Title
Genomic and Molecular Characterization of Brain Tumors in Asian and Non-Asian Patients of Los Angeles: A Single Institution Analysis.

Permalink
https://escholarship.org/uc/item/41m2175p

Journal
Brain tumor research and treatment, 5(2)

ISSN
2288-2405

Authors
Duong, Courtney
Nguyen, Thien
Sheppard, John P
et al.

Publication Date
2017-10-31

DOI
10.14791/btrt.2017.5.2.64

Peer reviewed
INTRODUCTION

Worldwide, less than 2% of new cancer diagnoses are of the brain and central nervous system [1,2]. Five-year survival rates among brain cancer patients have been reported as a little over a third. Differences in clinical outcomes between brain tumor patients of different races remain poorly understood.

Brain tumor epidemiology in specific races has been documented, and studies into the mechanisms of mutation by race and pathology are well-established [1,4-31]. However, differences in clinical outcomes between brain tumor patients of different races are still being elucidated [25,32,33]. A prior study showed a higher probability of worse outcomes in Asian/Pacif-
ic Islanders than in their white counterparts [25]. While these reports evaluated outcomes in a single tumor pathology, studies evaluating the survival between patients of different racial backgrounds against several tumor types are rare.

To optimize treatment for patients with brain tumors, racial differences in progression-free survival (PFS) and overall survival (OS) should be considered. Patients of certain racial backgrounds may need additional consideration despite identical mutational composition as their counterparts because of different underlying genotypic variations [33]. Compared to the white population, the Asian cohort had a higher incidence of isocitrate dehydrogenase (IDH), suggesting additional consideration for glioblastoma (GBM) treatment in Asian patients [33]. The majority of existing studies focus on Asian populations, who compose 5.6% (n=17,320,856) of the total United States population [5,25,34-36]. At our institution, Asians comprise over 10% of the brain tumor population, nearly double the national percentage [37]. To further explore differences within this population group, we assessed differences in genetic markers and survival outcomes in patients of either Asian or non-Asian descent diagnosed with brain tumors.

MATERIALS AND METHODS

Inclusion criteria
A retrospective chart review was performed. Patients who had undergone brain tumor resection from March 2013 (year in which the electronic chart system was established at our institution) through January 2017 were included. Patients with "unknown" race were excluded. This study was approved by our center’s Medical Institutional Review Board.

Data collection
Patient demographics (age, sex, race, and ethnicity), treatment variables, and survival outcomes were collected. The entire population was stratified by race, with the subgroups as “white,” “black,” “Hispanic or Latino,” and “Asian.” Patients in the Asian category were separately grouped by ethnicity. Categorization was chosen based on examples from the most recent United States Census Bureau data [36,37]. Treatment variables included operation duration, extent of resection (gathered from operative report), chemotherapy, and radiation modality and dosage. Primary outcomes were length of stay, discharge disposition, recurrence rate, PFS, and OS.

Mutational statuses and diagnoses were gathered from pathology reports. For patients diagnosed with GBM specifically, statuses were gathered for IDH, phosphate and tensin homologue (PTEN), tumor protein p53 (p53), chromosome 1p and chromosome 19q (1p/19q), epidermal growth factor receptor (EGFR), type III epidermal growth factor receptor (EGFRVIII), overall antigen Ki-67 (Ki67) percentages, and methylation mutational statuses. World Health Organization (WHO) grade, glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA), and S100 mutational statuses were accumulated for meningioma patients. Patients were then organized by tumor histological subtype.

Statistical analysis
Wilcoxon signed-rank and Pearson’s tests were performed. Correlation analyses were performed to identify relationships between race and all variables of interest for GBM and meningioma patients. Statistical analyses were performed using SAS, version 9.3 (SAS Institute, Cary, NC, USA). A p-value less than 0.05 was considered statistically significant.

RESULTS

General population
A total of 452 patients were included in the study. Demographics of both cohorts are summarized in Table 1. Whites comprised 71% of the cohort (n=323), Asian 16% (n=70), Hispanic or Latino 9% (n=40), black 4% (n=18), and unspecified 0.2% (n=1). Pathologies stratified by race are summarized in Table 2. The Asian-only population consisted of: Filipino 17% (n=12), Chinese 14% (n=10), Korean 10% (n=7), Vietnamese 4% (n=3), Pacific Islander 3% (n=2), Japanese 3% (n=2), Burmese 1% (n=1), and unspecified 47% (n=33). Tumor pathologies in the Asian-only cohorts included are summarized in Table 3.

Glioblastoma
We identified 65 GBM patients in total across all races. Of patients diagnosed with GBM, non-Asian patients comprised 89% of the cohort (n=58) with the remaining 11% (n=7) being Asian patients. There were no statistically significant differences between the groups in PTEN loss (p=0.705), p53 (p=0.086), 1p/19q loss (p=0.282), EGFR amplification (p=0.709), EGFRVIII (p=0.118), overall Ki67 (p=0.695), O6-methylguanine methyltransferase (MGMT) gene promoter methylation status (p=0.090), or other gathered variables (Table 4).

Table 1. Demographics of all populations

| Population | Age (years, SD, range) | Sex, % (n) |
|------------|------------------------|------------|
| General    | 54.8, 14.5, 18–90      | 52.4 (242) |
| Glioblastoma | 54.1, 13.1, 28–69    | 38.8 (64)  |
| Meningioma | 57.5, 14.7, 18–90      | 71.9 (133) |

SD, standard deviation
Table 2. Summary of pathologies by race

| Pathology              | White or Caucasian | Black or African American | Hispanic or Latino | Asian |
|------------------------|--------------------|---------------------------|--------------------|-------|
| GBM/gliosarcoma        | 30.5 (141)         | 0.2 (1)                   | 3.1 (14)           | 3.1 (14) |
| Low-grade glioma       | 5.8 (27)           | 0 (0)                     | 0 (0)              | 0.9 (4)  |
| High-grade glioma      | 8.2 (38)           | 0.2 (1)                   | 0 (0)              | 1.5 (7)   |
| Meningioma             | 22.9 (106)         | 3.1 (14)                  | 5.6 (26)           | 8.4 (38)  |
| Metastases             | 2.4 (11)           | 0.4 (2)                   | 0 (0)              | 1.5 (7)   |

All values given in percentage and (n). GBM, glioblastoma

Table 3. Summary of pathologies by Asian ethnicity

| Pathology              | Pacific Islander | Burmese | Korean | Filipino | Vietnamese | Chinese | Japanese | Unspecified |
|------------------------|------------------|---------|--------|----------|------------|---------|----------|-------------|
| GBM/gliosarcoma        | 0 (0)            | 0 (0)   | 2.86 (2) | 2.86 (2) | 1.43 (1)   | 2.86 (2) | 0 (0)    | 10.00 (7)   |
| Low-grade glioma       | 1.43 (1)         | 0 (0)   | 0 (0)   | 0 (0)    | 0 (0)      | 0 (0)   | 0 (0)    | 4.29 (3)    |
| High-grade glioma      | 1.43 (1)         | 0 (0)   | 0 (0)   | 1.43 (1) | 0 (0)      | 0 (0)   | 0 (0)    | 7.14 (5)    |
| Meningioma             | 0 (0)            | 1.43 (1) | 7.14 (5) | 11.83 (8) | 1.43 (1)   | 10.00 (7) | 2.86 (2) | 20.00 (14)  |
| Metastases             | 0 (0)            | 0 (0)   | 0 (0)   | 1.43 (1) | 1.43 (1)   | 1.43 (1) | 0 (0)    | 5.71 (4)    |

All values given in percentage and (n). GBM, glioblastoma

**Meningioma**

A total of 185 meningioma patients were included. Non-Asian patients comprised 79% of the group (n=146) while Asian patients composed the last 21% of meningioma patients (n=39). There were no statistically significant differences between these groups in WHO grade (p=0.643), histological subtype (p=0.783), GFAP (p=0.197), EMA (p=0.057), S100 (p=0.549), Ki67 (p=0.592), or other collected variables (Table 4).

**DISCUSSION**

Differences in races, specifically Asians in contrast to other groups, in respect to brain tumor epidemiology has already been well studied [1,4-31]. Due to the considerable Asian patient population at our institution, we endeavored to compare races within the cohort. We performed a retrospective chart analysis of patients, who underwent brain tumor resection at our institution. Race and all collected variables were tested in both GBM and meningioma patients. Survival outcomes were measured in those two cohorts against our collected variables.

Though several studies have reported significant proclivities between tumor pathologies and certain races, there were no statistically significant differences between race and tumor pathologies in our population cohort [1,4-31,38-42]. Maile et al. [8] studied 35,663 patients in England and found that the general white population had the highest occurrence of GBM among other races. They also reported Pakistanis had two times the incidence of brain neoplasms compared to that of Bangladeshis (p<0.001) [8]. However Brown et al. [4] found that in a cohort of 2,096 pediatric patients, age-specific incidence of tumor pathology was not statistically different between races. In that report, even when stratified by age, there were no significant differences or correlations between race and tumor pathology [4].

In our patients with GBM, there was no significant difference between Asians and non-Asians for any of our variables. PFS and OS between the two groups were not statistically distinct from one another. There are several studies that document the mutational statuses of GBM, with some demonstrating disparities in PFS and OS between races [23,25,26,28,32,33,35,43-68]. Dai et al. [33] performed a meta-analysis of GBM patients which included studies from Europe, North America, and Asia. In their study of 3,464 patients, IDH mutation associated mortality rate decreased nearly two times more in Euro-

Table 4. Elements investigated in pathology cohorts

|                     | Glioblastoma | Meningioma |
|---------------------|--------------|------------|
| Age                 | 0.0703       | 0.3581     |
| Sex                 | 0.0986       | 0.7487     |
| Chemotherapy        | 0.2547       | 0.9903     |
| Radiation           | 0.6093       | 0.5779     |
| Surgery duration    | 0.5631       | 0.3395     |
| Extent of resection | 0.2671       | 0.0918     |
| Length of stay      | 0.3900       | 0.1118     |
| Discharge disposition | 0.2397   | 0.8238     |
| Follow up duration  | 0.8293       | 0.4121     |
| Recurrence          | 0.6294       | 0.1580     |
| Progression-free survival | 0.4048 | 0.9662     |
| Overall survival    | 0.8183       | 0.3711     |
ean populations than it did in Asian populations [33]. Addi-
tional multivariate analysis between race, treatment modalities,
and mutational variation is one approach that warrants further
study to understand PFS and OS. A study by Wu et al. [28] ex-
amined MGMT methylation in GBM patients of different ethnic
groups and found no statistically significant differences between
these groups with mutational statuses and OS. Because MGMT
methylation results in higher sensitivity to chemotherapeutic
agents, the lack of differences between methylation scores of
various ethnic groups should contribute to similar PFS or OS
among races [69-72]. This is consistent with our analysis of
races in the GBM population. Emerging racial disparities al-
ready published in GBM patients could be used in large meta-
analysis studies to continue this line of research.

In addition, we examined correlates between race and other
prognostic markers in patients with meningioma. While we
found no significant correlations, several studies show a pro-
clivity of meningiomas with certain ethnicities [5,73-75]. Das
et al. [5] published an article on 48,001 patients from a Singa-
porean hospital and found that Chinese patients had the highest
rate of meningioma occurrence. According to their study,
over 90% of their malignant meningiomas were expressed in
Chinese patients [5]. Despite the ethnic propensity for me-
ningioma they found, PFS and OS in patients are comparable
between ethnicities [5]. Analyses of mutational statuses and
their effects as confounding factors in the survival outcomes of
these patients propose a valid area of research that should be ex-
plored more in depth. This model of analysis has already been
well-applied to GBM research.

Our study was a retrospective review, which incurs several
limitations. Data was gathered in a limited setting; therefore,
the tested variables are not as homogenous as a prospective
study. Patients with unspecified race or unknown mutational
statuses, although still included here, could not be further dis-
tinguished. Additionally, we reported from a single institution,
while several similar studies acquired their cohort from a large,
national database [6-8,13,25,32,34,38,61,76]. Therefore, our
sample population may be limited in both size and location.
Socio-economic status of patients has been acknowledged to
affect rates of brain tumor occurrence and may be a confound-
ing variable [13,20-22,28,32,42,76-83]. While our analysis only
used univariate statistics, future studies analyzing confound-
ing factors, such as age, in survival rates are the next approach-
es in identifying racial disparities.

Our single institution study facilitated the acquisition of so-
co-economic status, which in our future studies could eluci-
date the role of socio-economic status on OS and PFS. Addi-
tional multivariate analysis includes investigating the role of
mutational statuses as confounding factors in race and survival
outcome correlations. Racial disparities have been documented
in a few studies similar to the one performed by the authors.
Continued evaluation of those disparities is necessary to as-
sure standardized treatment across all races.

In conclusion, while there are few studies assessing survival
outcomes of different racial cohorts with various tumor pa-
thologies, patients with the same mutational configuration
may not have the same treatment response between varying
racial backgrounds. Additional studies using larger cohorts,
such as the Surveillance, Epidemiology, and End Results data-
base, are necessary for more decisive results.

Conflicts of Interest

The authors have no financial conflicts of interest.

Acknowledgments

Lawrence K. Chung is supported by an American Medical Association
27 (AMA) Foundation Seed Grant and an AGA Carolyn L. Kuckein Stu-
dent Research Fellowship. Isaac Yang was partially supported by a Vision-
ary Fund Grant, an Eli and Edythe Broad Center of Regenerative Medicine
and Stem Cell Research UCLA Scholars in Translational Medicine Pro-
gram Award, the Jason Dessel Memorial Seed grant, the UCLA Honberger
Endowment Brain Tumor Research Seed Grant, and the STOP CANCER
Research Career Development Award.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mor-
tality worldwide: sources, methods and major patterns in GLOBO-
CAN. 2012. Int J Cancer 2013;136:E359-86.
2. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Re-
view (CSR) 1975-2014. Bethesda, MD: National Cancer Institute. (Ac-
cessed July 28, 2017, at https://seer.cancer.gov/csr/1975_2014/).
3. Chen JG, Zhu J, Zhang YH, et al. Cancer survival in Qidong between
1972 and 2011: a population-based analysis. Mol Clin Oncol 2017;6:
944-54.
4. Brown M, Schrot R, Bauer K, Dodge J. Incidence of first primary cen-
nal nervous system tumors in California, 2001-2005: children, adoles-
cents and teens. J Neurooncol 2009;94:263-73.
5. Das A, Tang WY, Smith DR. Meningiomas in Singapore: demographic
and biological characteristics. J Neurooncol 2000;47:153-60.
6. Dubrow R, Darefsky AS. Demographic variation in incidence of adult
glioma by subtype, United States, 1992-2007. BMC Cancer 2011;11:325.
7. Gittleman H, Ostrom QT, Farah PD, et al. Descriptive epidemiology of
pituitary tumors in the United States, 2004-2009. J Neurosurg 2014;121:
527-35.
8. Malek EJ, Barnes I, Finlayson AE, Sayeed S, Ali R. Nervous system and
intracranial tumour incidence by ethnicity in England, 2001-2007: a
descriptive epidemiological study. PLoS One 2016;11:e0154347.
9. Kohler BA, Ward E, McCarthy BJ, et al. Annual report to the nation on
the status of cancer, 1975-2007, featuring tumors of the brain and other
nervous system. J Natl Cancer Inst 2011;103:714-36.
10. Linabery AM, Ross JA. Trends in childhood cancer incidence in the
U.S. (1992-2004). Cancer 2008;112:416-32.
11. Howard SC, Metzger ML, Willimas JA, et al. Childhood cancer epide-
miology in low-income countries. Cancer 2008;112:461-72.
12. Heshmat MY, Kov i J, Simpson C, Kennedy J, Fan KJ. Neoplasms of
the central nervous system. Incidence and population selectivity in the
Washington DC, metropolitan area. Cancer 1976;38:2135-42.
13. Ohgaki H, Kleihues P. Epidemiology and etiology of gliomas. Acta
Neuropathol 2005;109:93-108.
14. Davis FG, McCarthy B, Jukich P. The descriptive epidemiology of brain
tumors. Neuroimaging Clin N Am 1999;9:381-94.
15. Fan KJ, Pezeshkpour GH. Ethnic distribution of primary central nervous system tumors in Washington, DC, 1971 to 1985. J Natl Med Assoc 1992;84:858-63.
16. Jukich PJ, McCarthy BJ, Surawicz TS, Freels S, Davis FG. Trends in incidence of primary brain tumors in the United States, 1985-1994. Neuro Oncol 2001;3:141-51.
17. Kuratsu J, Takeshima H, Ushio Y. Trends in the incidence of primary intracranial tumors in Kumamoto, Japan. Int J Clin Oncol 2001;6:183-91.
18. McLendon RE, Robinson JS Jr, Chambers DB, Grufterman S, Burger PC. The glioblastoma multiforme in Georgia, 1977-1981. Cancer 1985;56:894-7.
19. Stiller CA, Nectoux J. International incidence of childhood brain and spinal tumours. Int J Epidemiol 1994;23:458-64.
20. Deorah S, Lynch CF, Sibenaller ZA, Ryken TC. 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.
21. Chakrabarti I, Cockburn M, Cozen W, Wang YP, Preston-Martin S. A population-based description of glioblastoma multiforme in Los Angeles County, 1974-1999. Cancer 2005;104:2798-806.
22. Preston-Martin S. Descriptive epidemiology of primary tumors of the brain, cranial nerves and cranial meninges in Los Angeles County. Neuroepidemiology 1989;8:283-95.
23. Barnholtz-Sloan JS, Sloan AE, Schwartz AG. Racial differences in survival after diagnosis with primary malignant brain tumor. Cancer 2003;98:603-9.
24. Sadetzki S, Modan B, Chetrit A, Freedman L. An iatrogenic epidemic of benign meningioma. Am J Epidemiol 2000;151:266-72.
25. Thumma SR, Fairbanks RK, Lamoreaux WT, et al. Effect of pretreatment clinical factors on overall survival in glioblastoma multiforme: a Surveillance Epidemiology and End Results (SEER) population analysis. World J Surg Oncol 2012;10:75.
26. Barnholtz-Sloan JS, Maldonado JL, Williams VL, et al. Racial/ethnic differences in survival among elderly patients with a primary glioblastoma. J Neurooncol 2007;85:171-80.
27. Robertson JT, Gunter BC, Somes GW. Racial differences in the incidence of gliomas: a retrospective study from Memphis, Tennessee. Br J Neurosurg 2002;16:562-6.
28. Wu CC, Wang TJ, Jani A, et al. A modern radiotherapy series of survival in Hispanic patients with glioblastoma. World Neurosurg 2016;88:260-9.
29. Sze M, Butow P, Bell M, et al. Migrant health in cancer: outcome disparities and the determinant role of migrant-specific variables. Oncologist 2015;20:523-31.
30. Grenade C, Phelps MA, Villalona-Calero MA. Race and ethnicity in cancer therapy: what have we learned? Clin Pharmacol Ther 2014;95:403-12.
31. Allard JE, Maxwell GL. Race disparities between black and white women in the incidence, treatment, and prognosis of endometrial cancer. Cancer Control 2009;16:53-6.
32. Aizer AA, Ancukiewicz M, Nguyen PL, Shih HA, Loeffler JS, Oh KS. Underutilization of radiation therapy in patients with glioblastoma: predictive factors and outcomes. Cancer 2014;120:238-43.
33. Dai Y, Ning X, Han G, Li W. Assessment of the association between isocitrate dehydrogenase 1 mutation and mortality risk of glioblastoma patients. Mol Neurobiol 2016;53:1501-8.
34. Jung KW, Yoo H, Kong HJ, Won YJ, Park S, Lee SH. Population-based survival data for brain tumors in Korea. J Neurooncol 2012;109:301-7.
35. Mukasa A, Takayanagi S, Saito K, et al. Significance of IDH mutations varies with tumor histology, grade, and genetics in Japanese glioma patients. Cancer Sci 2012;103:587-92.
36. Hoeffel EM, Rastogi S, Kim MO, Shahid H. The Asian population: 2010. Asian Origins 2010: US census bureau. 2010. (Accessed March 23, 2016, at https://www.census.gov/prod/cen2010/briefs/c2010br-11.pdf).
37. Humes KR, Jones NA, Ramirez RR. Overview of Race and Hispanic Origin: 2010. US census bureau. 2010. (Accessed March 23, 2016, at https://www.census.gov/prod/2010pubs/c2010br-02.pdf).
38. Nomura K. Epidemiology of germ cell tumors in Asia of pineal region tumor. J Neurooncol 2001;54:211-7.
39. Araki C, Matsumoto S. Statistical reevaluation of pinealoma and related tumors in Japan. J Neurosurg 1969;30:146-9.
40. Oi S, Matsuzawa K, Chou JU, Kim DS, Kang JK, Cho BK. Identical characteristics of the patient populations with pineal region tumors in Japan and in Korea and therapeutic modalities. Childs Nerv Syst 1998;14:36-40.
41. Surawicz TS, Davis F, Freels S, Laws ER Jr, Menck HR. Brain tumor survival: results from the National Cancer Data Base. J Neurooncol 1998;40:151-60.
42. Ostrom QT, Gittleman H, Xu J, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2009-2013. Neuro Oncol 2016;18(suppl_5):v1-75.
43. Sanson M, Marie Y, Paris S, et al. Isocitrate dehydrogenase 1 codon 132 mutation is an important prognostic biomarker in gliomas. J Clin Oncol 2009;27:4150-4.
44. Weller M, Felsberg J, Hartmann C, et al. Molecular predictors of progression-free and overall survival in patients with newly diagnosed glioblastoma: a prospective translational study of the German Glioma Network. J Clin Oncol 2009;27:5743-50.
45. Hartmann C, Hentschel B, Wick W, et al. Patients with IDH1 wild type anaplastic astrocytomas exhibit worse prognosis than IDH1-mutated glioblastomas, and IDH1 mutation status accounts for the unfavorable prognostic effect of higher age: implications for classification of gliomas. Acta Neuropathol 2010;120:707-18.
46. Parsons DW, Jones S, Zhang X, et al. An integrated genomic analysis of human glioblastoma multiforme. Science 2008;321:1807-12.
47. Carrillo JA, Lai A, Nghiempbu PL, et al. Relationship between tumor enhancement, edema, IDH1 mutational status, MGMT promoter methylation, and survival in glioma. Am J Neuroradiol 2012;33:1349-55.
48. Juratli TA, Kirsch M, Geiger K, et al. The prognostic value of IDH mutations and MGMT promoter status in secondary high-grade gliomas. J Neurooncol 2012;110:325-33.
49. Phillips JP, Aranda D, Ellison DW, et al. PDGFRA amplification is common in pediatric and adult high-grade astrocytomas and identifies a poor prognostic group in IDH1 mutant glioblastoma. Brain Pathol 2013;23:565-73.
50. Shin HJ, Lee YS, Hong YK, Kang CS. Correlation between the prognostic value and the expression of the stem cell marker CD133 and isocitrate dehydrogenase1 in glioblastomas. J Neurooncol 2013;115:333-41.
51. Labussière M, Boisselier B, Mokhtari K, et al. Combined analysis of TERT, EGFR, and IDH status defines distinct prognostic glioblastoma classes. Neurology 2014;83:1200-6.
52. Molenaar RJ, Verbaan D, Lamba S, et al. The combination of IDH1 mutations and MGMT methylation status predicts survival in glioblastoma better than either IDH1 or MGMT alone. Neuro Oncol 2014;16:1263-73.
53. Bleeker FE, Atai NA, Lamba S, et al. The prognostic IDH1 (R132H mutation is associated with reduced NADP+-dependent IDH activity in glioblastoma. Acta Neurochir 2010;151:947-94.
54. Killela PJ, Pirozzi CJ, Healy P, et al. Mutations in IDH1, IDH2, and in the TERT promoter define clinically distinct subgroups of adult malignant gliomas. Oncotarget 2014;5:1515-25.
55. Castells X, Acebes JJ, Majos C, et al. Development of robust discriminant equations for assessing subtypes of glioblastoma biopsies. Br J Cancer 2012;106:1816-25.
56. Stancheva G, Goranova T, Laleva M, et al. IDH1/IDH2 but not TP53 mutations predict prognosis in Bulgarian glioblastoma patients. Biomol Res Int 2014;2014:654727.
57. Takahashi Y, Nakamura H, Makino K, et al. Prognostic value of isocitrate dehydrogenase 1, O6-methylguanine-DNA methyltransferase promoter methylation, and 1p/19q co-deletion in Japanese malignant glioma.
patients. World J Surg Oncol 2013;11:284.

58. Wang XW, Boisselier B, Rossetto M, et al. Prognostic impact of the iso-
citrate dehydrogenase 1 single-nucleotide polymorphism rs11554137 in malignant gliomas. Cancer 2013;119:806-13.

59. Yan W, Zhang W, You G, et al. Correlation of IDH1 mutation with clinicopathologic factors and prognosis in primary glioblastoma: a re-
port of 118 patients from China. PLoS One 2012;7:e30339.

60. Zhang W, Zhang J, Yan W, et al. Whole-genome microRNA expression profiling identifies a 5-microRNA signature as a prognostic biomarker in Chinese patients with primary glioblastoma multiforme. Cancer 2013; 119:814-24.

61. Das A, Tan WL, Teo J, Smith DR. Glioblastoma multiforme in an Asian population: evidence for a distinct genetic pathway. J Neurooncol 2002;60:117-25.

62. Watanabe K, Tachibana O, Sata K, Yonekawa Y, Kliehues P, Ohgaki H. Overexpression of the EGF receptor and p53 mutations are mutually exclusive in the evolution of primary and secondary glioblastomas. Brain Pathol 1996;6:217-23; discussion 223-4.

63. Ng HK, Lo SY, Huang DP, Poon WS. Paraffin section p53 protein immu-
nohistochemistry in neuroectodermal tumors. Pathology 1994;26:1-5.

64. Wang Y, Pan L, Sheng XF, Chen S, Dai JZ. Nimotuzumab, a human-
ized monoclonal antibody specific for the EGFR, in combination with temozolomide and radiation therapy for newly diagnosed glioblasto-
ma multiforme: first results in Chinese patients. Asia Pac J Clin Oncol 2016;12:e23-9.

65. Yang H, Wei D, Yang K, Tang W, Luo Y, Zhang J. The prognosis of MGMT promoter methylation in glioblastoma patients of different race: a meta-analysis. Neurochem Res 2014;39:2277-87.

66. Lehrer S, Green S, Ramanathan L, Rosenzweig K, Labombardi V. No consistent relationship of glioblastoma incidence and cytomegalovirus seropositivity in whites, blacks, and Hispanics. Anticancer Res 2012;32:1113-5.

67. Krishnamachari B, Il'yasova D, Scheurer ME, et al. A pooled multisite
analysis of the effects of atopic medical conditions in glioma risk in different ethnic groups. Ann Epidemiol 2015;25:270-4.

68. Tang J, Shao W, Dorak MT, et al. Positive and negative associations of human leukocyte antigen variants with the onset and progression of adult glioblastoma multiforme. Cancer Epidemiol Biomarkers Prev 2005;14:2404-4.

69. Esteller M, Hamilton SR, Burger PC, Baylin SB, Herman JG. Inactiva-
tion of the DNA repair gene O6-methylguanine-DNA methyltransfer-
ase by promoter hypermethylation is a common event in primary hu-
nan neoplasia. Cancer Res 1999;59:793-7.

70. Hegi ME, Liu L, Herman JG, et al. Correlation of O6-methylguanine
methyltransferase (MGMT) promoter methylation with clinical out-
comes in glioblastoma and clinical strategies to modulate MGMT activ-
ity. J Clin Oncol 2008;26:4189-99.

71. Kitange GJ, Carlson BL, Mladek AC, et al. Evaluation of MGMT pro-
moter methylation status and correlation with temozolomide response in orthotopic glioblastoma xenograft model. J Neurooncol 2009;92:23-
31.

72. Amatu A, Sartore-Bianchi A, Moutinho C, et al. Promoter CpG island
hypermethylation of the DNA repair enzyme MGMT predicts clinical response to dacarbazine in a phase II study for metastatic colorectal cancer. Clin Cancer Res 2013;19:2265-72.

73. Kepes J. Meningiomas. Biology, Pathology and Differential Diagnosis. New York: Masson; 1982.

74. Bondy M, Ligon BL. Epidemiology and etiology of intracranial menin-
giomas: a review. J Neurooncol 1996;29:197-205.

75. Rachlin JR, Rosenblum ML. Etiology and biology of meningiomas. In: A-Fetty O, editor. Meningiomas. NY: Raven Press; 1991. p.27-35.

76. Sadetzki S, Zach I, Chetrit A, et al. Epidemiology of gliomas in Israel: a nationwide study. Neuroepidemiology 2008;31:264-9.

77. Pashaki AS, Hamed EA, Mohamadian K, Abassi M, Safaei AM, Torka-
man T. Efficacy of high dose radiotherapy in post-operative treatment of glioblastoma multiforme—a single institution report. Asian Pac J Cancer Prev 2014;15:2793-6.

78. Gurney JG, Kadan-Lottick N. Brain and other central nervous system tumors: rates, trends, and epidemiology. Curr Opin Oncol 2001;13:160-
6.

79. Ohgaki H, Kliehues P. Population-based studies on incidence, survival rates, and genetic alterations in astrocytic and oligodendrogial gliomas. J Neuropathol Exp Neurol 2005;64:479-89.

80. Elia-Pasquet S, Provost D, Jaffre A, et al. Incidence of central nervous system tumors in Gironde, France. Neuroepidemiology 2004:23:110-7.

81. Fleury A, Menegoz F, Grosclaude P, et al. Descriptive epidemiology of cerebral gliomas in France. Cancer 1997;79:1195-202.

82. Iwamoto FM, Reiner AS, Nayak L, Panageas KS, Elkin EB, Abrey LE. Prognosis and patterns of care in elderly patients with glioma. Cancer 2009;115:5534-40.

83. Formenti SC, Meyerowitz BE, Ell K, et al. Inadequate adherence to ra-
diotherapy in Latina immigrants with carcinoma of the cervix. Poten-
tial impact on disease free survival. Cancer 1995;75:1135-40.