AOSNP-ADAPTR

Adapting Diagnostic Approaches for Practical Taxonomy in Resource-Restrained Regions

The Asian Oceanian Society of Neuropathology

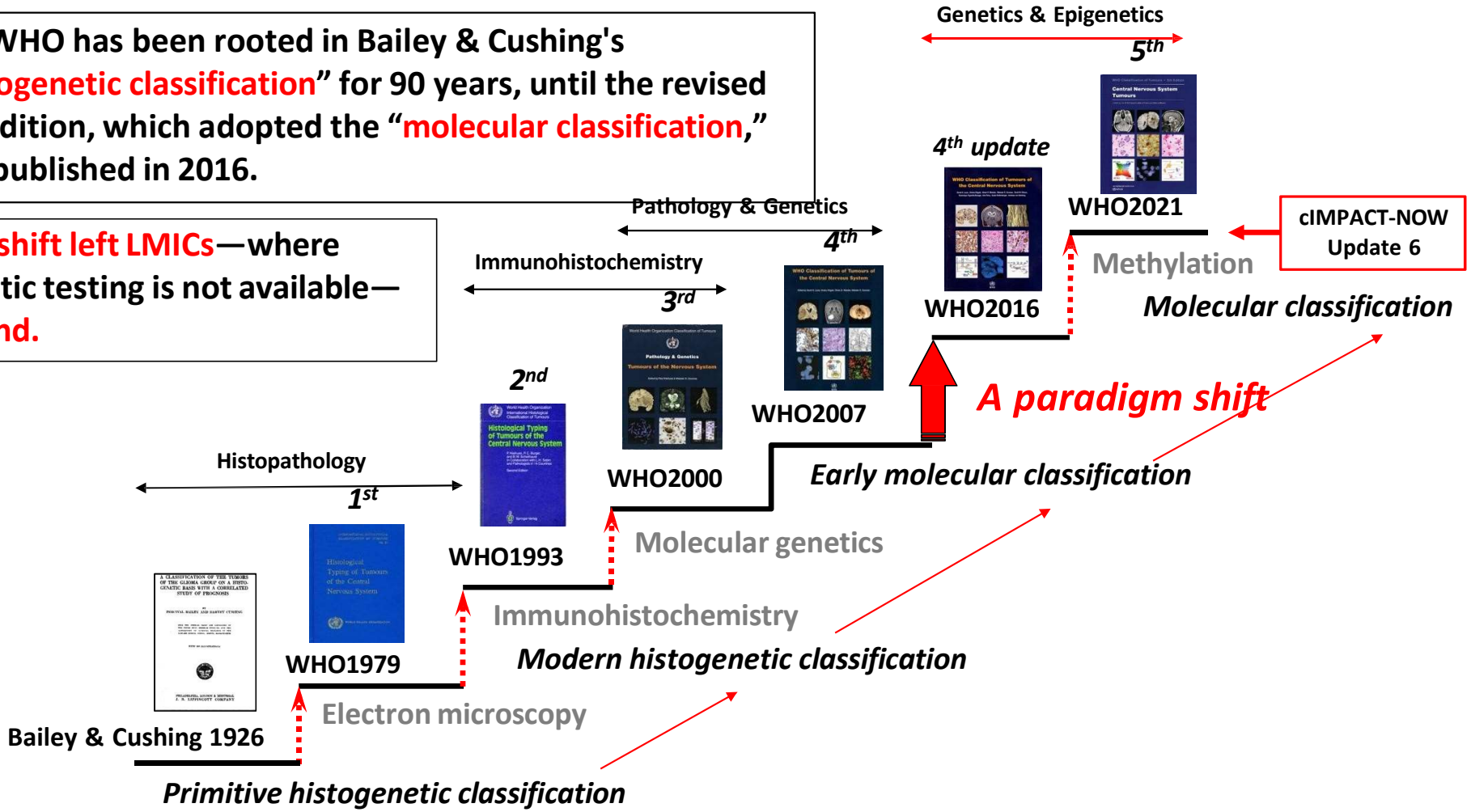
(AOSNP)

Background

WHO classification of tumors of CNS

The WHO has been rooted in Bailey & Cushing's "histogenetic classification" for 90 years, until the revised 4th edition, which adopted the "molecular classification," was published in 2016.

This shift left LMICs—where genetic testing is not available—behind.



Why AOSNP-ADAPTR: the need

More than 10 years:

Joint Neuropathology workshop with the Asian Society for Neuro-Oncology (ASNO) and the Asian Oceanian Society of Neuropathology (AOSNP)

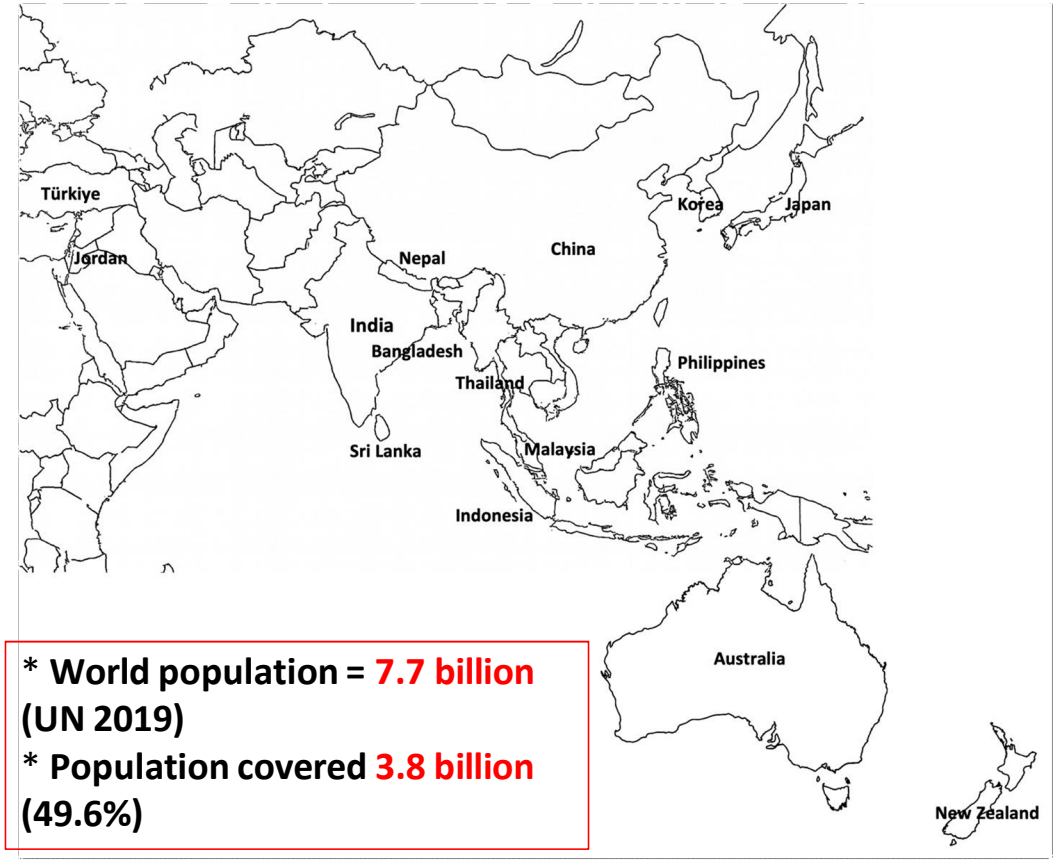
ASNO 2023 Bali

The most frequently asked question from local pathologists: What type of antibodies should we have in our laboratory?

- Implementation of CNS5 diagnosis in lower- and middle-income countries (LMICs) poses critical challenges .

- Mainly attributable to
  - High **costs**
  - Lack of **infrastructure**
  - Shortage of **personnel**
    - skilled technicians and trained neuropathologists

AOSNP members



*** World population = 7.7 billion (UN 2019)**
*** Population covered 3.8 billion (49.6%)**

***IHME /GHDx (The Institute For Health Metrics And Evaluation/Global Health Data); 2019**

Countrie/region	Income Level*	Population (in millions)
SOUTH ASIA		
India	LMIC	1400
Bangladesh	LMIC	159.3
Nepal	LMIC	30.4
Sri Lanka	LMIC	21.9
SOUTHEAST ASIA		
Indonesia	LMIC	259.5
Malaysia	UMIC	31.3
Philippines	LMIC	112.1
Thailand	UMIC	70.1
Singapore	UMIC	5.7
EAST ASIA		
China	UMIC	1400
Korea	HIC	53.4
Taiwan, China	HIC	23.6
Japan	HIC	127.8
WESTERN ASIA		
Turkey	UMIC	81.4
Jordan	UMIC	11.6
AUSTRALASIA		
Australia	HIC	24.6
New Zealand	HIC	4.5
TOTAL		3817.2

***New World Bank country classifications by income level: 2022-2023**

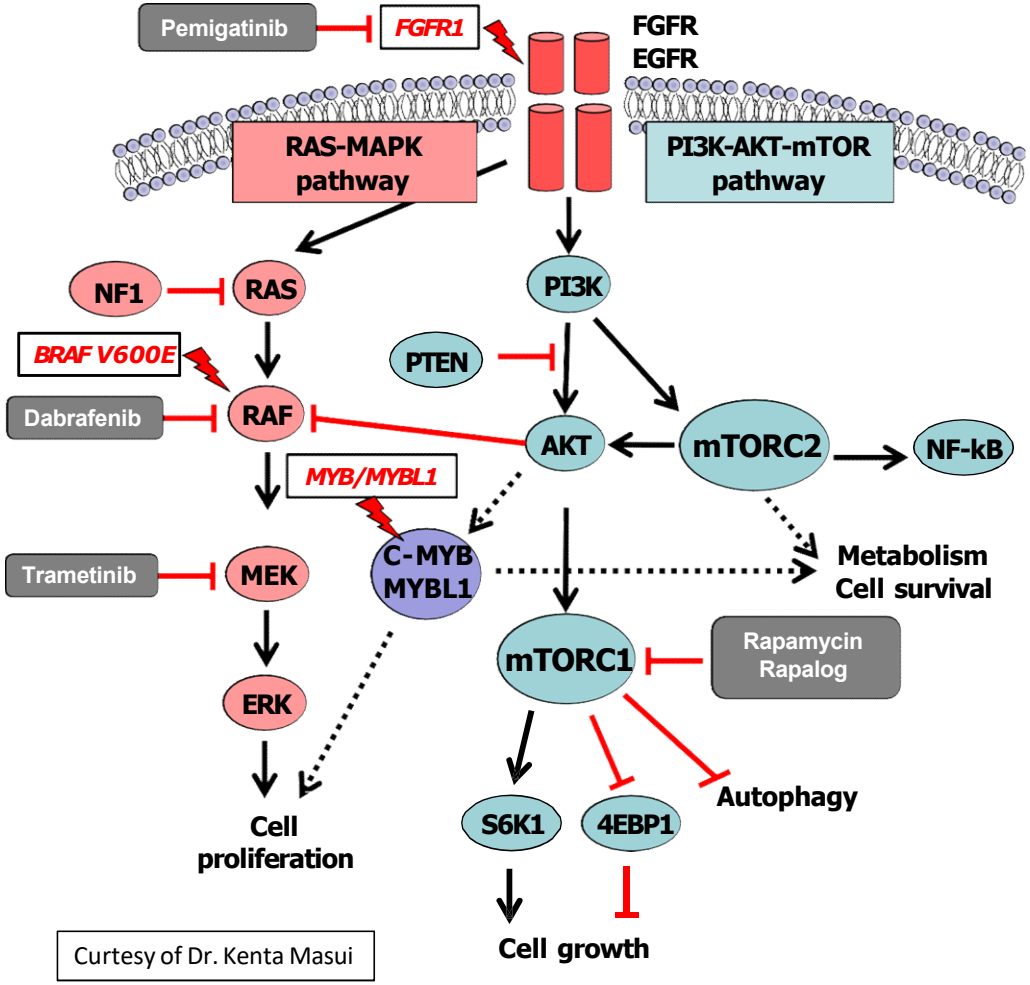
Pediatric malignancies in LMICs

- Each year, approximately 429,000 children and adolescents under 20 years of age develop cancer, and nearly 90% of these cases occur in low- and middle-income countries (LMICs). Notably, about 80% of children with central nervous system (CNS) tumors also live in LMICs (Lam CG, *Science*, 2019).

- The cure rate for childhood cancers in LMICs remains below 30%, in stark contrast to >80% in high-income countries (HICs) (Seah T, *Pediatric Blood & Cancer*, 2019).

- Children with CNS tumors are presumed to have a similarly poor—if not worse—prognosis in LMICs; however, the true situation remains unclear due to the absence of robust national cancer registries in many of these regions.

Genetic alterations in low-grade gliomas



Curtesy of Dr. Kenta Masui

- Genetic alterations in LGGs involve MAPK pathway
- About 2/3 of the genetic alterations in LGGs are *BRAF* p.V600E mutation
- Mutation-specific antibody, VE1, and
- BRAF/MEK inhibitors are available

Small-molecule inhibitors for gliomas

- BRAF MEK
- FGFR1
- ALK/ROS1/NTRK
- EGFR MET
- CDK 4/6
- mTOR

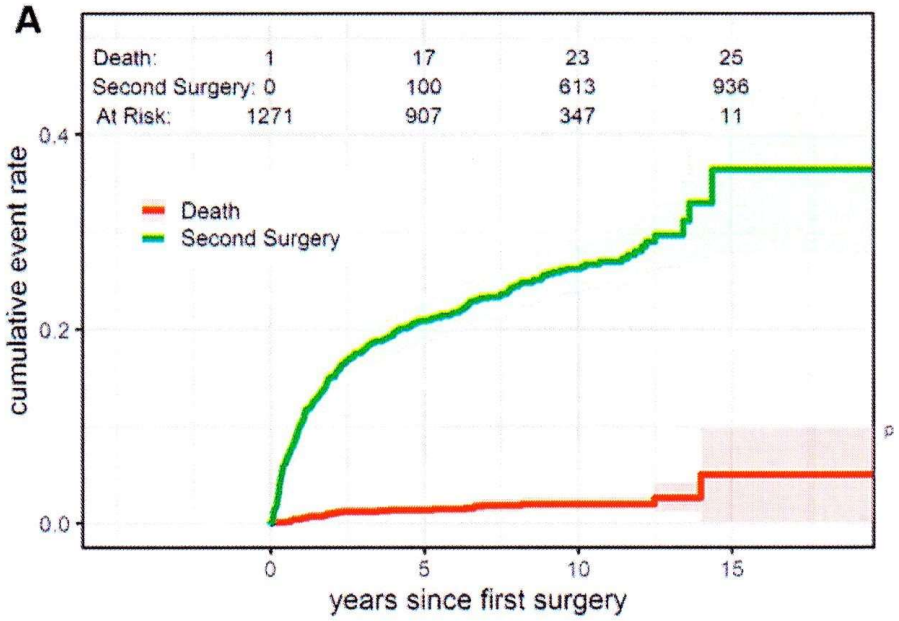
The patients in LMICs have limited access to genetic testing and they do not have a chance to get the target therapies based on those tests.

JNS PEDIATRICS CLINICAL ARTICLE

Long-term follow-up of surgical intervention pattern in pediatric low-grade gliomas: report from the German SIOP-LGG 2004 cohort

J Neurosurg Pediatr July 22, 2022

CONCLUSIONS: Neurosurgery is a key element of pediatric LGG treatment. In almost 50% of the patients, however, at least some tumor burden will remain during long-term follow-up. This study found that most of these patients reached a stable disease status without further surgeries.



Among 1225 patients<18 years old, 613 reached complete remission.

FIG. 4. Sankey chart visualizing the resection grade at the first and subsequent surgeries in relation to the radiological outcome at last imaging follow-up for 1225 patients with completely documented surgical records and radiological outcome. Figure is available in color online only.

- **Inhibitors are not available**
- **Radiotherapy is not applicable**
- **Surgery remains the first and only option**

Creation of ADAPTR

AOSNP-ADAPTR aim

Bridging the gap between WHO CNS5 and resource-restrained settings to help local pathologists approach it with simplified tools without altering the WHO classification.

We are not creating a parallel system.

We are providing a step-by-step guide for each resource level to help pathologists achieve the WHO CNS5 standard.

Our recommendations, which utilize surrogate markers, are evidence-based.

ADAPTR Committees

AOSNP-ADAPTR: The Asian Oceanian Society of Neuropathology (AOSNP) Committee for Adapting Diagnostic Approaches for Practical Taxonomy in Resource-Restrained Regions (ADAPTR)

Steering Committee

	Chair	Co-chair	Steering Member		
	Takashi Komori	Chitra Sarkar	Maysa Al-Hussaini	Michael Buckland	Ho-Keung Ng
			Sung-Hye Park	Vani Santosh	Tarik Tihan

Advisory Board

International Neuropathology Advisor	David N. Louis	Pieter Wesseling	Catriona McLean
Neuro-oncology Advisor	Rakesh Jalali	Zarnie Lwin	
Neurosurgery Advisor	Yonehiro Kanemura		
Neuroradiology Advisor	Sona A. Pungavkar		
Molecular Oncology Advisor	Koichi Ichimura		

Working Committee (WC)

	Chair	Co-chair	Steering Member	Working Member			
WC1: Adult type diffuse gliomas	Vani Santosh	Ho-Keung Ng	Takashi Komori	Shilpa Rao	Junji Shibahara		
WC2: Pediatric-type diffuse low-grade gliomas	Vani Santosh	Sung-Hye Park	Tarik Tihan	Se Hoon Kim	Yue-Shan Piao	Shilpa Rao	
WC3: Circumscribed astrocytic gliomas	Tarik Tihan	Buckland M	Takashi Komori	Sonika Dahiya	Se Hoon Kim	Yue-Shan Piao	
WC4: Pediatric-type diffuse high-grade gliomas	Sung-Hye Park	Maysa Al-Hussaini	Ho-Keung Ng	Geeta Chacko	Sonika Dahiya	Shinya Tanaka	
WC4: Ependymal tumors	Michael Buckland	Ho-Keung Ng	Vani Santosh	Geeta Chacko	Kenta Masui	Junji Shibahara	Laveniya Satgunaseelan
WC5: Embryonal tumors	Maysa Al-Hussaini	Chitra Sarkar	Sung-Hye Park	Yue-Shan Piao	Vaishali Suri	Shilpa Rao	

An official support from the International Society of Neuropathology (ISN).

ICN 2023

« Back

Scientific session - Neurooncology

Session 23 - Neurooncology

AOSNP Guidelines for Adapting Diagnostic Approaches for Practical Taxonomy in Resource-Limited Regions (AOSNP-ADAPTR)

The 20th International Congress of Neuropathology
（ICN2023 Berlin）
2023.09.13-16

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DOI: 10.1111/bpa.13201

COMMENTARY

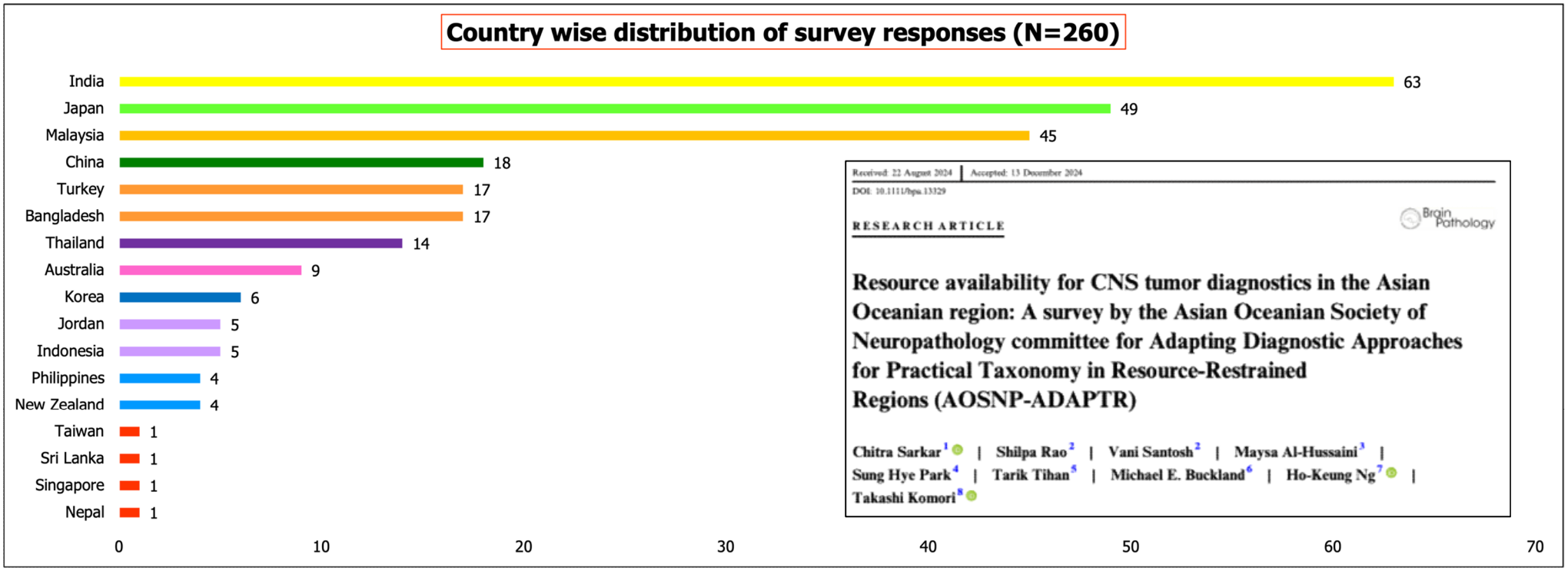
Brain Pathology

Announcing the Asian Oceanian Society of Neuropathology guidelines for Adapting Diagnostic Approaches for Practical Taxonomy in Resource-Restrained Regions (AOSNP-ADAPTR)

M. E. Buckland[1] | C. Sarkar[2] | V. Santosh[3] | M. Al-Hussaini[4] | S. H. Park[5] | T. Tihan[6] | H. K. Ng[7] | T. Komori[8]

AOSNP-ADAPTR Survey results

- Devised a Google survey form to give us an idea about resource availability in different regions/countries in the Asian Oceanian region.
- Circulated to Regional Neuropathology/Pathology Societies
- Responses obtained from Neuropathologists/General Pathologists practicing Neuropathology



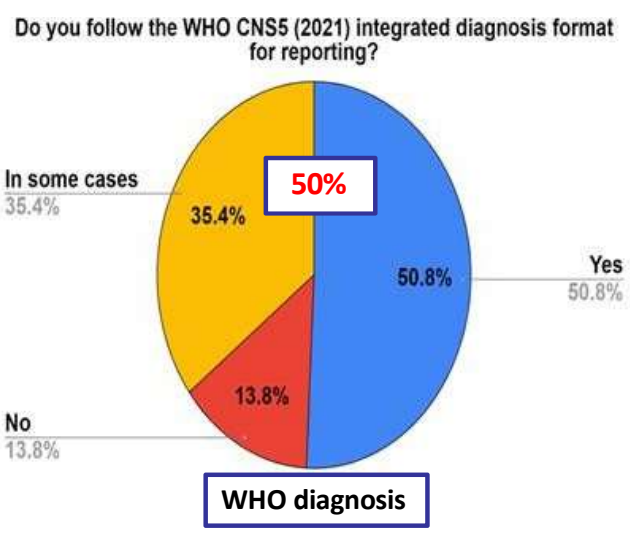
Received: 22 August 2024 | Accepted: 13 December 2024
DOI: 10.1111/bpa.13329

RESEARCH ARTICLE

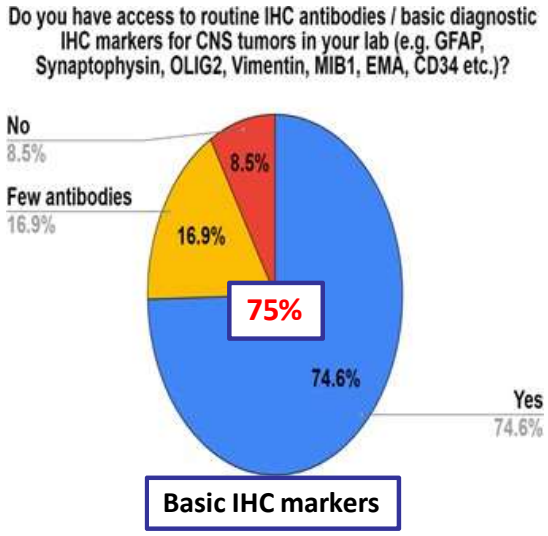
Brain Pathology

Resource availability for CNS tumor diagnostics in the Asian Oceanian region: A survey by the Asian Oceanian Society of Neuropathology committee for Adapting Diagnostic Approaches for Practical Taxonomy in Resource-Restrained Regions (AOSNP-ADAPTR)

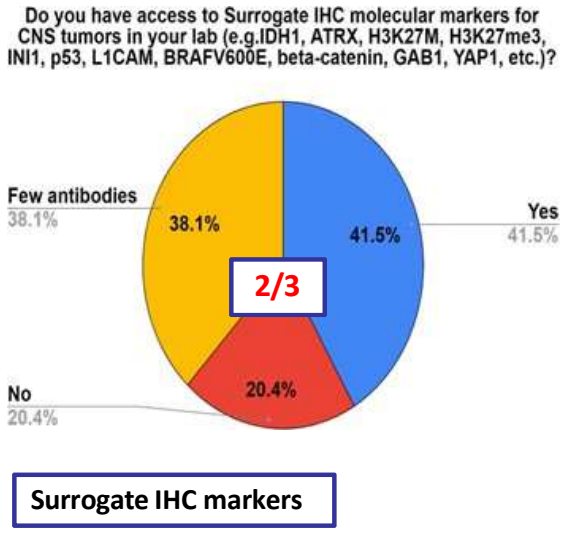
Chitra Sarkar[1] | Shilpa Rao[2] | Vani Santosh[2] | Maysa Al-Hussaini[3] | Sung Hye Park[4] | Tarik Tihan[5] | Michael E. Buckland[6] | Ho-Keung Ng[7] | Takashi Komori[8]



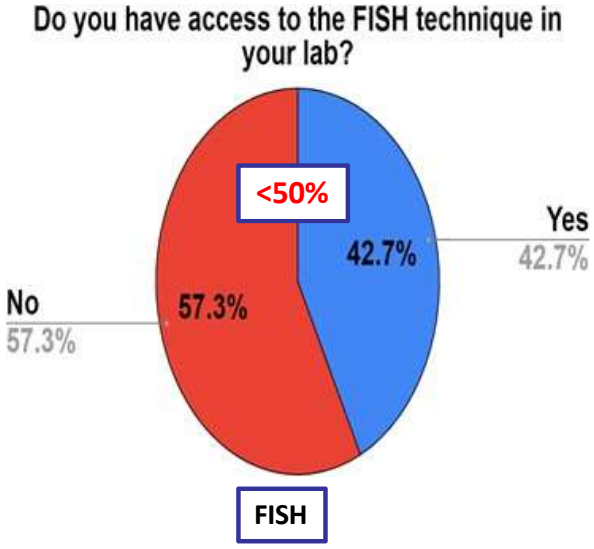
WHO diagnosis



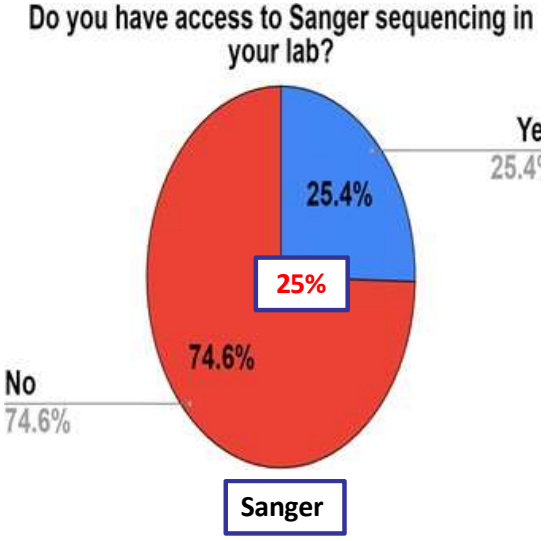
Basic IHC markers



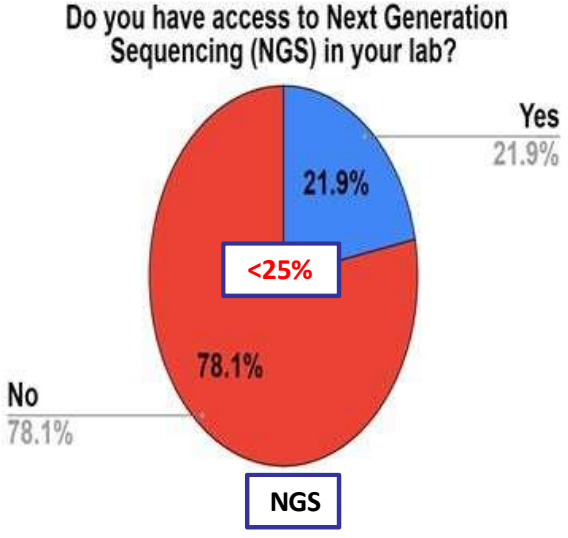
Surrogate IHC markers



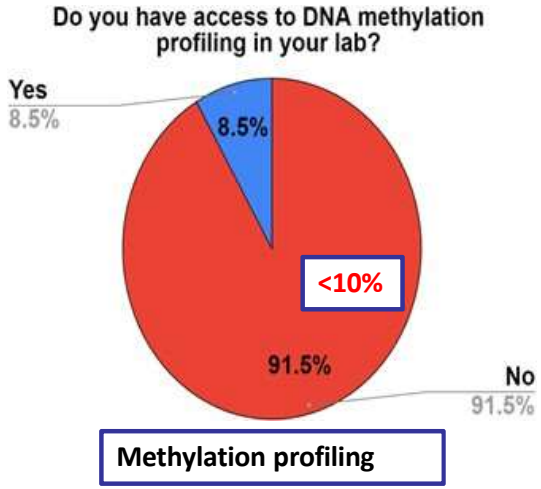
FISH



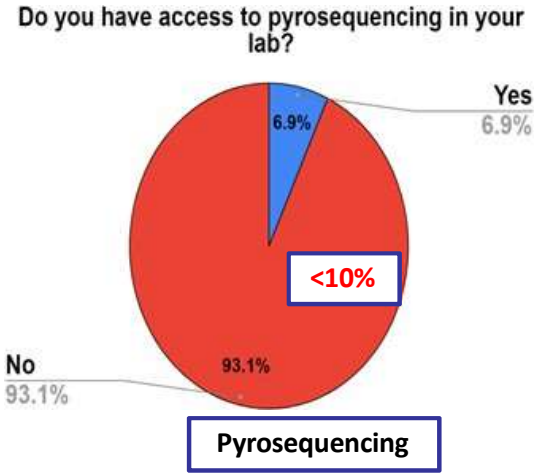
Sanger



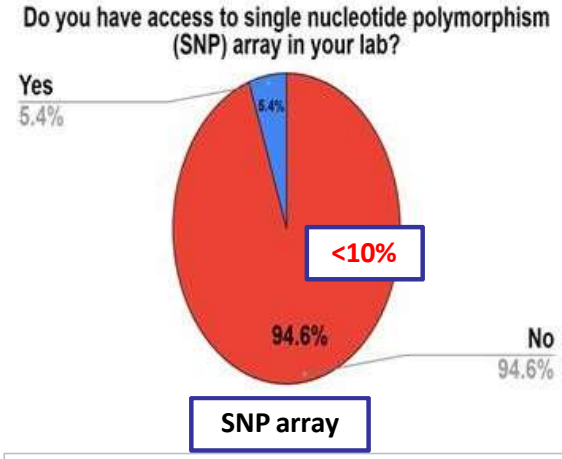
NGS



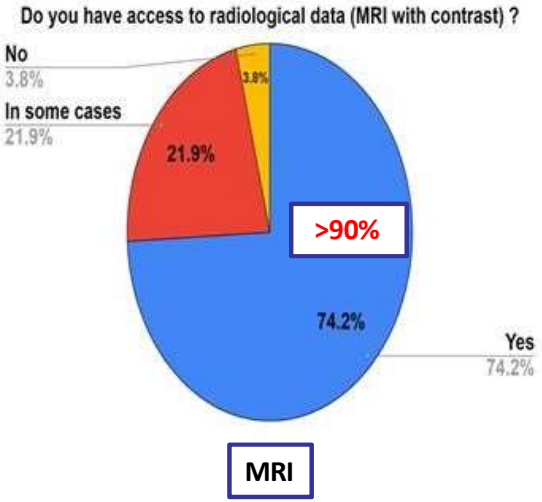
Methylation profiling



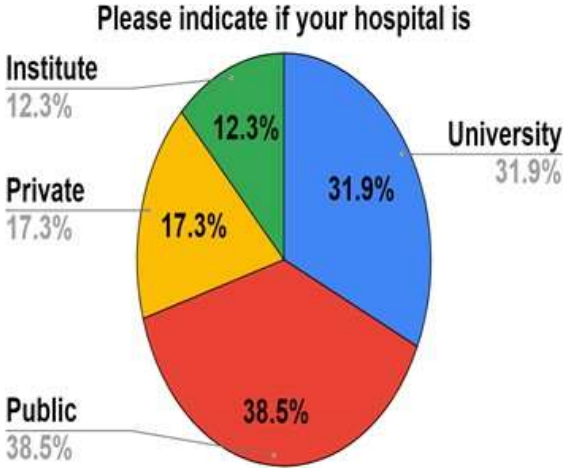
Pyrosequencing

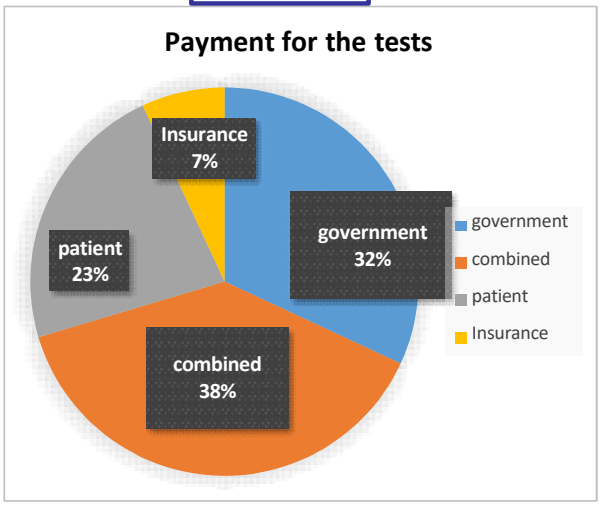


SNP array



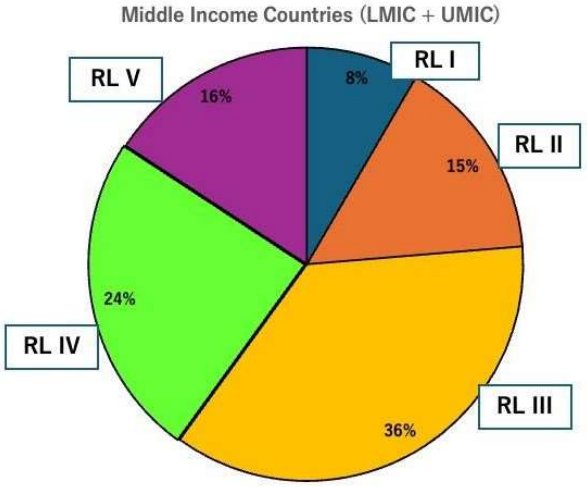
MRI



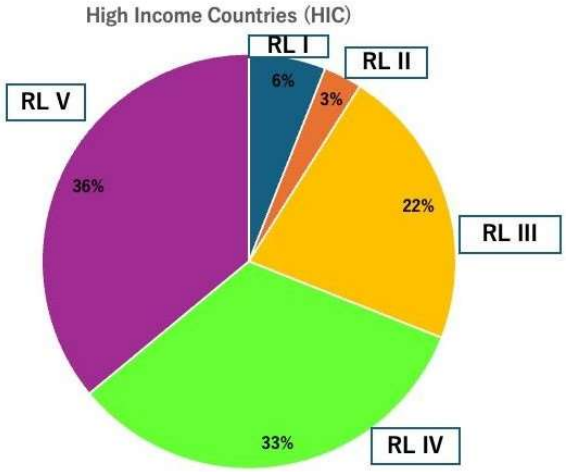


Resource Levels

RL I: Conventional histology
RL II: Basic immunohistochemistry (IHC)
: RL: III: Advanced molecular IHC (primary target)
RL IV: Basic molecular testing
RL V: Advanced molecular diagnostics



60% of Middle-Income Countries belong to RL I, II, and III.



70% of High-Income Countries belong to RL IV and V

ADAPTR's principle: three pillars

1. A comprehensive list of optimal immunohistochemical molecular markers tailored to each resource level.

2. A histology-oriented integrated diagnosis format across various resource levels.

3. Diagnostic flowcharts suitable for resource-limited regions.

Immunohistochemical markers to each level

A hierarchy of resource levels (RLs) has been defined based on the diverse range of local resource availability: adult-type diffuse gliomas

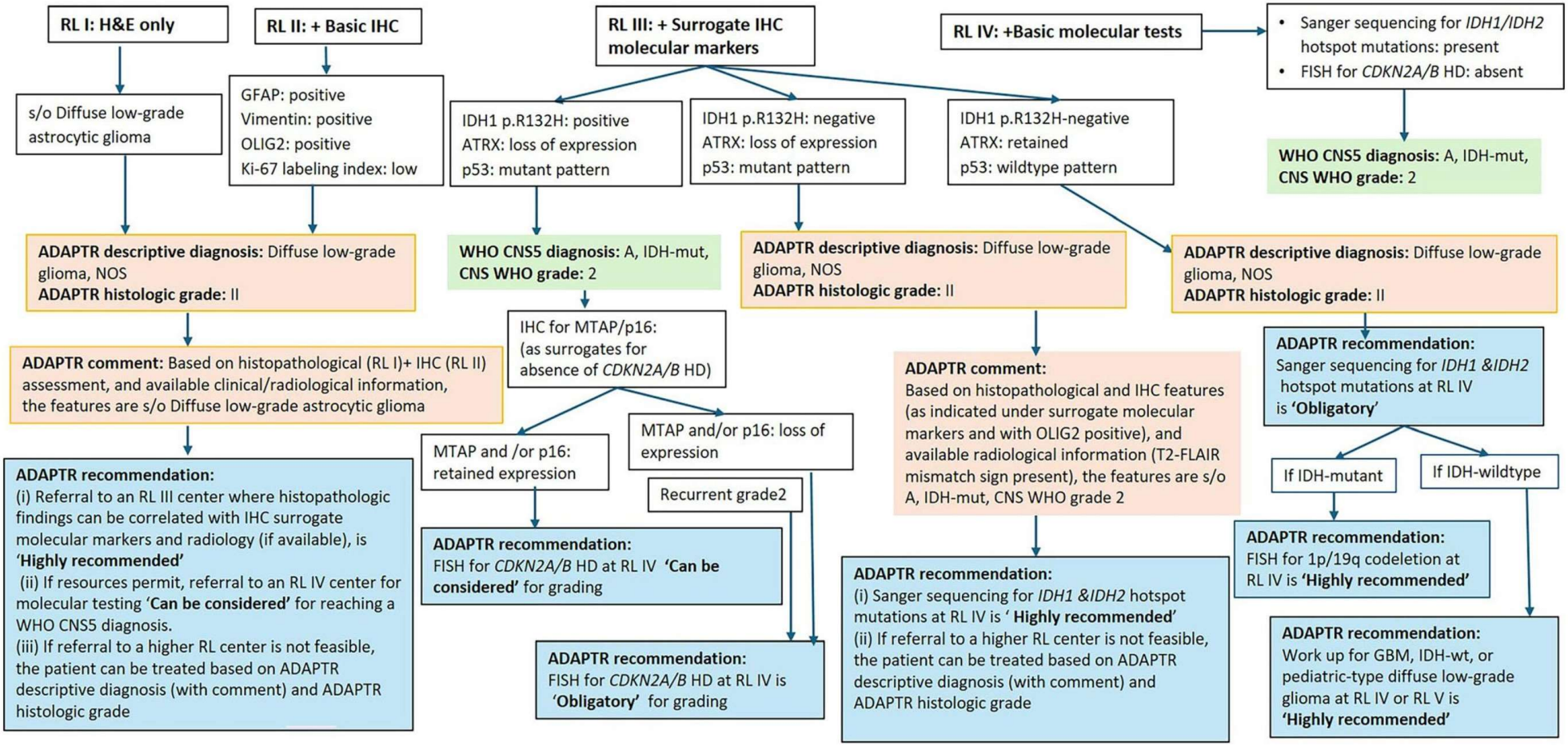
Resource Level (RL)	Available Resources
Resource Level I (RL-I)	Conventional histology techniques and some special stains (e.g., reticulin, PAS)
Resource Level II (RL-II)	Standard / basic IHC markers available such as GFAP, synaptophysin, vimentin, EMA, OLIG2, CD34, Ki-67/MIB-1, etc.
Resource Level III (RL-III)	+Advanced IHC markers available (specific or surrogate markers for key molecular events) e.g. IDH1 p.R132H, ATRX, p53, BRAF VE1, EZHIP, H3K27me3, H3K27M, L1CAM, NFkB, YAP1, INI-1, BRG1, LIN28A, etc.
Resource Level IV (RL-IV)	+ Basic molecular testing methods such as FISH and Sanger Sequencing e.g. 1p/ 19q, EGFR, MYC, MYCN, PTEN, CDKN2A/2B, etc. These methods may allow the appropriate classification of many CNS tumors to WHO CNS5 standards
Resource Level V (RL-V)	+ Basic molecular testing methods such as FISH and Sanger Sequencing e.g. 1p/ 19q, EGFR, MYC, MYCN, PTEN, CDKN2A/2B, etc. These methods may allow the appropriate classification of many CNS tumors to WHO CNS5 standards

Histopathology-oriented Integrated diagnosis format

Age of the patient	
Tumor location	
Clinical features	
Imaging features	
Histopathological features	
IHC information	
Molecular test information	
Diagnosis	WHO CNS5 diagnosis **OR** ADAPTR descriptive diagnosis with comment, as applicable
Grade	CNS WHO grade **OR** ADAPTR histologic grade, as applicable
ADAPTR recommendations	Highly recommended: Obligatory: Can be considered:

Santosh V. Brain Pathology. 2025;e70046. https://doi.org/10.1111/bpa.70046
Supple Table 1

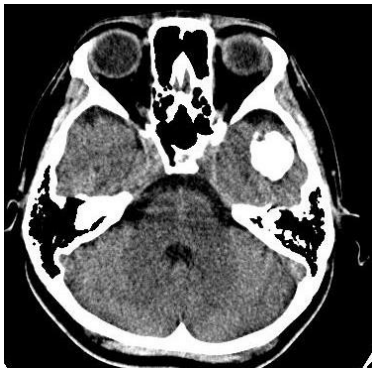
ADAPTR diagnostic flow chart at different resource levels for Astrocytoma, IDH-mutant, CNS WHO grade 2 (Cerebral hemispheric, typical histology)

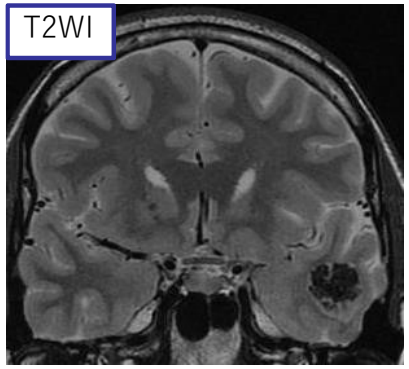


Santosh V. Brain Pathology. 2025;e70046. https://doi.org/10.1111/bpa.70046

Practical diagnostic approach

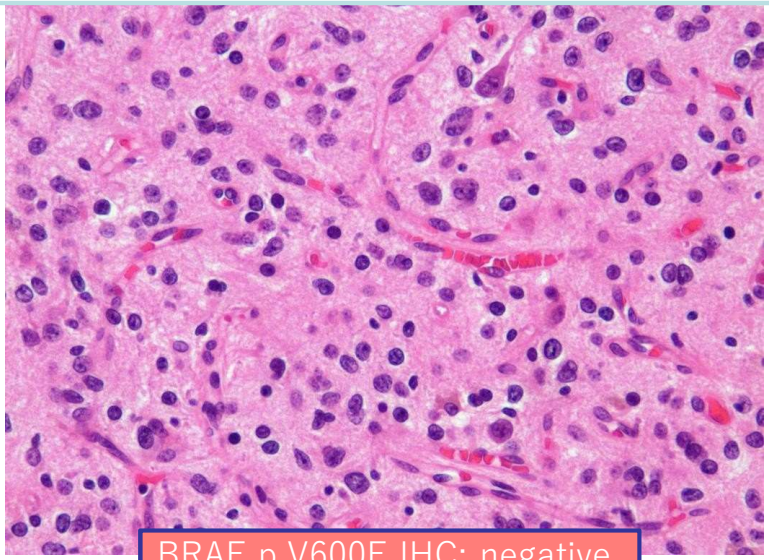
Pediatric-type low-grade diffuse astrocytomas

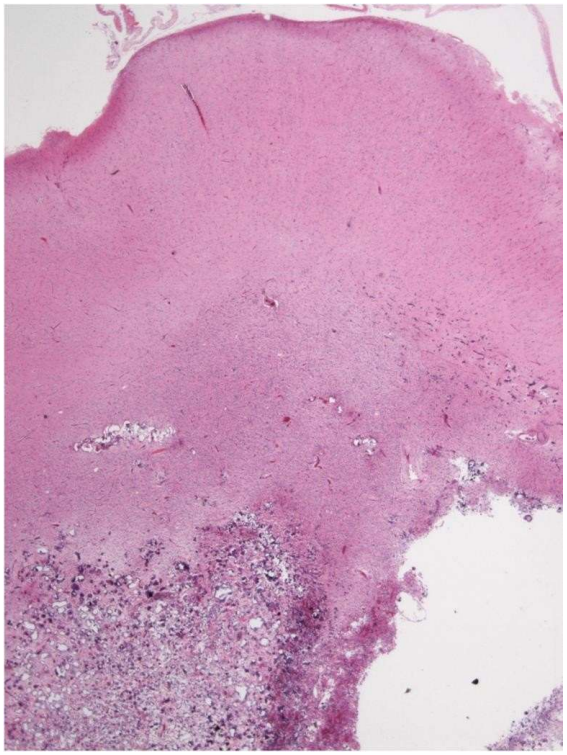




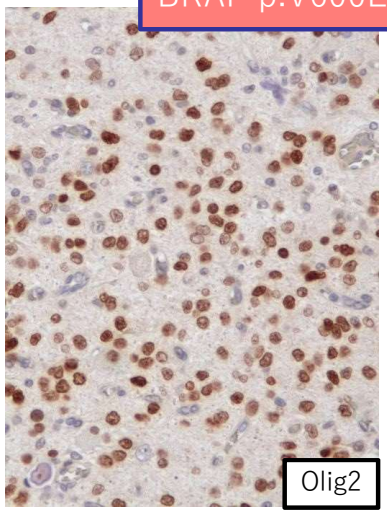
A 16-year-old male with complex partial seizures: lt. temporal lobe tumor

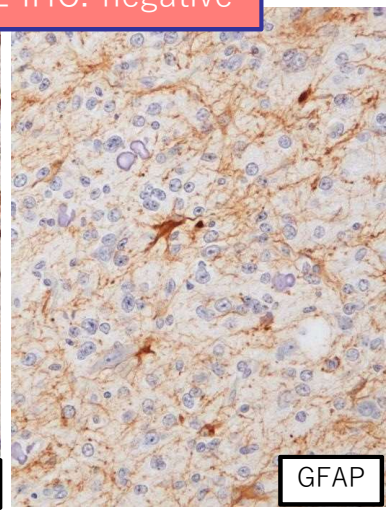
polymorphous low-grade neuroepithelial tumor of the young (PLNTY)





BRAF p.V600E IHC: negative





Histology-oriented integrated diagnosis, Resource Level III

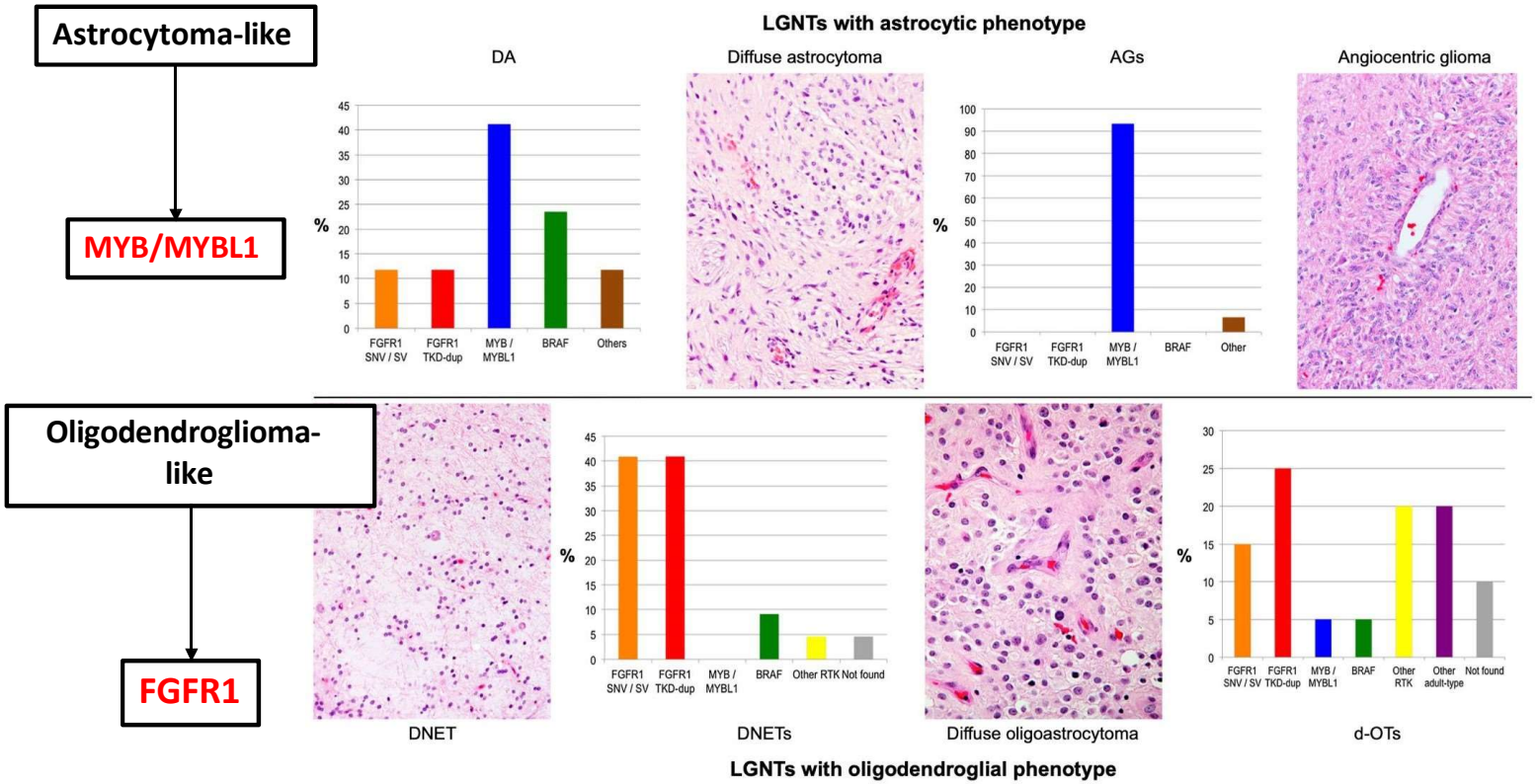
Age & gender of the patient	16 years, male
Tumor location	Left temporal lobe
Imaging features	A well-demarcated mass without contrast enhancement; hypointense on T1 and T2 imaging. Solid calcification on CT.
Histologic grade	I
Histopathological diagnosis	**Oligodendroglioma, s/o PLNTY**
Basic diagnostic markers	Extensive OLIG2 and CD34 immunoreactivities. Ki-67 labeling index < 3%, IDH1 p.R132H negative, ATRX retained, p53 negative.
Surrogate molecular markers	BRAF p.V600E negative
Molecular information	Not available
WHO CNS 5 diagnosis	**Pediatric-type diffuse low-grade glioma, NOS**
CNS WHO grade	Not applicable
AOSNP-ADAPTR conclusion: s/o polymorphous low-grade neuroepithelial tumor of the young (PLNTY), histological grade I, probably with *FGFR2* or *FGFR3* fusions or other MAPK pathway alterations, cerebral hemisphere	
AOSNP-ADAPTR recommendations for resource-restricted settings: (i) To confirm the WHO CNS5 diagnosis, molecular workup should be carried out, particularly for *FGFR2* or *FGFR3* fusions, which is mutually exclusive for *BRAF* p.V600E mutation. (ii) The patient could be treated as a grade I tumor in a resource-restricted setting.	**Needs frozen material!**

Acta Neuropathol (2016) 131:833–845
DOI 10.1007/s00401-016-1539-z

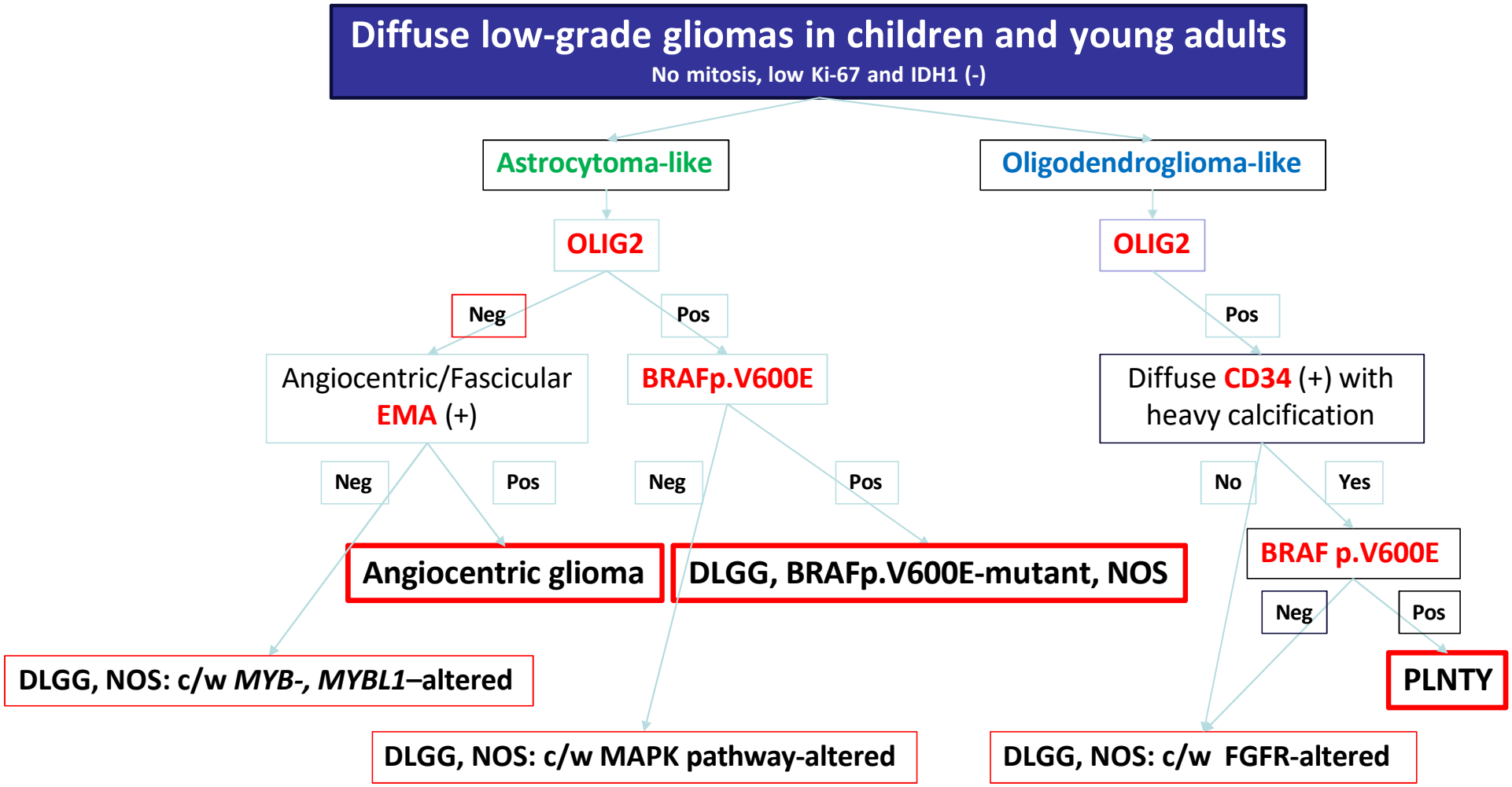
ORIGINAL PAPER

Genetic alterations in uncommon low-grade neuroepithelial tumors: *BRAF*, *FGFR1*, and *MYB* mutations occur at high frequency and align with morphology

Ibrahim Qaddoumi[1] · Wilda Orisme[2] · Ji Wen[2] · Teresa Santiago[2] · Kirti Gupta[2] · James D. Dalton[2] ·



Histology-oriented flow chart at RL III for PLGGs



Conclusions

Summary

1. We aim to develop a feasible testing protocol tailored to each resource level that remains reliable and aligned with WHO CNS5.
2. By structuring our recommendations according to available resources, pathologists can achieve appropriate and consistent diagnoses using the diagnostic methods accessible in their setting.
3. The approach relies mainly on IHC, with FISH or Sanger sequencing required only in select situations that impact prognosis or treatment.
4. We recommend that frozen tissue always be stored, as it truly serves as a "gift for the future."
5. Ultimately, ADAPTR provides practical guidance to help general pathologists worldwide navigate WHO NOS diagnoses in their daily brain tumor practice.