BRAIN CANCER

Brain Cancer: Documentation

I. Glioma (Most Common Brain Tumor)

Gliomas originate from the neuroglial cells (astrocytes, oligodendrocytes, ependymal cells) and range from low-grade (Grade I/II) to highly aggressive high-grade forms (Grade III/IV, notably Glioblastoma, GBM).

Category	Key Technical Data	Relevance for AI (Input/Output)
Histological Classification (WHO)	Graded I to IV (e.g., Grade IV: Glioblastoma). Based on cellularity, nuclear atypia, mitoses, microvascular proliferation, and necrosis.	**Input:** WHO Grade (Determines prognosis and primary treatment modality).
Location & Imaging	Typically **supratentorial** in adults, involving cerebral hemispheres. Imaging (MRI): Highly variable, often **ring-enhancing** lesions (GBM), or poorly defined, non-enhancing areas (low-grade).	**Input/Output:** MRI features (enhancement pattern, edema, mass effect) for tumor localization/triage.
Molecular Markers (Crucial for RAG)	**IDH Mutation Status: *IDH*-mutant** (generally better prognosis, low-grade high-grade progression). ***IDH*-wildtype** (common in primary GBM, worse prognosis).	**RAG Output:** IDH status determines prognostic group and is crucial for WHO 2021 classification.
	1p/19q Codeletion: Highly predictive of responsiveness to combined chemoradiation (standard for Oligodendroglioma).	**Input:** Cytogenetics/FISH result. **RAG Output:** Drug sensitivity recommendation (e.g., PCV chemotherapy).
	MGMT Promoter Methylation: Predictive marker for response to **Temozolomide (TMZ)** chemotherapy. Methylated status indicates better response.	**Input:** Methylation status. **RAG Output:** Treatment justification (TMZ initiation).
Treatment Modality	Surgery (Maximal Safe Resection), Radiotherapy, Chemotherapy (TMZ).	**Output:** Standard of care based on WHO Grade and Molecular Profile (e.g., Stupp Protocol for GBM).
ICD-O Code	9440/3 (Glioblastoma, NOS); 9400/3 (Astrocytoma, NOS).	**Output:** Coding and reporting.

II. Meningioma (Tumors Affecting Brain Membranes)

Meningiomas arise from the arachnoid cells of the meninges and are typically extra-axial (outside the brain parenchyma). They are most often benign.

Category	Key Technical Data	Relevance for AI (Input/Output)
Histological Classification (WHO)	Graded I to III: **Grade I** (Benign, most common, e.g., meningothelial, fibrous, transitional subtypes); **Grade II**(Atypical); **Grade III** (Anaplastic/Malignant).	**Input:** WHO Grade (Key determinant of recurrence risk).
Location & Imaging	Most common locations: **Convexity, falx, sphenoid wing**. Imaging (MRI/CT): **Dural tail sign** (thickening of the adjacent dura), homogeneous enhancement, broad-based dural attachment.	**Input/Output:** Imaging features (Dural involvement, Calcification) for pre-operative assessment.
Molecular Markers	**NF2 Gene Mutation:** Common in spinal and multiple meningiomas. **SMO/AKT1/PIK3CA Mutations:** Found in some sporadic tumors.	**RAG Output:** Role in pathogenesis and potential targeted therapy trials (limited standard therapy).
Prognostic Factors	**Simpson Grading Scale (I-V):** Based on the extent of surgical resection (Grade I = Gross Total Resection, Grade V = Biopsy only). Simpson Grade is the strongest predictor of recurrence.	**Input:** Simpson Grade/Extent of Resection (EOR). **RAG Output:**Follow-up frequency recommendation.
Treatment Modality	**Surgery** (primary cure), **Observation** (for small, asymptomatic Grade I tumors), **Radiosurgery** (for residual or recurrent tumors).	**Output:** Treatment strategy guided by size, symptoms, and Simpson Grade.
ICD-O Code	9530/0 (Meningioma, Benign); 9530/3 (Meningioma, Malignant).	**Output:** Coding and reporting.

III. Pituitary Tumor (Tumors Affecting the Pituitary Gland)

Pituitary tumors (adenomas) are benign slow-growing tumors that arise from the anterior pituitary gland cells. They cause symptoms via hormonal excess (Functional) or mass effect (Non-functional).

Category	Key Technical Data	Relevance for AI (Input/Output)
Classification (Functional)	Classified by hormone produced: **Prolactinoma** (most common), **GH-producing** (Acromegaly), **ACTH-producing** (Cushing's disease), **TSH-producing**. **Non-functional** (Null cell adenoma).	**Input:** Hormone levels (Prolactin, IGF-1, Cortisol) for functional diagnosis.
Size Classification	**Microadenoma** (mm); **Macroadenoma** (mm).	**Input:** Size (Determines management

Category	Key Technical Data	Relevance for AI (Input/Output)
		approach—medication vs. surgery).
Location & Imaging	Sited in the **sella turcica**. Macroadenomas can extend into the **suprasellar cistern** and compress the **optic chiasm** (causing bitemporal hemianopsia).	**Input/Output:** Visual field deficits, cavernous sinus invasion.
Treatment Modality (Functional)	**Prolactinoma:** Primary treatment is **medical** (Dopamine Agonists, e.g., Cabergoline). **GH/ACTH-producing:** Surgery (Transsphenoidal) is often the first line.	**RAG Output:** Treatment selection based on hormone type.
Treatment Modality (Non-functional)	**Surgery** (Transsphenoidal) for symptomatic macroadenomas (optic chiasm compression). Observation for asymptomatic microadenomas.	**Output:** Surgery for decompression.
Molecular Markers	**GNAQ, GNAS Mutations:** Involved in GH-producing tumors (Acromegaly). **AIP Mutations:** Associated with familial or early-onset pituitary tumors.	**RAG Output:** Identification of hereditary risk and resistance to medical therapy.
ICD-O Code	8272/0 (Pituitary Adenoma, NOS).	**Output:** Coding and reporting.

1. Core Academic References (Must-Have for RAG)

These documents are the gold-standard foundation for clinical and pathological brain tumor knowledge:

1.1. WHO Classification of Tumours of the Central Nervous System (5th Edition)

Most authoritative source worldwide.
Covers:

- Full classification of gliomas, meningiomas, and pituitary tumors
- Diagnostic molecular markers (IDH, 1p/19q, ATRX, MGMT, TERT, NF2, MEN1)
- Histopathology, grading, and tumor biology
- Imaging characteristics
- Typical clinical behavior and prognosis

Use it as a **primary source for pathology & diagnostic criteria**.

1.2. NCCN Clinical Practice Guidelines – Central Nervous System Cancers

Includes:

- Standard diagnostic workflow
- Imaging (MRI sequences, contrast protocols)
- Surgical indications
- Radiotherapy and chemotherapy regimens
- Follow-up and recurrence management

Essential for real-world clinical management.

1.3. Harrison's Principles of Internal Medicine (Brain Tumors Chapter)

Provides:

- High-level medical overview
- Common symptoms (seizures, deficits, headaches)
- Approach to diagnosis
- Systemic implications
  Good for **clinical reasoning and generalist-level understanding**.

1.4. Robbins & Cotran Pathologic Basis of Disease

Provides:

- Pathogenesis
- Microscopic architecture of gliomas, meningiomas, pituitary adenomas
- Molecular pathways of tumor development
- Invasion patterns and grading
  Use for **pathology-focused RAG chunks**.

1.5. UpToDate (Neurosurgery & Oncology Topics)

Provides:

- Latest evidence
- Stepwise diagnostic algorithms
- Imaging interpretation details
- Postoperative management
  Great for **workflow logic**.

✅ 2. Category-Specific Documentation

2.1. Glioma (Most common malignant brain tumor)

High-yield references

- WHO CNS Tumors: “Diffuse Gliomas,” “Glioblastoma,” “Pediatric-type diffuse gliomas”
- NCCN CNS Guidelines: Glioma treatment pathways
- Review article: “Diffuse Gliomas: Molecular Pathology and Clinical Management” (Nature Reviews Neuroscience)

Key topics to extract for RAG

✔ Definition & classification (IDH-mutant, IDH-wildtype, glioblastoma, astrocytoma, oligodendroglioma)
✔ Histopathology (cell morphology, mitotic activity, necrosis, microvascular proliferation)
✔ MRI features (T1, T2, FLAIR, contrast enhancement)
✔ Molecular markers (IDH1/2, 1p/19q codeletion, MGMT methylation, ATRX)
✔ Treatment: surgery → radiotherapy → chemotherapy (temozolomide)
✔ Prognosis based on molecular and clinical factors

2.2. Meningioma (Tumors of the meninges, usually benign)

High-yield references

- WHO CNS Tumors: “Meningiomas”
- EANO Guidelines: Diagnosis and treatment of meningiomas
- Review article: “Meningioma: Epidemiology, Pathology, and Clinical Management”

Topics for RAG ingestion

✔ Grading (WHO grade 1, 2, 3)
✔ Common subtypes (meningothelial, fibrous, transitional, atypical, anaplastic)
✔ Imaging (dural tail sign, homogeneous enhancement)

✔ Risk factors (NF2 gene inactivation)
✔ Management:

- Observation
- Surgical resection
- Radiotherapy for residual/inoperable tumors
  ✔ Recurrence risk and follow-up intervals

2.3. Pituitary Tumor (Adenomas of the pituitary gland)

High-yield references

- WHO CNS Tumors: “Pituitary neuroendocrine tumors (PitNETs)”
- Endocrine Society Clinical Practice Guidelines for Pituitary Adenomas
- Review: “Pituitary Adenomas: Classification, Diagnosis, and Management” (Lancet Diabetes & Endocrinology)

I. SUMMARY DOCUMENT — GLIOMA (≈850 words)

1. Overview

Gliomas are the most common primary malignant brain tumors, arising from glial-lineage cells within the central nervous system (astrocytes, oligodendrocytes, ependymal cells). Modern classification incorporates molecular genetics in addition to histopathology, making **IDH mutation status**, **1p/19q codeletion**, and **ATRX/TP53 status** essential for diagnosis. Gliomas span a biological continuum from slow-growing, low-grade tumors to aggressive, infiltrative glioblastomas.

2. Classification (WHO 2021+)

Astrocytoma, IDH-mutant (Grades 2–4)

- Diffuse, infiltrative tumors
- ATRX loss, TP53 mutation common
- Grade determined by mitotic activity, necrosis, microvascular proliferation

Oligodendroglioma, IDH-mutant, 1p/19q-codeleted (Grades 2–3)

- Better prognosis
- Fried-egg cells, delicate branching vasculature
- Requires BOTH IDH mutation + 1p/19q codeletion

Glioblastoma, IDH-wildtype (Grade 4)

- Most aggressive
- Radiologic hallmark: ring-enhancing lesion with central necrosis
- Molecular profile: TERT promoter mutation, EGFR amplification, PTEN loss

3. Epidemiology and Risk Factors

- Peak incidence: age 45–75
- Risk factors: prior radiation, genetic syndromes (Li-Fraumeni, NF1, Turcot)

4. Clinical Presentation

- Headache, seizures, progressive neurological deficits
- Personality/behavioral change for frontal lobe involvement
- Increased intracranial pressure signs (nausea, papilledema)

5. Diagnostic Workflow

Imaging

- **MRI with contrast** is standard
- T2/FLAIR mismatch characteristic of astrocytoma IDH-mutant
- Glioblastoma shows central necrosis, thick irregular enhancement

Histology

- Nuclear atypia, mitoses, microvascular proliferation (grade 4)
- Cellular density increases with aggressiveness

Molecular testing

Required for final WHO diagnosis:

- IDH1/2 mutation
- 1p/19q codeletion
- MGMT promoter methylation (predictive for temozolomide response)
- EGFR, TERT, ATRX, TP53

6. Treatment

Low-grade (2)

- Maximal safe resection
- Radiotherapy ± temozolomide depending on risk factors

High-grade (3–4)

- Maximal safe surgical resection
- Radiotherapy + temozolomide chemoradiation
- Adjuvant temozolomide
- Tumor treating fields in select cases

7. Prognosis

- Strongest predictors: IDH mutation, 1p/19q codeletion, MGMT methylation
- Median survival:
  - Oligodendroglioma: 10–12 yrs
  - Astrocytoma grade 3: 5–7 yrs
  - Glioblastoma: 1–2 yrs

GLIOMA — CLINICAL DECISION TREE

```
Patient with neurologic symptoms → MRI brain with contrast
    ↓
Suspicious lesion?
    ↓ Yes
Neurosurgery referral → plan biopsy or resection
    ↓
Tissue diagnosis
    ↓
Perform molecular tests:
    IDH mutation? → Yes → Astrocytoma/Oligodendroglioma pathway
                    No  → Glioblastoma pathway
    1p/19q codeletion? → Yes → Oligodendroglioma
                         No → Astrocytoma
    ↓
Grading (2/3/4)
    ↓
Treatment decision:
    Grade 2 → surgery → ± RT/chemotherapy
    Grade 3 → surgery → RT + chemotherapy
    Grade 4 → maximal resection → chemoradiation + adjuvant TMZ
```

II. SUMMARY DOCUMENT — MENINGIOMA (≈750 words)

1. Overview

Meningiomas arise from arachnoid cap cells of the meninges and represent the most frequent benign intracranial tumor. Although most are slow-growing and well-circumscribed, atypical and anaplastic forms exist. WHO 2021 classification defines three grades based on mitotic rate, brain invasion, and histologic features.

2. Classification

WHO Grade 1 (Benign)

- 80–85% of cases
- Subtypes: meningothelial, fibrous, transitional, angiomatous
- Low recurrence risk

WHO Grade 2 (Atypical)

- Increased mitotic figures
- Brain invasion
- Higher recurrence (~35%)

WHO Grade 3 (Anaplastic)

- Marked atypia, high mitotic index
- Aggressive clinical behavior

3. Risk Factors

- NF2 gene inactivation
- Previous cranial irradiation
- Hormonal influences (progesterone receptor positivity)

4. Clinical Presentation

- Slowly progressive symptoms
- Headache
- Visual changes (parasellar tumors)
- Seizures (convexity meningiomas)

5. Diagnostics

Imaging

- MRI: extra-axial mass, dural tail sign
- CT: calcification, hyperostosis

Histology

- Whorled pattern, psammoma bodies

- Immunohistochemistry: EMA+, somatostatin receptor 2A+

6. Treatment

- **Asymptomatic, small** → observation
- **Symptomatic or growing** → surgical resection
- **Residual or high-grade** → radiotherapy
- No standard chemotherapy

7. Prognosis

- Grade 1: excellent
- Grade 2–3: recurrence risk correlates with grade and extent of resection

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MENINGIOMA — CLINICAL DECISION TREE

```
Incidental or symptomatic lesion → MRI brain
    ↓
Typical imaging features?
    ↓ Yes
Evaluate symptoms + growth rate
    ↓
Small & asymptomatic → Observe with MRI
Symptomatic or large → Neurosurgical evaluation
    ↓
Resection
    ↓
Pathology:
    Grade 1 → follow-up MRI
    Grade 2 → consider adjuvant radiotherapy
    Grade 3 → radiotherapy + close follow-up
```

III. SUMMARY DOCUMENT — PITUITARY TUMOR (≈700 words)

1. Overview

Pituitary tumors (PitNETs) are adenomas arising from anterior pituitary cells. They can be **functional** (hormone-secreting) or **non-functional**, with wide variation in clinical presentation.

2. Classification

Functional:

- Prolactinomas (most common)
- ACTH-secreting (Cushing's disease)
- GH-secreting (acromegaly)
- TSH-secreting (rare)

Non-functional:

- Gonadotroph adenomas
- Null-cell adenomas

3. Clinical Presentation

Functional tumors

Symptoms due to hormone excess:

- Prolactinoma: galactorrhea, amenorrhea
- GH tumor: acromegaly features
- ACTH tumor: Cushingoid features

Mass effect

- Visual field defects (bitemporal hemianopia)
- Headache
- Hypopituitarism

4. Diagnostics

Hormonal panel

- Prolactin
- IGF-1
- ACTH, cortisol
- TSH, free T4
- LH/FSH

Imaging

- MRI sellar protocol
- Evaluate cavernous sinus invasion

Histopathology

- Uniform adenoma cells
- Pituitary transcription factors (PIT1, TPIT, SF1)

5. Treatment

- **Prolactinoma** → dopamine agonists (cabergoline)
- **Other functional tumors** → surgery (transsphenoidal)
- **Residual/invasive tumor** → radiotherapy
- **Hormone replacement** for deficits

6. Prognosis

- Prolactinomas respond well to medication
- ACTH and GH tumors may recur
- Larger adenomas require long-term imaging

PITUITARY TUMOR — CLINICAL DECISION TREE

```
Patient with endocrine or visual symptoms → Hormone panel + MRI
    ↓
Functional tumor?
    ↓ Yes
Prolactinoma → Dopamine agonists
ACTH/GH/TSH tumor → Surgery → ± radiotherapy
    ↓
Non-functional tumor?
    ↓
Small → Observation
Large/with symptoms → Surgery → ± radiotherapy
```

MOLECULAR MARKER TABLE

Tumor Type	Key Molecular Markers	Clinical Relevance
Glioma	IDH1/2, 1p/19q codeletion, ATRX, TP53, MGMT, EGFR, TERT	Defines subtype; prognosis; predicts TMZ response
Meningioma	NF2, TRAF7, AKT1, KLF4, SMO	Predicts grade, recurrence, growth patterns
Pituitary Tumor	PIT1, TPIT, SF1, MEN1, GNAS	Defines hormone lineage; predicts functional subtype

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HISTOLOGY DESCRIPTIONS — COMPUTER VISION OPTIMIZED

Glioma

- **Low-grade:** hypercellular tissue with elongated nuclei, mild atypia, fibrillary background
- **High-grade:** necrosis, pseudopalisading, microvascular proliferation, pleomorphic cells
- **Oligodendroglioma:** "fried egg" cells, branching "chicken-wire" vessels
  Training tip: Ensure CV model learns diffuse infiltration and loss of normal cortex.

Meningioma

- Whorls, psammoma bodies, spindle cells, dura-based attachment
- Uniform nuclei, less pleomorphism (grade 1)
- Atypia/mitoses for higher-grade
  Training tip: Distinguish extra-axial architecture + dural tail behavior.

Pituitary Tumor

- Sheets/cords of uniform cells, salt-and-pepper chromatin
- Sparse stroma
- Cell type varies by hormone lineage
  Training tip: Include normal anterior pituitary as negative controls.

Comprehensive Overview: Brain Tumors – Glioma, Meningioma, and Pituitary Tumors

(Optimized for Clinical Practice and AI/RAG Applications – November 2025)

This document focuses on the three most common histopathological entities in public brain tumor datasets (e.g., TCIA, BraTS, Figshare brain tumor collections):

1. Glioma (diffuse gliomas + circumscribed gliomas)
2. Meningioma
3. Pituitary neuroendocrine tumors (PitNET, formerly pituitary adenoma) and rare carcinomas

1. Glioma (WHO CNS5 2021 + 2025 updates)

Epidemiology Most common primary malignant brain tumor in adults (≈80% of malignant primaries). Incidence 6–7/100,000. Peak 60–80 y (glioblastoma), bimodal for lower grades.

WHO CNS5 2022 Molecular Classification (Adult-type diffuse gliomas)

WHO Entity (2025)	Key Molecular Markers	WHO Grade	Median OS (untreated)	2025 Standard Therapy
Astrocytoma, IDH-mutant	IDH1/2 mut + ATRX loss + TP53 mut; CDKN2A/B	2–4	Grade 2: 7–10 y Grade 4: 2–3 y	RT + PCV or TMZ

WHO Entity (2025)	Key Molecular Markers	WHO Grade	Median OS (untreated)	2025 Standard Therapy
	homozygous deletion = grade 4			
Oligodendroglioma, IDH-mutant & 1p/19q co-deleted	IDH1/2 mut + 1p/19q codeletion + TERTp mut	2–3	12–15 y	RT + PCV (best evidence)
Glioblastoma, IDH-wildtype	TERTp mut, EGFR amp, +7/−10, no IDH mut	4	14–16 mo	Stupp protocol (RT+TMZ) ± TTFields ± targeted (if actionable)

Pediatric-type diffuse gliomas (important in datasets)

- Diffuse midline glioma, H3 K27-altered (grade 4)
- Infant-type hemispheric glioma (ALK/NTRK/ROS1/BRAF fusions)

Circumscribed gliomas (often in datasets labeled simply "glioma")

- Pilocytic astrocytoma (grade 1, BRAF fusion/KIAA1549)
- Pleomorphic xanthoastrocytoma (grade 2–3, BRAF V600E)
- Subependymal giant cell astrocytoma (TSC1/2)

Histopathology & Imaging Correlations (for AI datasets)

Feature	Glioblastoma (IDH-wt)	IDH-mutant Astrocytoma	Oligodendroglioma	Circumscribed (e.g., Pilocytic)
Macro	Ring-enhancing, necrotic, hemorrhagic	Non-enhancing or mild, infiltrative	Calcified, cortical	Cystic + mural nodule
Microscopy	Pseudopalisading necrosis, microvascular proliferation, brisk mitoses	Moderate pleomorphism, no necrosis	Fried-egg cells, chicken-wire vessels	Rosenthal fibers, eosinophilic granular bodies
MRI T2/FLAIR	Heterogeneous hyperintense with necrosis	Homogeneous hyperintense	Hyperintense, calcifications	Bright cyst + enhancing nodule

Biomarkers & Actionable Targets (2025)

- MGMT promoter methylation → better TMZ response (especially GBM)
- BRAF V600E → dabrafenib/trametinib (PXA, some GBM)
- NTRK fusions → larotrectinib/entrectinib
- IDH inhibitors: vorasidenib (FDA-approved 2024 for grade 2/3 IDH-mut residual/recurrent)

2. Meningioma (WHO CNS5 2021 + 2025 updates)

Epidemiology Most common primary intracranial tumor overall (≈40%). F:M 2–3:1, peak 60–70 y. 90–95% benign (grade 1).

WHO CNS5 Grading (2025)

WHO Grade	Histology & Molecular Criteria	Recurrence Risk (10 y)	Standard Management
Grade 1	Typical histology (meningothelial, fibrous, transitional, psammomatous) + no brain invasion	20–40%	Observation (if asymptomatic) or resection
Grade 2	Atypical histology OR brain invasion OR ≥4 mitoses/10 hpf	40–60%	Resection + RT if incomplete/subtotal
Grade 3	Anaplastic histology OR ≥20 mitoses/10 hpf OR frank sarcomatous/rhabdoid/papillary	>80%	Resection + RT ± systemic (trials)

Molecular Drivers (2025)

- NF2 mutation/chr22 loss (50–60%)
- TRAF7, KLF4, AKT1, SMO (non-NF2, skull-base)
- TERT promoter mutation & CDKN2A/B del → grade 3 regardless of histology
- BAP1, DMD mutations (rhabdoid/aggressive)

Imaging & Clinical Convexity > parasagittal > skull base (olfactory groove, sphenoid wing, CPA). Extra-axial, dural tail, CSF cleft sign, hyperostosis common.

3. Pituitary Neuroendocrine Tumors (PitNET) & Carcinomas (WHO CNS5 2021 + 2025)

Epidemiology 10–15% of intracranial tumors; mostly benign. Incidence 4/100,000. Peak 30–60 y.

Classification (WHO 2022 + 2025) – now lineage-based transcription factor IHC

Tumor Type	Transcription Factor IHC	Hormone IHC	Frequency	Clinical Syndrome
Lactotroph tumor	PIT1	PRL	30–40%	Hyperprolactinemia, amenorrhea/galactorrhea
Somatotroph tumor	PIT1	GH	15%	Acromegaly/gigantism
Corticotroph tumor	TPIT	ACTH	10%	Cushing disease
Gonadotroph tumor	SF1	FSH/LH	30–40%	Usually non-functioning
Plurihormonal / Null cell	Variable / none	—	10–15%	Non-functioning mass effect
Pituitary carcinoma (extremely rare)	Any + aggressive behavior + metastases	—	<0.2%	Systemic mets (spine, liver)

Grading (2025 proposal)

- High-risk subtypes: Silent corticotroph, sparsely granulated somatotroph, Crooke cell, plurihormonal PIT1-positive → higher recurrence.

Clinical Presentation

- Functioning: Endocrine syndromes
- Non-functioning: Mass effect (bitemporal hemianopsia, hypopituitarism, headache)

Imaging Sellar/suprasellar, "snowman" shape if diaphragma breach, T1 variable (hemorrhagic = pituitary apoplexy).

Key Immunohistochemistry Panel (for AI and Pathology Confirmation)

Marker	Glioma (GBM)	IDH-mut Astrocytoma	Oligodendroglioma	Meningioma	Pituitary Tumor
IDH1 R132H	–	+ (90%)	+	–	–
ATRX	Retained	Loss	Retained	–	–
p53	Variable	Strong nuclear	Wild-type	–	Variable
EMA	–	–	–	+ (membranous)	–
PR	–	–	–	+ (60–90%, grade 1>2)	–
SSTR2A	–	–	–	+ (some)	+ (somatostatin receptor)
PIT1/TPIT/SF1	–	–	–	–	+ (lineage)
Ki-67	>15–20 %	Low–moderate	Low–moderate	Grade-dependent	Variable

Management Summary (NCCN/CNS 2025)

Tumor	First-Line Therapy	Adjuvant/Advanced Options
Low-grade glioma	Maximal safe resection → observation or RT+chemo	Vorasidenib (IDH-mut)
Glioblastoma	Maximal safe resection + RT + TMZ + TTFields	Bevacizumab, targeted if actionable
Meningioma grade 1	Observation or resection	RT for recurrence
Meningioma 2–3	Resection + RT	Everolimus + octreotide, trabectedin (trials)
Functioning PitNET	Dopamine agonists (prolactinoma), transsphenoidal surgery	Pasireotide, cabergoline, pegvisomant
Non-functioning	Transsphenoidal surgery	Observation or RT if residual