# Glioma classification

- Brain tumor classification using MRI images and deep learning techniques
- Exploring neonatal brain tumors: a narrative review about epidemiology, classification, and management
- Current Research Trends in Glioblastoma: Focus on Receptor Tyrosine Kinases
- Real-time brain tumour diagnoses using a novel lightweight deep learning model
- Inferred developmental origins of brain tumors from single-cell RNA-sequencing data
- Peripheral biomarkers predict survival in patients with glioblastoma treated with temozolomide
- Semisupervised adaptive learning models for IDH1 mutation status prediction
- Reclassification of pineal tumor as high-grade astrocytoma with piloid features through methylation profiling: illustrative case

---

They are initially classified, based on their cell of origin, into astrocytoma, oligodendroglioma, or ependymoma. Then, the establishment of the degree of malignancy according to the World Health Organization (WHO) classification criteria allows the organization of these tumors into grades ranging from I to IV.

---

The World Health Organization Classification of Tumors of the Central Nervous System 2021, also known as WHO 5th edition, introduces substantial changes, especially within the glioma category, and separates adult-type and pediatric-type glial tumors into different categories for the first time. In addition, another category of glial tumors, “Circumscribed Astrocytic Gliomas” was also created. This group includes pilocytic astrocytoma, pleomorphic xanthoastrocytoma, subependymal giant cell astrocytoma, chordoid glioma, astroblastoma, and the highly nebulous novel entity high-grade astrocytoma with piloid features [1)].

---

With the advance of genomics research, there has been a new breakthrough in the molecular classification of gliomas. Glioblastoma (WHO grade IV) could be subtyped to proneural, neural, classical, and mesenchymal according to the mRNA expression. Low-grade gliomas (WHO grade Ⅱ and Ⅲ) could be divided into 5 types using 1p/19q co-deletion, isocitrate dehydrogenase(IDH) mutation, and TERTp (promotor region) mutation. In 2016,the markers such as IDH1 mutation were introduced into the diagnosis of gliomas. Genotype and phenotype were integrated to diagnose gliomas [2)].

---

Axial and nonaxial diffusivities, anisotropy indices in the normal-appearing white matter and their interhemispheric differences demonstrated microstructural differences between IDH and TERT mutations, with the potential for classification methods [3)].

---

Currently, classification of neoplasms, especially regarding gliomas, is established on molecular mutations in isocitrate dehydrogenase (IDH) genes and the presence of 1p/19q co-deletion [4)]

To propose a deep learning-based approach for the automated classification of glioma histopathology images. Two classification methods, the ensemble method based on 2 binary classifiers and the multiclass method using a single multiclass classifier, were implemented to classify glioma images into astrocytoma, oligodendroglioma, and glioblastoma, according to the 5th edition of the World Health Organization classification of central nervous system tumors, published in 2021.

Jose L et al. tested 2 different deep neural network architectures (VGG19 and ResNet50) and extensively validated the proposed approach based on The Cancer Genome Atlas data set (n = 700). We also studied the effects of stain normalization and data augmentation on the glioma classification task.

With the binary classifiers, the model could distinguish astrocytoma and oligodendroglioma (combined) from glioblastoma with an accuracy of 0.917 (area under the curve [AUC] = 0.976) and astrocytoma from oligodendroglioma (accuracy = 0.821, AUC score = 0.865). The multiclass method (accuracy = 0.861, AUC score = 0.961) outperformed the ensemble method (accuracy = 0.847, AUC = 0.933) with the best performance displayed by the ResNet50 architecture.

With the high performance of the model (>80%), the proposed method can assist pathologists and physicians to support examination and differential diagnosis of glioma histopathology images, with the aim to expedite personalized medical care [5)]

## IDH-mutant glioma

IDH-mutant glioma

## WHO grade 1 glioma

WHO grade 1 glioma

## WHO grade 2 glioma

WHO grade 2 glioma

## WHO grade 3 glioma

WHO grade 3 glioma

## WHO grade 4 glioma

WHO grade 4 glioma

## Low-grade glioma

Low-grade glioma

## High-grade glioma

High-grade glioma

## Gliomas, glioneuronal tumors, and neuronal tumors

Gliomas, glioneuronal tumors, and neuronal tumors:

Adult-type diffuse gliomas

- Astrocytoma IDH-mutant
- Oligodendroglioma IDH-mutant and 1p/19q-codeleted
- Glioblastoma IDH-wildtype

Pediatric-type diffuse low-grade gliomas

- Diffuse astrocytoma MYB or MYBL1 altered
- Angiocentric glioma
- Polymorphous low-grade neuroepithelial tumor of the young
- Diffuse low-grade glioma, MAPK pathway-altered

Pediatric-type diffuse high-grade gliomas

- Diffuse midline glioma, H3 K27-altered
- Diffuse hemispheric glioma, H3 G34-mutant
- Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype
- Infant-type hemispheric glioma

Circumscribed astrocytic gliomas

- Pilocytic astrocytoma

- High-grade astrocytoma with piloid features
- Pleomorphic xanthoastrocytoma
- Subependymal giant cell astrocytoma
- Chordoid glioma
- Astroblastoma MN1-altered

Glioneuronal and neuronal tumors

- Ganglioglioma
- Desmoplastic infantile ganglioglioma / desmoplastic infantile astrocytoma
- Dysembryoplastic neuroepithelial tumor
- Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters
- Papillary glioneuronal tumor
- Rosette-forming glioneuronal tumor
- Myxoid glioneuronal tumor
- Diffuse leptomeningeal glioneuronal tumor
- Gangliocytoma
- Multinodular and vacuolating neuronal tumor
- Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)
- Central neurocytoma
- Extraventricular neurocytoma
- Cerebellar liponeurocytoma

# Glioma biology

The tumors classified as gliomas include a wide variety of histologies including the more common (astrocytoma, glioblastoma), as well as the less common histologies (oligodendroglioma, mixed oligoastrocytoma, pilocytic astrocytoma). Recent efforts at the comprehensive genetic characterization of various primary brain tumor types have identified a number of common alterations and pathways common to multiple tumor types. Common pathways in glioma biology include growth factor receptor tyrosine kinases and their downstream signaling via the Mitogen activated protein kinase cascade or PI3K signaling, loss of apoptosis through p53, cell cycle regulation, angiogenesis via VEGF signaling and invasion. However, in addition to these common general pathway alterations, a number of specific alterations have been identified in particular tumor types, and a number of these have direct therapeutic implications. These include mutations or fusions in the BRAF gene seen in

pilocytic astrocytomas (and gangliogliomas). In oligodendrogliomas, mutations in IDH1 and codeletion of chromosomes 1p/19q co-deletion are associated with improved survival with upfront use of combined chemotherapy and radiation, and these tumors also have unique mutations of CIC and FUBP1 genes. Low-grade gliomas are increasingly seen to be divided into two groups based on IDH mutation status, with astrocytomas developing through IDH mutation followed by p53 mutation, while poor prognosis low-grade gliomas and primary glioblastomas (Glioblastomas) are characterized by EGFR amplification, loss of PTEN, and loss of cyclin-dependent kinase inhibitors. Glioblastomas can be further characterized based on gene expression and gene methylation patterns into three or four distinct subgroups. Prognostic markers in diffuse gliomas include IDH mutation, 1p19q co-deletion, and MGMT methylation, and MGMT is also a predictive marker in elderly patients with glioblastoma treated with temozolomide monotherapy [6].

## Glioma grade

see Glioma grade.

## Biomarkers

see Glioma biomarker

## Localization

Supratentorial glioma

Infratentorial glioma.

#### Multifocal

see Multiple gliomas

see Multifocal glioma.

see Low-grade glioma and high-grade glioma.

Their various degrees of malignancy form the basis of the World Health Organisation (WHO) grading system:

Pilocytic astrocytoma is the most benign form of glioma (WHO Grade I), followed by a heterogeneous group of so-called “Low-grade gliomas” (WHO Grade II) that comprises oligodendroglioma, astrocytoma and oligoastrocytoma.

Anaplastic glioma (WHO Grade III) is a malignant and aggressive form of glioma but lacks the malignant characteristics of the glioblastoma (WHO IV), the most aggressive and most common glioma [7].

Collective tissue banking, large-scale genomic, transcriptomics and methylomic expression profiling, and discoveries such as isocitrate dehydrogenase gene mutation and the C-phosphate-G island methylation phenotype have improved glioma classification schemes.

Furthermore, the discovery of glioma stem cells has both enhanced and complicated our understanding. Gene signatures describing a proneural versus mesenchymal subtype within glioblastoma multiforme is reflected in both parental tumour as well as glioma stem cells and correlates with differential prognosis and response to radiation and chemotherapy [8].

1)
Köy Y, Tihan T. Circumscribed astrocytic gliomas: Contribution of molecular analyses to histopathology diagnosis in the WHO CNS5 classification. Indian J Pathol Microbiol. 2022 May;65(Supplement):S33-S41. doi: 10.4103/ijpm.ijpm_1019_21. PMID: 35562132.
2)
Hua W, Mao Y. [Advance of molecular subtyping and precise treatment for gliomas]. Zhonghua Wai Ke Za Zhi. 2017 Jan 1;55(1):63-66. doi: 10.3760/cma.j.issn.0529-5815.2017.01.016. Chinese. PubMed PMID: 28056258.
3)
Halilibrahimoğlu H, Polat K, Keskin S, Genç O, Aslan O, Öztürk-Işık E, Yakıcıer C, Danyeli AE, Pamir MN, Özduman K, Dinçer A, Özcan A. Associating IDH and TERT Mutations in Glioma with Diffusion Anisotropy in Normal-Appearing White Matter. AJNR Am J Neuroradiol. 2023 Apr 27. doi: 10.3174/ajnr.A7855. Epub ahead of print. PMID: 37105678.
4)
Casili G, Paterniti I, Campolo M, Esposito E, Cuzzocrea S. The Role of Neuro-Inflammation and Innate Immunity in Pathophysiology of Brain and Spinal Cord Tumors. Adv Exp Med Biol. 2023;1394:41-49. doi: 10.1007/978-3-031-14732-6_3. PMID: 36587380.
5)
Jose L, Liu S, Russo C, Cong C, Song Y, Rodriguez M, Di Ieva A. Artificial Intelligence-Assisted Classification of Gliomas Using Whole-Slide Images. Arch Pathol Lab Med. 2022 Nov 29. doi: 10.5858/arpa.2021-0518-OA. Epub ahead of print. PMID: 36445697.
6)
Cohen AL, Colman H. Glioma biology and molecular markers. Cancer Treat Res. 2015;163:15-30. doi: 10.1007/978-3-319-12048-5_2. Review. PubMed PMID: 25468223.
7)
Schucht P, Beck J, Seidel K, Raabe A. Extending resection and preserving function: modern concepts of glioma surgery. Swiss Med Wkly. 2015 Feb 4;145:w14082. doi: 10.4414/smw.2015.14082. eCollection 2015. PubMed PMID: 25651063.
8)
Morokoff A, Ng W, Gogos A, Kaye A. Molecular subtypes, stem cells and heterogeneity: Implications for personalised therapy in glioma. J Clin Neurosci. 2015 May 6. pii: S0967-5868(15)00101-0. doi: 10.1016/j.jocn.2015.02.008. [Epub ahead of print] Review. PubMed PMID: 25957782.