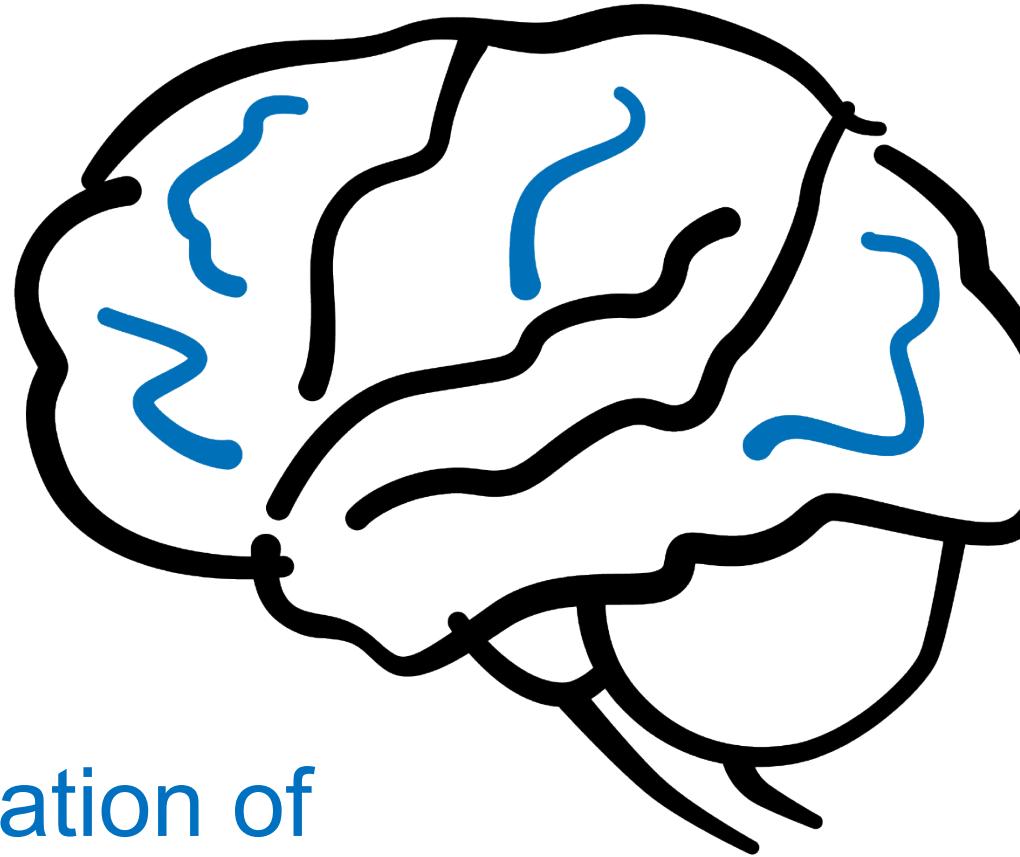




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The 2021 Classification of Brain Tumors: pediatric implications

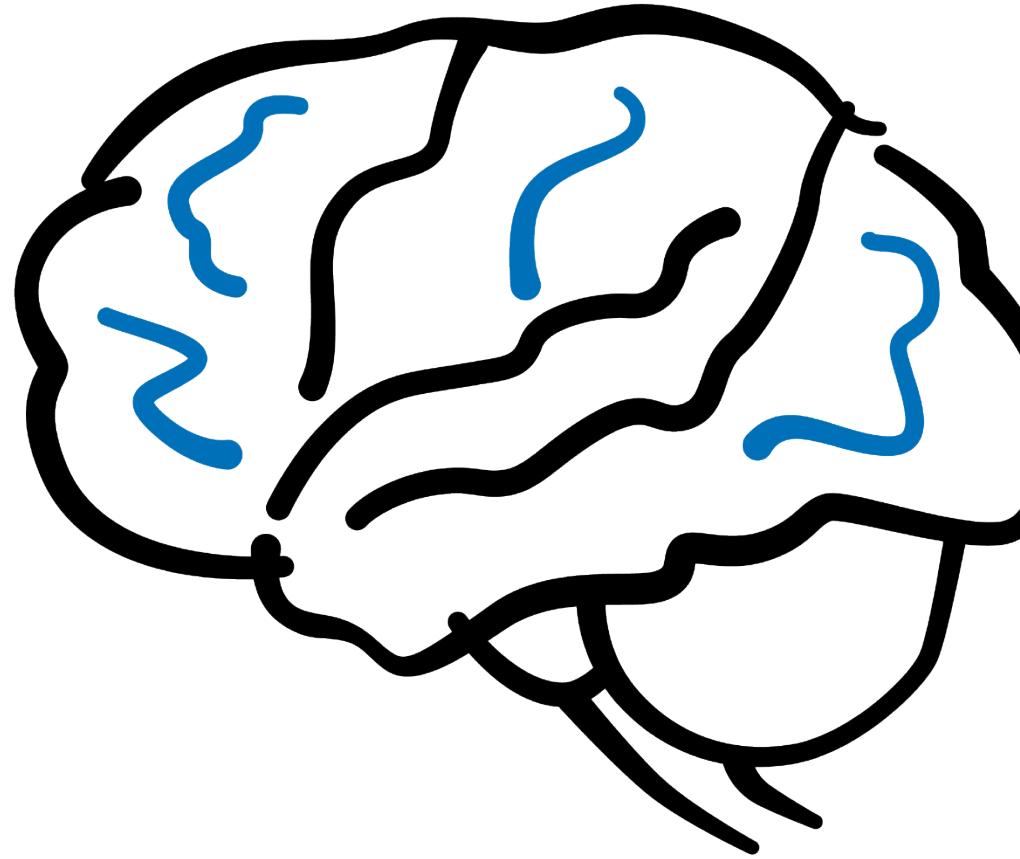
Ulrike Löbel

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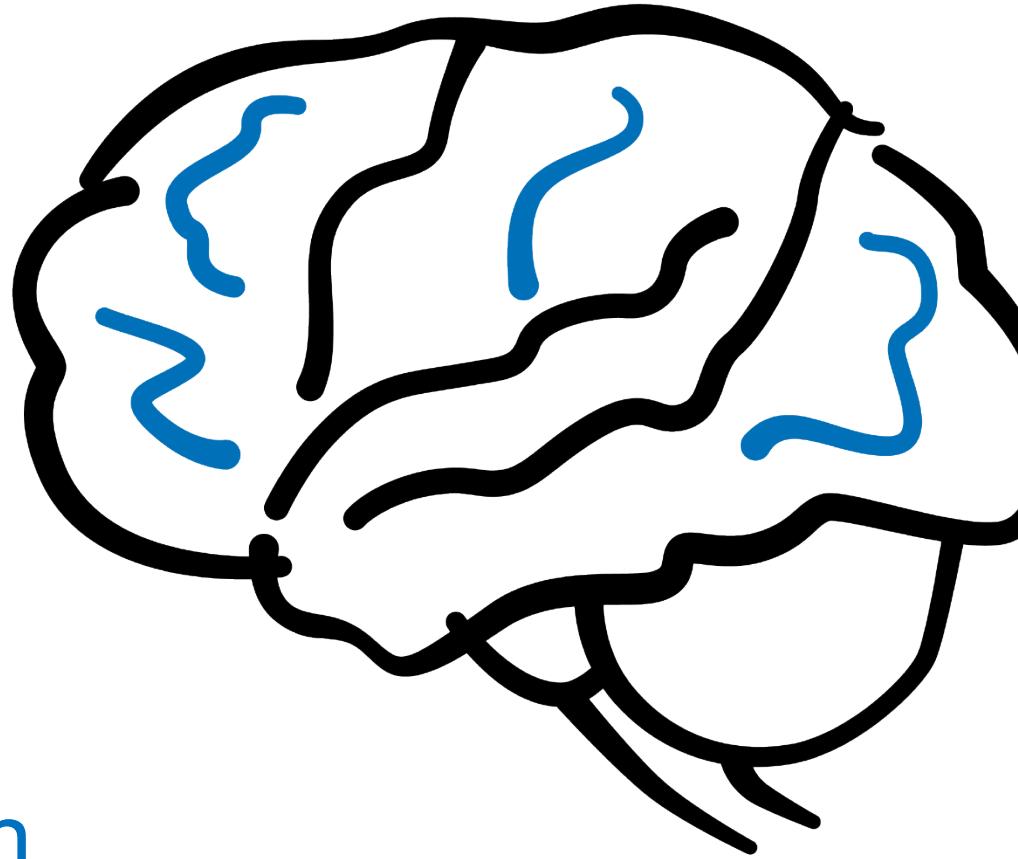


I have no conflicts of interest to disclose.



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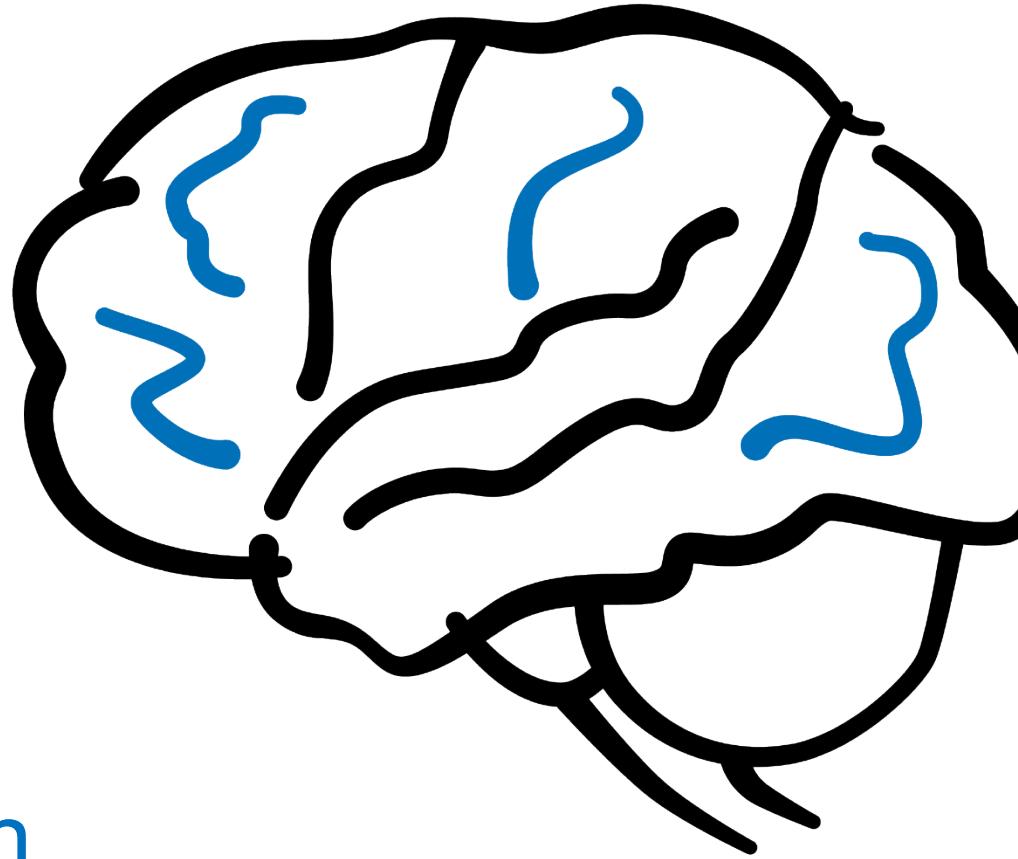


- 1. Brief introduction**
- 2. Specific tumor types**



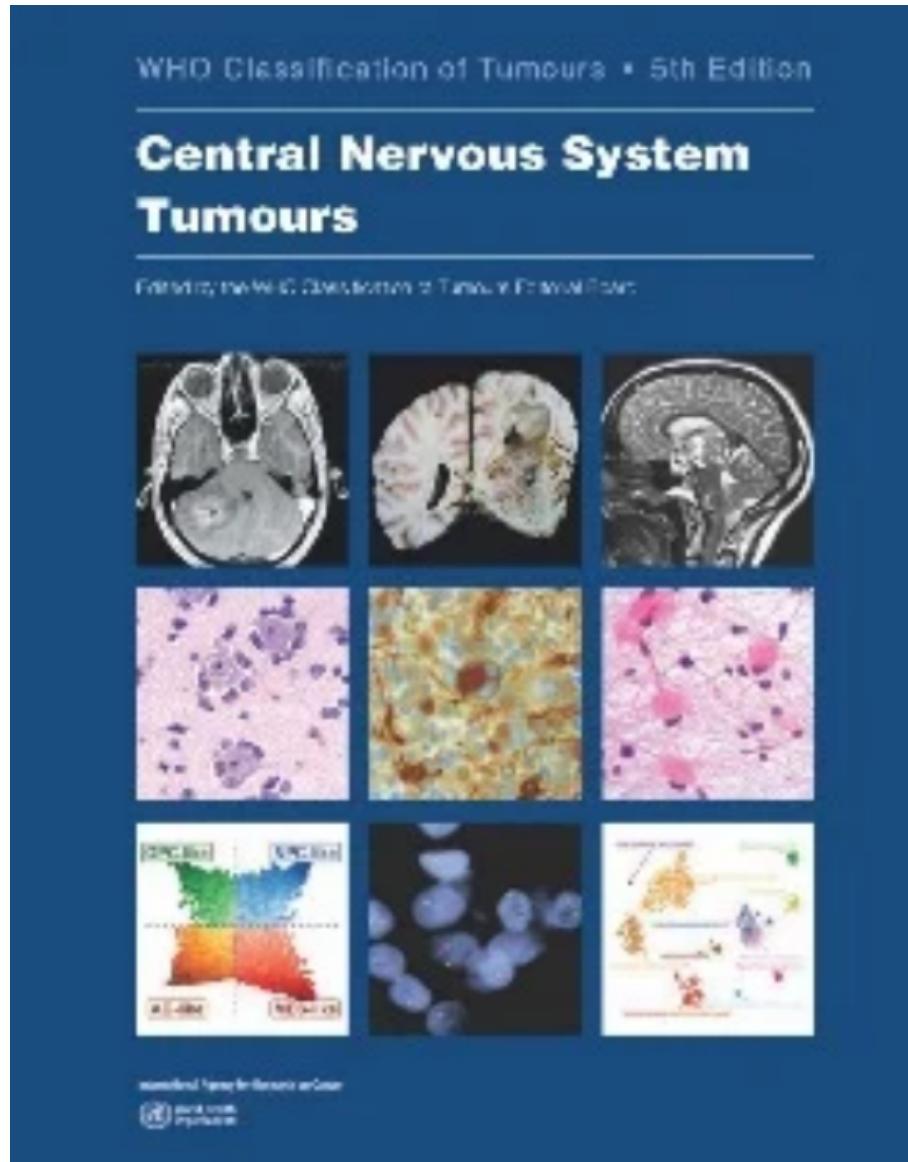
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- 1. Brief introduction**
- 2. Specific tumor types**

WHO classification of CNS tumours 2021



WHO classification of CNS tumours 2021

Table 1 2021 WHO Classification of Tumors of the Central Nervous System. Provisional Entity

World Health Organization Classification of Tumors of the Central Nervous System, Provisional Entity
Gliomas, glioneuronal tumors, and neuronal tumors
Adult-type diffuse gliomas
Astrocytoma, IDH-mutant
Oligodendrogioma, IDH-mutant, and 1p/19q-codeleted
Glioblastoma, IDH-wildtype
Pediatric-type diffuse low-grade gliomas
Diffuse astrocytoma, <i>MYB</i> - or <i>MYBL1</i> -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, <i>MN1</i> -altered
Glioneuronal and neuronal tumors
Ganglioglioma
Desmoplastic infantile ganglioglioma / desmoplastic infantile astrocytoma
Dysembryoplastic neuroepithelial tumor
Diffuse glioneuronal tumor with oligodendrogloma-like features and nuclear <i>cl</i>
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
Ependymal tumors
Supratentorial ependymoma
Supratentorial ependymoma, ZFTA fusion-positive
Supratentorial ependymoma, <i>YAP1</i> fusion-positive
Posterior fossa ependymoma
Posterior fossa ependymoma, group PFA
Posterior fossa ependymoma, group PFB
Spinal ependymoma
Spinal ependymoma, <i>MYCN</i> -amplified
Myxopapillary ependymoma
Subependymoma

Table 1 Continued

World Health Organization Classification of Tumors of the Central Nervous System
Choroid plexus tumors
Choroid plexus papilloma
Atypical choroid plexus papilloma
Choroid plexus carcinoma
Embryonal tumors
Medulloblastoma
Medulloblastoma, molecularly defined
Medulloblastoma, <i>WNT</i> -activated
Medulloblastoma, <i>SHH</i> -activated and <i>TP53</i> -wildtype
Medulloblastoma, <i>SHH</i> -activated and <i>TP53</i> -mutant
Medulloblastoma, non- <i>WNT</i> /non- <i>SHH</i>
Medulloblastoma, histologically defined
Other CNS embryonal tumors
Atypical teratoid/rhabdoid tumor
Cribriform neuroepithelial tumor
Embryonal tumor with multilayered rosettes
CNS neuroblastoma, <i>FOXR2</i> -activated
CNS tumor with <i>BCOR</i> internal tandem duplication
CNS embryonal tumor
Pineal tumors
Pineocytoma
Pineal parenchymal tumor of intermediate differentiation
Pineoblastoma
Papillary tumor of the pineal region
Desmoplastic myxoid tumor of the pineal region, <i>SMARCB1</i> -mutant
Cranial and paraspinal nerve tumors
Schwannoma
Neurofibroma
Perineurioma
Hybrid nerve sheath tumor
Malignant melanotic nerve sheath tumor
Malignant peripheral nerve sheath tumor
Paraganglioma
Meningiomas
Meningioma
Mesenchymal, non-meningotheelial tumors
Soft tissue tumors
Fibroblastic and myofibroblastic tumors
Solitary fibrous tumor
Vascular tumors
Hemangiomas and vascular malformations
Hemangioblastoma
Skeletal muscle tumors
Rhabdomyosarcoma
Uncertain differentiation
Intracranial mesenchymal tumor, <i>FET-CREB</i> fusion-positive
CIC-rearranged sarcoma
Primary intracranial sarcoma, <i>DVCER1</i> -mutant
Ewing sarcoma

Table 1 Continued

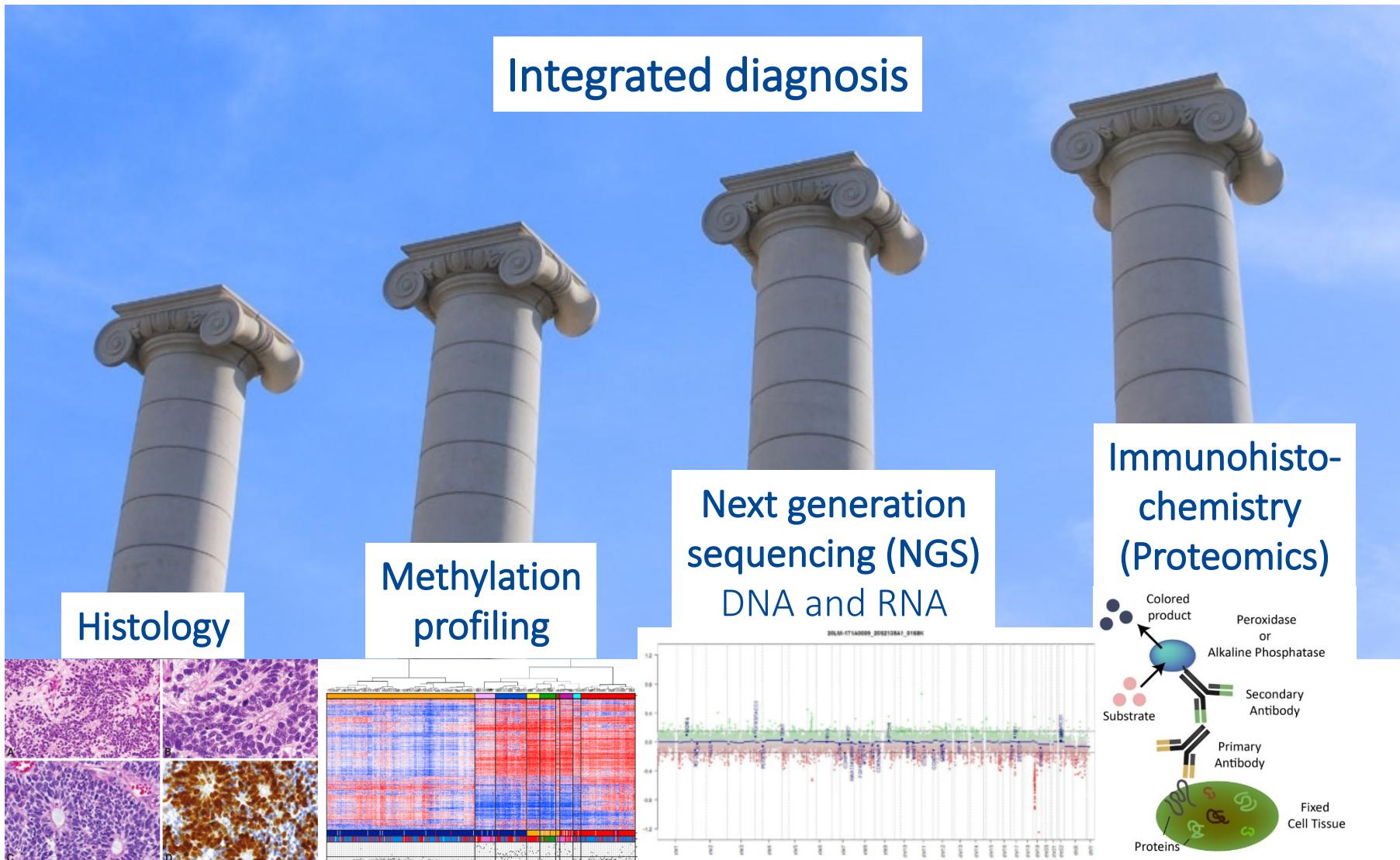
World Health Organization Classification of Tumors of the Central Nervous System, fifth edition
Chondro-osseous tumors
Chondrogenic tumors
Mesenchymal chondrosarcoma
Chondrosarcoma
Notochordal tumors
Chondroma (including poorly differentiated chondroma)
Melanocytic tumors
Diffuse meningeal melanocytic neoplasms
Meningeal melanocytosis and meningeal melanomatosis
Circumscribed meningeal melanocytic neoplasms
Meningeal melanocytoma and meningeal melanoma
Hematolymphoid tumors
Lymphomas
CNS lymphomas
Primary diffuse large B-cell lymphoma of the CNS
Immuno deficiency-associated CNS lymphoma
Lymphomatoid granulomatosis
Intravascular large B-cell lymphoma
Miscellaneous rare lymphomas in the CNS
MALT lymphoma of the dura
Other low-grade B-cell lymphomas of the CNS
Anaplastic large cell lymphoma (<i>ALK</i> +/ <i>ALK</i> -)
T-cell and NK/T-cell lymphomas
Histiocytic tumors
Erdheim-Chester disease
Rosai-Dorfman disease
Juvenile xanthogranuloma
Langerhans cell histiocytosis
Histiocytic sarcoma
Germ cell tumors
Mature teratoma
Immature teratoma
Teratoma with somatic-type malignancy
Germinoma
Embryonal carcinoma
Yolk sac tumor
Choriocarcinoma
Mixed germ cell tumor
Tumors of the sellar region
Adamantinomatous craniopharyngioma
Papillary craniopharyngioma
Pituicytoma, granular cell tumor of the sellar region, and spindle cell oncocytoma
Pituitary adenoma/PitNET
Pituitary blastoma
Metastases to the CNS
Metastases to the brain and spinal cord parenchyma
Metastases to the meninges
Abbreviations: CNS, central nervous system; IDH, isocitrate dehydrogenase; NK, natural killer; PitNET, pituitary neuroendocrine tumor; SHH, sonic hedgehog.

2021 newly recognised tumour types

Newly Recognized Tumor Types	
Paediatric-type diffuse gliomas	Diffuse astrocytoma, <i>MYB-</i> or <i>MYBL1</i> -altered
	Polymorphous low-grade neuroepithelial tumor of the young
	Diffuse low-grade glioma, MAPK pathway-altered
	Diffuse hemispheric glioma, H3 G34-mutant
	Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype
	Infant-type hemispheric glioma
	High-grade astrocytoma with piloid features
Glioneuronal tumours	<i>Diffuse glioneuronal tumor with oligodendrogioma-like features and nuclear clusters</i> (provisional)
	Myxoid glioneuronal tumor
	Multinodular and vacuolating neuronal tumor
Ependymomas	Supratentorial ependymoma, <i>YAP1</i> fusion-positive
	Posterior fossa ependymoma, group PFA
	Posterior fossa ependymoma, group PFB
	Spinal ependymoma, <i>MYCN</i> -amplified
	<i>Cribiform neuroepithelial tumor</i> (provisional type)
Embryonal tumours	CNS neuroblastoma, <i>FOXR2</i> -activated
	CNS tumor with <i>BCOR</i> internal tandem duplication
Pineal region	Desmoplastic myxoid tumor of the pineal region, <i>SMARCB1</i> -mutant
	<i>Intracranial mesenchymal tumor, FET-CREB fusion positive</i> (provisional type)
others	<i>CIC</i> -rearranged sarcoma
	Primary intracranial sarcoma, <i>DICER1</i> -mutant
	Pituitary blastoma

Novel diagnostic methods

Integrated diagnosis



Images from: Louis et al. 2007 IARC, Pajtler et al. 2015 Cancer Cell, www.rockland-inc.com, careers.acrt.com

Novel diagnostic methods

Immunohisto-
chemistry

GFAP

Synaptophysin

EMA

BCOR

INI-1

SMARCA4

Lin28a

H3K27M

L1CAM

P65

FOXR2

CD45.

CD99

Myogenin

Next generation sequencing (NGS)

Gene	ROI	Gene	ROI	Gene	ROI	Gene	ROI
ACVR1	Exons 3-11	CREBBP	Exons 1-31	HIST2H3C	Exon 1	NRAS	Exons 2-4
AKT1	Exons 2-14	CTNNB1	Exons 2-15	HRAS	Exons 2-6	OTX2	Exons 3-5
ALK	Exons 20-29	DAXX	Exons 2-8	IDH1	Exons 3-10	PDGFRA	Exons 2-23
AMER1	Exon 2	DDX1	Exons 1-26	IDH2	Exons 1-11	PHOX2B	Exons 1-3
APC	Exons 1-16	DDX3X	Exons 1-17	IGF1R	Exons 1-21	PIK3CA	Exons 2-21
ARID1A	Exons 1-20	DICER1	Exons 2-27	IGF2	Exons 2-5	PIK3R1	Exons 2-16
ARID1B	Exons 1-20	DROSHA	Exons 3-35	KIT	Exons 1-21	PMS2	Exons 1-15
ASXL1	Exons 1-4,4a-13	EGFR	Exons 1-28	KRAS	Exons 2-4	PPM1D	Exons 1-6
ATM	Exons 2-63	ERBB2	Exons 1-27	MAP2K1	Exons 1-11	PTCH1	Exons 1,1a,1b-23
ATRX	Exons 1-35	EZH2	Exons 2-20	MAP2K2	Exons 1-11	PTEN	Exons 1-9
BCOR	Exons 2-15	FBXW7	Exons 1,1a,1b-11	MDM2	Exons 1-11	PTPN11	Exons 1-15
BRAF	Exons 11,15	FGFR1	Exons 1-2,2a-18	MDM4	Exons 2-11	RB1	Exons 1-27
CCND1	Exons 1-5	FGFR2	Exons 2-7,7a-17,17a,17b-18	MET	Exons 2-21	RELA	Exon 3
CCND2	Exons 1-5	FGFR3	Exons 1-18	MLH1	Exons 1-19	SETD2	Exons 1-21
CCNE1	Exons 2-12	FGFR4	Exons 11-18	MSH2	Exons 1-16	SMARCA2	Exons 2-34
CDK12	Exons 1-14	FRS2	Exons 6-10	MSH6	Exons 1-10	SMARCA4	Exons 2-36
CDK4	Exons 2-8	FUBP1	Exons 1-20	MYC	Exons 1-3	SMARCB1	Exons 1-9
CDK6	Exons 2-8	GLI2	Exons 1-13	MYCL	Exons 1-3	SMO	Exons 1-12
CDKN2A	Exons 1,1a-3,3a	H3F3A	Exons 2-4	MYCN	Exons 2-3	SUFU	Exons 1-11,11a-12
CDKN2B	Exons 1-2	HIST1H3B	Exon 1	MYOD1	Exons 1-3	TERT	Exons 1-16
CHEK2	Exons 2-15	HIST1H3C	Exon 1	NF1	Exons 1-58	TP53	Exons 2-10,10a-11
CIC	Exons 1-20	HIST2H3A	Exon 1	NF2	Exons 1-15,15a-16	TSC1	Exons 3-23

Integrated diagnosis

Integrated Diagnosis

Medulloblastoma, WNT-activated, classic, WHO 4

CNS WHO grade

4

Genetically defined

Medulloblastoma: WNT, SHH, group 3/4

Histologically defined

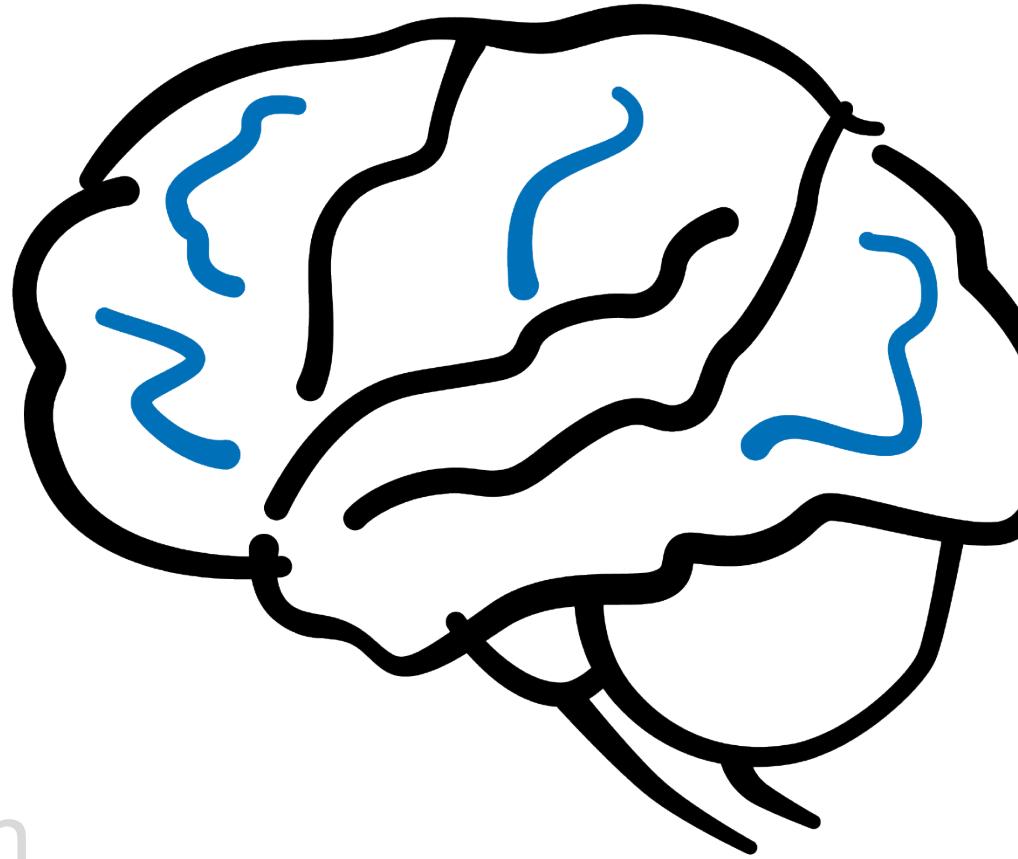
Medulloblastoma: classic, large-cell/anaplastic,
desmoplastic/nodular, extensiv-nodular (MBEN)

NOS/NEC



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1. Brief introduction
2. Specific tumor types

Gliomas, glioneuronal and neuronal tumours

Families in this group:

1. Adult-type diffuse gliomas
2. Paediatric-type diffuse HGG
3. Paediatric-type diffuse LGG
4. Circumscribed astrocytic tumours
5. Glioneuronal and neuronal tumours
6. Ependymal tumours

World Health Organization Classification of Tumors of the Central Nervous System, fifth edition

Gliomas, glioneuronal tumors, and neuronal tumors

Adult-type diffuse gliomas

Astrocytoma, IDH-mutant

Oligodendrogioma, 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 oligodendrogioma-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

Ependymal tumors

Supratentorial ependymoma

Supratentorial ependymoma, *ZFTA* fusion-positive

Supratentorial ependymoma, *YAP1* fusion-positive

Posterior fossa ependymoma

Posterior fossa ependymoma, group PFA

Posterior fossa ependymoma, group PFB

Spinal ependymoma

Spinal ependymoma, *MYCN*-amplified

Myxopapillary ependymoma

Subependymoma

Gliomas, glioneuronal and neuronal tumours

1. Adult-type diffuse gliomas

2016

Diffuse astrocytoma, IDH-mutant

Gemistocytic astrocytoma, IDH-mutant

Diffuse astrocytoma, IDH-wildtype

Diffuse astrocytoma, NOS

Anaplastic astrocytoma, IDH-mutant

Anaplastic astrocytoma, IDH-wildtype

Anaplastic astrocytoma, NOS

Glioblastoma, IDH-wildtype

Giant cell glioblastoma

Gliosarcoma

Epithelioid glioblastoma

Glioblastoma, IDH-mutant

Glioblastoma, NOS

Oligodendrogloma, IDH-mutant, 1p/19q-codeleted

Oligodendrogloma, NOS

Anaplastic oligodendrogloma, IDH-mutant, 1p/19q-codeleted

Anaplastic oligodendrogloma, NOS

Oligoastrocytoma, NOS

Anaplastic oligoastrocytoma, NOS

2021

Astrocytoma, **IDH-mutant**

(WHO CNS grades 2, 3, 4)

Glioblastoma, **IDH-wildtype**

(WHO CNS grade 4)

Oligodendrogloma, **IDH-mutant**, and **1p/19q-codeleted**

(WHO CNS grades 2, 3)

Gliomas, glioneuronal and neuronal tumours

2. Paediatric-type diffuse HGG

Pediatric-type diffuse high-grade gliomas	WHO CNS grade
Diffuse midline glioma, H3 K27-altered	4
Diffuse hemispheric glioma, H3 G34-mutant	4
Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype	
Infant-type hemispheric glioma	

Gliomas, glioneuronal and neuronal tumours

2. Paediatric-type diffuse HGG

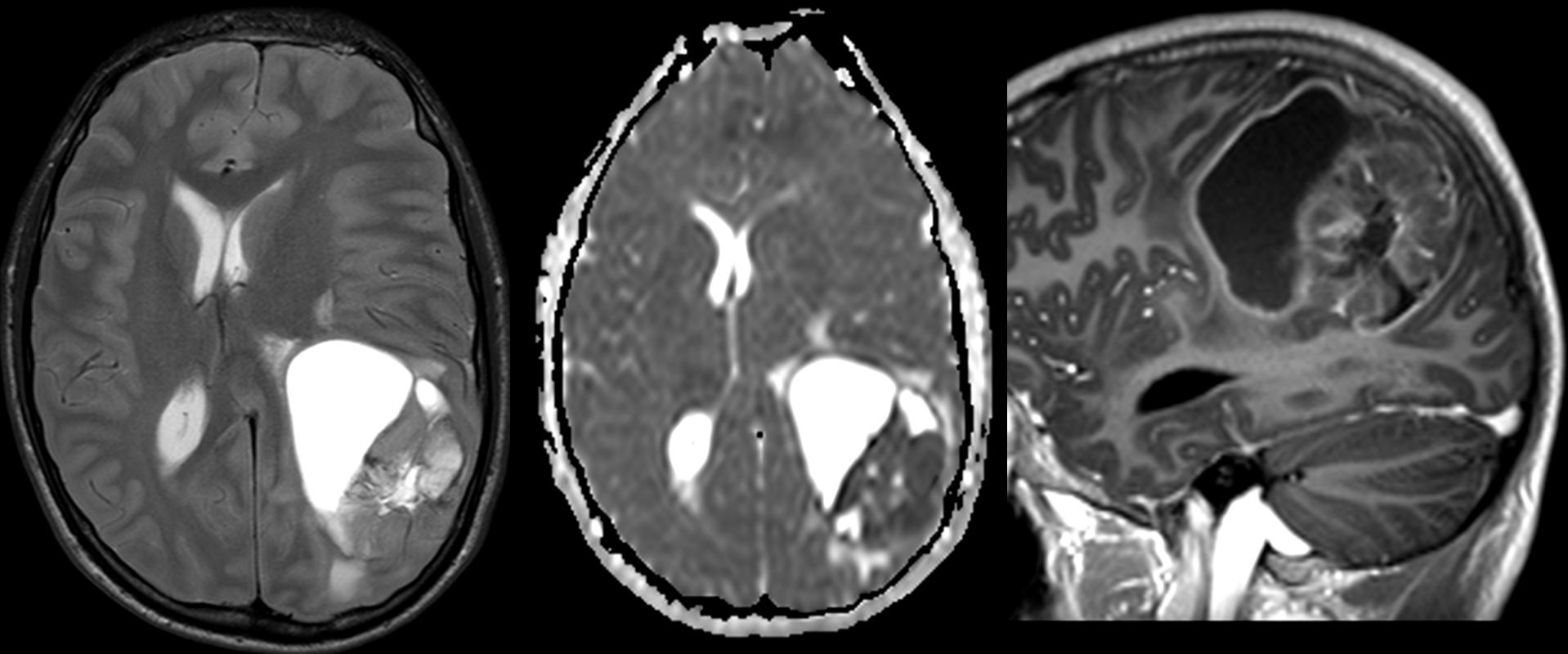
New tumour type: Diffuse hemispheric tumour, H3 G34-mutant



Gliomas, glioneuronal and neuronal tumours

2.Paediatric-type diffuse HGG

New tumour type: Diffuse hemispheric tumour, H3 G34-mutant

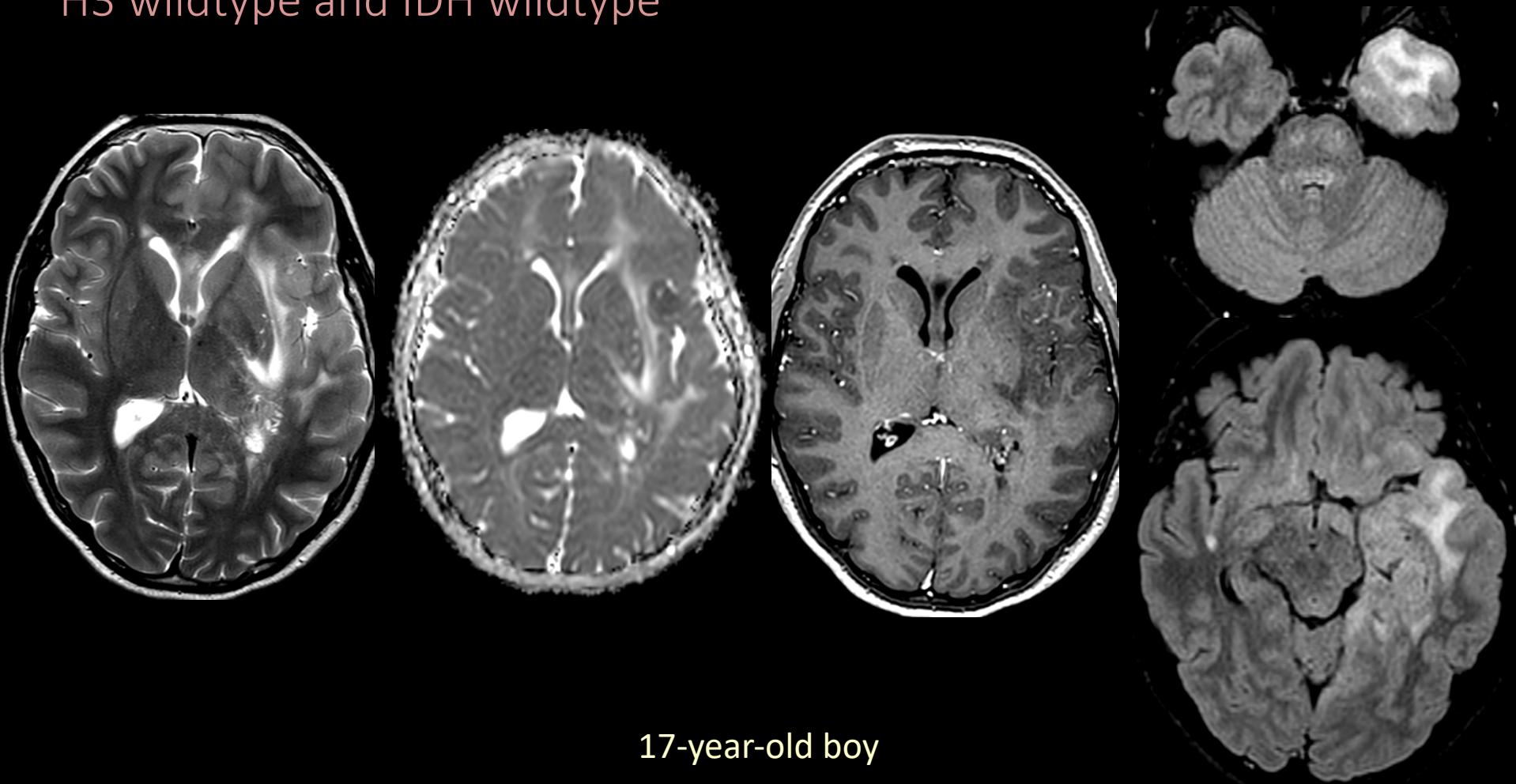


18-year-old boy

Gliomas, glioneuronal and neuronal tumours

2. Paediatric-type diffuse HGG

New tumour type: Diffuse paediatric-type high-grade glioma, H3 wildtype and IDH wildtype



17-year-old boy

Gliomas, glioneuronal and neuronal tumours

2.Paediatric-type diffuse HGG

Diffuse paediatric-type high-grade glioma, H3wt and IDHwt

Essential diagnostic criteria

A high-grade glioma HGG
AND

WT for IDH1/Histone 3
AND

a typical methylation class
(pHGG RTK1, pHGG RTK2, or pHGG
MYCN) OR

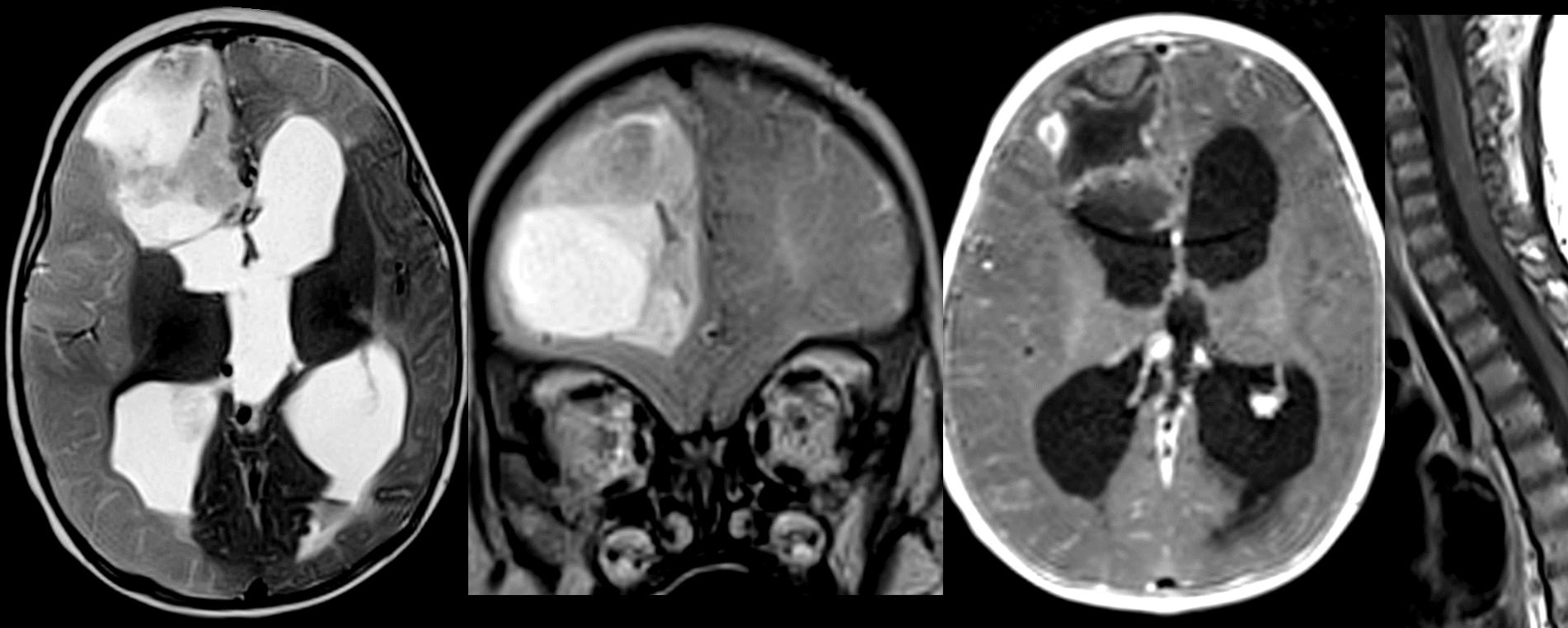
a typical genetic variant
(PDGFRA alteration, EGFR alteration,
or MYCN amplification)

Gliomas, glioneuronal and neuronal tumours

2. Paediatric-type diffuse HGG

New tumour type: Infant-type hemispheric glioma

- Fusion genes involving ALK, ROS1, NTRK1/2/3, or MET



Infant-type hemispheric glioma, TRIM24-MET fusion
3-month-old boy

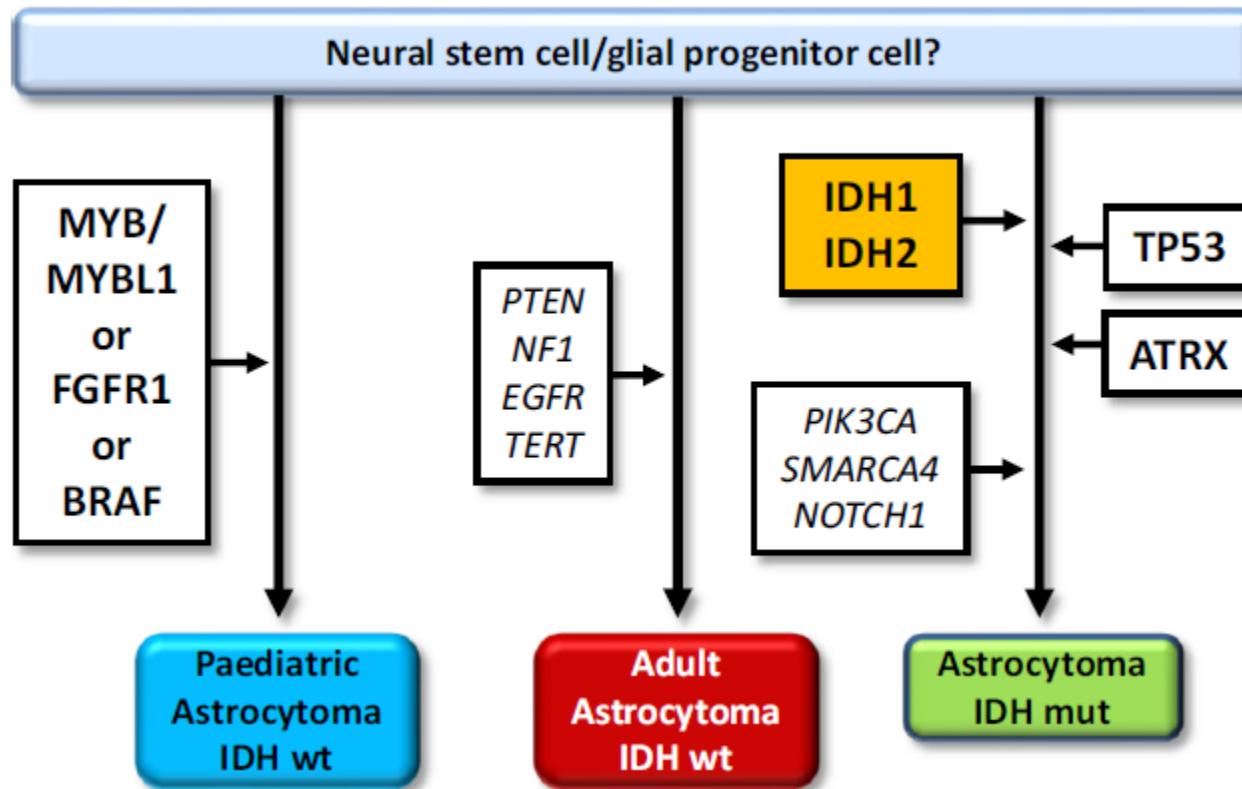
Gliomas, glioneuronal and neuronal tumours

3. Paediatric-type diffuse LGG

Pediatric-type diffuse low-grade gliomas	WHO CNS grade
Diffuse astrocytoma, <i>MYB</i> - or <i>MYBL1</i> -altered	1
Angiocentric glioma	
Polymorphous low-grade neuroepithelial tumor of the young	1
Diffuse low-grade glioma, MAPK pathway-altered	

→ Angiocentric glioma is a paediatric-type tumour

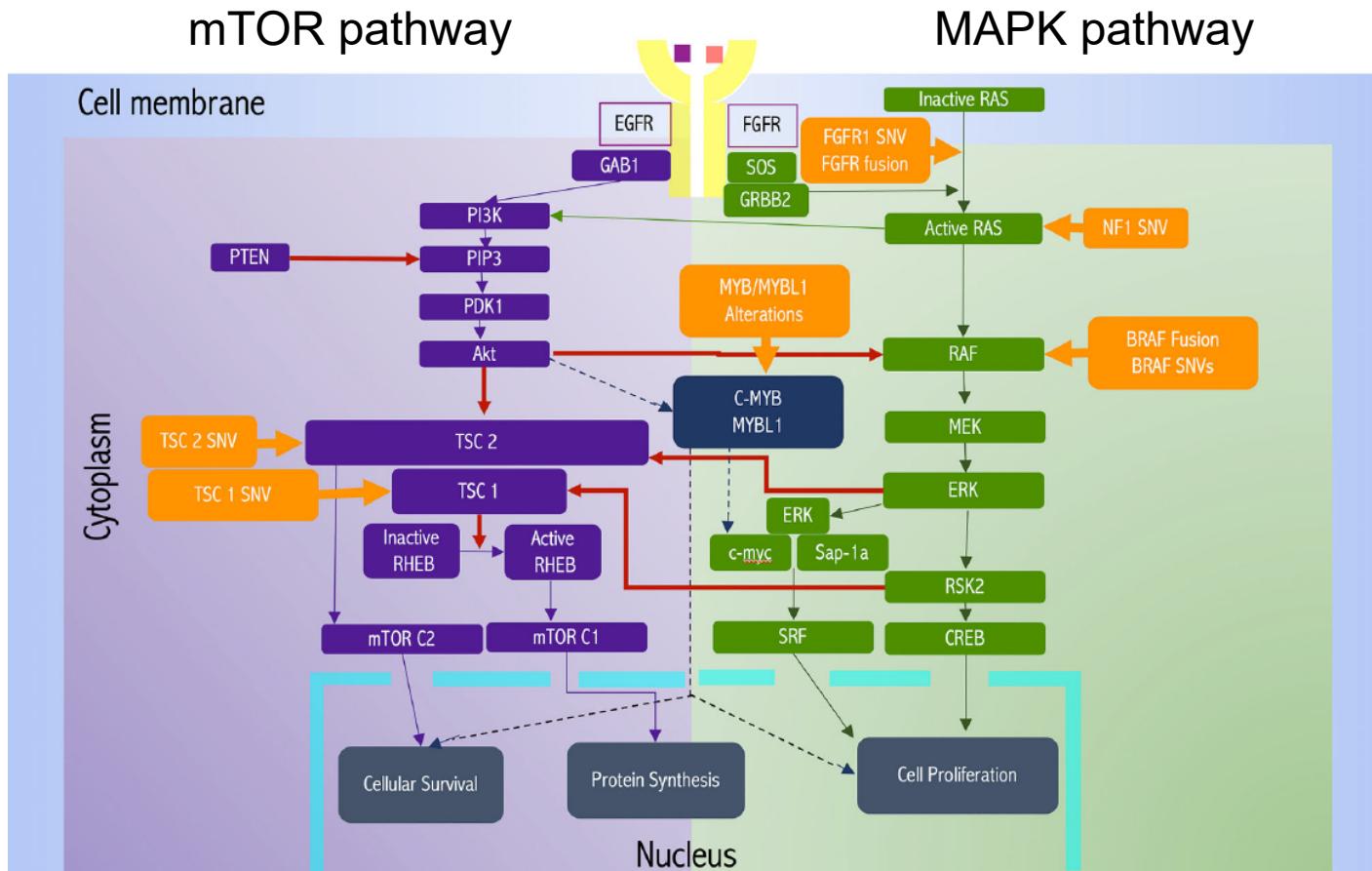
Gliomas, glioneuronal and neuronal tumours



→ Pediatric high-grade diffuse astrocytic tumors are distinct from their adult counterparts

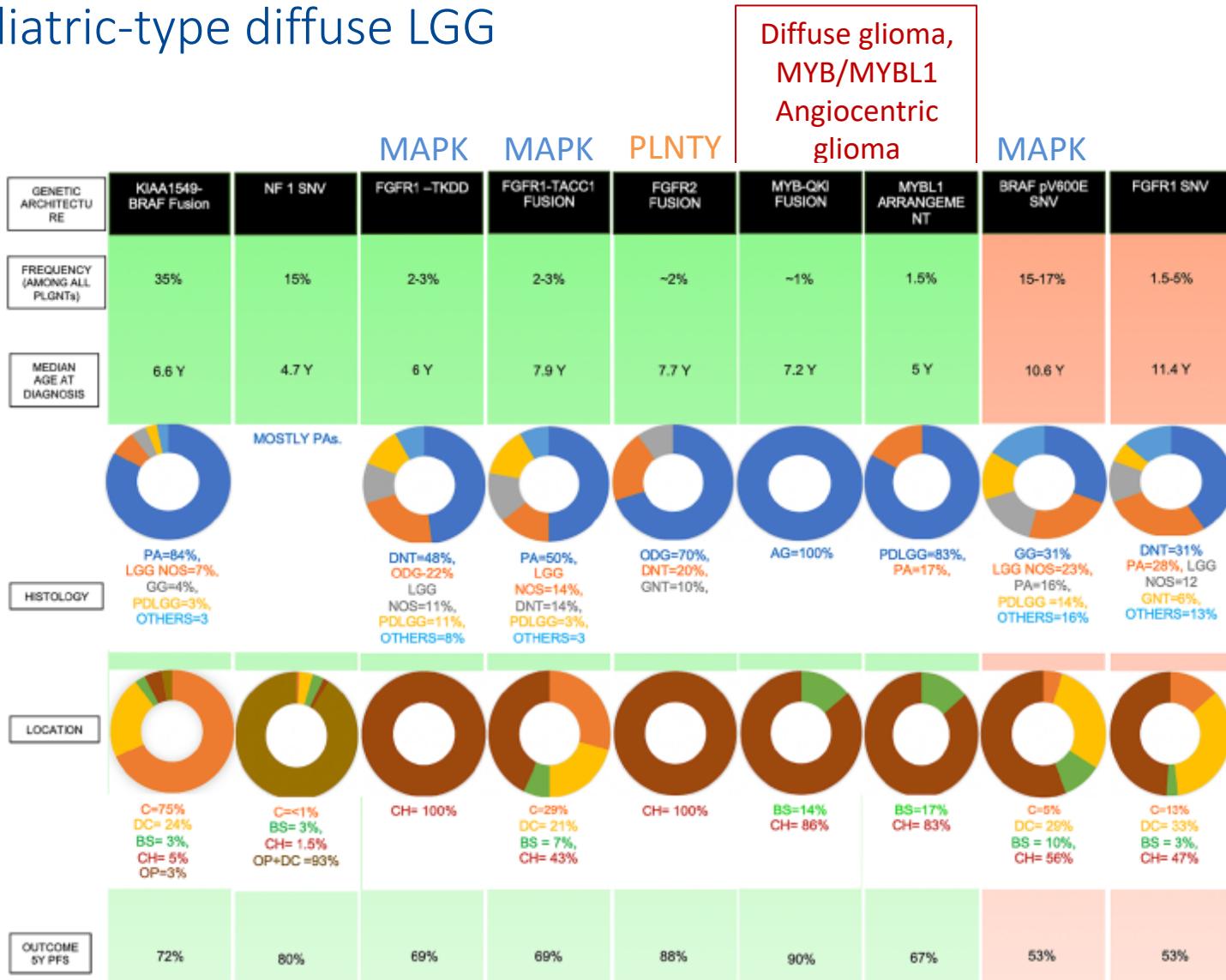
Gliomas, glioneuronal and neuronal tumours

3. Paediatric-type diffuse LGG



Gliomas, glioneuronal and neuronal tumours

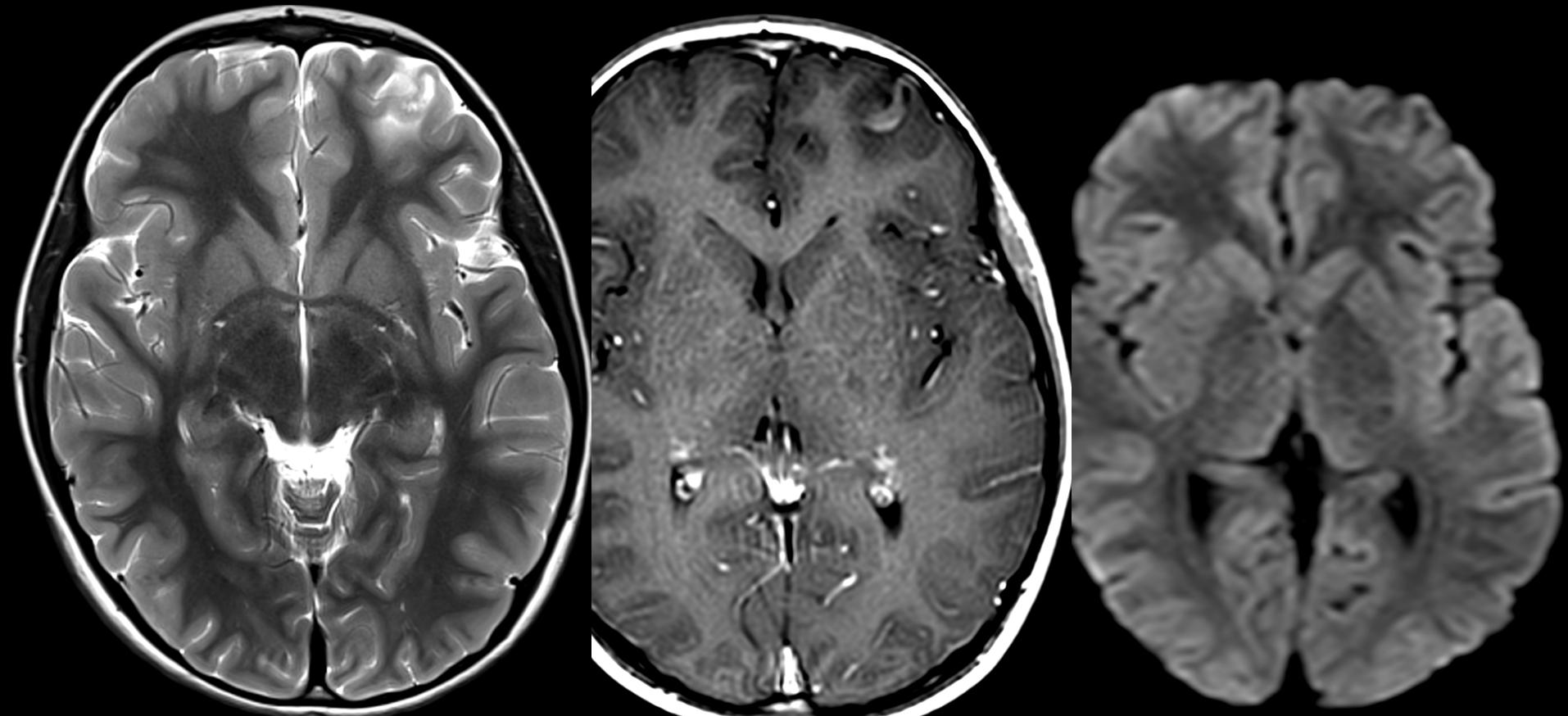
3. Paediatric-type diffuse LGG



Gliomas, glioneuronal and neuronal tumours

3.Paediatric-type diffuse LGG

Angiocentric glioma, MYB-QKI fusion

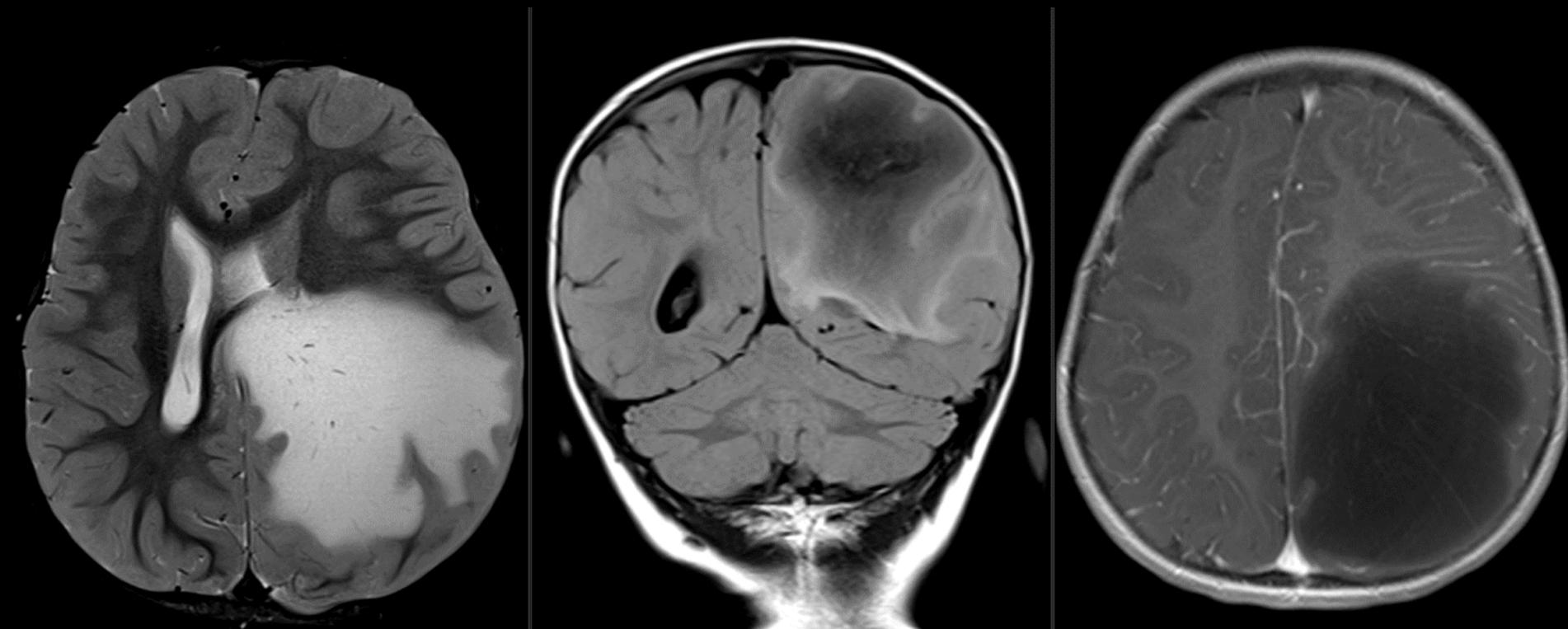


8-year-old boy

Gliomas, glioneuronal and neuronal tumours

3.Paediatric-type diffuse LGG

New tumour type: Diffuse glioma, MYBL1/MYB-altered



18-month-old girl

Gliomas, glioneuronal and neuronal tumours

4. Circumscribed astrocytic tumours

Circumscribed astrocytic gliomas

Pilocytic astrocytoma

High-grade astrocytoma with piloid features

Pleomorphic xanthoastrocytoma

Subependymal giant cell astrocytoma

Chordoid glioma

Astroblastoma, *MN1*-altered

Gliomas, glioneuronal and neuronal tumours

5. Glioneuronal and neuronal tumours

Glioneuronal and neuronal tumors

Ganglioglioma

Desmoplastic infantile ganglioglioma / desmoplastic infantile astrocytoma

Dysembryoplastic neuroepithelial tumor

Diffuse glioneuronal tumor with oligodendrogloma-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

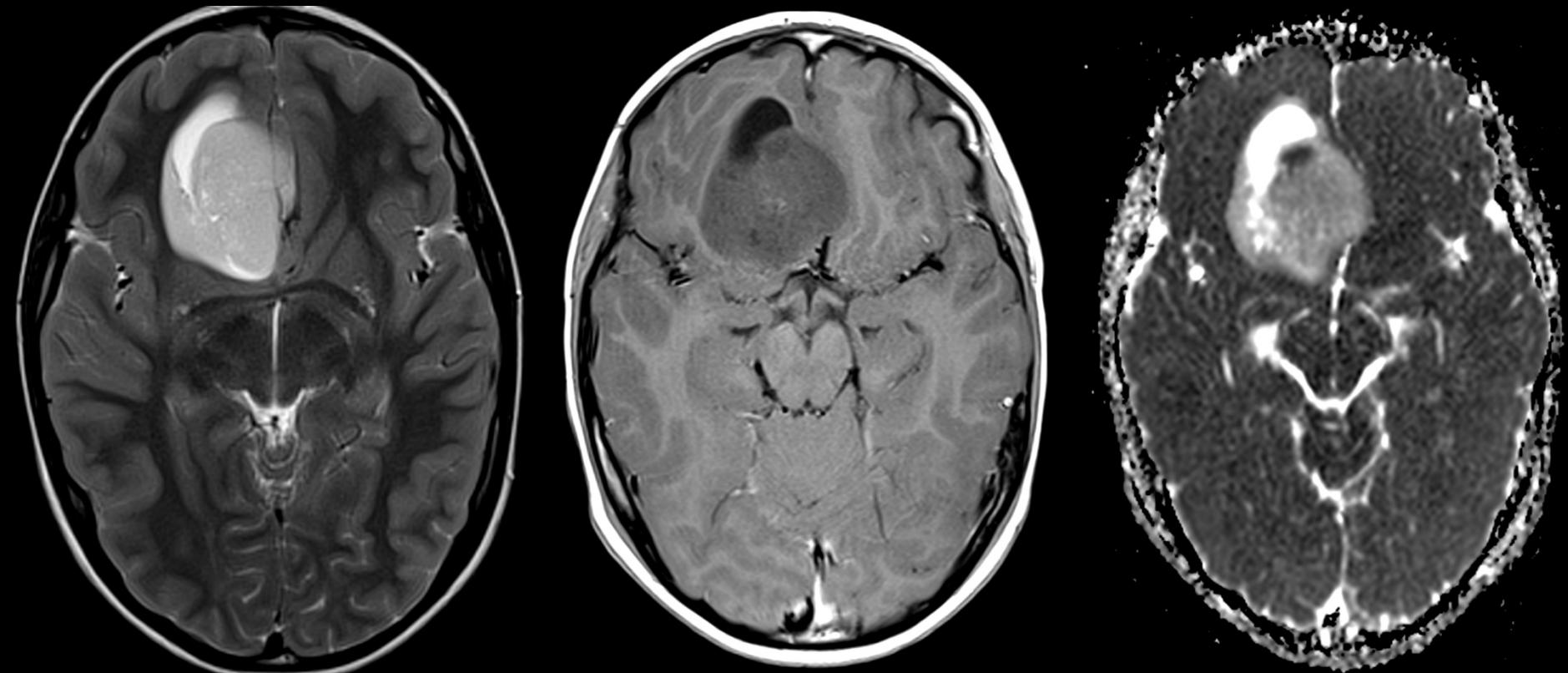
Extraventricular neurocytoma

Cerebellar liponeurocytoma

Gliomas, glioneuronal and neuronal tumours

5.Glioneuronal and neuronal tumours

Provisional tumour type: Diffuse Glioneuronal Tumours with Oligodendrogioma-like features and Nuclear Clusters (DGONC)

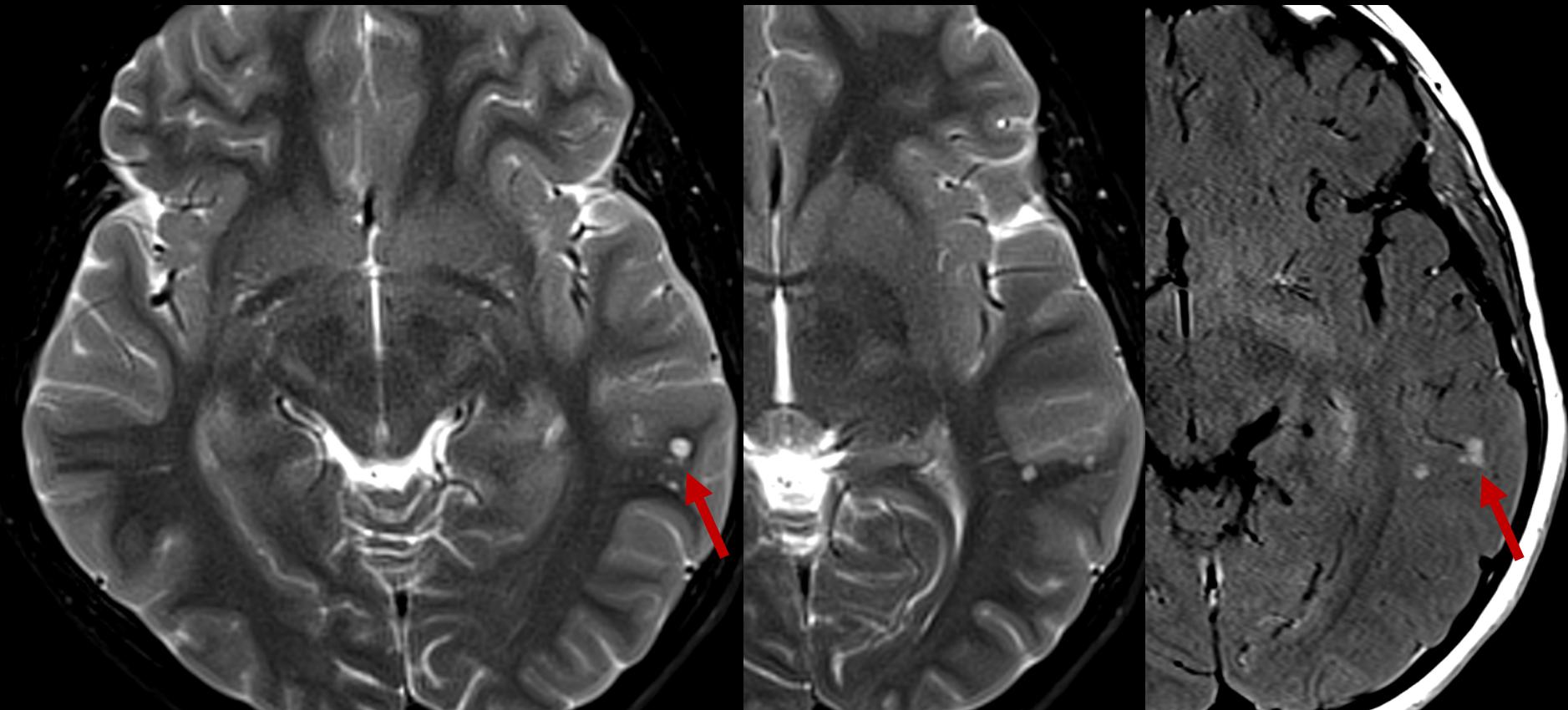


11-year-old boy

Gliomas, glioneuronal and neuronal tumours

5.Glioneuronal and neuronal tumours

New tumour type: Multinodular and vacuolating neuronal tumour

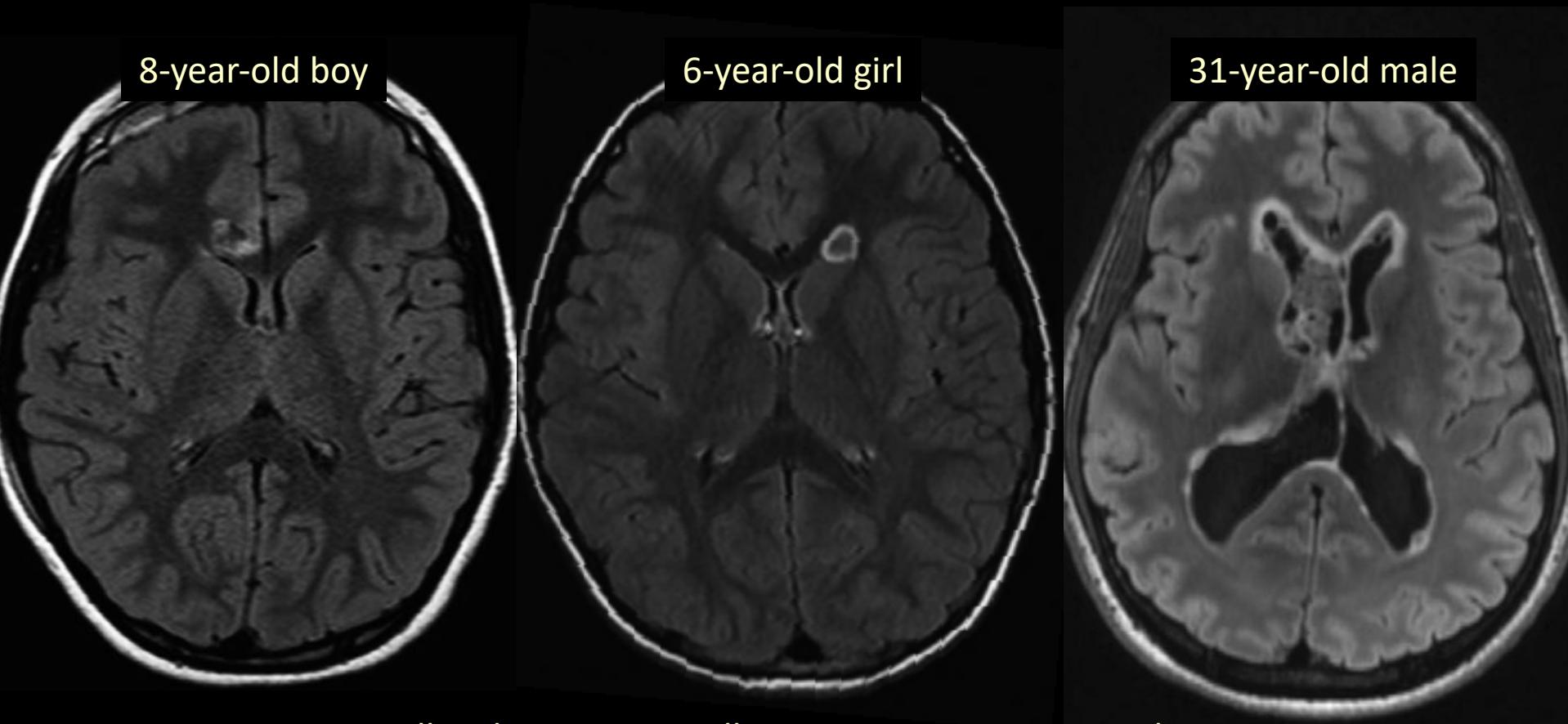


12-year-old girl
(presumed diagnosis)

Gliomas, glioneuronal and neuronal tumours

5.Glioneuronal and neuronal tumours

New tumour type: Myxoid glioneuronal tumour



Septum pellucidum, corpus callosum, no restriction or enhancement

Gliomas, glioneuronal and neuronal tumours

6. Ependymal tumours

2016

Subependymoma
Myxopapillary ependymoma
Ependymoma
Papillary ependymoma
Clear cell ependymoma
Tanycytic ependymoma
Ependymoma, *RELA* fusion-positive
Anaplastic ependymoma

2021

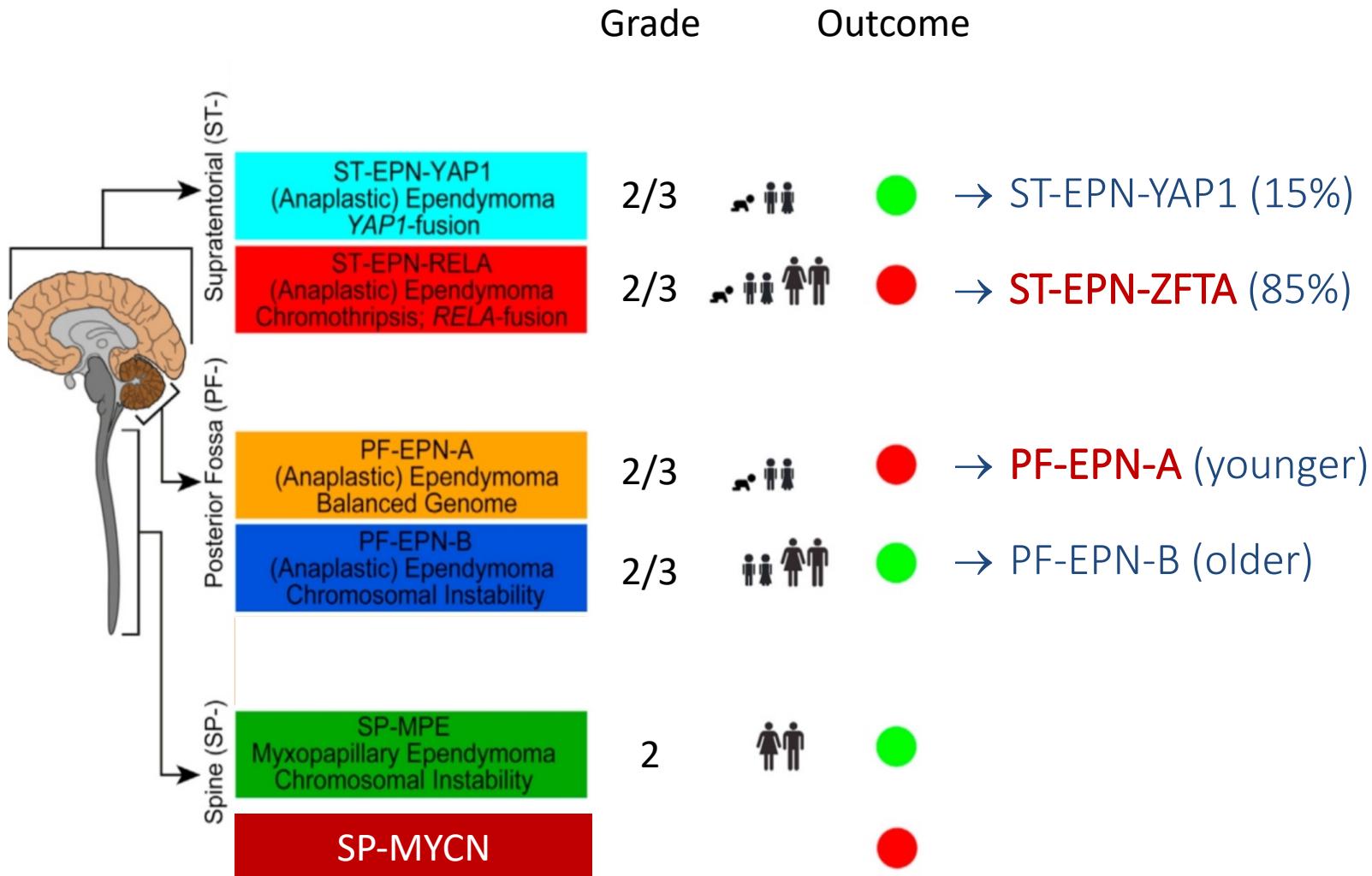
Supratentorial ependymoma
Supratentorial ependymoma, *ZFTA* fusion-positive
Supratentorial ependymoma, *YAP1* fusion-positive
Posterior fossa ependymoma
Posterior fossa ependymoma, group PFA
Posterior fossa ependymoma, group PFB
Spinal ependymoma
Spinal ependymoma, *MYCN*-amplified
Myxopapillary ependymoma
Subependymoma

RELA → *c11orf95* → ZFTA-fusion positive
ZFTA = zinc finger translocation associated

“new designation for C11orf95, which is considered more representative of the tumour type than RELA because it may be fused with partners more than RELA”

Gliomas, glioneuronal and neuronal tumours

6. Ependymal tumours

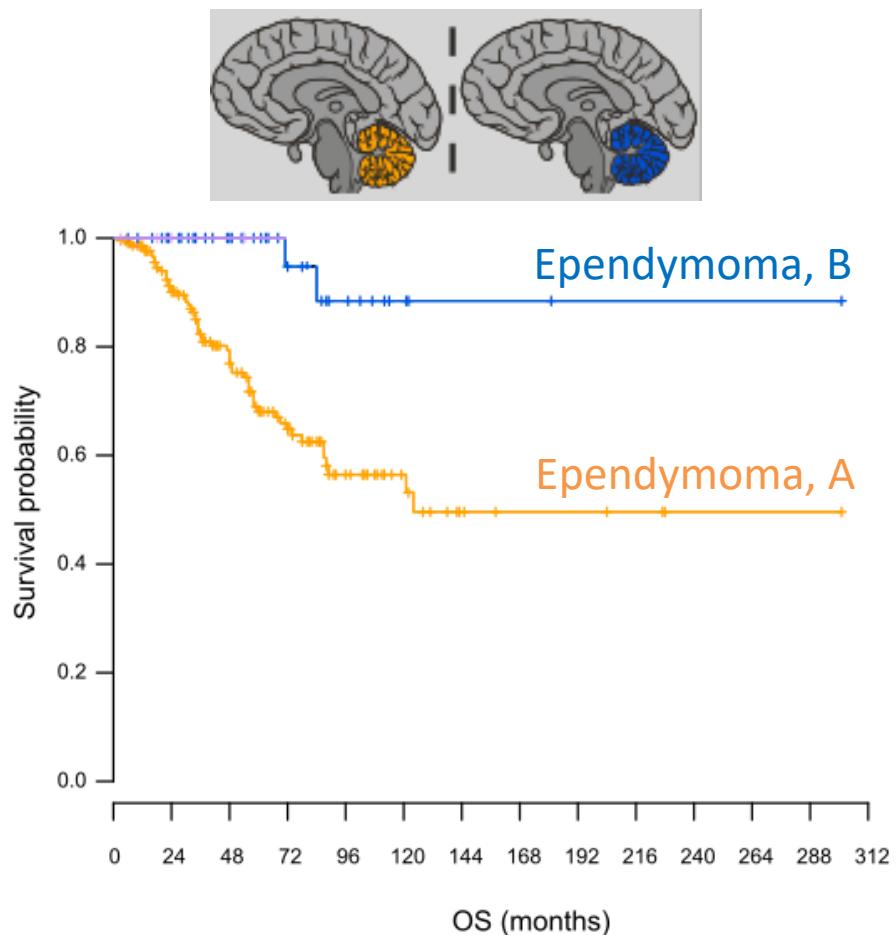
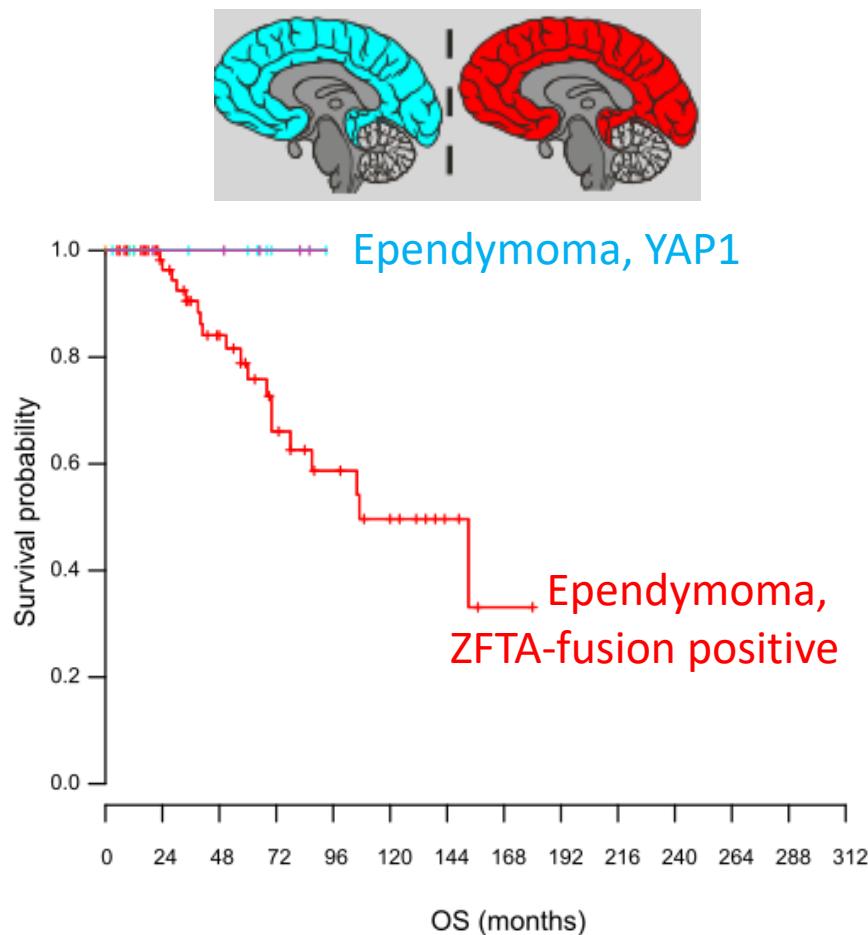


Modified after: Pajtler et al. 2015 Cancer Cell

Gliomas, glioneuronal and neuronal tumours

6. Ependymal tumours

- Correlation to patient outcome

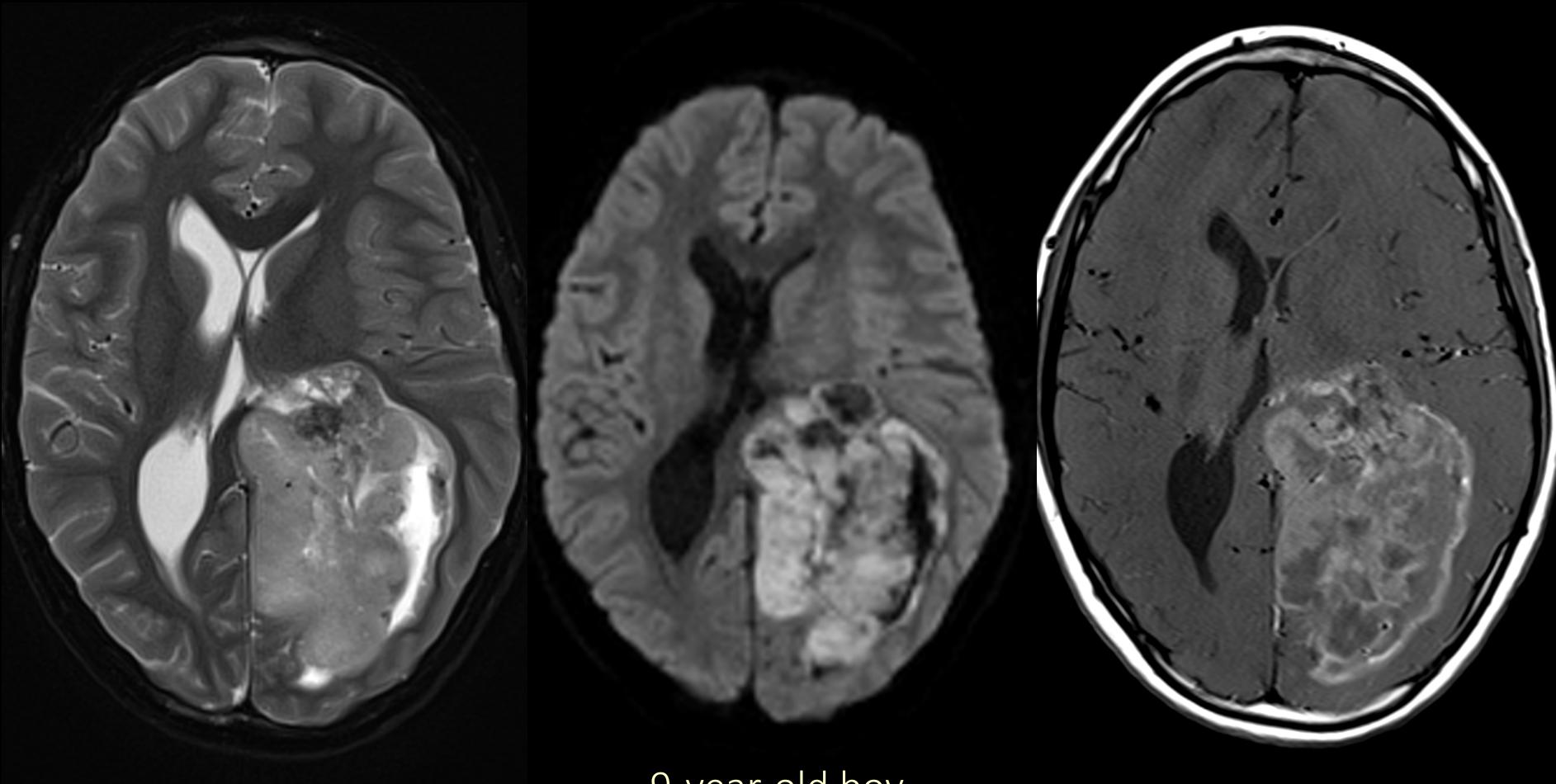


Modified from: Pajtler et al. 2015 Cancer Cell

6. Ependymal tumours

6.Ependymal tumours

Modified tumour type: Ependymoma, ZFTA-fusion positive

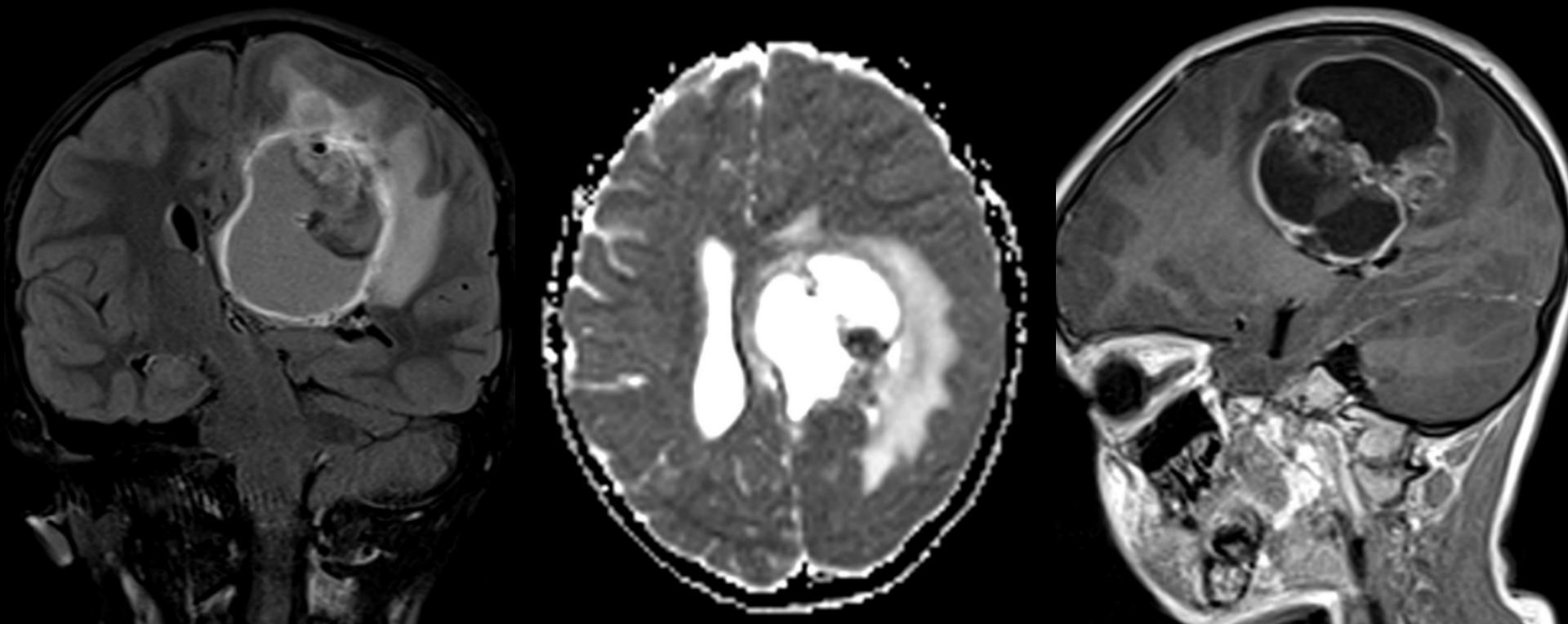


9-year-old boy
Can mimick ETMR but enhancement

6. Ependymal tumours

6.Ependymal tumours

Modified tumour type: Ependymoma, ZFTA-fusion positive

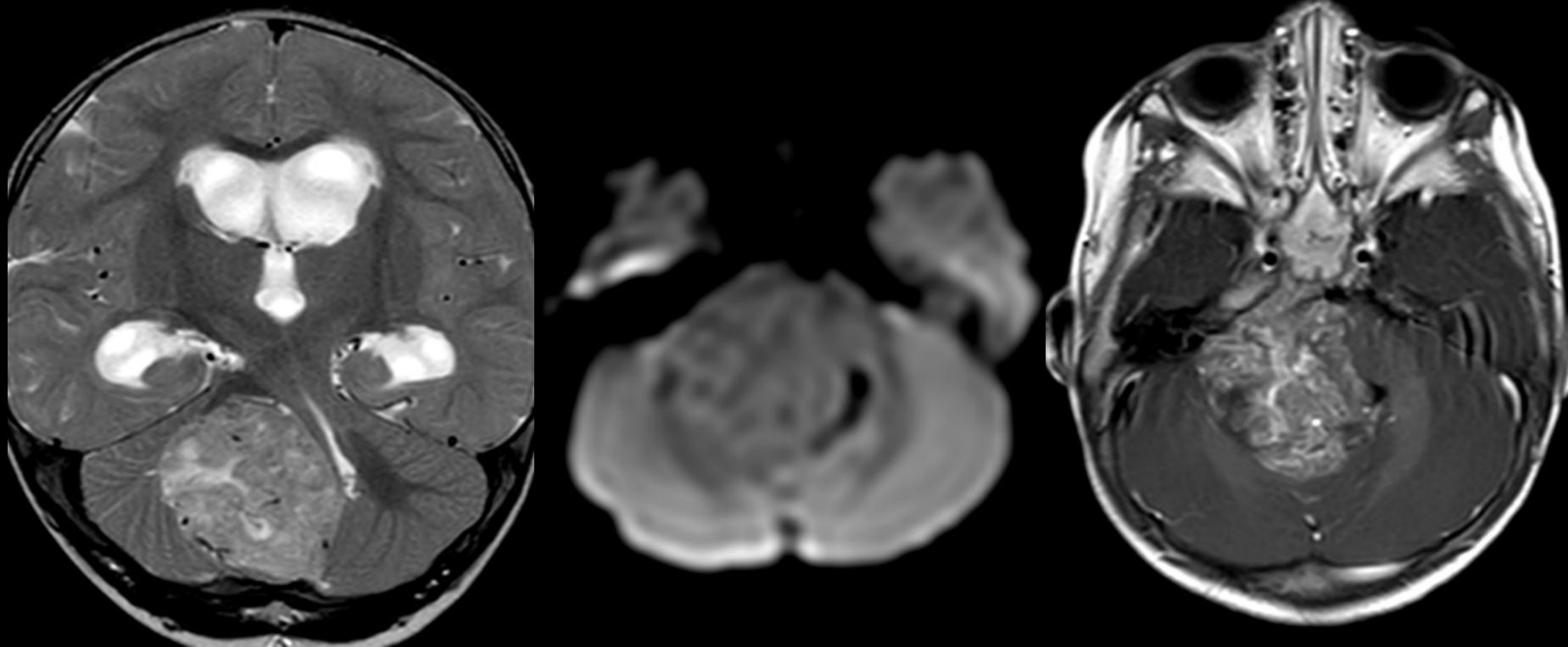


6-year-old girl

6. Ependymal tumours

6.Ependymal tumours

Modified tumour type: Ependymoma, PF-A

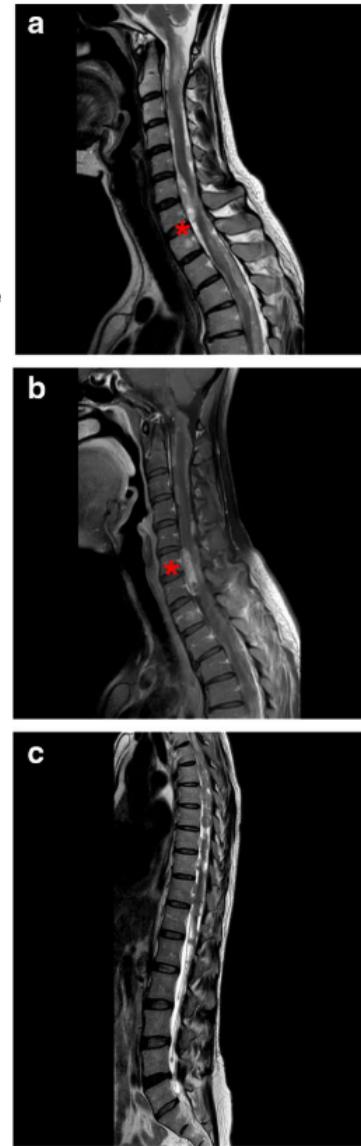
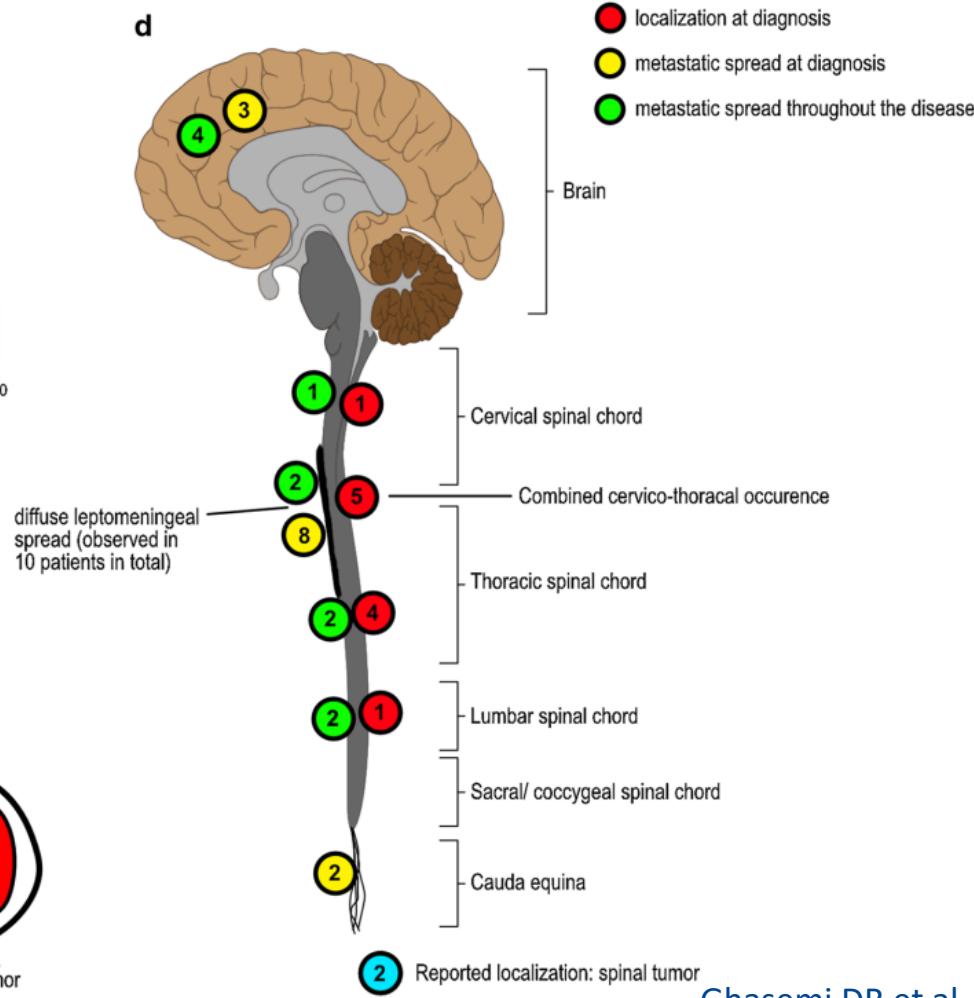
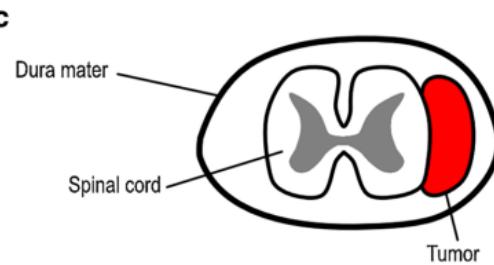
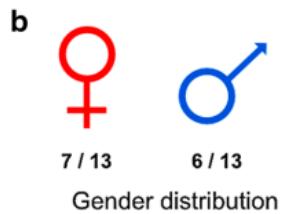
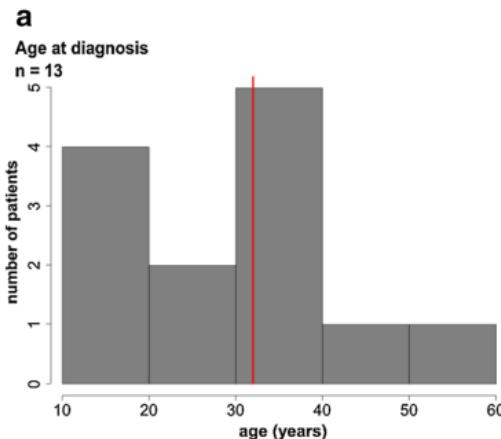


14-month-old girl

Gliomas, glioneuronal and neuronal tumours

6. Ependymal tumours

New type: Spinal ependymoma, MYCN



Embryonal tumours

→ Medulloblastoma

Medulloblastomas, molecularly defined

Medulloblastoma, WNT-activated

Medulloblastoma, SHH-activated and *TP53*-wildtype

Medulloblastoma, SHH-activated and *TP53*-mutant

Medulloblastoma, non-WNT/non-SHH

Medulloblastomas, histologically defined

Other CNS embryonal tumors

→ Atypical teratoid/rhabdoid tumor

Cribiform neuroepithelial tumor

→ Embryonal tumor with multilayered rosettes *DICER1*

CNS neuroblastoma, FOXR2-activated

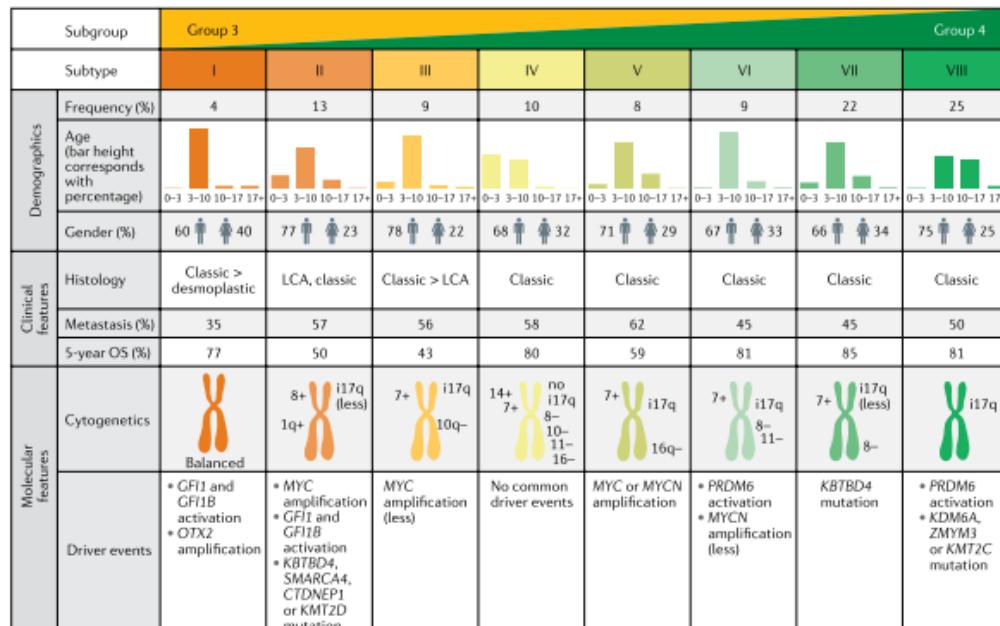
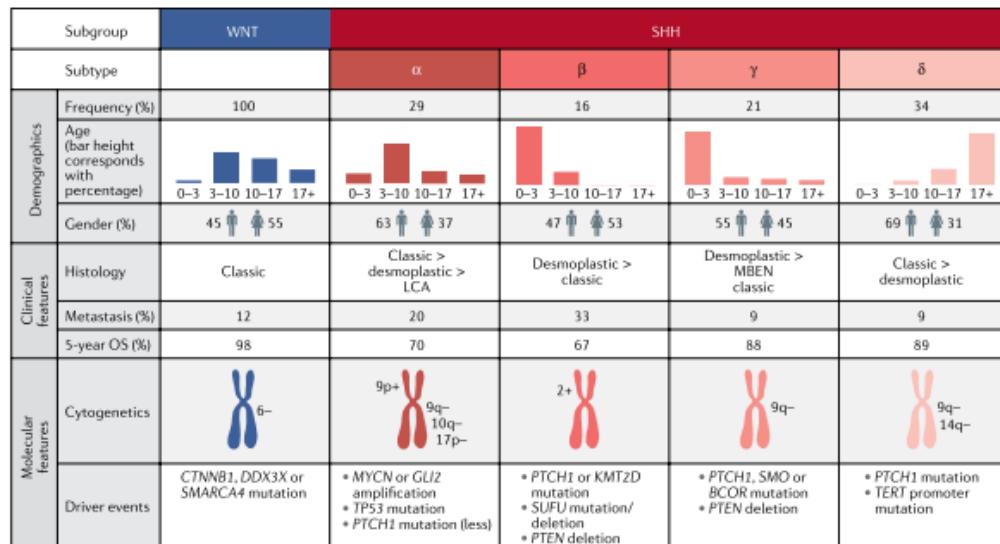
CNS tumor with BCOR internal tandem duplication

CNS embryonal tumor

Embryonal tumours

1. Medulloblastoma

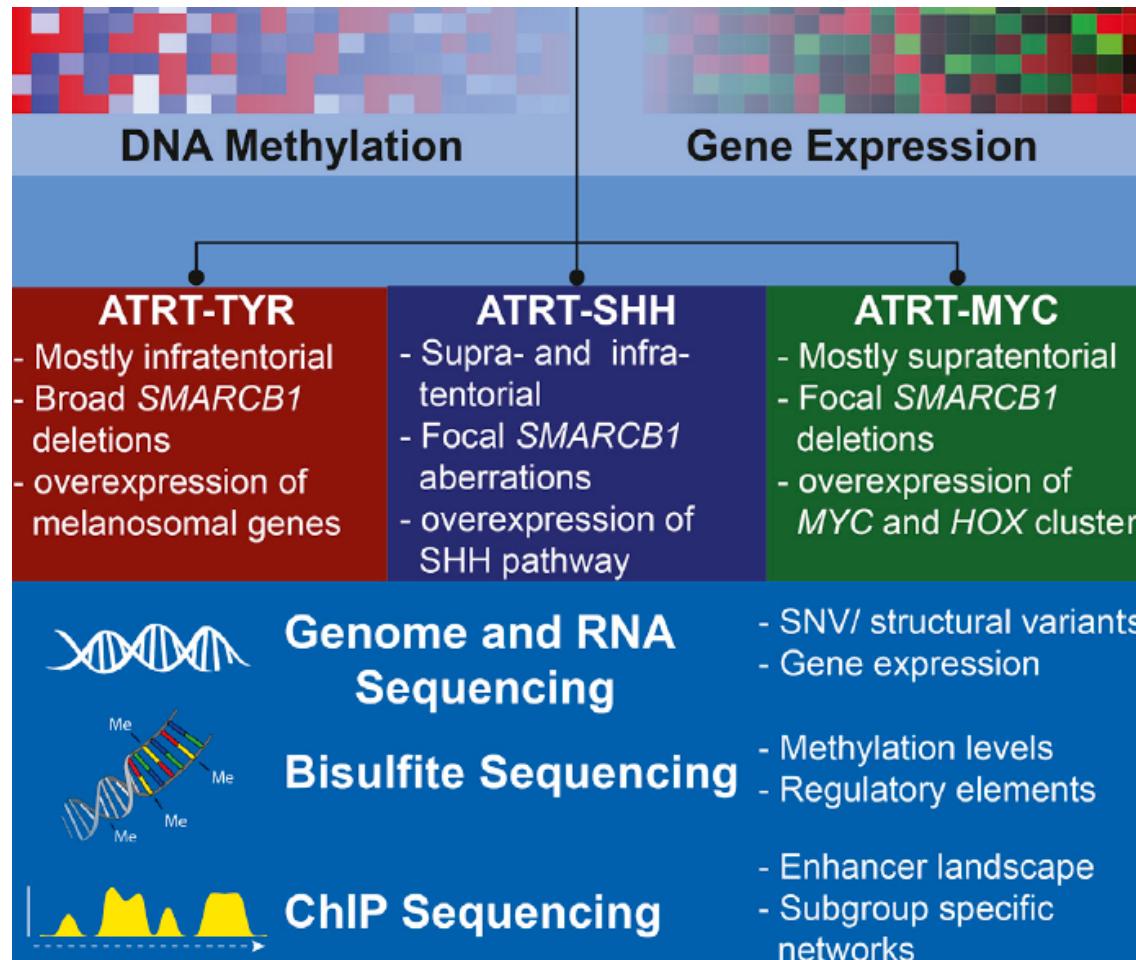
4 main tumour types,
new subgroups for
SHH and group 3/4



Embryonal tumours

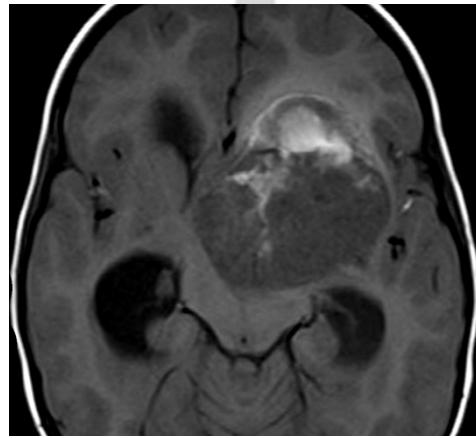
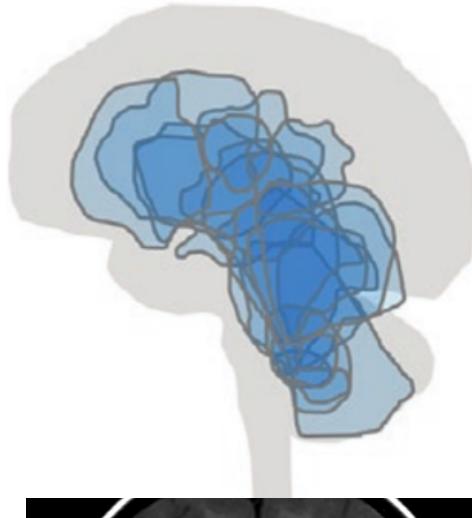
2. Other embryonal tumours

AT/RT: *SMARCB1* (or *SMARCA4*) alterations, 3 new subgroups



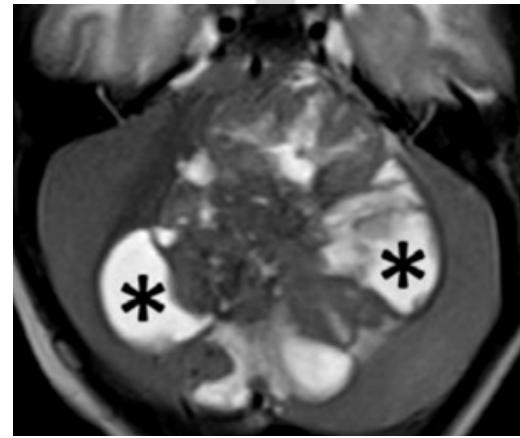
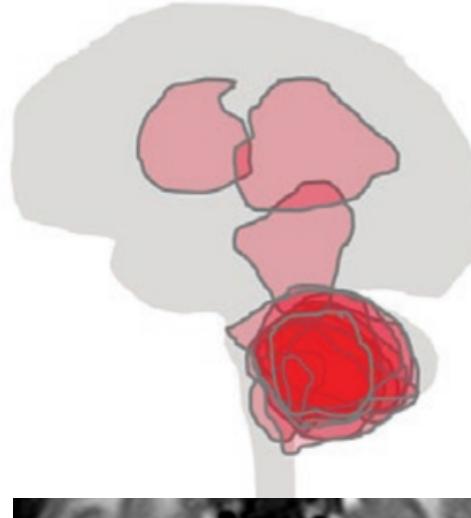
Embryonal tumours

ATRT-SHH



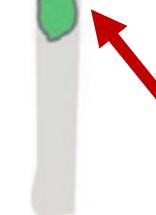
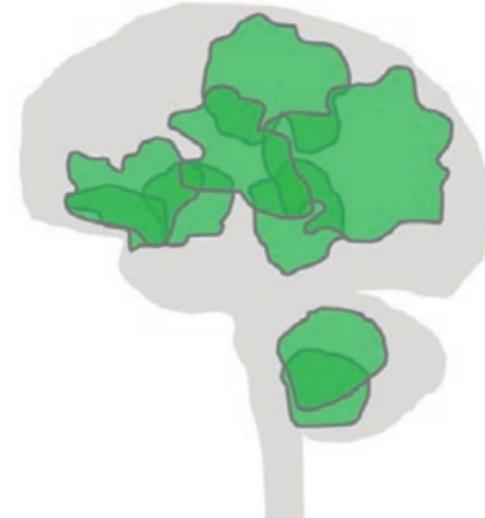
29% no CE

ATRT-TYR



94% periph. cysts

ATRT-MYC



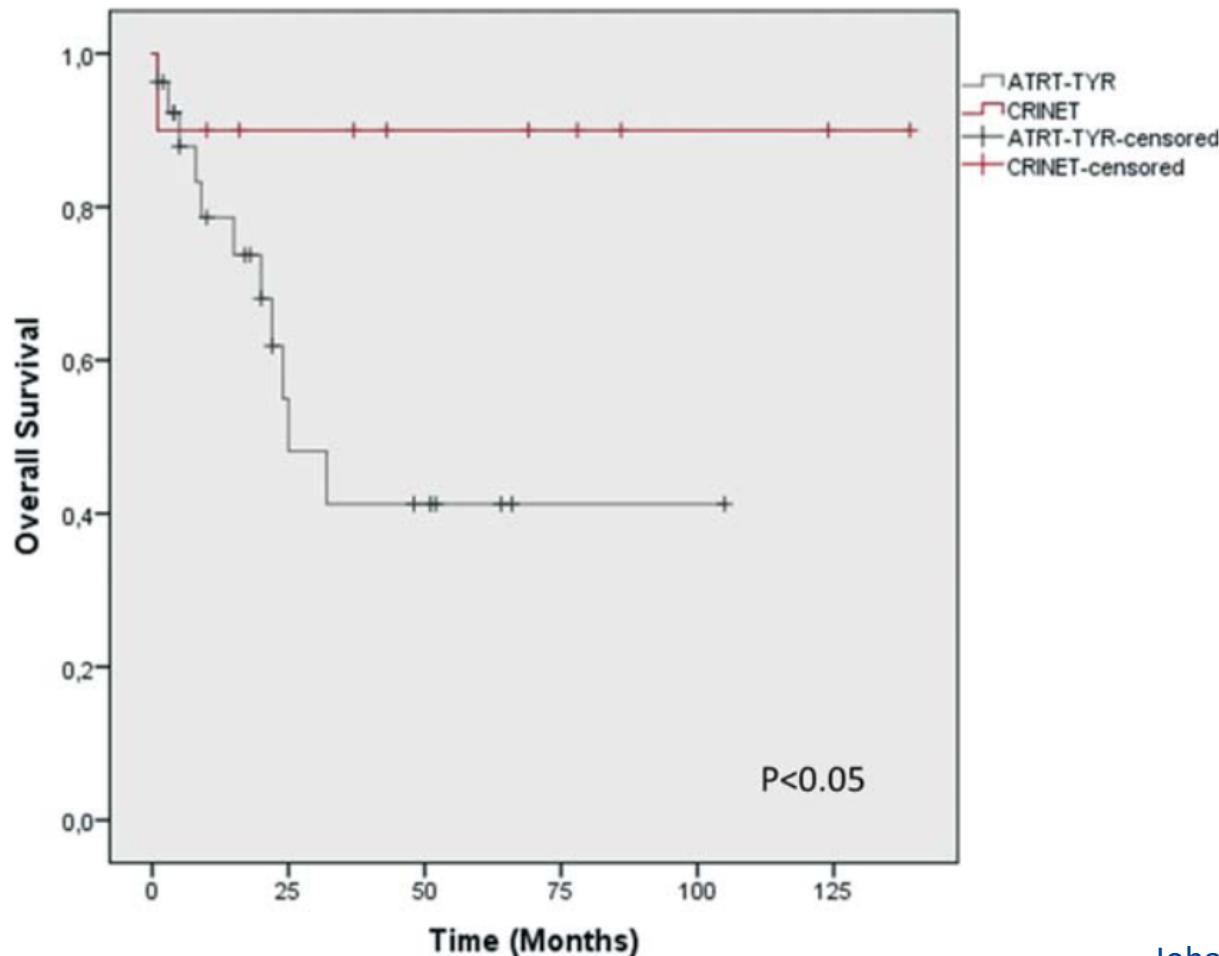
Spinal

Embryonal tumours

2. Other embryonal tumours

New tumour type: Cribriform neuroepithelial tumor (CRINET)

SMARCB1

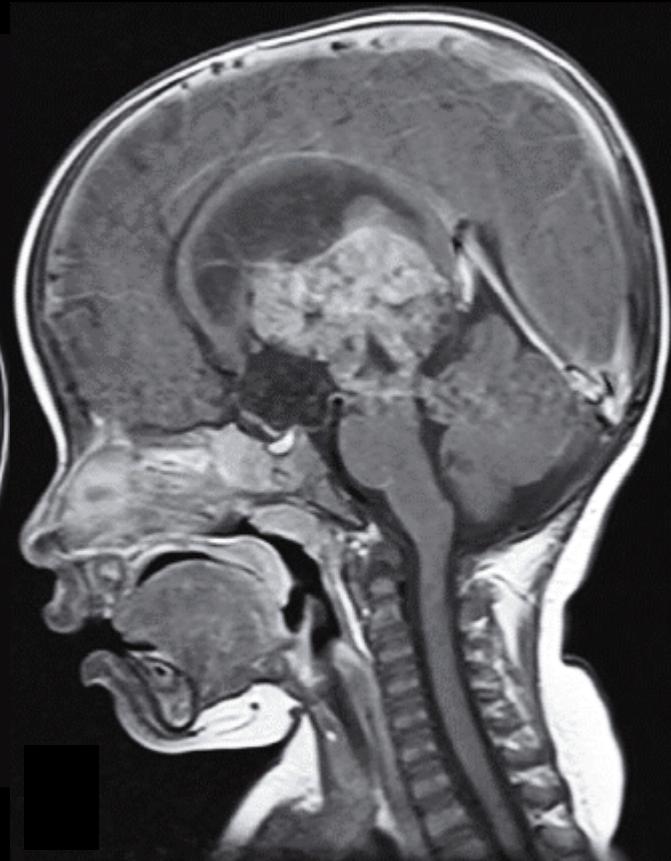
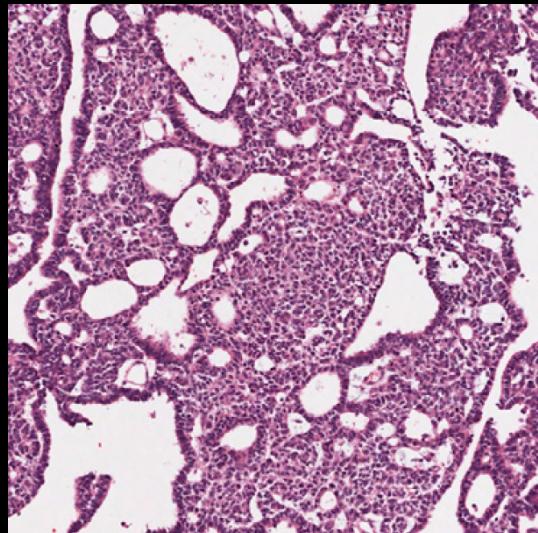


6. Ependymal tumours

2. Other embryonal tumours

New tumour type: Cribriform neuroepithelial tumor (CRINET)

SMARCB1



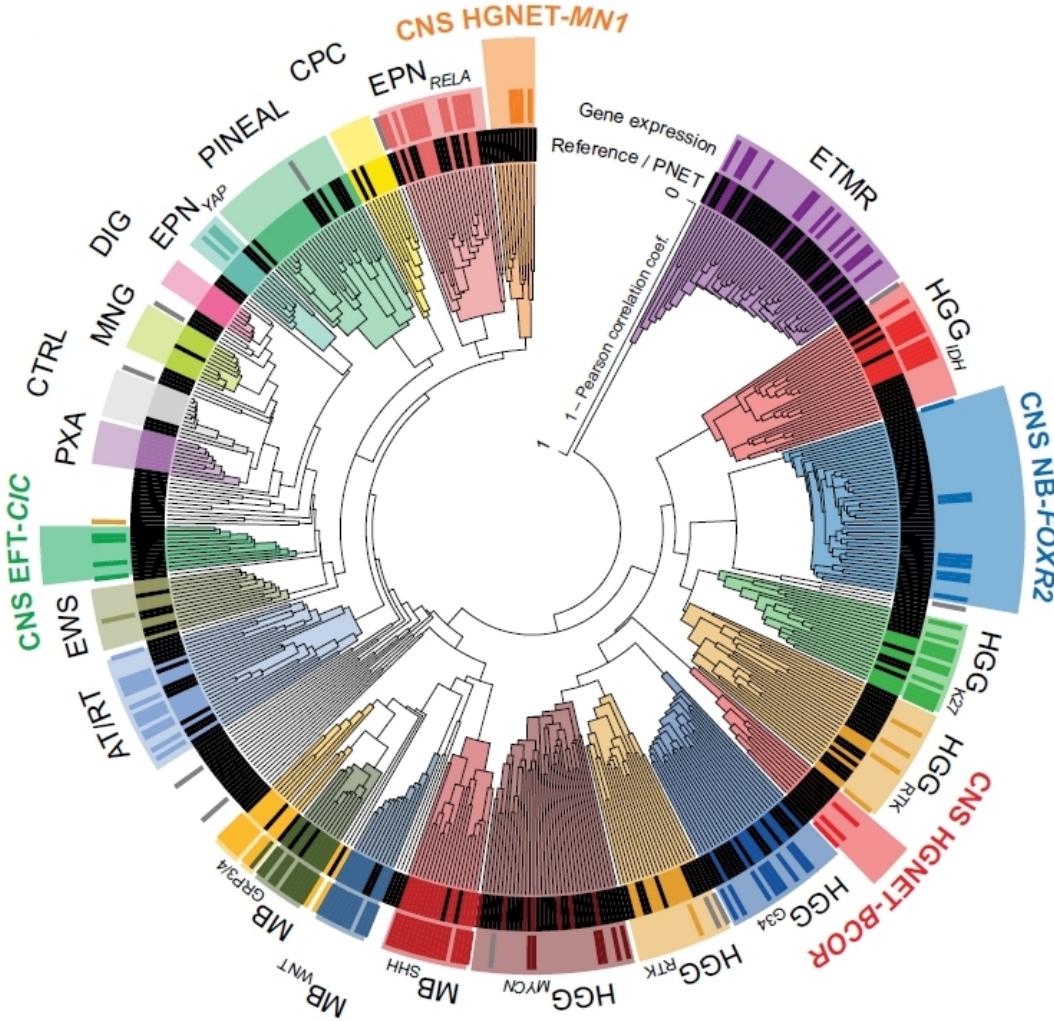
14-month-old boy
2-week history of gait imbalance

Imaging may mimick choroid plexus tumours

Images from: Park et al. 2012 Neuropathol

Embryonal tumours

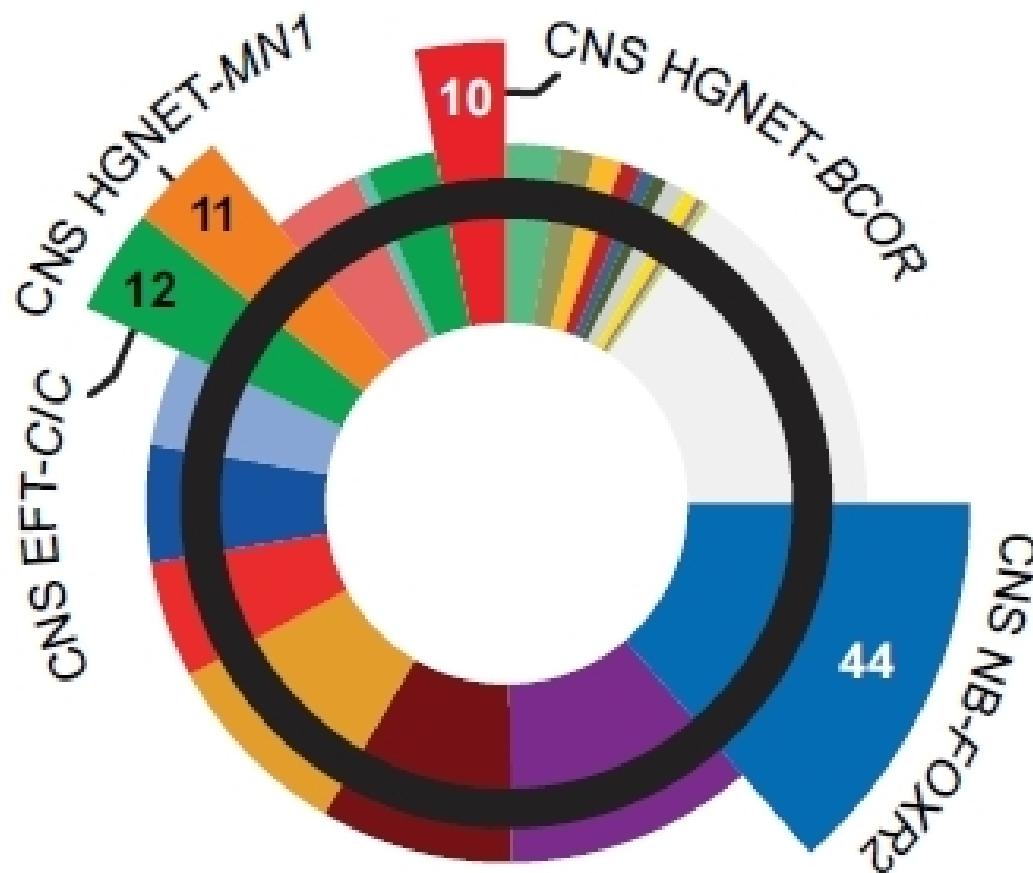
PNET



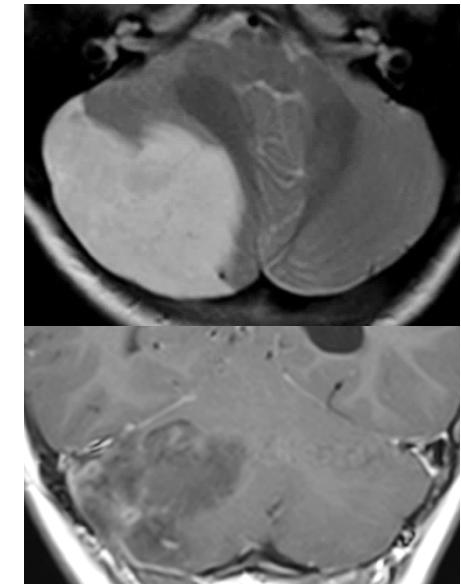
323 CNS-PNET and 211 reference samples

Sturm et al. 2016 Cancer Cell

Embryonal tumours

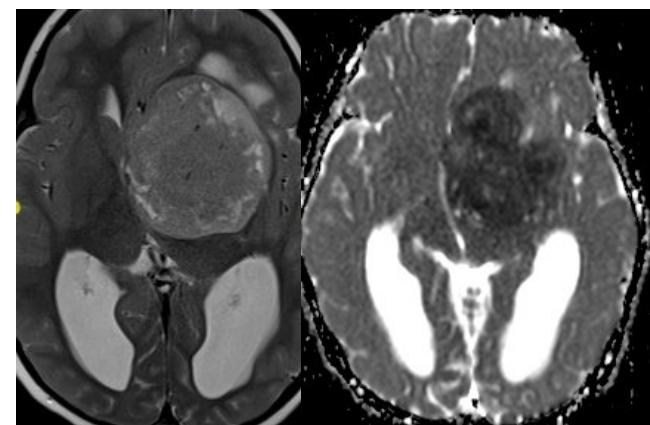


CNS tumour with BCOR internal tandem duplication



5 year-old boy

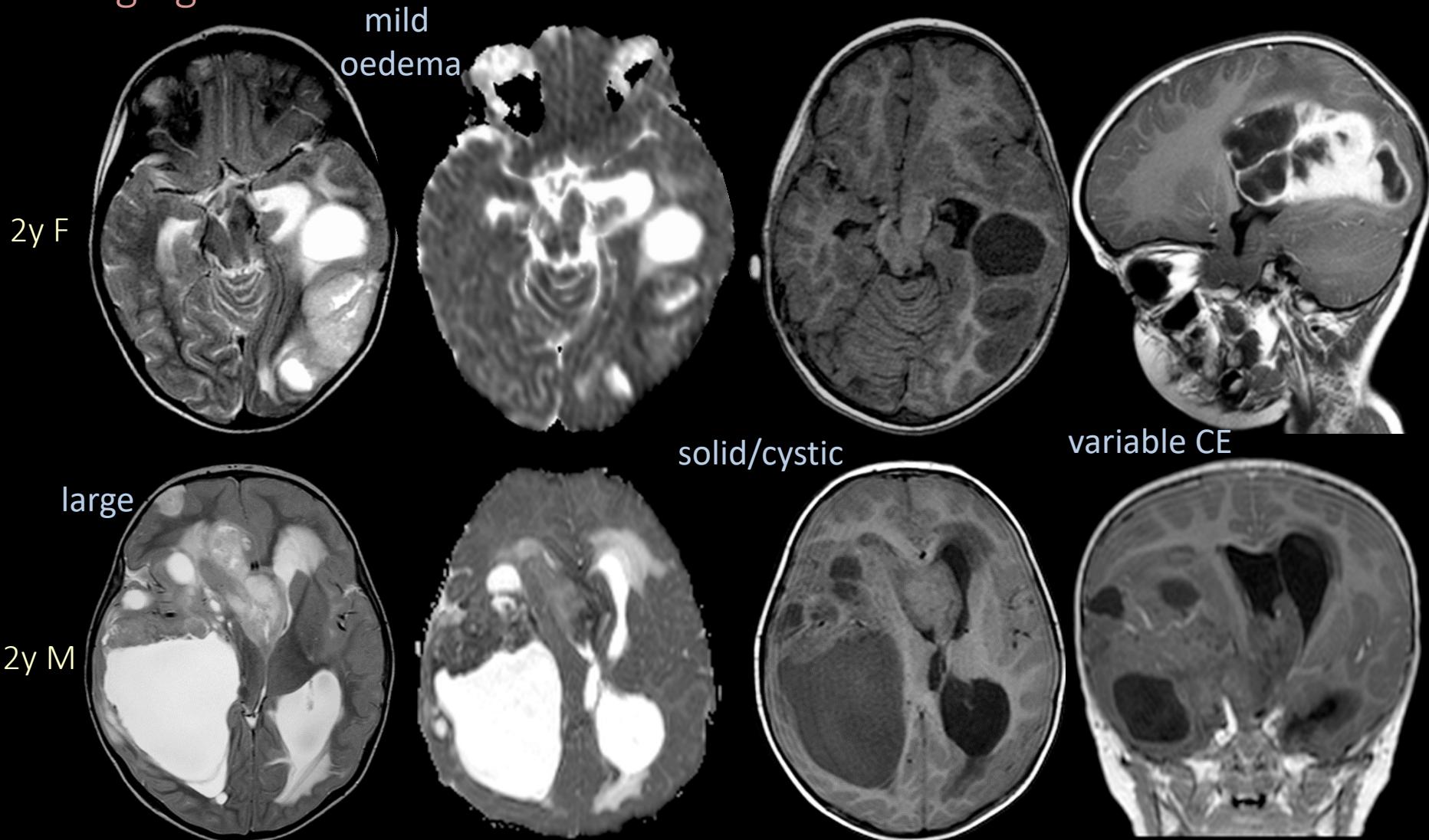
CNS neuroblastoma, FOXR2



5 year-old boy

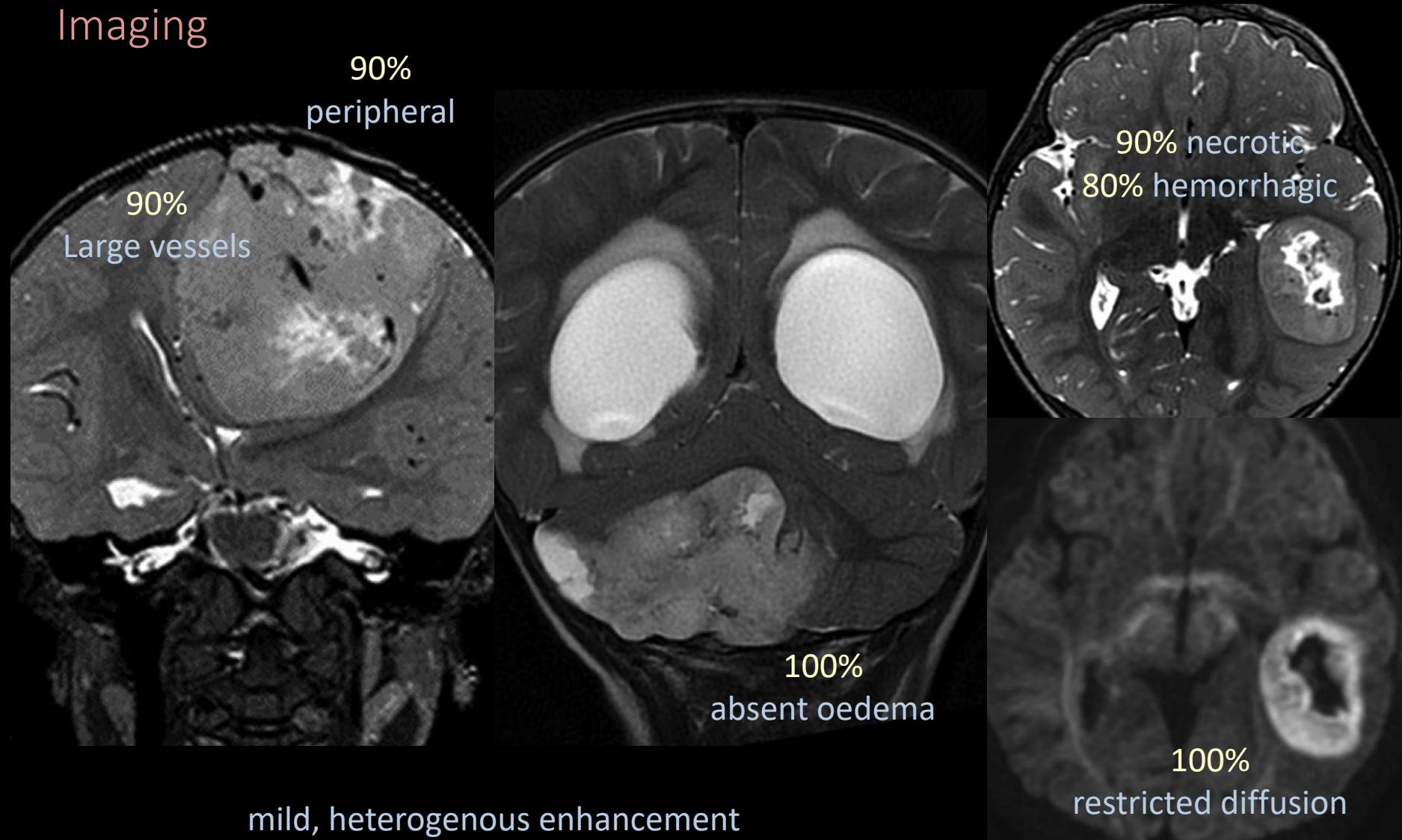
CNS Neuroblastoma, *FOXR2*-activated

Imaging



CNS tumour with BCOR internal tandem duplication

Imaging

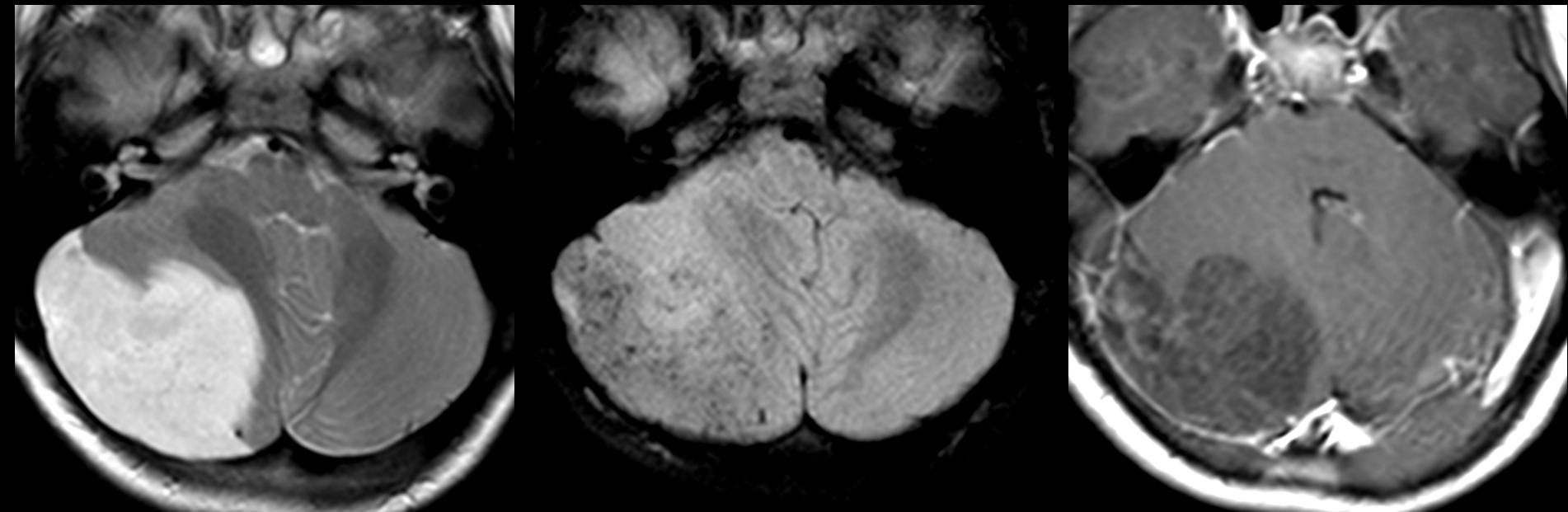


Data and images from: Cardoen et al. 2022 AJNR

CNS tumour with BCOR internal tandem duplication

Outcome is not great

Can also occur in brainstem and spinal cord

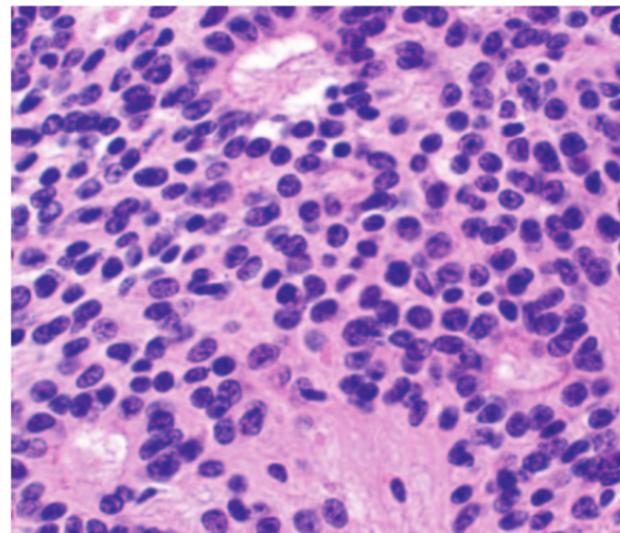
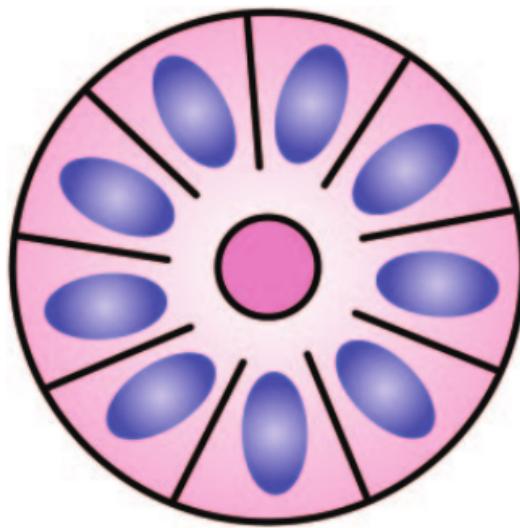


5-year-old boy

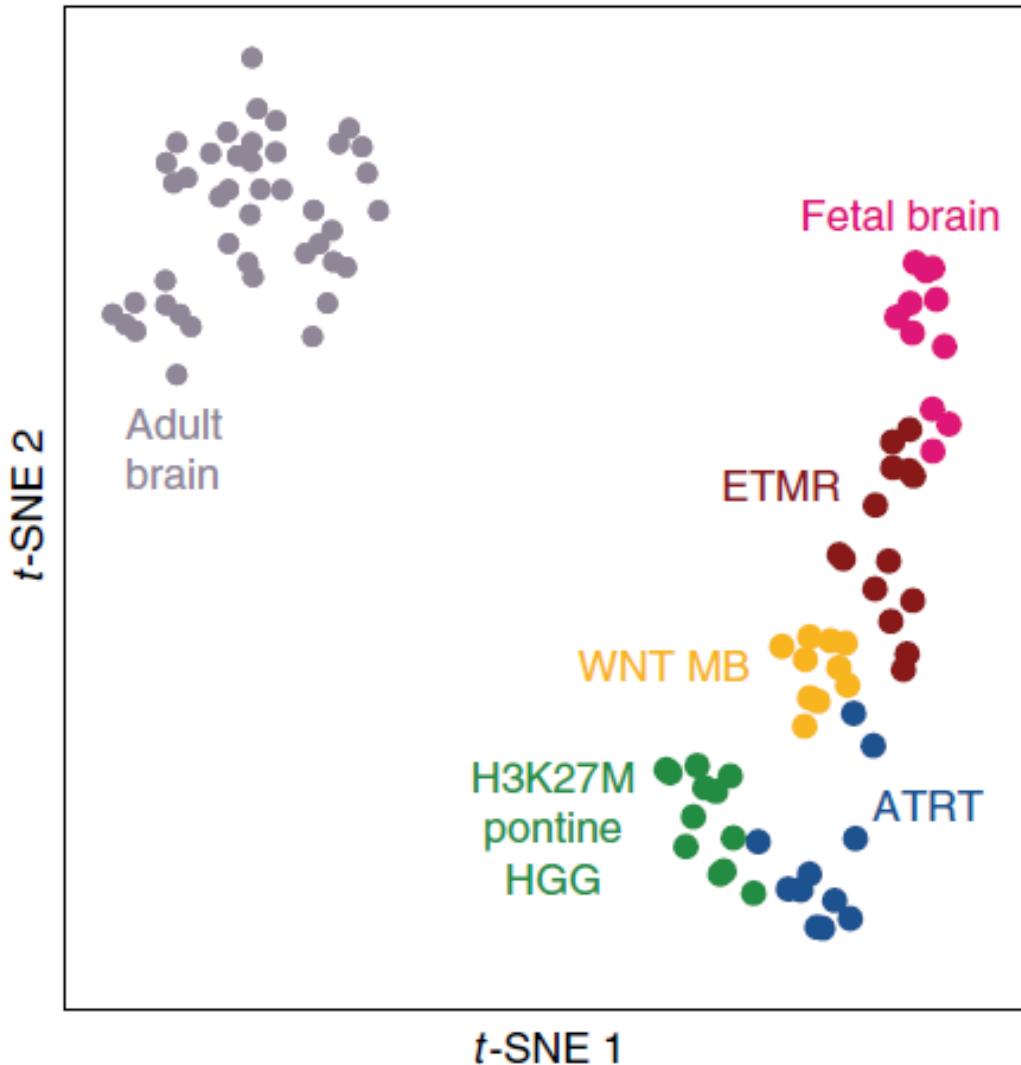
Embryonal tumours

Embryonal tumour with multi-layered rosettes, ETMR

- Alterations of **C19MC** locus at 19q13.42
- Additional mutation: *DICER1* (Cancer predisposition syndrome)
- rapid growth and are associated with an aggressive clinical course, with reported survival times averaging 12 months



Embryonal tumours



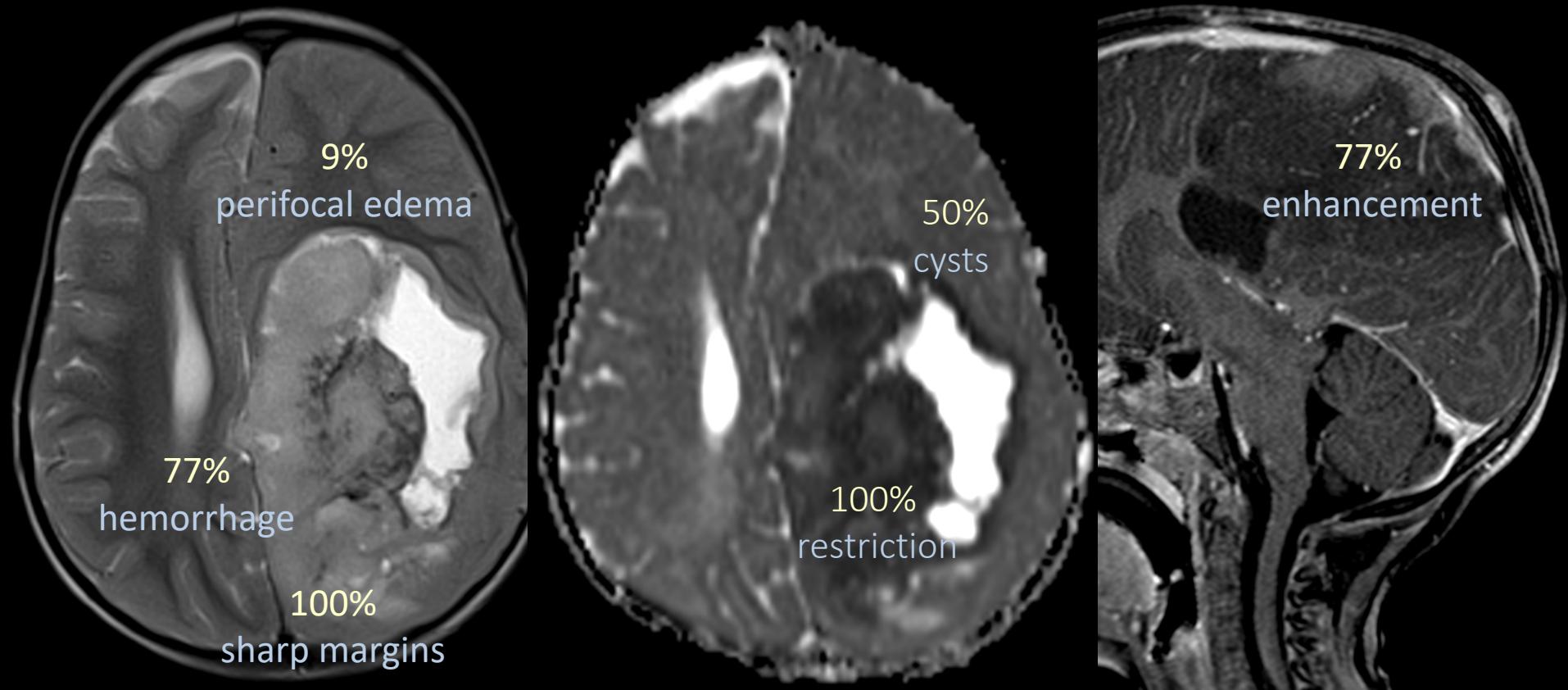
ETMRs cluster with the developmental cell populations of the fetal brain

Origin:
Prenatal radial glial cells that undergo oncogenic transformation and persist in the developing brain

Embryonal tumours

2. Other embryonal tumours

Known tumour type: ETMR



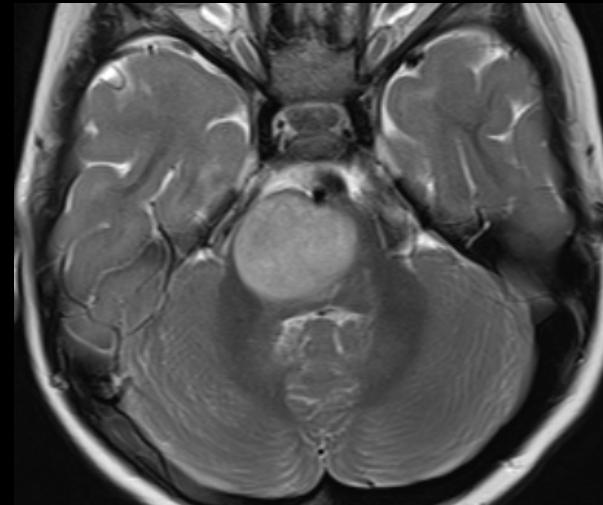
2-year-old girl

Data from Nowak et al. 2014 AJNR, 22 patients with ependymoblastoma*

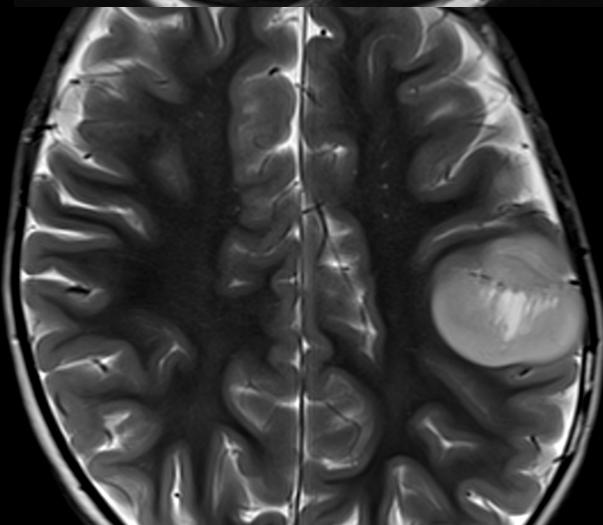
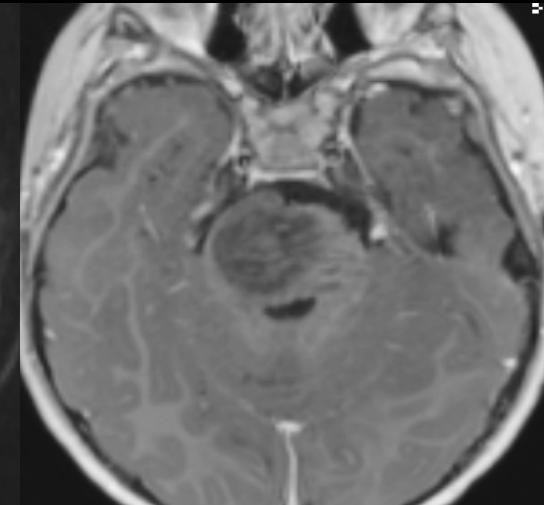
Embryonal tumours

2. Other embryonal tumours

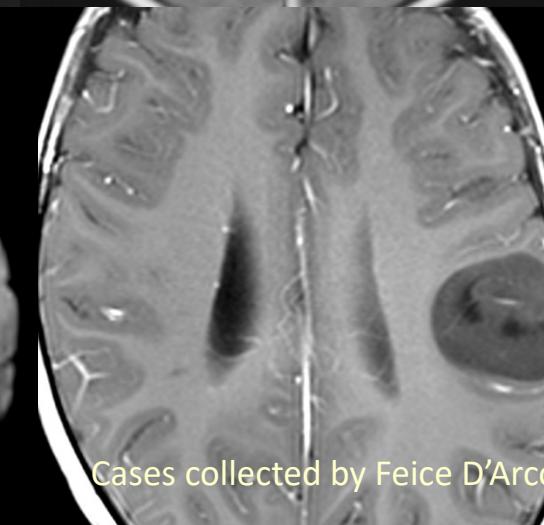
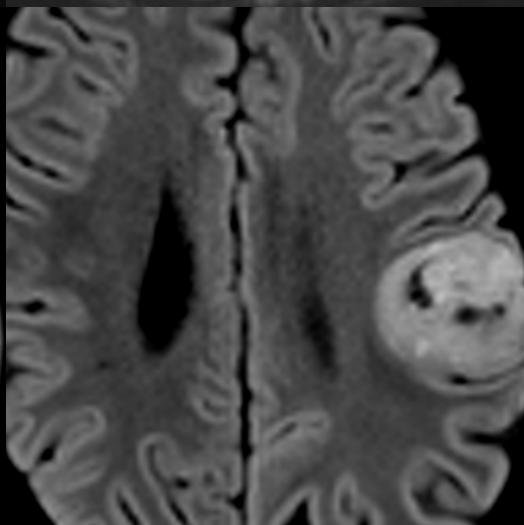
Known tumour type: ETMR



2-year-old girl

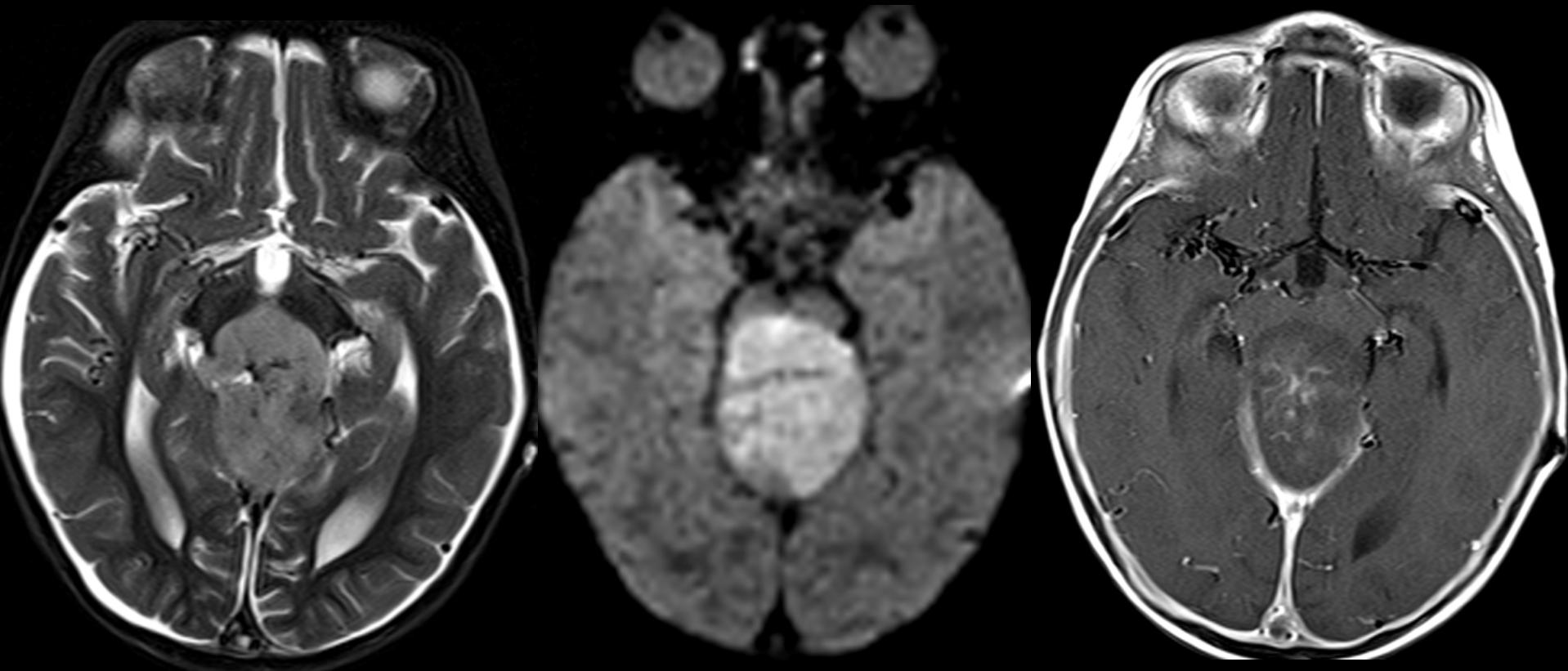


2-year-old girl



5. ETMR

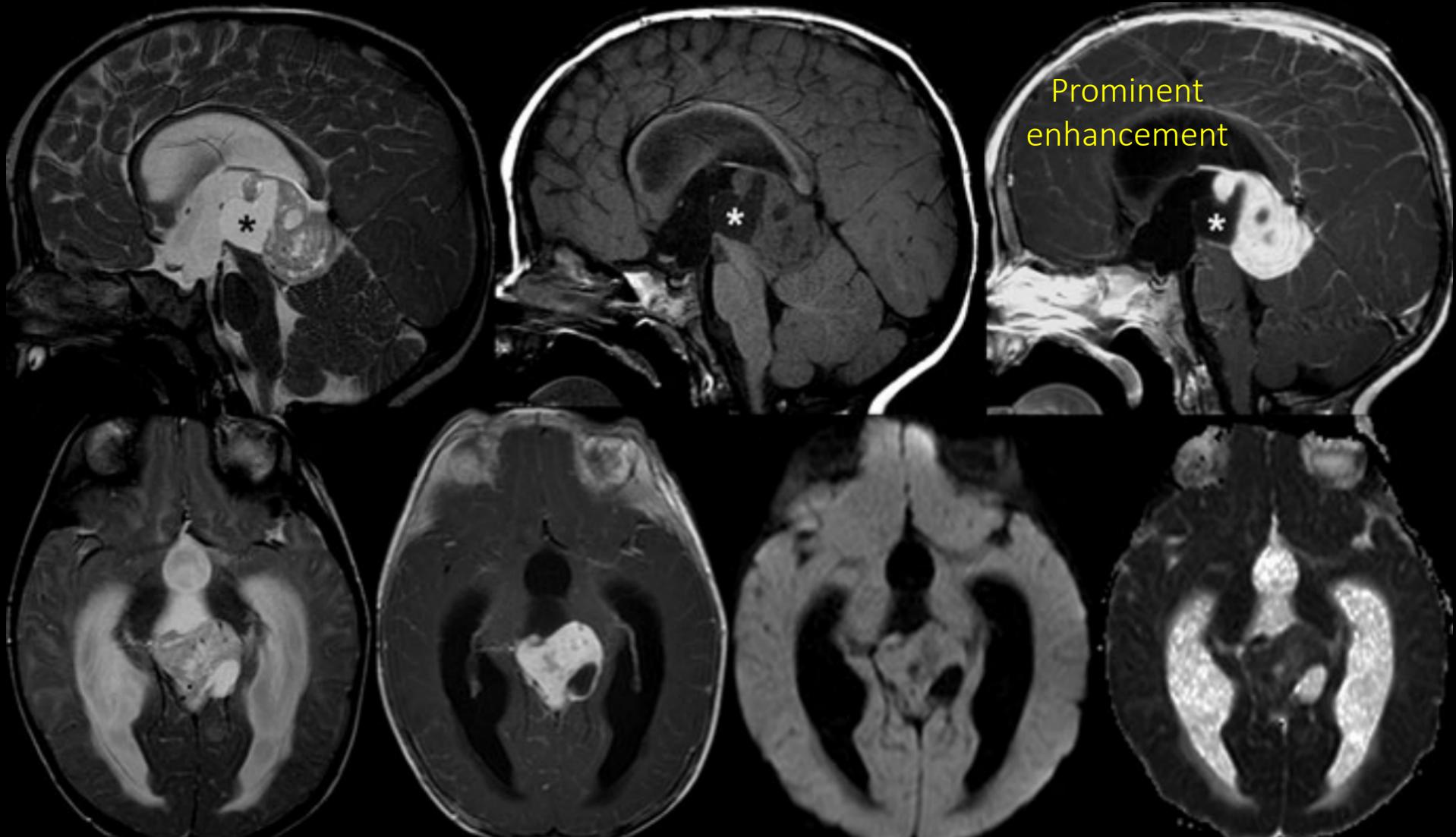
Pineal region



21-month-old girl

Pineal tumours

Pineoblastoma



Pineal tumours

Desmoplastic myxoid tumour of the pineal region, SMARCB1-mutant

Acta Neuropathologica (2020) 139:277–286
<https://doi.org/10.1007/s00401-019-02094-w>

ORIGINAL PAPER

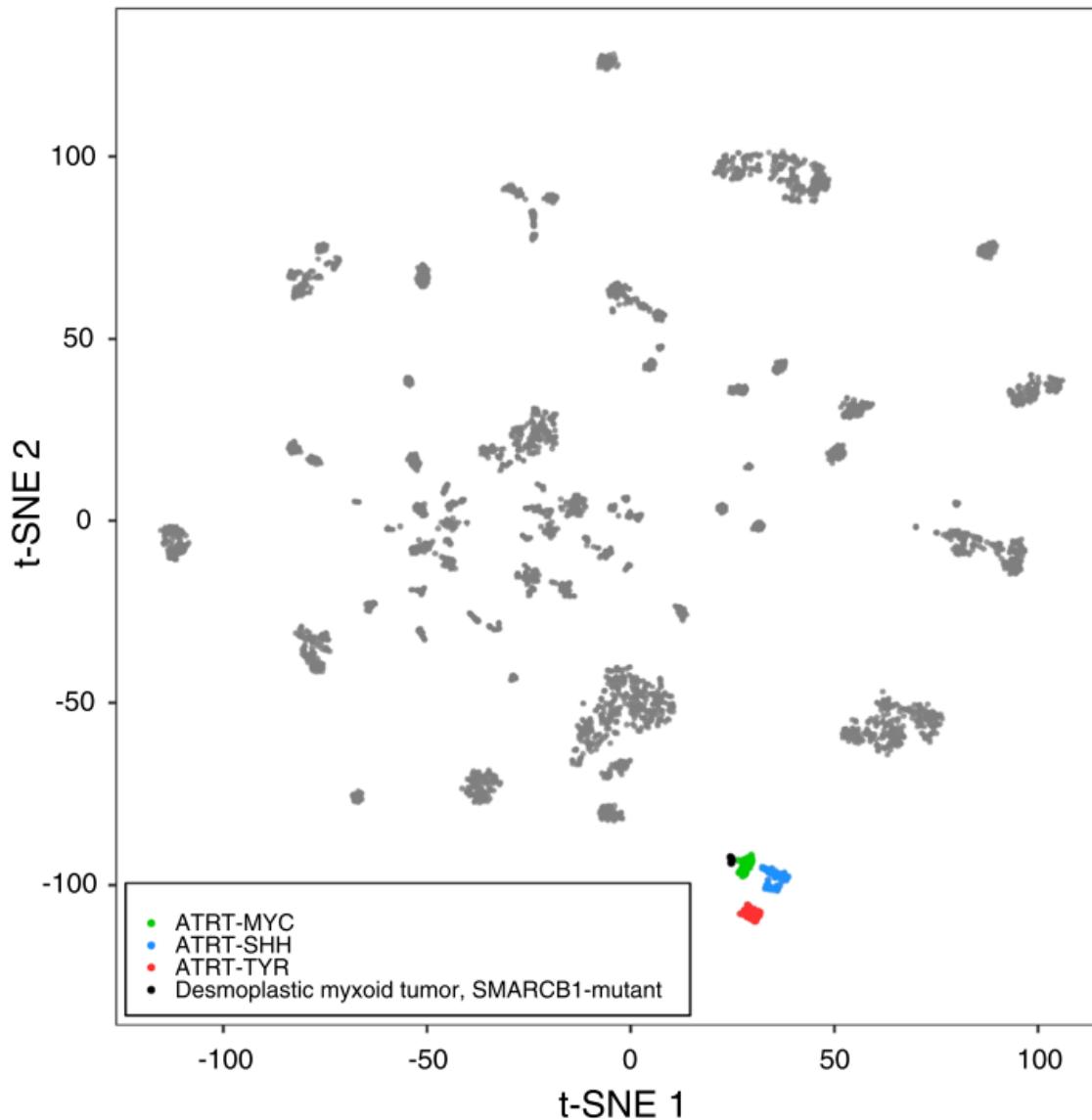


Desmoplastic myxoid tumor, SMARCB1-mutant: clinical, histopathological and molecular characterization of a pineal region tumor encountered in adolescents and adults

Christian Thomas¹ · Annika Wefers^{2,3} · Susanne Bens⁴ · Karolina Nemes⁵ · Abbas Agaimy⁶ · Florian Oyen⁷ · Silke Vogelgesang⁸ · Fausto J. Rodriguez⁹ · Francesca M. Brett¹⁰ · Roger McLendon¹¹ · Istvan Bodi¹² · Fanny Burel-Vandenbos¹³ · Kathy Keyvani¹⁴ · Stefan Tippelt¹⁵ · Frantz R. Poulsen¹⁶ · Eric S. Lipp¹⁷ · Caterina Giannini¹⁸ · Guido Reifenberger^{19,20} · Klaus Kuchelmeister²¹ · Torsten Pietsch²¹ · Uwe Kordes⁷ · Reiner Siebert⁴ · Michael C. Fröhwald⁵ · Pascal D. Johann^{22,23} · Martin Sill^{22,23} · Marcel Kool^{22,23} · Andreas von Deimling^{2,3} · Werner Paulus¹ · Martin Hasselblatt¹

Pineal tumours

Desmoplastic myxoid tumour of the pineal region, *SMARCB1*-mutant



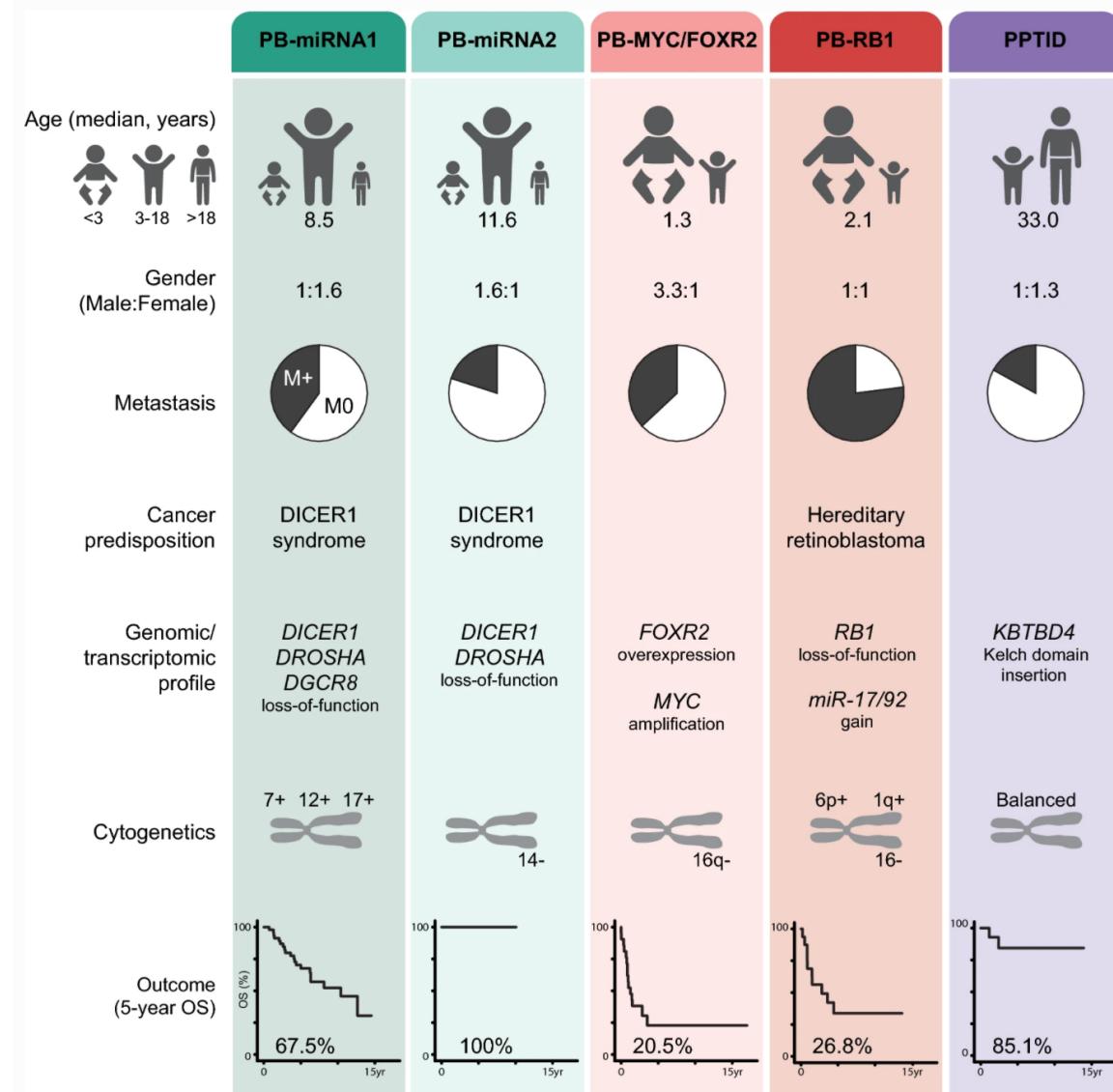
- Distinct tumour of the pineal region
- Epigenetic similarities with **ATRT-MYC**
- Adolescents and adults
- Intermediate prognosis

Pineal tumours

Pineoblastoma

5 new subgroups

PB-MC/FOXR2 and
PB-RB1 have worst
outcome



Summary

1. Incorporation of novel diagnostic techniques (proteomics, methylation, NGS)
 2. Integrated diagnosis
 3. Restructuring
 4. Multiple new tumour types and subtypes
 5. Adult and paediatric-type tumours
 - Are different diseases
 6. Need to redefine imaging appearances and differential diagnoses
-
- It gets more complicated
 - New definitions of imaging characteristics will be needed

Thank you

Great Ormond Street Hospital for Children NHS Foundation Trust

NHS

GOSH London

Paediatric Neuroradiology

Kshitij Mankad, Asthik Biswas,
Olivia Carney, Felice D'Arco,
Sniya Sudhakar

Pathology

Tom Jacques

& Jan