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Brain tumors

Epidemiology & Pathology

BIO 389

Hertler / Gramatzki

General concepts

Primary brain tumors

Hemispheres > cerebellar
Shortened Survival

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

Secondary brain tumors

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

General concepts

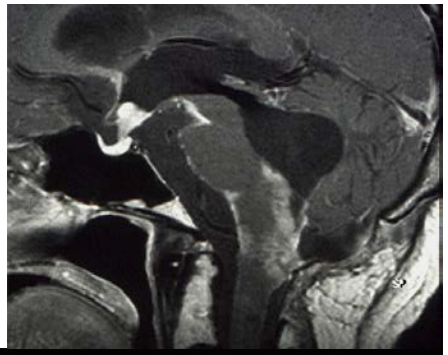
Primary brain tumors	Secondary brain tumors
	Hemispheres > cerebellar Survival
• Different cells from brain structures • WHO classification • Specific therapy	• Different cells from primary tumor • TNM classification • Therapy according to primary tumor

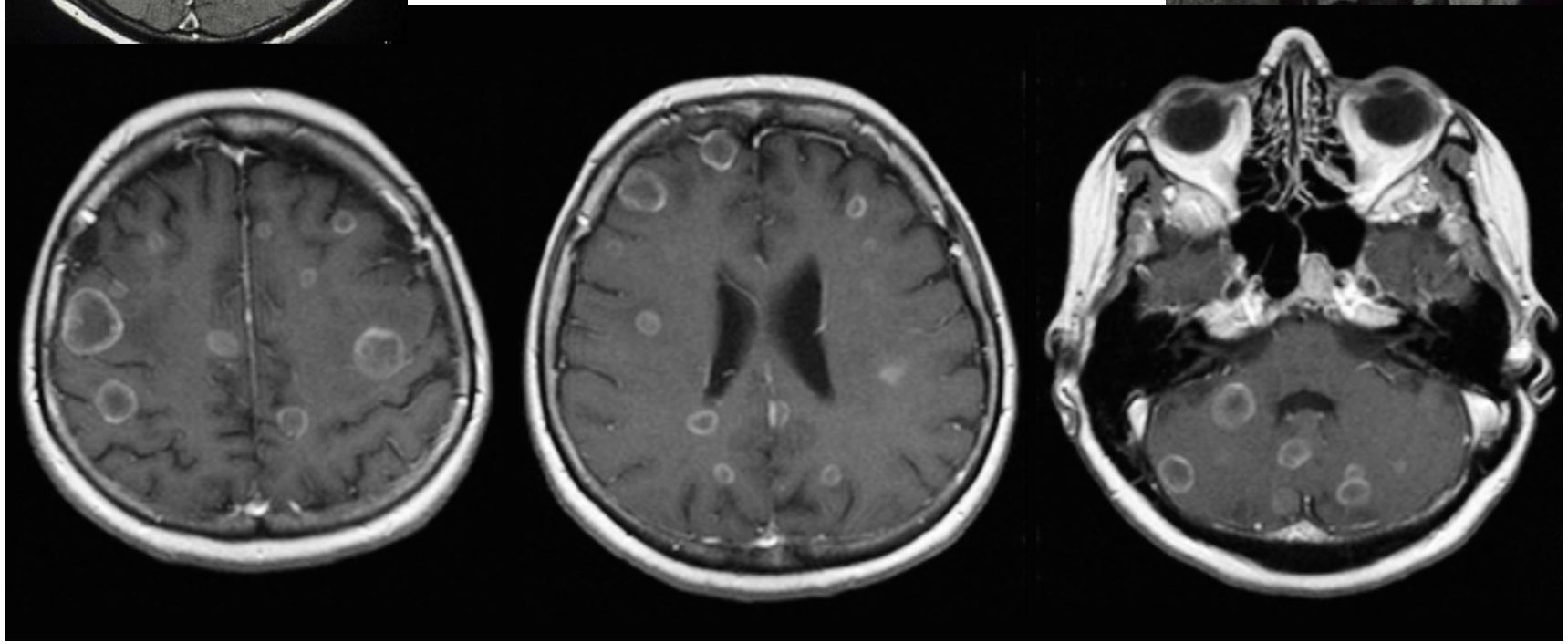
CNS metastasis from solid tumors

	Incidence Clinical (%)	Autopsy (%)	**Median interval from diagnosis** (months)	**Range** (months)
Lung cancer				
small cell	30-45	30-70	2.6	0-15
adenocarcinoma	24-30	50	2	0-66
squamous cell	30	40	0.2	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

80% hemispheres
15% cerebellum
5% brain stem





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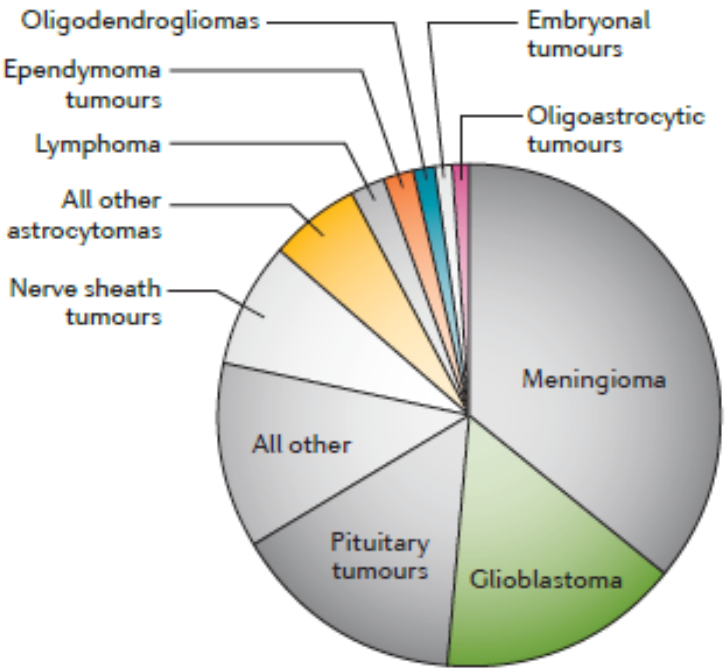
Epidemiology

Etiology:

- Sporadic
- Genetic
- Radiation
- *Immunosuppression*



Ostrom CBTRUS 2014

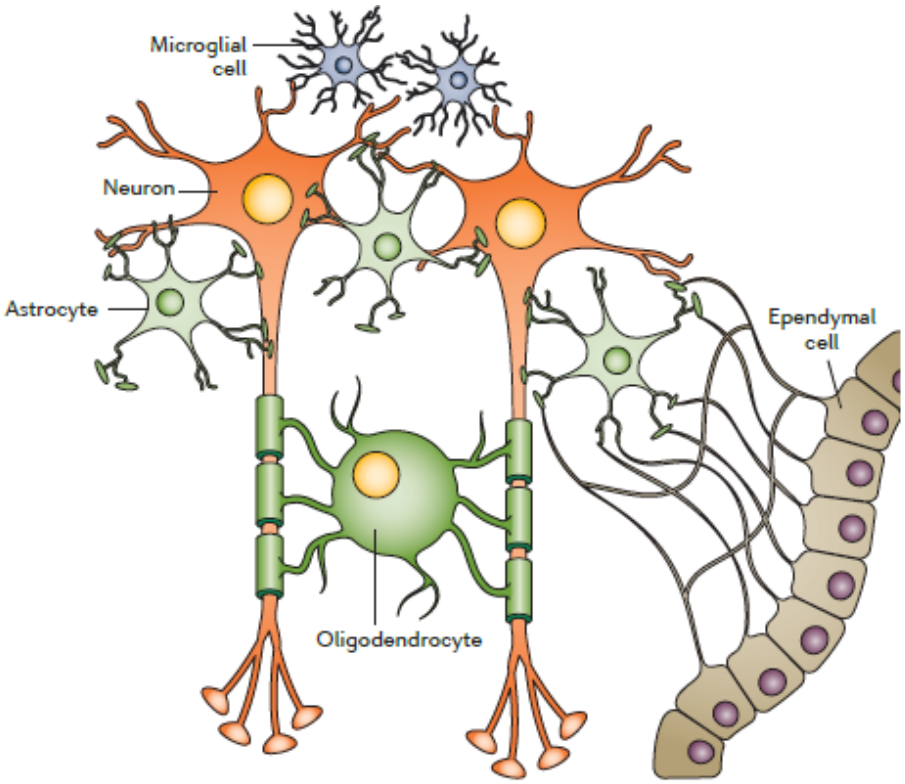


Figure 2 | **Brain cells and brain tumours.** Neurons form extensive networks and serve the main control functions of the brain, including regulation of homeostasis, circadian rhythms and all higher nervous system functions. Astrocytes form the main connective tissue of the brain. Oligodendrocytes serve 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.

Weller Nat Rev Dis Prim 2015

UniversitätsSpital Zürich

WHO classification 2007

TUMOURS OF NEUROEPITHELIAL TISSUE

Astrocytic tumours	
Pilocytic astrocytoma	9421/1[1]
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
Choroid plexus tumours	
Choroid plexus papilloma	9390/0
Atypical choroid plexus papilloma	*9390/1**
Choroid plexus carcinoma	9390/3
Other neuroepithelial tumours	
Astroblastoma	9430/3
Chordoid glioma of the third ventricle	9444/1
Angiocentric glioma	*9431/1**
Neuronal and mixed neuronal-glial tumours	
Dysplastic gangliocytoma of cerebellum (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 (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 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)	9540/3
Epithelioid	9540/3
MPNST with divergent mesenchymal and / or epithelial differentiation	9540/3
Melanotic	9540/3

TUMOURS OF THE MENINGES

Tumours 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
Mesenchymal tumours	
Lipoma	8850/0
Angiolipoma	8861/0
Hibernoma	8880/0
Liposarcoma (intracranial)	8850/3
Solitary fibrous tumour	8815/0
Fibrosarcoma	8810/3
Malignant fibrous histiocytoma	8830/3
Leiomyoma	8890/0
Leiomyosarcoma	8890/3
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	
Diffuse melanocytosis	8728/0
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

[1] 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 /0 for benign tumours, /3 for malignant tumours and /1 for borderline or uncertain behaviour.

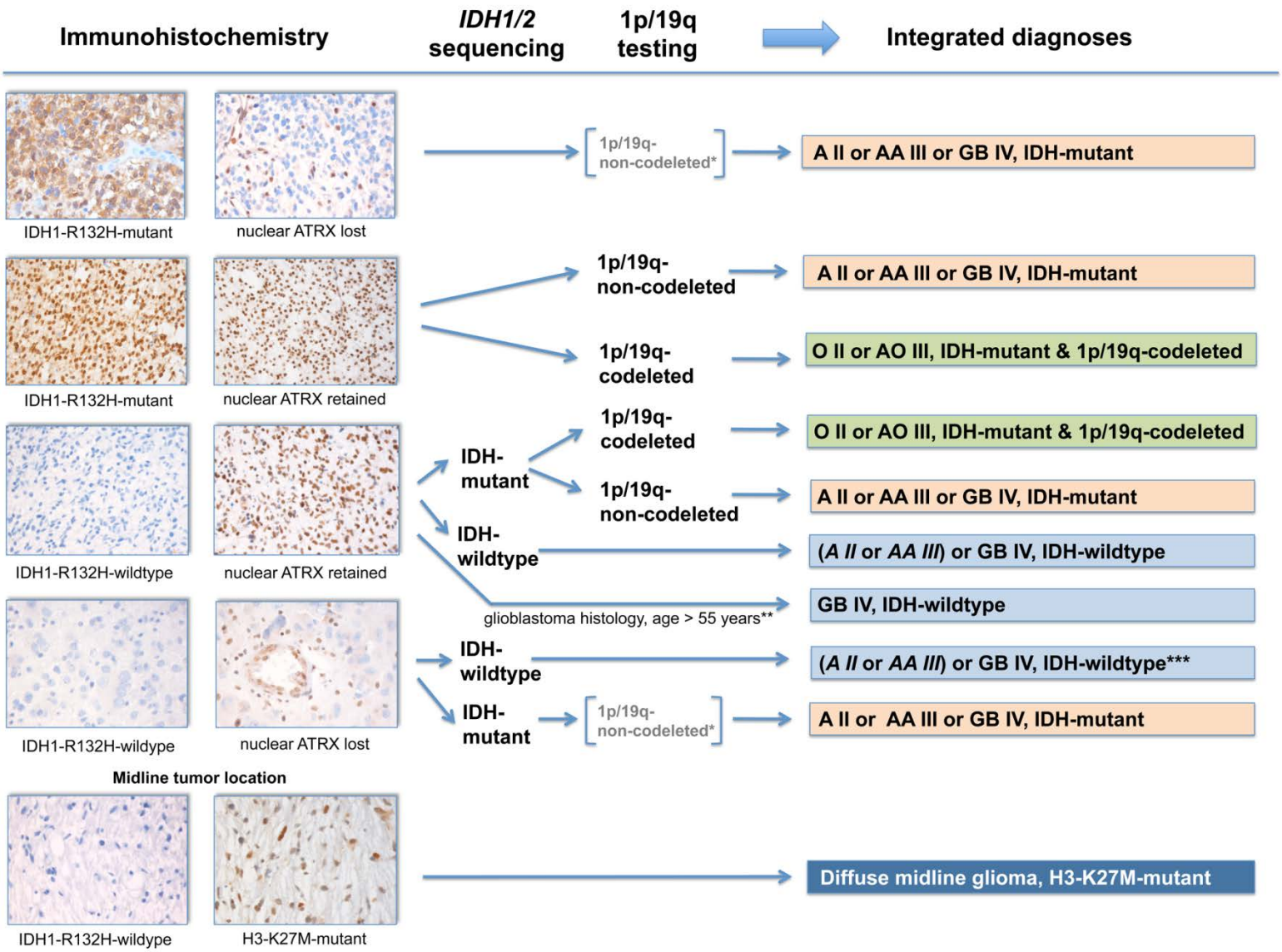
* The italicised numbers are provisional codes proposed for the 4th edition of ICD-O. While they are expected to be incorporated into the next ICD-O edition, they currently remain subject to change.

Louis et al., Acta Neuropathologica 2007

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§
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)	• *IDH1* or *IDH2* mutation • *TP53* mutation • *ATRX* mutation	Observation or radiotherapy or alkylating agent chemotherapy
Oligodendroglioma	II	43	89.6 (88.5–90.7)	62.8 (60.5–65.1)	• *IDH1* or *IDH2* mutation • *TERT* promoter mutation • *CIC* mutation • 1p/19q co-deletion	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)	• *IDH1* or *IDH2* mutation • *TP53* mutation • *ATRX* mutation	Radiotherapy or alkylating agent chemotherapy or both
Anaplastic oligodendroglioma	III	49	68.6 (65.9–71.2)	39.3 (35.7–42.8)	• *IDH1* or *IDH2* mutation • *TERT* promoter mutation • *CIC* mutation • 1p/19q co-deletion	Radiotherapy or alkylating agent chemotherapy or both
Glioblastoma	IV	64	14.8 (14.3–15.2)	2.6 (2.3–2.9)	• *EGFR* amplification • +7q/–10q genotype • *PTEN* mutation • *EGFRvIII* expression	Radiotherapy plus concomitant and maintenance temozolomide
Ependymoma	I–III	44	89.7 (88.4–90.9)	79.2 (76.8–81.3)	• *RELA–C11orf95* or *YAP1* fusions (supratentorial) • g-CIMP (posterior fossa) • *NF2* mutation (spinal intramedullary)	Radiotherapy

The new diagnostic approach

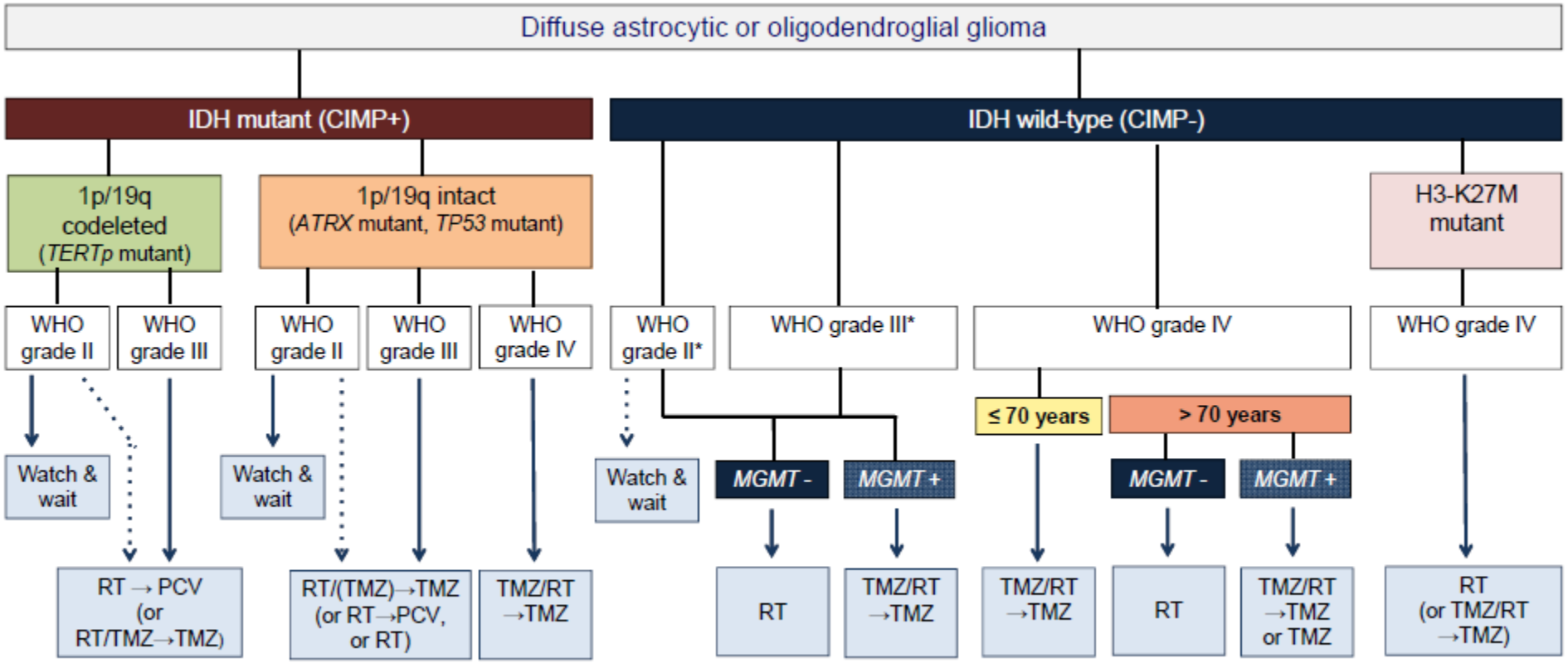


WHO classification of tumors of the nervous system

- 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



* Refers to the provisional entities of diffuse astrocytoma, IDH wildtype, and anaplastic astrocytoma, IDH wildtype.

The 2017 EANO guideline, *Lancet Oncology*

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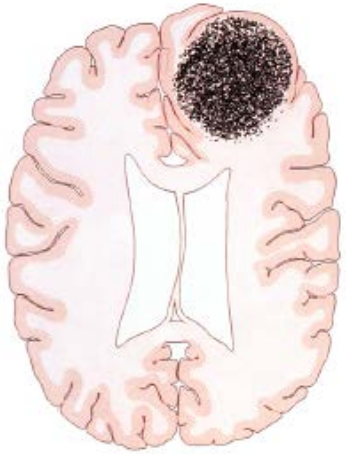
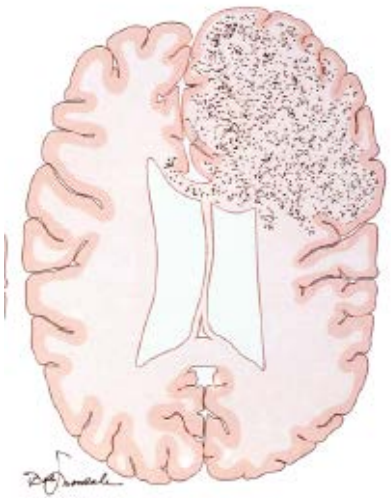
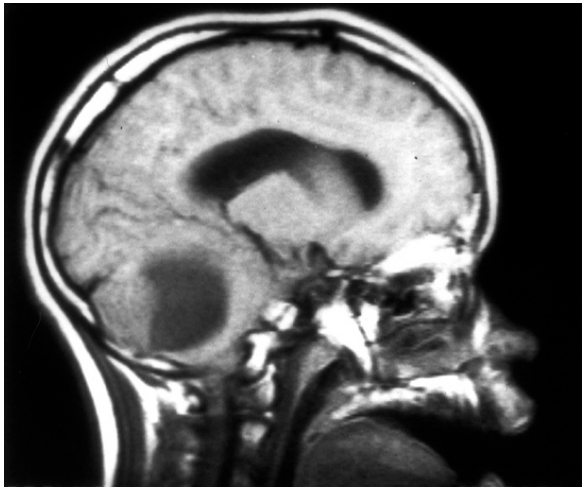
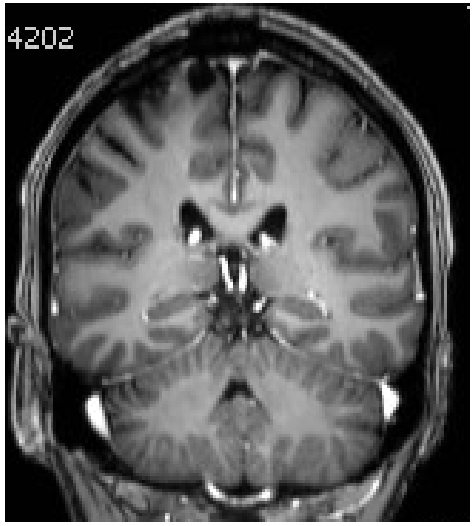
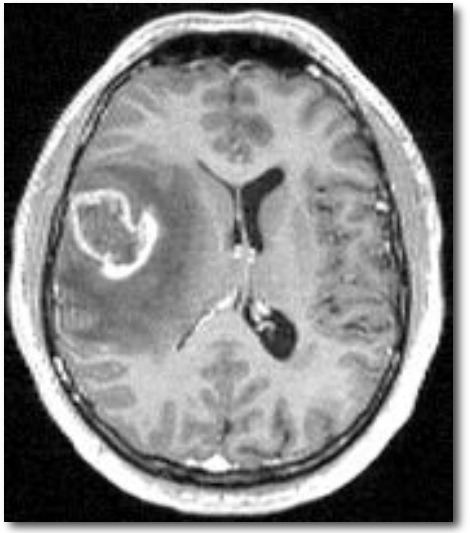
Gliomas











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Spindle cell oncocytoma of the adenohypophysis	*8291/0**

METASTATIC TUMOURS

Louis et al., Acta Neuropathologica 2007

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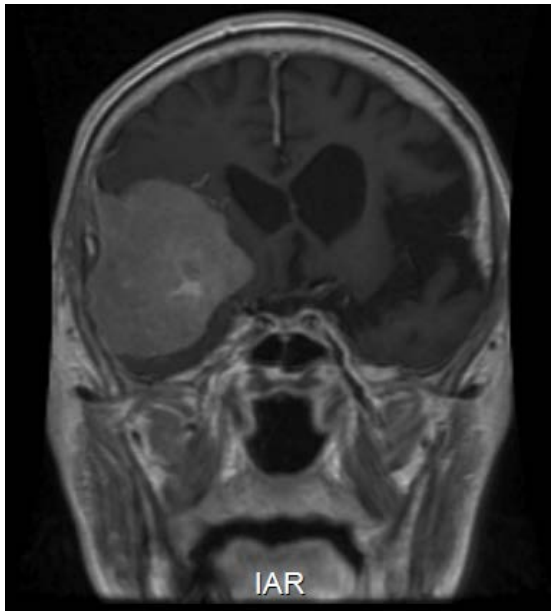
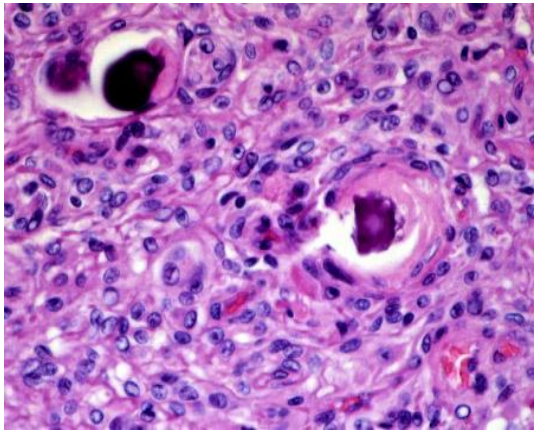
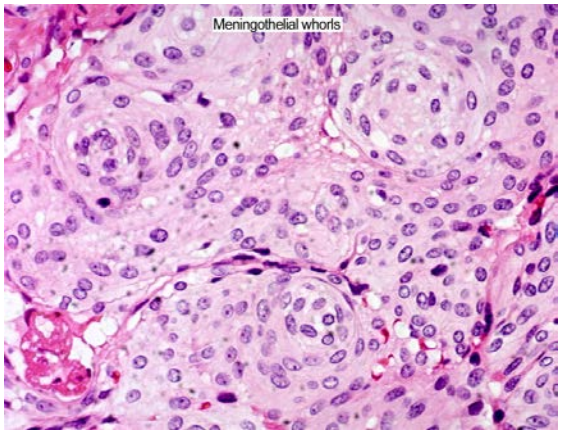
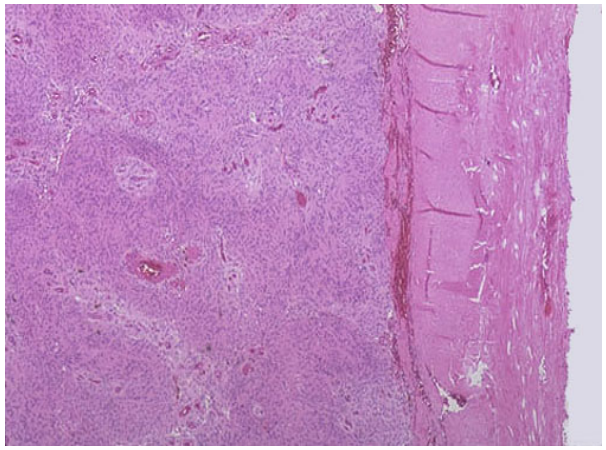
Meningioma









Most common non-malignant primary brain tumor

- WHO I > 90% -> non-infiltrative
- WHO II&III -> infiltrative atypical or anaplastic

-> No established chemotherapy