

## The Last Classification of Tumors of the Central Nervous System by the 2016 World Health Organization

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### Abstract

Scientific advances are progressing at a dizzying pace in all over the world. Parallel to technological progress, enormous advances are recorded in also medicine. No doubt that one of these advances is in neuroscience even is the first.

Parallel to these realities almost every day a new journal is participated in the publishing life. Moreover, the journals are published in the electronic environment also facilitate information access. I believe in that this new journal, International Journal of Clinical Neurology and Brain Research (IJCNBR) will very valuable contributes to humanity.

So, I hope that, to begin with the last updated "2016 World Health Organization Classification of Tumors of the Central Nervous System" will be useful.

**Keywords:** Tumors; Central Nervous System

### Introduction

For the past century, the classification of brain tumors has been based largely on concepts of histogenesis that tumors can be classified according to their microscopic similarities with different putative cells of origin and their presumed levels of differentiation. The characterization of such histological similarities has been primarily dependent on light microscopic features in haematoxylin and eosin-stained sections, immunohistochemical expression of lineage associated proteins and ultrastructural characterization [1].

Studies over the past two decades have clarified the genetic basis of tumorigenesis in the common and some rarer brain tumor entities, raising the possibility that such an understanding may contribute to classification of these tumors [2].

In 2014, a meeting held in Haarlem, the Netherlands, under the auspices of the International Society of Neuropathology, established guidelines for how to incorporate molecular findings into brain tumor diagnoses, setting the stage for a major revision of the 2007 CNS WHO classification [3]. The current update (2016 CNS WHO) thus breaks with the century-old principle of diagnosis based entirely on microscopy by incorporating molecular parameters into the classification of CNS tumor entities [4].

To do so required an international collaboration of 117 contributors from 20 countries and deliberations on the most controversial issues at a three-day consensus conference by a Working Group of 35 neuropathologists, neurooncological clinical advisors and scientists from 10 countries [1].

### Classification

The 2016 CNS WHO is summarized in Table 1 and officially represents an update of the 2007 4th Edition rather than a formal 5th Edition. At this point, a decision to undertake the 5th Edition series of WHO Blue Books has not been made, but given the considerable progress in the fields, both the Hematopoietic/Lymphoid and CNS tumor volumes were granted permission for 4th Edition updates. The 2016 update contains numerous differences from the 2007 CNS WHO [5]. A synopsis of tumor grades for selected entities is reprinted from [4], with permission from the WHO and given by Louis, *et al* [1] in Table 2.

### Discussion

The 2016 CNS WHO represents a substantial step forward over its 2007 ancestor in that, for the first time, molecular parameters are used to establish brain tumor diagnoses. It is hoped that these more objective and more precisely defined entities will allow for improved tailoring of patient therapy, better classification for clinical trials and experimental studies, and more precise categorization for epidemiological purposes. Moreover, while the classification has left some "wastebasket" categories, it allows for more focused study of these less defined groups that will eventually lead to clarification of their status. In addition, while the classification still enables diagnoses to be made in the absence of molecular data in many situations, those settings are clearly designated, allowing distinction of molecularly defined and non-molecularly defined groups. In the long run, it is believed that the 2016 CNS WHO will facilitate the clinical, experimental and epidemiological studies that will lead to improvements in the lives of patients with brain tumors [1].

## WHO classification of tumours of the central nervous system

<b>Diffuse astrocytic and oligodendroglial tumours</b>		<b>Neuronal and mixed neuronal-glial tumours</b>	
Diffuse astrocytoma, IDH-mutant	9400/3	Dysembryoplastic neuroepithelial tumour	9413/0
Gemistocytic astrocytoma, IDH-mutant	9411/3	Gangliocytoma	9492/0
<i>Diffuse astrocytoma, IDH-wildtype</i>	9400/3	Ganglioglioma	9505/1
Diffuse astrocytoma, NOS	9400/3	Anaplastic ganglioglioma	9505/3
Anaplastic astrocytoma, IDH-mutant	9401/3	Dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease)	9493/0
<i>Anaplastic astrocytoma, IDH-wildtype</i>	9401/3	Desmoplastic infantile astrocytoma and ganglioglioma	9412/1
Anaplastic astrocytoma, NOS	9401/3	Papillary glioneuronal tumour	9509/1
Glioblastoma, IDH-wildtype	9440/3	Rosette-forming glioneuronal tumour	9509/1
Giant cell glioblastoma	9441/3	<i>Diffuse leptomeningeal glioneuronal tumour</i>	
Gliosarcoma	9442/3	Central neurocytoma	9506/1
<i>Epithelioid glioblastoma</i>	9440/3	Extraventricular neurocytoma	9506/1
Glioblastoma, IDH-mutant	9445/3*	Cerebellar liponeurocytoma	9506/1
Glioblastoma, NOS	9440/3	Paraganglioma	8693/1
Diffuse midline glioma, H3 K27M–mutant	9385/3*	<b>Tumours of the pineal region</b>	
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	9450/3	Pineocytoma	9361/1
Oligodendroglioma, NOS	9450/3	Pineal parenchymal tumour of intermediate differentiation	9362/3
Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted	9451/3	Pineoblastoma	9362/3
<i>Anaplastic oligodendroglioma, NOS</i>	9451/3	Papillary tumour of the pineal region	9395/3
<i>Oligoastrocytoma, NOS</i>	9382/3	<b>Embryonal tumours</b>	
<i>Anaplastic oligoastrocytoma, NOS</i>	9382/3	Medulloblastomas, genetically defined	
<b>Other astrocytic tumours</b>		Medulloblastoma, WNT-activated	9475/3*
Pilocytic astrocytoma	9421/1	Medulloblastoma, SHH-activated and <i>TP53</i> -mutant	9476/3*
Piloxyoid astrocytoma	9425/3	Medulloblastoma, SHH-activated and <i>TP53</i> -wildtype	9471/3
Subependymal giant cell astrocytoma	9384/1	Medulloblastoma, non-WNT/non-SHH <i>Medulloblastoma, group 3</i>	9477/3*
Pleomorphic xanthoastrocytoma	9424/3	<i>Medulloblastoma, group 4</i>	
Anaplastic pleomorphic xanthoastrocytoma	9424/3	Medulloblastomas, histologically defined	
<b>Ependymal tumours</b>		Medulloblastoma, classic	9470/3
Subependymoma	9383/1	Medulloblastoma, desmoplastic/nodular	9471/3
Myxopapillary ependymoma	9394/1	Medulloblastoma with extensive nodularity	9471/3
Ependymoma	9391/3	Medulloblastoma, large cell / anaplastic	9474/3
Papillary ependymoma	9393/3	Medulloblastoma, NOS	9470/3
Clear cell ependymoma	9391/3	Embryonal tumour with multilayered rosettes, C19MC-altered	9478/3*
Tanycytic ependymoma	9391/3	<i>Embryonal tumour with multilayered     rosettes, NOS</i>	9478/3
Ependymoma, <i>RELA</i> fusion–positive	9396/3*	Medulloepithelioma	9501/3
Anaplastic ependymoma	9392/3	CNS neuroblastoma	9500/3
<b>Other gliomas</b>		CNS ganglioneuroblastoma	9490/3
Chordoid glioma of the third ventricle	9444/1	CNS embryonal tumour, NOS	9473/3
Angiocentric glioma	9431/1	Atypical teratoid/rhabdoid tumour	9508/3
Astroblastoma	9430/3	<i>CNS embryonal tumour with rhabdoid features</i>	9508/3
<b>Choroid plexus tumours</b>		<b>Tumours of the cranial and paraspinal nerves</b>	
Choroid plexus papilloma	9390/0	Schwannoma	9560/0
Atypical choroid plexus papilloma	9390/1	Cellular schwannoma	9560/0
Choroid plexus carcinoma	9390/3	Plexiform schwannoma	9560/0

Melanotic schwannoma	9560/1	Osteochondroma	9210/0
Neurofibroma	9540/0	Osteosarcoma	9180/3
Atypical neurofibroma	9540/0		
Plexiform neurofibroma	9550/0	<b>Melanocytic tumours</b>	
Perineurioma	9571/0	Meningeal melanocytosis	8728/0
Hybrid nerve sheath tumours		Meningeal melanocytoma	8728/1
Malignant peripheral nerve sheath tumour	9540/3	Meningeal melanoma	8720/3
Epithelioid MPNST	9540/3	Meningeal melanomatosis	8728/3
MPNST with perineurial differentiation	9540/3		
<b>Meningiomas</b>		<b>Lymphomas</b>	
Meningioma	9530/0	Diffuse large B-cell lymphoma of the CNS	9680/3
Meningothelial meningioma	9531/0	Immunodeficiency-associated CNS lymphomas	
Fibrous meningioma	9532/0	AIDS-related diffuse large B-cell lymphoma	
Transitional meningioma	9537/0	EBV-positive diffuse large B-cell lymphoma, NOS	
Psammomatous meningioma	9533/0	Lymphomatoid granulomatosis	9766/1
Angiomatous meningioma	9534/0	Intravascular large B-cell lymphoma	9712/3
Microcystic meningioma	9530/0	Low-grade B-cell lymphomas of the CNS	
Secretory meningioma	9530/0	T-cell and NK/T-cell lymphomas of the CNS	
Lymphoplasmacyte-rich meningioma	9530/0	Anaplastic large cell lymphoma, ALK-positive	9714/3
Metaplastic meningioma	9530/0	Anaplastic large cell lymphoma, ALK-negative	9702/3
Chordoid meningioma	9538/1	MALT lymphoma of the dura	9699/3
Clear cell meningioma	9538/1		
Atypical meningioma	9539/1	<b>Histiocytic tumours</b>	
Papillary meningioma	9538/3	Langerhans cell histiocytosis	9751/3
Rhabdoid meningioma	9538/3	Erdheim–Chester disease	9750/1
Anaplastic (malignant) meningioma	9530/3	Rosai–Dorfman disease	
		Juvenile xanthogranuloma	
		Histiocytic sarcoma	9755/3
<b>Mesenchymal, non-meningothelial tumours</b>			
Solitary fibrous tumour / haemangiopericytoma**		<b>Germ cell tumours</b>	
Grade 1	8815/0	Germinoma	9064/3
Grade 2	8815/1	Embryonal carcinoma	9070/3
Grade 3	8815/3	Yolk sac tumour	9071/3
Haemangioblastoma	9161/1	Choriocarcinoma	9100/3
Haemangioma	9120/0	Teratoma	9080/1
Epithelioid haemangioendothelioma	9133/3	Mature teratoma	9080/0
Angiosarcoma	9120/3	Immature teratoma	9080/3
Kaposi sarcoma	9140/3	Teratoma with malignant transformation	9084/3
Ewing sarcoma / PNET	9364/3	Mixed germ cell tumour	9085/3
Lipoma	8850/0		
Angiolipoma	8861/0	<b>Tumours of the sellar region</b>	
Hibernoma	8880/0	Craniopharyngioma	9350/1
Liposarcoma	8850/3	Adamantinomatous craniopharyngioma	9351/1
Desmoid-type fibromatosis	8821/1	Papillary craniopharyngioma	9352/1
Myofibroblastoma	8825/0	Granular cell tumour of the sellar region	9582/0
Inflammatory myofibroblastic tumour	8825/1	Pituicytoma	9432/1
Benign fibrous histiocytoma	8830/0	Spindle cell oncocyoma	8290/0
Fibrosarcoma	8810/3		
Undifferentiated pleomorphic sarcoma / malignant fibrous histiocytoma	8802/3	<b>Metastatic tumours</b>	
Leiomyoma	8890/0		
Leiomyosarcoma	8890/3		
Rhabdomyoma	8900/0		
Rhabdomyosarcoma	8900/3		
Chondroma	9220/0		
Chondrosarcoma	9220/3		
Osteoma	9180/0		

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) [742A]. Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. The classification is modified from the previous WHO classification, taking into account changes in our understanding of these lesions. \*These new codes were approved by the IARC/WHO Committee for ICD-O. *Italics*: Provisional tumour entities. \*\*Grading according to the 2013 WHO Classification of Tumours of Soft Tissue and Bone.

**Table 1:** The 2016 World Health Organization Classification of Tumors of the Central Nervous System. Note that the WHO classifications use spellings that are hybrid between American and British English. The present review, however, has used American English spellings. The italicized entries are provisional, i.e., the WHO Working Group felt there was insufficient evidence to recognize these as distinct disease entities at this time. Reprinted from [4] with permission from the WHO by Louis, *et al.* [1].

## Grading of selected CNS tumors according to the 2016 CNS WHO

**Table 2:** Reprinted from [4], with permission from the WHO by Louis *et al.* [1].

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