



## **Brain tumors**

# Epidemiology & Pathology

**BIO 389** 

Hertler / Gramatzki

## **General concepts**

### **Primary brain tumors**

### **Secondary brain tumors**

Hemispheres > cerebellar Shortened Survival

- Different cells from brain structures
- WHO classification
- Specific therapy

- Different cells from primary tumor
- TNM classification
- Therapy according to primary tumor

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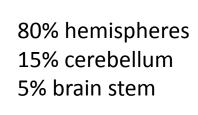
	Incidence Clinical (%)	Autopsy (%)	Median interval from diagnosis (months)	Range (months)
Lung cancer small cell adenocarcinoma squamous cell	30-45 24-30 30	30-70 50 40	2.6 2 0.2	0-15 0-66 0-31
Breast cancer	10-20	20-40	23	0-121
Melanoma	20-45	40-90	36	3-83
Renal cell cancer	20	20	39	19-119
Colon cancer	4	6-10	22	0-48

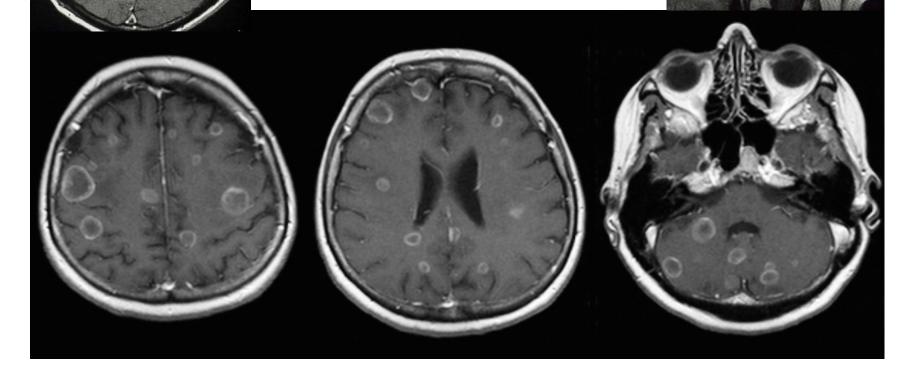




# Local versus whole brain versus systemic treatment approach to metastasis to the

central nervous system





## **General concepts**

## **Primary brain tumors**

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Hemispheres > cerebellar Shortened Survival

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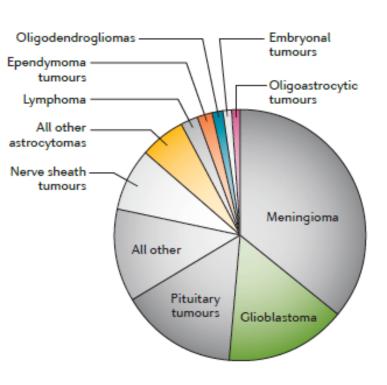


## **Epidemiology**



### **Etiology:**

- Sporadic
- Genetic
- Radiation
- Immunosuppression



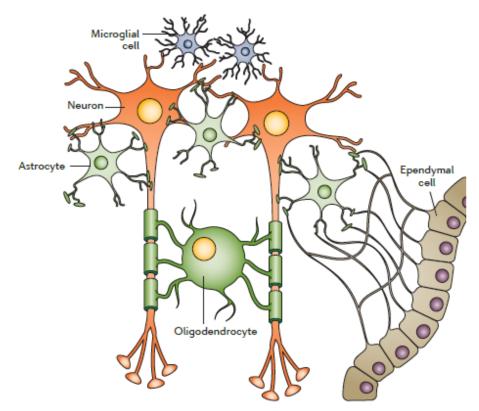


Figure 2 | Brain cells and brain tumours. Neurons form extensive networks and serve the main control functions of the brain, including regulation of homeostasis, circadian rhythms and all higher nervous system functions. Astrocytes form the main connective tissue of the brain. Oligodendrocytes serve the specific function of wrapping central nervous system axons with myelin. Microglial cells exert limited immune function and may have roles in tissue repair and restoration. Neurons are postmitotic cells, and astrocytic and oligodendroglial cells have limited proliferative capacity. It is now believed that gliomas are most likely derived from precursors of intrinsic brain cells rather than from dedifferentiated neurons, astrocytes, and oligodendroglial or microglial cells.







TUMOUR	S OF NE	UROEPITHE	LIALTISSUE

Astrocytic tumours	
Pilocytic astrocytoma	9421/11
Pilomyxoid astrocytoma	9425/3*
Subependymal giant cell astrocytoma	9384/1
Pleomorphic xanthoastrocytoma	9424/3
Diffuse astrocytoma	9400/3
Fibrillary astrocytoma	9420/3
Protoplasmic astrocytoma	9410/3
Gemistocytic astrocytoma	9411/3
Anaplastic astrocytoma	9401/3
Glioblastoma	9440/3
Giant cell glioblastoma	9441/3
Gliosarcoma	9442/3
Gliomatosis cerebri	9381/3
Oligodendroglial tumours	
Oligodendroglioma	9450/3
Anaplastic oligodendroglioma	9451/3
Oligoastrocytic tumours	
Oligoastrocytoma	9382/3
Anaplastic oligoastrocytoma	9382/3
Ependymal tumours	
Subependymoma	9383/1
Myxopapillary ependymoma	9394/1
Ependymoma	9391/3
Cellular	9391/3
Papillary	9393/3
Clear cell	9391/3
Tanycytic	9391/3
Anaplastic ependymoma	9392/3
, mapassa spenajinoma	O O O E O

Choroid plexus papilloma	9390/0
Atypical choroid plexus papilloma	9390/1*
Choroid plexus carcinoma	9390/3
Other neuroepithelial tumours	

Other neuroepithelial tumours	
Astroblastoma	9430/3
Chordoid glioma of the third ventricle	9444/1
Angiocentric glioma	9431/1*

<sup>&</sup>lt;sup>1</sup> Morphology code of the International Classification of Diseases for Oncology (ICD-O) (616A) and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded i0 for benign tumours, /3 for malignant tumours and /1 for bordefine

Neuronal and mixed neuronal-glial tumo Dysplastic gangliocytoma of cerebellum	ours
(Lhermitte-Duclos)	9493/0
Desmoplastic infantile astrocytoma/	
ganglioglioma	9412/1
Dysembryoplastic neuroepithelial tumour	9413/0
Gangliocytoma	9492/0
Ganglioglioma	9505/1
Anaplastic ganglioglioma	9505/3
Papillary glioneuronal tumor	9509/1*
Rosette-forming glioneuronal tumour	
of the fourth ventricle	9509/1*
Central neurocytoma	9506/1
Extraventricular neurocytoma	9506/1*
Cerebellar liponeurocytoma	9506/1*
Paraganglioma of the filum terminale	8680/1
Tumours of the pineal region	
Pineocytoma	9361/1
Pineal parenchymal tumour of	
intermediate differentiation	9362/3
Pineoblastoma	9362/3
Papillary tumour of the pineal region	9395/3*
Embryonal tumours	
Medulloblastoma	9470/3
Desmoplastic/nodular medulloblastoma	9471/3
Medulloblastoma with extensive	
nodularity	9471/3*
Anaplastic medulloblastoma	9474/3*
Large cell medulloblastoma	9474/3
CNS primitive neuroectodermal tumours (F	PNETs)
CNS PNET, NOS	9473/3
CNS neuroblastoma	9500/3
CNS ganglioneuroblastoma	9490/3
Medulloepithelioma	9501/3
Ependymoblastoma	9392/3
Atypical teratoid / rhabdoid tumour	9508/3
TUMOURS OF CRANIAL AND PAR	ASPINA

	OF	CRANIAL	AND	PARASPINAL
NERVES				

Schwannoma (Neurilemoma, neurinoma)	9560/0
Cellular	9560/0
Plexiform	9560/0
Melanotic	9560/0
Neurofibroma	9540/0
Plexiform	9550/0

Perineurioma	9571/0
Intraneural perineurioma	9571/0
Soft tissue perineurioma	9571/0
Malignant peripheral nerve sheath tumour (MPNST) Epithelioid MPNST with divergent mesenchymal and / or epithelial differentiation Melanotic	9540/3 9540/3 9540/3 9540/3

#### **TUMOURS OF THE MENINGES**

umours of meningothelial cells	
Meningioma	9530/0
Meningothelial	9531/0
Fibrous (fibroblastic)	9532/0
Transitional (mixed)	9537/0
Psammomatous	9533/0
Angiomatous	9534/0
Microcystic	9530/0
Secretory	9530/0
Lymphoplasmacyte-rich	9530/0
Metaplastic	9530/0
Chordoid	9538/1
Clear cell	9538/1
Atypical	9539/1
Papillary	9538/3
Rhabdoid	9538/3
Anaplastic (malignant)	9530/3
lesenchymal tumours	
ipoma	8850/0
ngiolipoma	8861/0

8880/0

8850/3

8815/0

8810/3

8830/3 8890/0 8890/3

	Malignant fibrous histiocytoma
ASPINAL	Leiomyoma
	Leiomyosarcoma

Hibernoma

Fibrosarcoma

Liposarcoma (intracranial)

Solitary fibrous tumour

Rhabdomyoma	8900/0
Rhabdomyosarcoma	8900/3
Chondroma	9220/0
Chondrosarcoma	9220/3
Osteoma	9180/0
Osteosarcoma	9180/3
Osteochondroma	9210/0
Haemangioma	9120/0
Epithelioid haemangioendothelioma	9133/1

Haemangiopericytoma	9150/1
Angiosarcoma	9120/3
Kaposi sarcoma	9140/3

## Primary melanocytic lesions 8728/0 Diffuse melanocytosis 8728/1 Melanocytoma 8728/1 Malignant melanoma 8720/3 Meningeal melanomatosis 8728/3

Other neoplasms related to the meninges
Haemangioblastoma 9161/1

#### LYMPHOMAS AND HAEMOPOIETIC NEOPLASMS

Malignant lymphomas	9590/3
Plasmacytoma	9731/3
Granulocytic sarcoma	9930/3

#### **GERM CELL TUMOURS**

Germinoma	9064/3
Embryonal carcinoma	9070/3
Yolk sac tumour	9071/3
Choriocarcinoma	9100/3
Teratoma	9080/1
Mature	9080/0
Immature	9080/3
Teratoma with malignant transformation	9084/3
Mixed germ cell tumours	9085/3

#### **TUMOURS OF THE SELLAR REGION**

Craniopharyngioma	9350/1
Adamantinomatous	9351/1
Papillary	9352/1
Granular cell tumour	9582/0
Pituicytoma	9432/1*
Spindle cell oncocytoma	
of the adenohypophysis	8291/0*

#### METASTATIC TUMOURS

<sup>\*</sup>The fallicised numbers are provisional codes proposed for the 4th edition of ICD-O. While they are expected to be incorporated into the next ICD-O edition, they currently remain subject to change.



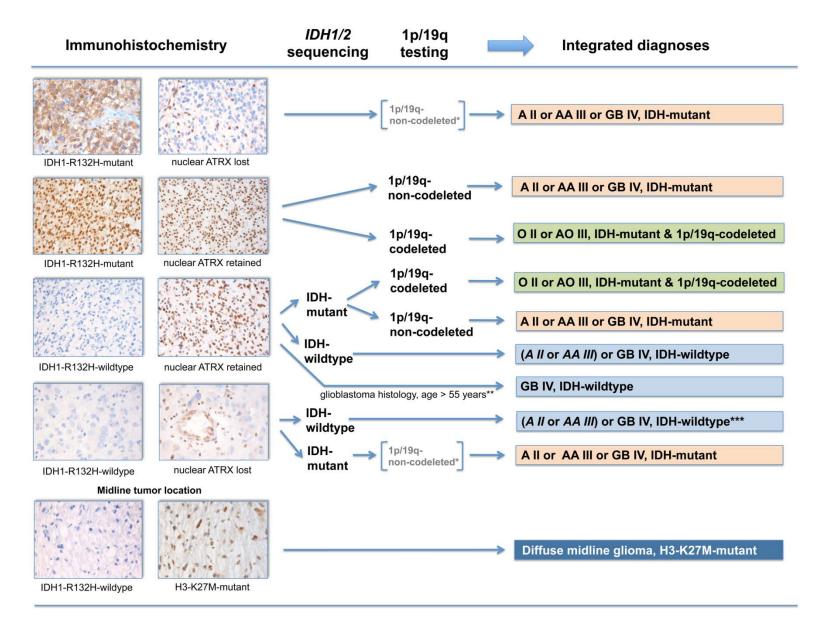
## **Clinical and Biological Features of Gliomas**

Tumour type	WHO grade	Median age at diagnosis* (years)	Survival rate at 2 years* (%; 95% CI)	Survival rate at 10 years* (%; 95% CI)	Common molecular lesions‡	Standard of care <sup>§</sup>
Pilocytic astrocytoma	I	13	96.6 (95.9–97.2)	91.9 (90.5–93.0)	MAPK activation, most commonly due to BRAF fusion or mutation	Observation or carboplatin-based or vincristin-based chemotherapy if resection is not feasible
Diffuse astrocytoma	II	48	61.1 (59.9–62.4)	37.0 (35.4–38.6)	<ul> <li>IDH1 or IDH2 mutation</li> <li>TP53 mutation</li> <li>ATRX mutation</li> </ul>	Observation or radiotherapy or alkylating agent chemotherapy
Oligodendroglioma	II	43	89.6 (88.5–90.7)	62.8 (60.5–65.1)	<ul> <li>IDH1 or IDH2 mutation</li> <li>TERT promoter mutation</li> <li>CIC mutation</li> <li>1p/19q co-deletion</li> </ul>	Observation or radiotherapy or alkylating agent chemotherapy or both
Anaplastic astrocytoma	III	53	43.3 (41.6–45.0)	19.0 (17.3–20.7)	<ul><li>IDH1 or IDH2 mutation</li><li>TP53 mutation</li><li>ATRX mutation</li></ul>	Radiotherapy or alkylating agent chemotherapy or both
Anaplastic oligodendroglioma	III	49	68.6 (65.9–71.2)	39.3 (35.7–42.8)	<ul> <li>IDH1 or IDH2 mutation</li> <li>TERT promoter mutation</li> <li>CIC mutation</li> <li>1p/19q co-deletion</li> </ul>	Radiotherapy or alkylating agent chemotherapy or both
Glioblastoma	IV	64	14.8 (14.3–15.2)	2.6 (2.3–2.9)	<ul> <li>EGFR amplification</li> <li>+7q/–10q genotype</li> <li>PTEN mutation</li> <li>EGFRvIII expression</li> </ul>	Radiotherapy plus concomitant and maintenance temozolomide
Ependymoma	I–III	44	89.7 (88.4–90.9)	79.2 (76.8–81.3)	<ul> <li>RELA–C11orf95 or YAP1 fusions (supratentorial)</li> <li>g-CIMP (posterior fossa)</li> <li>NF2 mutation (spinal intramedullary)</li> </ul>	Radiotherapy



## The new diagnostic approach







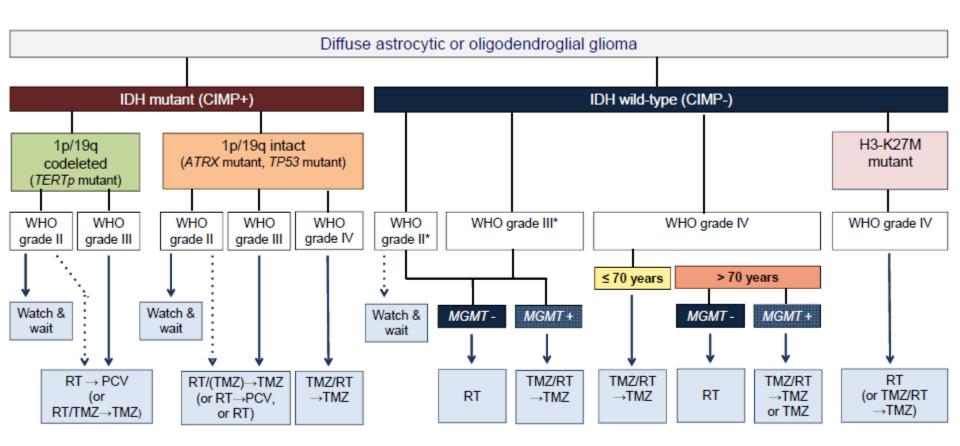


# WHO classification of tumors of the nervous system

- based on histology
- histogenetic classification
- grading of malignancy I-IV
- And molecular pathological criteria
- Goal: prognostic value for clinical guidance



## Molecular Marker-based Therapeutic Approach to Gliomas

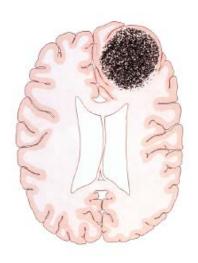


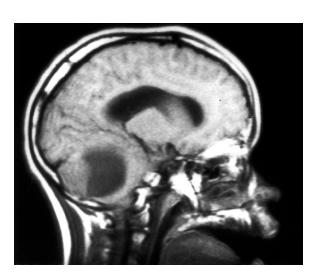
<sup>\*</sup> Refers to the provisional entities of diffuse astrocytoma, IDH wildtype, and anaplastic astrocytoma, IDH wildtype.

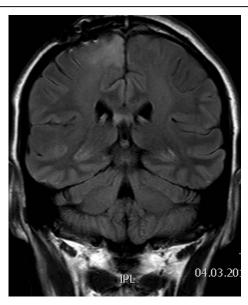


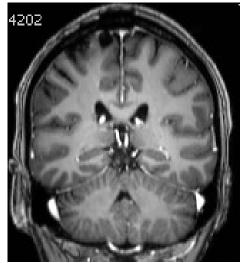
# Gliomas

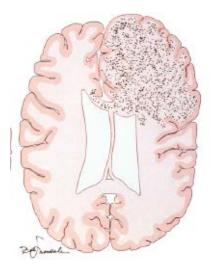


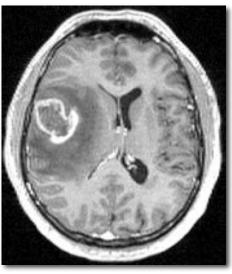
















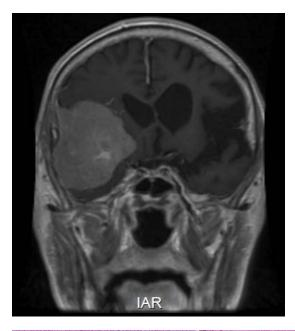


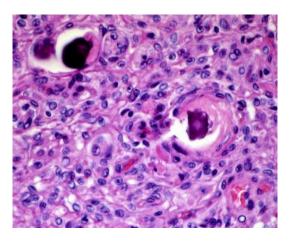
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Behaviour is coded /0 for benign tumours, /3 for malignant tumours a	and /1 for borderline	Neurofibroma	9540/0				
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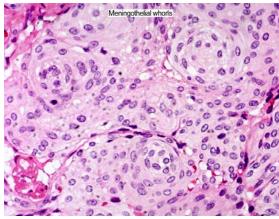


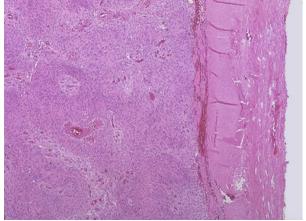
# Meningioma











### Most common non-malignant primary brain tumor

- WHO I > 90% -> non-infiltrative
- WHO II&III -> infiltrative atypical or anaplastic
- -> No established chemotherapy