Int J Clin Exp Pathol 2015;8(9):11485-11494
www.ijcep.com /ISSN:1936-2625/IJCEP0013634

Original Article

TERT promoter mutated WHO grades II and III gliomas are located preferentially in the frontal lobe and avoid the midline

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Received July 29, 2015; Accepted August 28, 2015; Epub September 1, 2015; Published September 15, 2015

Abstract: The *promoter region of telomerase reverse transcriptase* (*TERT*p) and *isocitrate dehydrogenase* (*IDH*) have been regarded as biomarkers with distinct clinical and phenotypic features. Investigated the possible correlations between tumor location and genetic alterations would enhance our understanding of gliomagenesis and heterogeneity of glioma. We examined mutations of *TERTp* and *IDH* by direct sequencing and fluorescence *in-situ* hybridization in a cohort of 225 grades II and III diffuse gliomas. Correlation analysis between molecular markers and tumor locations was performed by Chi-square tests/Fisher's exact test and multivariate logistic regression analysis. We found gliomas in frontal lobe showed higher frequency of *TERTp* mutation (P=0.0337) and simultaneously mutations of *IDH* and *TERTp* (*IDH*^{mut}-*TERTp*^{mut}) (P=0.0281) than frequency of biomarkers mutation of tumors in no-Frontal lobes, while lower frequency of *TERT*p mutation (P<0.0001) and simultaneously wild type of *IDH* and *TERT*p (*IDH*^{wt}-*TERTp*^{wt}) (P<0.0001) in midline than no-midline lobes. Logistic regression analysis indicated that locations of tumors associated with *TERTp* mutation (OR=0.540, 95% CI 0.324-0.900, P=0.018) and status of combinations of *IDH* and *TERTp* (*IDH*^{mut}-*TERTp*^{mut} vs. *IDH*^{wt}-*TERTp* ^{wt} OR=0.162, 95% CI 0.075-0.350, P<0.001). In conclusion, grades II and III gliomas harboring *TERTp* mutation were located preferentially in the frontal lobe and rarely in midline. Association of *IDH-TERTp* status and tumor location suggests their potential values in molecular classification of grades II and III gliomas.

Keywords: Gliomas, heterogeneity, IDH mutation, TERT promoter mutation, tumor location

Introduction

Gliomas are the most common primary brain malignancies. They were classified by World Health Organization (WHO) into four grades according to the morphological resemblance of the neoplastic cells to normal glial tissues [1, 2]. While glioblastomas (grade IV) had the most dismal prognosis [3-5], grades II and III gliomas showed a relatively favorable but highly variable survival [2]. Although the great improve had been made on the diagnosis and treatment of grades II and III gliomas in the past decades, patients with grades II and III gliomas had an inevitable recurrence and mortal result.

It had been increasingly valued by researchers that gliomas with diverse genetic abnormalities might arise from distinct cell types of origin and might be an important cause of tumor heterogeneity [6, 7]. The association between genetic signature and tumor location is important for understanding the spatial origin of tumorigenesis, sub-classifying this kind of aggressive cancers and developing more intensive treatment measures to prolong the life of patients with grades II and III gliomas.

In the recent years, *isocitrate dehydrogenase* (*IDH*) mutation has been linked with special location distribution in diffuse gliomas. Appro-

ximately 70% to 80% of grades II and III diffuse gliomas and secondary glioblastomas, excluding ependymoma and pilocytic astrocytomas, harbor mutations at codon 132 (R132) of the *isocitrate dehydrogenase 1* gene (*IDH1*) or at codon 172 (R172) of the *isocitrate dehydrogenase 2* gene (*IDH2*) [5, 8-11]. Many studies reported the preferential localization of glioblastomas [12-14] and lower-grade diffuse astrocytic gliomas [5, 6, 9, 12, 15-19] with *IDH* mutation in frontal lobe, suggesting this kind of tumors may arise from distinct cell types of origin.

Concurrently, it is well known that the *promoter region of telomerase reverse transcriptase* (*TERT*p) is a driver event in cancer development [19]. Shortening of telomere repeats cap at the ends of eukaryotic chromosomes with each cell division trigger cell death or senescence eventually [20]. *TERT*p encodes catalytic subunits of telomerase which maintain telomere length, and delay cellular senescence [20, 21]. Tumors with *TERT*p mutation present distinct clinical and phenotypic features [19]. Analysis of the spatial distribution of *TERT*p mutation in grade II and III gliomas and combined analysis with the spatial distribution of *IDH* mutation may enhance the understanding of gliomagenesis. It would be a new perspective for neurosurgeons to consider grade II and III gliomas because of the association between genetic alterations and distinct prognosis of gliomas [22-25]. To our knowledge, there is no report about the regional distribution of *TERT*p mutation in WHO grade II and III gliomas. In this study, we examined the *TERT*p and *IDH* mutation of 225 WHO grade II and III gliomas, confirmed the brain lobes their located and analysis the associations of *TERTp* mutation, *IDH* mutation and tumor location.

Patients and methods

Patients and tissue samples

A total of 225 grades II and III gliomas with formalin-fixed paraffin-embedded tissues available and imaging studies (MRI) at the time of the diagnosis or in the preoperative period available were selected from the Department of Neurosurgery, Huashan hospital (Shanghai, China) between 2001 and 2011 and from the Department of Anatomical and Cellular Pathology, Prince of Wales Hospital (Hong Kong) between 1990 and 2012 [26, 27]. To confirm the tumors location perfectly, detailed radiological reports, operative reports and profiles of postoperative MRI were studied also. According to the 2007 WHO classification [2], there were 96 diffuse astrocytomas (WHO grade II; AII), 20 oligodendrogliomas (WHO grade II; OII), 47 oligoastrocytomas (WHO grade II; OAII), 54 anaplastic astrocytomas (WHO grade III; AAIII), 5 anaplastic oligodendrogliomas (WHO grade III; AOIII), 3 anaplastic oligoastrocytomas (WHO grade III; AOAIII). The cohort overlapped partly with previous studies [26, 27]. This study was approved by the Ethics Committee of Shanghai Huashan Hospital and the New Territories East Cluster-Chinese University of Hong Kong Ethics Committee.

Tumor location

To consider the tumor locations, imaging profiles (MRI) and the clinical files were retrospectively reviewed by two neurosurgeons that had no idea of the molecular status of the patient. If there were disagree with the tumor categorization between them, a senior neurosurgeon would have the right to judge the tumor involvement. To simplify the analysis, the tumors were primarily assigned into three kinds of locations: frontal, midline and others [28]. Frontal gliomas included only the tumors located entirely in frontal lobe. Midline location included corpus callosum, thalamencephalon, periventricular location, brainstem and thoracic spinal cord [7], where tumors entirely located in. Others lobes included insular lobe (including insular, frontotemporal-insular, temporal-insular and frontal-insular lobe), temporal lobe (including temporal, frontotemporal, tempoparietal, temporal-occipital lobe), parietal lobe (including parietal, frontoparietal, parietal-occipital lobe) and Occipital lobe & Cerebellum (including occipital lobe and cerebellum).

Mutational analysis of TERTp and IDH

Among the 225 grade II and III gliomas that had been detected *IDH* mutation, 213 grade II and III gliomas were examined for mutations of *TERTp*. Detection of *IDH1* and *IDH2* alterations of the mutational hotspot codons R132 and R172 and mutation analysis of *TERTp* were performed as previously described respectively [26, 27, 29]. Briefly, crude cell lysate extracted from dewaxed sections from representative

Table 1. Clinical and molecular data of 225 WHO grade II and III gliomas

Variables	All patients number (%)	*IDH* mutation positive/all (%)	*TERTp* mutation positive/all (%)
Age			
Median	40	39	44
Mean (±SD)	40.8±12.2	40.9±9.6	43.7±11.5
Range	3-79	23-79	13-70
Sex			
Male	140 (62.22)	91/140 (65)	35/131 (26.72)
Female	85 (37.78)	58/85 (68.24)	26/82 (31.71)
Pathology			
II	163 (72.44)	123/163 (75.46)	45/158 (28.48)
III	62 (27.56)	26/62 (41.93)	16/55 (35.56)
Location			
Frontal	83 (36.89)	67/83 (80.72)	30/81 (37.04)
Insular	13 (5.78)	10/13 (76.92)	4/13 (30.77)
Temporal	61 (27.11)	41/61 (67.21)	15/53 (28.3)
Parietal	35 (15.56)	25/35 (71.43)	9/33 (27.27)
O & C	6 (2.67)	1/6 (16.67)	0/6 (0)
C & C	6 (2.67)	3/6 (50)	0/6 (0)
Midline	21 (9.33)	2/21 (9.52)	2/21 (9.52)

Abbreviations: O & C, Occipital & Cerebellum; C & C, Corpus callosum & Cingulate gyrus. Frontal including tumors located entirely in frontal lobe; Midline including tumors located entirely in corpus callosum, thalamencephalon, periventricular location, brainstem and thoracic spinal cord; Insular including tumors involved in insular, frontotemporal-insular, temporal-insular and frontal-insular lobe; Temporal including tumors involved in temporal, frontotemporal, tempoparietal, temporal-occipital lobe; Parietal including tumors involved in parietal, frontoparietal, parietal-occipital lobe; O & C including tumors located entirely in occipital lobe and cerebellum; C & C including tumors located entirely in corpus callosum and cingulate gyrus.

tumor area with tumor content greater than 70% was used for subsequent polymerase chain reaction (PCR) analysis. Primers sequences (the forward primer IDH1F: 5'-CGGTCTTCAGAGAAGCCATT-3' and reverse primer IDH1-R: 5'-CACATTATTGCCAACATGAC-3'; forward primer IDH2-F: 5'-AGCCCATCATCTGCAAAAAC-3' and reverse primer IDH2-R 5'-CTAGGCGAGGAGCTCCAGT-3') were used to amplify fragments of PCR, while a 163 bp fragment spanning the two mutational hotspots (C228T and C250T) in promoter region of *TERTp* were amplified with TERT-F (5'-GTCCTGCCCCTTCACCTT-3') and TERT-R (5'-CAGCGCTGCCTGAAACTC-3'). Sequencing was performed using Big Dye Terminator Cycle Sequencing kit v1.1. The products were resolved in Genetic Analyzer 3130xl and analyzed by Sequencing Analysis software.

Statistical analysis

Fisher's exact test (or Chi-square tests when n>10) were performed to assess the genotype distribution of *IDH* and *TERTp* mutation in different tumor locations. Main effects multivariate logistic regression analysis was used to identify the factors associated with status of biomarker of this cohort of grade II and III gliomas. Gender (values: 1= female, 0= male), age (values: 1= group of patients ≤40 years old, 2≥40 years old), pathology (values: 1= GradeII, 2= Grade III) and locations of tumors (values: 1= Frontal, 2= Others lobe, 3= Midline) were selected as independent variables for the analysis of each biomarker status. Value of β, odds ratio (ORs), 95% confidence interval (95% CIs) and p-values of factors with status of each biomarkers status were calculated respectively. All statistical tests were two-sided, and the threshold for statistical significance was $P<0.05$. Analyses were conducted with SPSS for Windows version 20.0 (SPSS Inc, Chicago, IL, USA).

Results

Cohort characteristics and molecular data

IDH mutation was found in 149 of 225 (66.22%) cases examined, including one IDH1-R132S mutation, one IDH2-R172M mutation, three IDH2-R172K mutation and 144 IDH1-R132H mutations. *IDH* mutations were found in 65% (91/140) male patients and 68.24% (58/85) female patients. There were 117 patients younger than or equal to 40 years and 108 patients older than 40 years, with 72.12% (75/108) and 63.25% (74/117) harboring *IDH* mutations, respectively. Among the cohort, 68.75% (66/96) of AII, 90% (18/20) of OII and 82.98% (39/47) of OAII harbored *IDH* mutations. Grade III gliomas, including AAIII, AOIII and AOAIII showed *IDH* mutations in 41.94% (26/62) of cases (**Table 1** and Table S1).

Mutation in *TERTp* was found in 61 of 213 (28.64%) grade II and III gliomas examined. The

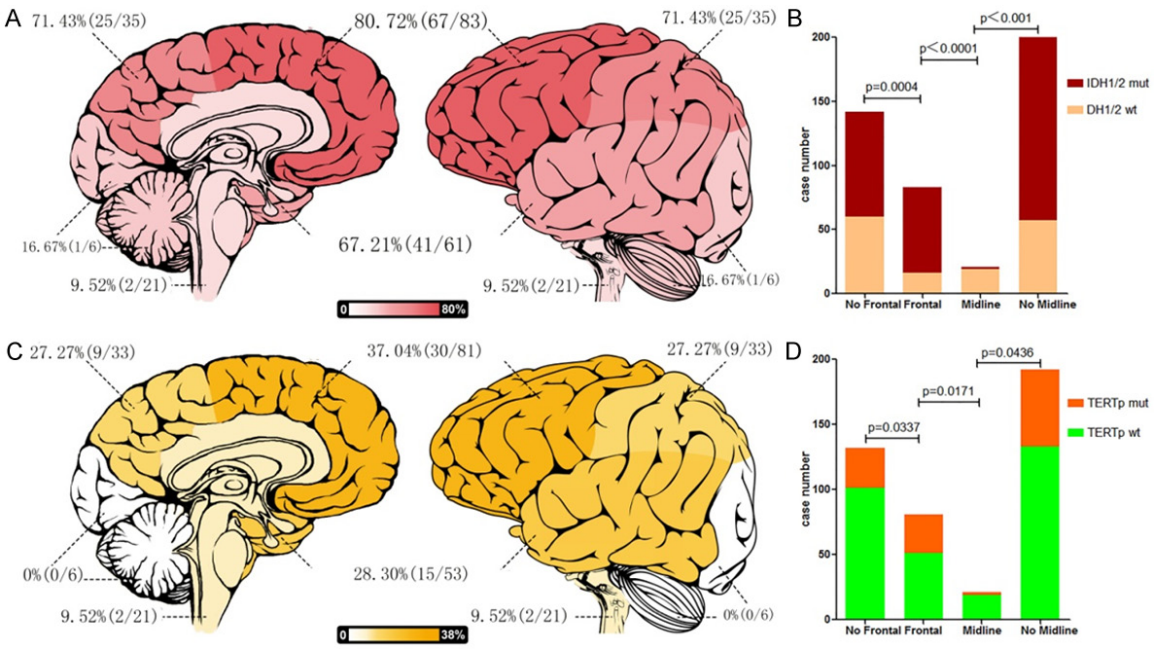

Figure 1. Correlations between locations distribution and molecular status of WHO grade II and III gliomas. The rate of IDH mutation (A) and TERT promoter mutation (C) of WHO grade II and III gliomas decreased gradually from frontal lobe to Midline. WHO grade II and III gliomas with IDH mutation (B) and TERT promoter mutation (D) is more preferentially located in Frontal and repulsively in midline. Footnotes: Frontal including tumors located entirely in frontal lobe; Midline including tumors located entirely in corpus callosum, thalamencephalon, periventricular location, brainstem and thoracic spinal cord; Insular lobe including tumors involved in insular, frontotemporal-insular, temporal-insular and frontal-insular lobe; Temporal lobe including tumors involved in temporal, frontotemporal, tempoparietal, temporal-occipital lobe; Parietal lobe including tumors involved in parietal, frontoparietal, parietal-occipital lobe; Occipital lobe & Cerebellum including tumors located entirely in occipital lobe and cerebellum.

Table 2. ORs, 95% CIs and *p*-values of classes of gliomas location according to status of *IDH*

Variables	β	*P*	OR	95% CI
Gender	-0.286	0.396	0.751	0.388-1.455
Age	-0.387	0.237	0.679	0.358-1.289
Pathology	-1.483	0.000	0.227	0.114-0.453
Location	-1.456	0.000	0.233	0.132-0.413

Abbreviations: CI, confidence interval; OR, odds ratio.

Table 3. ORs, 95% CIs and *p*-values of classes of gliomas location according to status of *TERTp*

Variables	β	*P*	OR	95% CI
Gender	0.092	0.774	1.097	0.584-2.061
Age	0.539	0.089	1.715	0.921-3.192
Pathology	0.025	0.946	1.025	0.504-2.085
Location	-0.616	0.018	0.540	0.324-0.900

Abbreviations: CI, confidence interval; OR, odds ratio.

mutations were found in 26.72% (35/131) of male patients and 31.7% (26/82) of female patients. There were110 patients younger than or equal to 40 years and 103 patients older than 40 years, with 19.42% (20/103) and 36.36% (40/110) showing *TERTp* mutation, respectively. Among the cohort, 14.89% (14/94) of AII, 73.68% (14/19) of OII, 37.78% (17/45) of OAII, 22.45% (11/49) of AAIII, 100% (3/3) of AOIII and 66.67% (2/3) of AOAIII harbored *TERTp* mutation respectively (**Table 1**).

Correlation between biomarker status and tumor location

To discover the tendency of the distributions of biomarker status on brain lobes, we calculated the approximate mutation rate of each biomarker across brain lobes. **Figure 1A** showed *IDH* mutation was identified in 67 of 83 (80.72%) frontal tumors, 10 of 13 (76.92%) insular tumors, 41 of 61 (67.21%) temporal tumors, 25 of 35 (71.43%) parietal tumors, 3 of

Table 4. Regional distribution of the tumors according to combined status of *IDH* and *TERTp*

	Number	Frontal P/N	no Frontal P/N	*P* (F vs. NF)	Midline P/N	no Midline P/N	P (M vs. NM)
IDH^{wt}-*TERTp*^{wt}	57	10/71	47/85	0.0002	17/4	40/152	<0.0001
IDH^{wt}-*TERTp*^{mut}	13	5/76	8/124	1.0000	2/19	7/185	0.6309
IDH^{mut}-*TERTp*^{wt}	95	41/40	54/78	0.2015	2/19	93/99	0.0004
IDH^{mut}-*TERTp*^{mut}	48	25/56	23/109	0.0281	0/21	48/144	0.0050

Abbreviations: P/N, numbers of gliomas with positive/negative biomarker mutation; *P* (F vs. NF), *P* values between Frontal and no-Frontal; P (M vs. NM), *P* values between Midline and no-Midline.

Table 5. ORs, 95% CIs and *p*-values of classes of gliomas location according to combined status of *IDH* and *TERTp*

Variables	β	*P*	OR	95% CI
IDH^{wt}-*TERTp*^{wt}			1	
IDH^{mut}-*TERTp*^{mut}				
Gender	-0.043	0.923	0.958	0.399-2.299
Age	0.190	0.665	1.209	0.513-2.852
Pathology	-1.395	0.009	0.248	0.087-0.709
Location	-1.819	0.000	0.162	0.075-0.350
IDH^{mut}-*TERTp*^{wt}& *IDH*^{wt}-*TERTp*^{mut}				
Gender	-0.135	0.720	0.874	0.417-1.830
Age	-0.024	0.948	0.976	0.479-1.991
Pathology	-0.774	0.049	0.461	0.213-0.998
Location	-1.411	0.000	0.244	0.131-0.453

Abbreviations: CI, confidence interval; OR, odds ratio.

6 (50%) corpus callosum & cingulate gyrus tumors, 1 of 6 (16.67%) occipital & cerebellar tumors and 2 of 21 (9.52%) midline tumors. We found from **Figure 1A** that there was a degressive tendency of mutation rate of *IDH* from Frontal to Midline. Chi-square test or Fisher's exact test had been used to find out that the rate of *IDH* mutation in the cohort of grade II and grade III gliomas were higher in the frontal lobe than non-frontal region (*P*=0.0004, Chi-square test) and lower in the midline than non-midline location (*P*<0.0001, Fisher's exact test) (**Figure 1B**). Results of binary logistic regress confirmed this discover. As shown in **Table 2**, Locations of tumors after adjustment for gender, age and pathology (β=-1.456, OR=0.233, 95% CI 0.132-0.413, *P*<0.001) was found to be independently associated with status of *IDH*1/2. With the values of β is negative, the rate of *IDH* mutation has a degressive tendency from Frontal to midline.

TERTp mutation was found in 37.04% (30/81) of frontal tumors, 30.77% (4/13) of insular tumors, 28.30% (15/53) temporal tumors, 9 of 33 (27.27%) parietal tumors, 0 of 6 (0%) corpus callosum & cingulate gyrus tumors, 0 of 6 (0%) occipital & cerebellar tumors and 2 of 21 (9.52%) midline tumors (**Figure 1C**). We found also that there was a degressive tendency of mutation rate of *TERTp* from Frontal to Midline. The rat of *TERTp* mutation in the cohort of grades II and grade III gliomas were higher in the frontal lobe than non-frontal region (*P*=0.0337, Chi-square tests) and lower in the midline than non-midline location (*P*= 0.0438, Fisher's exact test) (**Figure 1D**). Results of binary logistic regress confirmed this discover too. Locations of tumors after adjustment for gender, age and pathology (β=-0.616, OR=0.540, 95% CI 0.324-0.900, P=0.018) was found to be independently associated with status of *TERTp*. With the values of β is negative, the rate of *TERT*p mutation has a degressive tendency from frontal lobe to midline also (**Table 3**).

Distribution of grade II and III gliomas with combined status of IDH and TERTp

As the results shown above, *IDH* mutation and *TERTp* mutation in grades II and III gliomas shared similar spatial distributions across brain lobes. Therefore, we analyzed the regional distribution of the tumors according to *combined status of IDH and TERTp* (*IDH-TERTp*). Results of Chi-square test or Fisher's exact test identified that simultaneously mutations of *IDH* and *TERTp* (*IDH*^{mut}-*TERTp*^{mut}) subgroup was preferentially located in frontal lobe (*P*=0.0281) and simultaneously wild type of *IDH* and *TERTp* (*IDH*^{wt}-*TERTp*^{wt}) subgroup was preferentially located in midline regions (*P*<0.0001). We identified the rate of *IDH*^{mut}-*TERTp*^{wt} were lower in midline tumors (P=0.0004), but did not identify any other association between *IDH*^{mut}-*TERT*p^{wt}

Table 6. Correlations between locations distribution and molecular status of subgroups of WHO grade II and III gliomas

	Number	Frontal P/N	no Frontal P/N	*P* (F vs. NF)	Midline P/N	no Midline P/N	P (M vs. NM)
II							
TERTp	158	23/38	22/75	0.0468	0/11	45/102	0.0346
IDH1/2	163	56/6	67/34	0.0006	0/11	123/29	<0.0001
III							
TERTp	55	7/13	9/26	0.5434	2/8	14/31	0.7055
IDH1/2	62	11/10	15/26	0.2329	2/8	24/28	0.3316
Man							
TERTp	131	15/29	20/67	0.1750	2/15	33/81	0.2376
IDH1/2	140	40/5	52/43	<0.0001	2/15	90/33	<0.0001
Female							
TERTP	82	15/22	11/34	0.1191	0/4	26/52	0.3058
IDH1/2	85	27/11	31/16	0.6159	0/4	58/23	0.0087
>40							
TERTp	103	19/25	17/42	0.130	2/7	34/60	0.4894
IDH1/2	108	35/10	32/31	0.0051	1/8	66/33	0.0017
≤40							
TERTp	110	11/26	14/59	0.2122	0/12	25/73	0.0646
IDH1/2	117	32/6	50/29	0.0301	1/10	81/25	<0.0001

Abbreviations: P/N, numbers of gliomas with positive/negative biomarker mutation; *P* (F vs. NF), *P* values between Frontal and no-Frontal; P (M vs. NM), *P* values between Midline and no-Midline.

subgroup and *IDH*^{wt}-*TERTp*^{mut} subgroup with location (**Table 4**). To confirm the result, we used a main effects multivariate logistic regression analysis to identify if the *IDH-TERTp* status correlated with tumor locations. For dependent variables, the *IDH*^{mut}-*TERTp*^{mut} subgroup was set as 1, while subgroup of *IDH*^{mut}-*TERTp*^{wt} and *IDH*^{wt}-*TERTp*^{mut} were set as 2, *IDH*^{wt}-*TERTp*^{wt} subgroup was set as 3 (Table S1). As shown in **Table 6**, Locations of tumors after adjustment for gender, age and pathology (*IDH*^{mut}-*TERTp*^{mut} vs. *IDH*^{wt}-*TERTp*^{wt} β=-1.819, OR=0.162, 95% CI 0.075-0.350, *P*<0.001; *IDH*^{mut}-*TERTp*^{wt} & *IDH*^{wt}-*TERTp*^{mut} vs. *IDH*^{wt}-*TERTp*^{wt} β=-1.411, OR=0.244, 95% CI 0.131-0.453, *P*<0.001) was found to be independently associated with status of *IDH-TERTp*. The result of the regression analysis shown there was a depressive of rate of *IDH-TERTp* mutation from Frontal to Midline (**Table 5**).

Biomarker distribution in subgroups by age, gender and histology

We further evaluated the effects of age, gender and histology on the spatial distribution of molecular markers as shown in **Table 6**. In both age subgroups of patients above 40 years and patients at or under 40 years, *IDH* mutation frequency was significantly higher in frontal tumors and lower in midline tumors. For gender, the frequencies of *IDH* mutation were higher in frontal tumors and lower in midline tumors of male patients. Among the female patients, there was no statistical difference in *IDH* mutation rate between different tumor locations. There were not any associations between *TERTp* mutation and tumor locations in subgroups of gliomas classified by age and gender. Evaluating the cohort according to histological grade, biomarker-location associations were mainly identified in grade II tumors, with frontal tumors demonstrating higher rate of *IDH* mutation and *TERTp* mutation, and midline tumors showing lower rate of *IDH* mutation and *TERTp* mutation. Results of regression analysis shown pathology independently associated with *IDH*-1/2 mutation (β=-1.483, OR=0.227, 95% CI 0.114-0.453, *P*<0.001) (**Table 2**) and status of *IDH-TERTp* (*IDH*^{mut}-*TERTp*^{mut} vs. *IDH*^{wt}-*TERTp*^{wt} β=-1.395, OR=0.248, 95% CI 0.087-0.709, *P*=0.009; *IDH*^{mut}-*TERTp*^{wt} & *IDH*^{wt}-*TERTp*^{mut} vs. *IDH*^{wt}-*TERTp*^{wt} β=-0.774, OR=0.049, 95% CI 0.213-0.998, *P*=0.049) (**Table 5**).

Discussion

In this study, we found that WHO grade II and III gliomas located in frontal lobe were preferentially associated with *IDH*, *TERTp* and *IDH*^{mut}-*TERTp*^{mut}, while gliomas in midline were preferentially associated with *IDH*, *TERTp* and *IDH*^{wt}-*TERTp*^{wt}, evenly after adjustment for gender, age and pathology. It is in concordance with previous data [6, 15, 18] that frontal lobe was a preferential location for gliomas harboring *IDH* mutation as compared to other cerebral regions. Chen *et al*. recently reported that the glutaminergic neurotransmitter specialization of human neocortex, especially frontal lobe, created a metabolic niche favorable for the development of *IDH1* mutant tumors [30]. Their findings may explain the biological mechanisms for the preferential distribution of *IDH* mutated grades II and III gliomas in frontal lobes. Midline location in this study included corpus callosum, thalamencephalon, periventricular location, brainstem and thoracic spinal cord. The menchanism of the special distribution of gliomas in midline without *IDH* mutation remained undiscovered. In the subset analysis, association between *IDH* mutation and frontal localization was observed in male patients but not female patients. Given that the case numbers in the individual gender subsets of the cohort were small, further study evaluating the effect of gender on the regional distribution of *IDH* mutation in a larger cohort should be conducted.

We found that grades II and III gliomas in frontal lobe show high *TERTp* mutation rate, on the counterparts, low *TERTp* mutation rate in midline. To the best of our knowledge, this is the first study reported it. Dominik et al. had classified glioblastomas into six subgroups based on their global DNA methylation patterns [7]. They suggested there were a specific anatomically-defined subset of gliomas with H3F3A-K27M mutation almost exclusively arose from midline locations, which was consistent with results of several other researchers' studies [31, 32]. Our results of this report suggested that there might be an anatomically-defined subset of gliomas with biological character of *IDH*^{wt}-*TERTp*^{wt} in grades II and III diffuse gliomas located in midline. Although the biological mechanism of the special distribution of gliomas with *TERTp* mutation requires further elucidation, our results shed light on potential anatomical cellular origins of grades II and III gliomas and improved further research in this field.

As our previously study showed, *TERTp* mutation had been recognized as a dismal molecular marker in prognostic classification of diffuse gliomas [26]. Killela et al. had identified that gliomas exhibit *IDH*^{mut}-*TERTp*^{mut} had a best prognosis for exhibiting a median over survival (OS) of 125 months, while gliomas exhibit *TERTp* mutation alone with a poorest OS (11.5 months) in their cohort of gliomas [19]. In keeping with this study, Eckel-Passow et al. recently found that patients with *IDH*^{wt}-*TERTp*^{wt} and without co-deletion of 1p19q had poor OS than *IDH*^{mut}-*TERTp*^{mut} or IDH mutation alone, but better OS than *TERTp* mutation alone, after adjustment for age and grade [22]. Data of this study may imply neurosurgeons that grades II and III gliomas located in frontal lobe where is more accessible to surgery would be associated with different prognostic biomarkers. Moreover, our results suggest a gloomier prognosis of patients with grades II and III gliomas located in midline for being barely inaccessible to surgery and associated with poor prognostic biomarkers. So, there would be a more crucial need to design new therapeutic agents for grades II and III gliomas located in midline.

In conclusion, we have investigated the spatial distribution of grades II and III gliomas with specially status of *IDH*, *TERTp* and *IDH-TERTp*, suggested that there are some anatomically-defined subset of gliomas with special biomarkers, enhanced neurosurgeons' understanding of grades II and III gliomas in specific area of brain, and would stimulated more researchers to study in this field.

Acknowledgements

This work was supported by grant 13JC1408000 from the Science and Technology Commission of Shanghai Municipality, the Research Special Fund for Public Welfare Industry of Health (No. 201402008), and the National key clinical specialist construction Programs of China (Oncology). We thank Dr. Xiao-Qin Wang for helpful instructions about statistics treatment.

Disclosure of conflict of interest

None.

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Table S1. Details about clinical and molecular data of 225 WHO grade II and III gliomas

Serial number	Gender	Gender code	Age	Age code	Pathology	Pathology code	Location	Location code	Location code 2	TERTp	TERTp code	IDH1/2	IDH1/2 code	IDH-TERTp code
1	F	1	28	1	OII	1	Right Frontal	1	R	mutation	1	R132H	1	1
2	M	0	34	1	OAII	1	Left Parietal-occipital	2	L	mutation	1	R132H	1	1
3	F	1	40	1	OAII	1	Right Temporal	2	R	mutation	1	R132H	1	1
4	F	1	40	1	OAII	1	Left Frontal	1	L	mutation	1	R132H	1	1
5	M	0	47	2	OII	1	Left Frontal	1	L	mutation	1	R132H	1	1
6	M	0	41	2	OAII	1	Right Frontotemporal-insular	2	R	mutation	1	R132H	1	1
7	M	0	27	1	OAII	1	Left Frontal	1	L	mutation	1	R132H	1	1
8	F	1	44	2	OAII	1	Right Temporal	2	R	mutation	1	R132H	1	1
9	M	0	35	1	OAII	1	Left Frontal	1	L	mutation	1	R132H	1	1
10	M	0	23	1	AII	1	Right Frontal	1	R	mutation	1	R172K	1	1
11	F	1	30	1	OAII	1	Left Frontotemporal	2	L	mutation	1	R172K	1	1
12	M	0	38	1	OII	1	Right Temporal	2	R	mutation	1	R132H	1	1
13	M	0	66	2	AII	1	Right Frontal	1	R	mutation	1	R132H	1	1
14	M	0	37	1	OAII	1	Left Parietal	2	L	mutation	1	R132H	1	1
15	M	0	32	1	AII	1	Left Insula	2	L	mutation	1	R132H	1	1
16	M	0	55	2	AAIII	2	Left Temporal	2	L	mutation	1	R132H	1	1
17	M	0	48	2	OII	1	Right Frontal	1	R	mutation	1	R132H	1	1
18	M	0	45	2	OAII	1	Right Frontal	1	R	mutation	1	R132H	1	1
19	F	1	54	2	AII	1	Left Frontal	1	L	mutation	1	R132H	1	1
20	F	1	40	1	AII	1	Left Temporal	2	L	mutation	1	R132H	1	1
21	F	1	35	1	OAII	1	Left Parietal	2	L	mutation	1	R132H	1	1
22	M	0	50	2	OII	1	Bilateral Frontal	1	B	mutation	1	R132H	1	1
23	F	1	43	2	OII	1	Right Frontal	1	R	mutation	1	R132H	1	1
24	M	0	65	2	OII	1	Bilateral Frontal	1	B	mutation	1	R132H	1	1
25	F	1	58	2	AOIII	2	Bilateral Frontal	1	B	mutation	1	R132H	1	1
26	M	0	60	2	AOIII	2	Left Frontal	1	L	mutation	1	R132H	1	1
27	F	1	43	2	OII	1	Right Frontal	1	R	mutation	1	R132H	1	1
28	M	0	45	2	OAII	1	Left temporal-insular	2	L	mutation	1	R132H	1	1
29	F	1	51	2	OAII	1	Left Frontal	1	L	mutation	1	R132H	1	1
30	M	0	37	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2

31	F	1	42	2	OAII	1	Left Parietal	2	L	wild type	0	R132H	1	2
32	F	1	42	2	OII	1	Right Frontal	1	R	wild type	0	R132H	1	2
33	M	0	26	1	OAII	1	Right Frontal	1	R	wild type	0	R132H	1	2
34	M	0	57	2	OAII	1	Left Frontal	1	L	wild type	0	R132H	1	2
35	F	1	37	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
36	M	0	37	1	OAII	1	Right Temporal-occipital and Lateral ventricle	2	R	wild type	0	R132H	1	2
37	M	0	49	2	OII	1	Left Frontal	1	L	wild type	0	R132H	1	2
38	F	1	41	2	OAII	1	Bilateral Frontal	1	B	wild type	0	R132H	1	2
39	M	0	50	2	OAII	1	Right Frontal	1	R	ND	ND	R132H	1	ND
40	F	1	40	1	AII	1	Left Frontal	1	L	mutation	1	R132H	1	1
41	F	1	36	1	OII	1	Left Frontal	1	L	mutation	1	R132H	1	1
42	F	1	32	1	AII	1	Left Temporal	2	L	mutation	1	R132H	1	1
43	M	0	47	2	AII	1	Right Frontal	1	R	mutation	1	R132H	1	1
44	M	0	41	2	AAIII	2	Left Frontal	1	L	mutation	1	R132H	1	1
45	M	0	53	2	OII	1	Right Parietal	2	R	mutation	1	R132H	1	1
46	M	0	48	2	AII	1	Right Temporal	2	R	mutation	1	R132H	1	1
47	F	1	31	1	AII	1	Left Temporal	2	L	mutation	1	R132H	1	1
48	F	1	32	1	OII	1	Right Frontal	1	R	mutation	1	R132H	1	1
49	M	0	32	1	AOAIII	2	Right Frontal	1	R	mutation	1	R132H	1	1
50	F	1	34	1	AOIII	2	Left Frontoparietal	2	L	mutation	1	R132H	1	1
51	M	0	45	2	OAII	1	Right Frontal	1	R	mutation	1	R132H	1	1
52	F	1	49	2	OII	1	Bilateral Fronto-parietal	2	B	mutation	1	R132H	1	1
53	F	1	42	2	OII	1	Left Temporal	2	L	mutation	1	R132H	1	1
54	M	0	36	1	AOAIII	2	Bilateral Fronto-parietal	2	B	mutation	1	R132H	1	1
55	F	1	33	1	OAII	1	Left Frontal	1	L	mutation	1	R132H	1	1
56	M	0	49	2	OAII	1	Right Frontotem-poral-insular	2	R	mutation	1	R132H	1	1
57	F	1	58	2	AII	1	Right Frontal	1	R	mutation	1	wild type	0	2
58	F	1	36	1	AAIII	2	Right Frontal	1	R	mutation	1	wild type	0	2
59	M	0	50	2	AAIII	2	Left Temporal	2	L	mutation	1	wild type	0	2
60	F	1	46	2	AII	1	Cingulum	2	X	mutation	1	wild type	0	2
61	M	0	48	2	AAIII	2	Intraventricular	3	X	mutation	1	wild type	0	2
62	M	0	65	2	AAIII	2	Intraventricular	3	X	mutation	1	wild type	0	2

63	F	1	57	2	AII	1	Right Frontal	1	R	mutation	1	wild type	0	2
64	M	0	60	2	AAIII	2	Right Temporal	2	R	mutation	1	wild type	0	2
65	M	0	70	2	AAIII	2	Right Parietal	2	R	mutation	1	wild type	0	2
66	M	0	13	1	AAIII	2	Bilateral Parietal	2	B	mutation	1	wild type	0	2
67	F	1	54	2	AAIII	2	Right Frontal	1	R	mutation	1	wild type	0	2
68	M	0	48	2	AAIII	2	Right Frontal	1	R	mutation	1	wild type	0	2
69	M	0	46	2	AII	1	Right Temporal	2	R	mutation	1	wild type	0	2
70	F	1	45	2	AII	1	Left Parietal	2	L	wild type	0	R132H	1	2
71	M	0	38	1	AII	1	Right Frontal	1	R	wild type	0	R132H	1	2
72	F	1	46	2	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
73	M	0	39	1	AII	1	Right Frontal	1	R	wild type	0	R132H	1	2
74	M	0	58	2	AII	1	Right Temporal	2	R	wild type	0	R132H	1	2
75	M	0	32	1	AII	1	Left Parietal	2	L	wild type	0	R132H	1	2
76	M	0	34	1	AII	1	Left Frontotemporal-insular	2	L	wild type	0	R132H	1	2
77	F	1	52	2	OAII	1	Left Frontoparietal	2	L	wild type	0	R172K	1	2
78	F	1	42	2	OAII	1	Right Frontal	1	R	wild type	0	R132H	1	2
79	F	1	35	1	OAII	1	Bilateral Cerebellum	2	B	wild type	0	R132S	1	2
80	F	1	47	2	AII	1	Right Frontotemporal	2	R	wild type	0	R132H	1	2
81	M	0	26	1	AII	1	Right Frontal	1	R	wild type	0	R132H	1	2
82	M	0	41	2	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
83	M	0	49	2	AII	1	Right Frontal	1	R	wild type	0	R132H	1	2
84	M	0	38	1	OAII	1	Right Frontal	1	R	wild type	0	R132H	1	2
85	F	1	55	2	OII	1	Right Frontotemporal	2	R	wild type	0	R132H	1	2
86	M	0	79	2	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
87	M	0	28	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
88	F	1	46	2	OAII	1	Left Frontotemporal	2	L	wild type	0	R132H	1	2
89	M	0	54	2	AII	1	Right Frontotemporal	2	R	wild type	0	R132H	1	2
90	M	0	32	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
91	M	0	36	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
92	M	0	36	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
93	M	0	32	1	AII	1	Right Temporal	2	R	wild type	0	R132H	1	2
94	F	1	43	2	AII	1	Corpus callosum	2	X	wild type	0	R172M	1	2

95	M	0	31	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
96	M	0	29	1	AII	1	Left Insula	2	L	wild type	0	R132H	1	2
97	F	1	60	2	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
98	M	0	42	2	AII	1	Right Parietal	2	R	wild type	0	R132H	1	2
99	M	0	46	2	AII	1	Left Frontotem-poral	2	L	wild type	0	R132H	1	2
100	M	0	31	1	AII	1	Right Temporal	2	R	wild type	0	R132H	1	2
101	M	0	46	2	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
102	F	1	34	1	OAII	1	Left Frontal	1	L	wild type	0	R132H	1	2
103	M	0	68	2	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
104	F	1	45	2	AAIII	2	Left Temporal	2	L	wild type	0	R132H	1	2
105	M	0	49	2	AAIII	2	Right lateral ven-tricle trigonal	3	X	wild type	0	R132H	1	2
106	F	1	48	2	AAIII	2	Right Frontopa-rietal	2	R	wild type	0	R132H	1	2
107	M	0	51	2	AAIII	2	Left Frontal	1	L	wild type	0	R132H	1	2
108	M	0	41	2	AAIII	2	Left Frontal	1	L	wild type	0	R132H	1	2
109	M	0	39	1	AAIII	2	Right Frontal	1	R	wild type	0	R132H	1	2
110	M	0	31	1	AAIII	2	Left Frontotempo-ral-insular	2	L	wild type	0	R132H	1	2
111	F	1	42	2	OAII	1	Left Frontal	1	L	wild type	0	R132H	1	2
112	F	1	31	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
113	M	0	40	1	AAIII	2	Bilateral Frontal	1	B	wild type	0	R132H	1	2
114	M	0	43	2	OAII	1	Right Frontal	1	R	wild type	0	R132H	1	2
115	M	0	39	1	OAII	1	Left Temporal	2	L	wild type	0	R132H	1	2
116	M	0	38	1	AII	1	Left Parietal	2	L	wild type	0	R132H	1	2
117	M	0	28	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
118	F	1	50	2	AII	1	Right Parietal	2	R	wild type	0	R132H	1	2
119	F	1	49	2	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
120	F	1	33	1	AII	1	Right Insular	2	R	wild type	0	R132H	1	2
121	M	0	38	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
122	F	1	31	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
123	M	0	36	1	AII	1	Right Frontal	1	R	wild type	0	R132H	1	2
124	F	1	34	1	AAIII	2	Frontal and Cor-pus collosum	2	X	wild type	0	R132H	1	2
125	M	0	31	1	AAIII	2	Brainstem	3	X	wild type	0	R132H	1	2
126	F	1	46	2	AAIII	2	Left Frontal	1	L	wild type	0	R132H	1	2

127	F	1	46	2	AII	1	Left Parietal	2	L	wild type	0	R132H	1	2
128	F	1	35	1	AAIII	2	Left Frontotem-poral	2	L	wild type	0	R132H	1	2
129	M	0	37	1	AAIII	2	Left Parietal	2	L	wild type	0	R132H	1	2
130	M	0	38	1	AII	1	Right Temporal	2	R	wild type	0	R132H	1	2
131	M	0	60	2	AAIII	2	Corpus callosum	2	X	wild type	0	R132H	1	2
132	M	0	38	1	AII	1	Right Frontal	1	R	wild type	0	R132H	1	2
133	M	0	35	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
134	M	0	32	1	AII	1	Left Frontotempo-ral-insular	2	L	wild type	0	R132H	1	2
135	M	0	39	1	AII	1	Right Frontal	1	R	wild type	0	R132H	1	2
136	M	0	42	2	OAII	1	Left Parietal and Cental sulcus	2	L	wild type	0	R132H	1	2
137	M	0	29	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
138	F	1	24	1	AII	1	Bilateral Frontal	1	B	wild type	0	R132H	1	2
139	M	0	46	2	AII	1	Bilateral Frontal	1	B	wild type	0	R132H	1	2
140	F	1	39	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
141	M	0	27	1	AAIII	2	Right Frontal	1	R	wild type	0	R132H	1	2
142	F	1	36	1	AII	1	Right Parietal	2	R	wild type	0	R132H	1	2
143	M	0	39	1	AII	1	Right Temporal	2	R	wild type	0	R132H	1	2
144	F	1	34	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
145	F	1	33	1	OAII	1	Right Parietal-occipital	2	R	wild type	0	R132H	1	2
146	F	1	30	1	OAII	1	Left Frontoparietal	2	L	wild type	0	R132H	1	2
147	M	0	35	1	AII	1	Left Temporal	2	L	wild type	0	R132H	1	2
148	M	0	33	1	OII	1	Left Parietal	2	L	wild type	0	R132H	1	2
149	F	1	46	2	AOAIII	2	Right Frontal	1	R	wild type	0	R132H	1	2
150	M	0	36	1	OAII	1	Left Frontal-insular	2	L	wild type	0	R132H	1	2
151	M	0	32	1	OAII	1	Left Temporal	2	L	wild type	0	R132H	1	2
152	F	1	61	2	OAII	1	Right Frontal	1	R	wild type	0	R132H	1	2
153	F	1	47	2	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
154	F	1	25	1	OAII	1	Left Frontal	1	L	wild type	0	wild type	0	3
155	M	0	24	1	AII	1	Left Parietal	2	L	wild type	0	wild type	0	3
156	F	1	40	1	OAII	1	Right Occipital	2	R	wild type	0	wild type	0	3
157	F	1	28	1	AII	1	Left Cerebellum	2	L	wild type	0	wild type	0	3
158	F	1	21	1	AII	1	Right Thalamus	3	X	wild type	0	wild type	0	3

159	F	1	25	1	OAII	1	Right lateral ventricle trigonal	3	X	wild type	0	wild type	0	3
160	M	0	22	1	AII	1	Right Temporal	2	R	wild type	0	wild type	0	3
161	M	0	23	1	AII	1	Right Temporal	2	R	wild type	0	wild type	0	3
162	M	0	35	1	AII	1	Left Parietal	2	L	wild type	0	wild type	0	3
163	F	1	41	2	AII	1	Left Parietal	2	L	wild type	0	wild type	0	3
164	F	1	29	1	AII	1	Left Parietal	2	L	wild type	0	wild type	0	3
165	M	0	52	2	AAIII	2	Right Temporal	2	R	wild type	0	wild type	0	3
166	M	0	26	1	AAIII	2	Bilateral Frontal and Corpus Callosum	2	B	wild type	0	wild type	0	3
167	M	0	38	1	AAIII	2	Right lateral ventricle trigonal	3	X	wild type	0	wild type	0	3
168	M	0	53	2	AII	1	Left Frontotemporal	2	L	wild type	0	wild type	0	3
169	F	1	63	2	AAIII	2	Right Tempoparietal	2	R	wild type	0	wild type	0	3
170	M	0	65	2	AAIII	2	Left Parietal	2	L	wild type	0	wild type	0	3
171	M	0	45	2	AAIII	2	Left Frontal	1	L	wild type	0	wild type	0	3
172	M	0	34	1	AAIII	2	Left Frontal	1	L	wild type	0	wild type	0	3
173	F	1	44	2	AAIII	2	Left Frontal	1	L	wild type	0	wild type	0	3
174	M	0	50	2	AAIII	2	Left Frontotemporal	2	L	wild type	0	wild type	0	3
175	M	0	58	2	AAIII	2	Right Frontotemporal-insular	2	R	wild type	0	wild type	0	3
176	M	0	38	1	AAIII	2	Thoracic code T6-8	3	X	wild type	0	wild type	0	3
177	F	1	43	2	AAIII	2	Right Occipital	2	R	wild type	0	wild type	0	3
178	M	0	34	1	AII	1	Right Occipital	2	R	wild type	0	wild type	0	3
179	F	1	51	2	AII	1	Corpus callosum	2	X	wild type	0	wild type	0	3
180	M	0	48	2	AAIII	2	Right Cerebellum	2	R	wild type	0	wild type	0	3
181	M	0	51	2	AAIII	2	Right Basal ganglion	3	X	wild type	0	wild type	0	3
182	F	1	34	1	AAIII	2	Left Frontal	1	L	wild type	0	wild type	0	3
183	M	0	27	1	AAIII	2	Brainstem	3	X	wild type	0	wild type	0	3
184	M	0	33	1	AII	1	Intraventricular	3	X	wild type	0	wild type	0	3
185	M	0	40	1	AII	1	Right Temporal	2	R	wild type	0	wild type	0	3
186	M	0	14	1	AII	1	Right Temporal	2	R	wild type	0	wild type	0	3
187	M	0	45	2	AII	1	Right Temporal	2	R	wild type	0	wild type	0	3
188	M	0	48	2	AII	1	Left Thalamus, Basal ganglion and midbrain	3	X	wild type	0	wild type	0	3
189	F	1	46	2	AII	1	Left Parietal	2	L	wild type	0	wild type	0	3

190	M	0	58	2	AII	1	Right Insular	2	R	wild type	0	wild type	0	3
191	M	0	18	1	AAIII	2	Brainstem	3	X	wild type	0	wild type	0	3
192	M	0	59	2	AAIII	2	Left Parietal	2	L	wild type	0	wild type	0	3
193	M	0	34	1	AAIII	2	Left Thalamus	3	X	wild type	0	wild type	0	3
194	M	0	47	2	AII	1	Left Thalamus	3	X	wild type	0	wild type	0	3
195	M	0	36	1	AII	1	Right Thalamus	3	X	wild type	0	wild type	0	3
196	M	0	46	2	AII	1	Brainstem	3	X	wild type	0	wild type	0	3
197	M	0	47	2	AII	1	Left Thalamus	3	X	wild type	0	wild type	0	3
198	M	0	42	2	AAIII	2	Right Frontal	1	R	wild type	0	wild type	0	3
199	M	0	59	2	AAIII	2	Left temporal-insular	2	L	wild type	0	wild type	0	3
200	F	1	56	2	AII	1	Right Basal ganglion	3	X	wild type	0	wild type	0	3
201	F	1	65	2	AII	1	Right Frontal	1	R	wild type	0	wild type	0	3
202	M	0	3	1	AAIII	2	Right Temporal	2	R	wild type	0	wild type	0	3
203	F	1	13	1	OII	1	Left Temporal	2	L	wild type	0	wild type	0	3
204	M	0	12	1	OAII	1	Right Parietal	2	R	wild type	0	wild type	0	3
205	M	0	16	1	OAII	1	Right Frontal	1	R	wild type	0	wild type	0	3
206	M	0	7	1	OAII	1	Brainstem	3	X	wild type	0	wild type	0	3
207	M	0	8	1	OAII	1	Right Temporal	2	R	wild type	0	wild type	0	3
208	F	1	48	2	OAII	1	Right Frontal	1	R	wild type	0	wild type	0	3
209	M	0	55	2	OAII	1	Right Frontotemporal	2	R	mutation	1	R132H	1	1
210	M	0	28	1	OII	1	Left Temporal	2	L	mutation	1	R132H	1	1
211	M	0	27	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
212	F	1	33	1	AII	1	Left Frontal	1	L	wild type	0	R132H	1	2
213	F	1	63	2	AAIII	2	Right Frontal	1	R	wild type	0	wild type	0	3
214	F	1	31	1	AII	1	Thoracic code T8-10	3	X	wild type	0	wild type	0	3
215	M	0	37	1	AII	1	Right Frontoparietal	2	R	ND	ND	R132H	1	ND
216	M	0	40	1	AAIII	2	Left Temporal	2	L	ND	ND	R132H	1	ND
217	M	0	44	2	AAIII	2	Left Temporal	2	L	ND	ND	R132H	1	ND
218	M	0	39	1	OAII	1	Right Frontoparietal	2	R	ND	ND	R132H	1	ND
219	M	0	40	1	AAIII	2	Right Frontoparietal	2	R	ND	ND	R132H	1	ND
220	M	0	30.5	1	OII	1	Right Tempoparietal	2	R	ND	ND	wild type	0	ND
221	M	0	60	2	AOIII	2	Right Temporal	2	R	ND	ND	wild type	0	ND

222	M	0	28	1	AAIII	2	Right Temporal-occipital and Left Occipital	2	R	ND	ND	wild type	0	ND
223	F	1	62.5	2	AAIII	2	Left Temporal	2	L	ND	ND	wild type	0	ND
224	F	1	58	2	AII	1	Bilateral Frontal and Right Temporal	2	B	ND	ND	wild type	0	ND
225	F	1	38	1	AOIII	2	Left Frontal	1	L	ND	ND	wild type	0	ND

Abbreviations: Gender: F=female; M=male; Gender code: 1=F, 0=M; Age code: 1=younger than or qual to 40 years old, 2=older than 40 years old; Pathology: AII=astrocytoma WHO Grade II, OAII=oligoastrocytoma WHO Grade II, OII=oligodendroglioma WHO Grade II, AAIII=anaplastic astrocytoma WHO Grade III, AOAIII=anaplastic oligoastrocytoma WHO Grade III, AOIII=anaplastic oligodendroglioma WHO Grade III; Pathology code: 1=WHO Grade II, 2=WHO Grade III; Location code: 1=Frontal, 2=Others, 3=Midline; Location code 2: B=Bilateral, L=Left, R=Right, X=not determine; TERTp code: 1=mutation, 0=wild type; IDH1/2 code: 1=mutation, 0=wild type; IDH-TERTp code: 1=IDH^{mut}-$TERTp^{mut}$, 2=IDH^{mut}-$TERTp^{wt}$ and IDH^{wt}-$TERTp^{mut}$, 3=IDH^{wt}-$TERTp^{wt}$; ND=not detect.