemical and oil industry. In these circumstances no specific chemical has been identified and the possibility of multiple exposures has to be considered (McKinney, 2004).

Brain neoplasms in adults are a rare disease from which survival is generally poor compared to many other cancers. Reports of rising trends need to be cautiously interpreted as they may well be explained by changes in diagnostic and clinical practice. In childhood a different profile of neoplasm types is present and survival has improved over recent years and is higher than in adults. Apart from genetic predisposition, the most well established environmental risk factor for brain neoplasms is exposure to high doses of ionizing radiation (McKinney, 2004). Regarding risk factors, studies of inherited vulnerability and constitutive polymorphisms in genes pertinent to carcinogenesis (for example, DNA repair and detoxification genes and mutagen sensitivity) have exposed challenging findings (Wrensch, 2002). Studies continue to suggest that brain neoplasms might result from workstation, nutritional, and other individual and domestic contacts, but studies of cell phone use and power frequency electromagnetic fields have created little to support a causal connection with brain neoplasms; caveats remain. Progress in understanding primary brain neoplasms might result from studies of well-defined histologic and molecular neoplasm types incorporating assessment of potentially relevant information on subject vulnerability and environmental and nonintegrated endogenous factors (Wrensch, 2002).

Brain neoplasm classification: The World Health Organization (WHO) has revised the effect of neoplasm's categories on the central nervous system (CNS) neoplasms; in fact, based on the previous assumption that each type of neoplasm may originate from a particular cell type; thus, the system was depended on the histological features (Saberi, 2016). This categorization system did not consider other important factors such as anatomical location and neoplasm size; both were determined by surgical access and the uptake degree. The WHO model could guide the treatment and assessing overall prognosis in patients with brain neoplasms. Later, categorization systems resulted from scientific studies on brain neoplasm, clinical understanding of neoplasm biology, clinical response and prognosis have been initiated. Although most of malignant brain neoplasms with the same lethal effect are rare; however, certain cases may occur with good neoplasm response to treatment and recovery. Although current categories of WHO can decline the prediction of the treatment response of each individual neoplasm histologically at the same stage of treatment; however, they cannot provide a detailed guidance. Especially for those aimed at specific molecular or genetic pathways which start from the onset of neoplasms; there is clearly a need to improve the pattern of brain neoplasm classification, in order to provide a good treatment guideline and an assessment of response to treatment and then result in a clinically meaningful endpoint. It is unlikely to determine the grading of brain neoplasms only based on histological categories, to provide a meaningful endpoint for therapeutic trials. Especially those aimed at specific molecular or genetic pathways that cause the onset of neoplasms. So, neuroimaging techniques (Neuroimaging) as a substitute for the above procedure and the pursuit of biological origin neoplasms could show the potential information of biological differences between two neoplasms with similar type and in a stage with a very different response to treatment.

Magnetic resonance spectroscopy (MRS) of the human brain has been initiated since 20 years ago. All methods used in the clinic for evaluation of brain neoplasms are comprehensive. H-MRS techniques may help in many different diagnoses such as histological grading, the degree of influence, re-growth of neoplasms (neoplasm recurrence) and main treatment of cell and neoplasm cell necrosis induced by expansion of exposure of undetected neoplasms using the normal conventional MR imaging or combined with other advanced imaging techniques such as diffusion-weighted imaging (DWI), perfusion weighted imaging (PWI) and potential plans to improve the diagnostic accuracy for brain neoplasms (Gharib Salehi, 2016).

Conventional MRI and other biomedical imaging techniques are only used for unknown identity and localization the neoplasms; it can also be done by using routine biopsy; however, many neoplasms may be inaccessible for biopsy. Determination of neoplasm grading using MRS is a noninvasive diagnostic procedure. MRS is one of the modalities for assessing the type and grade of neoplasm, as well as a method for assessment of the neoplasm cells to radiotherapy. Neuroimaging of brain neoplasms using three magnetic imaging techniques based on physiological can be done. These methods have a major role in the transmission of clinical MR image of a special morphology to other imaging methods.

MRI technique is a valuable tool for quantitative metabolic abnormalities in the brain, prostate, breast and other organs. This method is routinely used in the clinical imaging, especially for cancer assessment and clinical. Methods of analysis and its impact on clinical applications of MRSI, as well as advanced techniques such as parallel imaging and high-speed methods, has resulted in the replacement of these new methods and conventional methods. Although the main focus is on H-MRS, the described principles are the same as other methods of compatible with nuclear MR, the revision of MRSI is expected for evaluating the critical assessment of clinical applications and determination of future development of future procedures, increasing the application of clinical usage of MRSI. It is likely that future technical development, would focus on the MRI scanners with very large field, new contrast agents using metabolically active compounds, and speed up the MRSI methods. Because this technology suggests unique sensitivity and specificity to explore the status and dynamics of metabolic tissue.

Physiology-based MRI: There are four important clinical application for this type of imaging. These methods are conducting for assessment of neoplasm grade and cellularity, postoperative injury, preneoplasmal edema and integrity of white matter tracts.

Glioma Grading by DWI: The grade of brain neoplasm is pivotal in the treatment decision and assessment of prognosis. Grade I gliomas encompass a unique group of gliomas—pilocytic astrocytoma, pleomorphic xanthoastrocytoma, subependymal giant cell astrocytoma—which all share a relatively benign biology and indolent clinical course. The remaining diffuse gliomas are subdivided into grades II–IV, which is the basis for our understanding of neoplasm biology and clinical outcome. Cellularity has been the target of quantitative assessment with DWI. The rationale of using DWI to quantify cellularity is founded on the evidence that water diffusivity within the extracellular compartment is inversely connected to the content and dilution of the constituents of the intracellular space.

Glioma Grading by PWI: In brain neoplasms, PWI proposes to measure the degree of neoplasm angiogenesis and capillary permeability,both of which are significant biologic markers of malignancy, grading, and prognosis, particularly in gliomas. Brain neoplasm vasculature plays critical roles not only in supplying nutrients and oxygen to neoplasm cells but also in providing a roadmap for neoplasm infiltration and complex feedback loop with neoplasm hypoxia and necrosis. It is of utmost importance to understand the complex biology of brain neoplasm angiogenesis to gain insight into the development of malignancy and strategies to combat neoplasm growth. To that end, various PWI methods strive to provide noninvasive and robust surrogate markers of neoplasm angiogenesis and capillary permeability (Saberi, 2016). The following sections focus on the 2 most widely used contrast-enhanced MR imaging methods—DSC and dynamic contrast-enhanced (DCE) PWI—to study and quantify brain neoplasm vasculature.

Glioma Grading by MRS: The clinical value of preoperative glioma grading based on metabolite ratios derived from 1H-MRS remains investigational despite several published reports on high diagnostic accuracy of 1H-MRS. Currently, the role of MRS in glioma grading in the clinical preoperative setting, especially in replacing surgical biopsy, has not been proved accurate enough to replace tissue diagnosis and grading. Several large case series have reported that 1H-MRS was very accurate in the differentiation of high- and low-grade. 1H-MRS is a influential noninvasive imaging technique that offers exclusive metabolic information on brain neoplasm biology that is not available from anatomic imaging. 1HMRS has shown a promising role in grading low and high-grade gliomas and also in differentiating active neoplasm from therapy-related necrosis. Several technical issues face 1H-MRS, however, including variable and non-standardized pulse sequences and the lack of standardized quantitation methods and diagnostic threshold for metabolite concentration that can be used in multi-institutional and multiple vendor platforms. Other issues include incomplete coverage of neoplasm tissue because of the limitation of spectral volume size and artifacts from bone and scalp tissues. Despite these challenges, 1H-MRS will continue to play an important role in providing noninvasive metabolic information on brain neoplasms that forms the basis for intense scientific research in technical refinements and remains a part of the clinical diagnostic armamentarium to improve brain neoplasm diagnosis.

2. CONCLUSION

Neuroimaging of brain neoplasms has evolved from a purely anatomy-based discipline to one that incorporates morphologic abnormality with physiologic alterations in extracellular compartment kinetics, cellular metabolism, and hemodynamics. Tremendous progress and widespread clinical use of physiology-based MRI have become an essential part of the diagnostic armamentarium to diagnose, guide surgery, monitor therapy response, and predict prognosis of patients with brain neoplasm. The incorporation of physiologic MR imaging, such as DWI, proton MRS, and PWI, as part of the mainstream clinical imaging protocol has empowered neuroradiologist to begin the process of combining radiology with biology in brain neoplasms to provide meaningful and clinically relevant end points and biomarkers for clinical trials and assessment of malignancy. Much work lies ahead, though, to validate and provide efficacy of these methods in improving diagnostic accuracy, affecting patient care, monitoring dynamic changes within brain neoplasm and healthy brain during treatment, and founding them as the arbiter of new treatment that may one day prove cure of brain neoplasm a reality.

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