ACRODeck

Low Grade Gliomas

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Introduction to ACRODeck

ACRODeck

- The goal of ACRODeck is to introduce standard treatments of oncologic malignancies for early radiation oncology residents

- Please note that there is often considerable variation in standard treatment recommendations

- Moreover, the landscape of oncology is ever-changing; for practice changing landmark studies and feedback, please email: resident@acro.org

Table of Contents

ACRODeck

1. Clinical Presentation and Differential Diagnosis
2. Initial Workup
3. Staging
4. Pathology
5. Treatment Summary
   - Risk Stratification
   - Surgery
   - Chemotherapy
   - Radiation
6. Prognosis
7. Review Questions

Clinical Presentation and Differential Diagnosis

In contrast to higher grade tumors, LGGs are more prevalent in the younger adult population

- As with any CNS lesion, the location of the lesion will determine the clinical presentation
  - LGGs most commonly present with seizures
  - Other symptoms may include neurologic deficits, headaches, altered mental status, motor and sensory deficits, nausea and vomiting

- Differential Diagnosis:
  - Glioma
  - Ependymoma
  - Lymphoma
  - Brain metastasis
  - Intracranial abscess
  - Empyema
  - Multiple sclerosis

Initial Workup

In contrast to higher grade tumors, most LGGs have minimal contrast enhancement

- H/P
- CBC and CMP
- MRI brain with and without contrast (obtain one within 24-48 hours of resection as well)
  - Classic findings: T2 hyperintense; minimal contrast enhancement (apart from pilocytic astrocytomas)

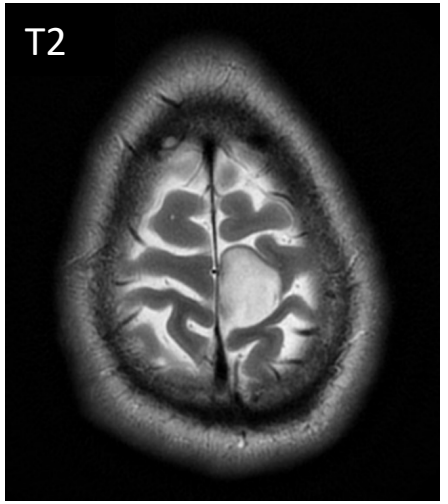
MRI Sequence	Appearance	Visualization of …
T1	Isointense/Hypointense	Anatomy
T1c	Minimal Contrast Enhancement	Pilocytic Astrocytomas
T2 / FLAIR	Hyperintense	Tumor

- Consider steroids and anti-epileptics
- Maximal safe resection
  - Molecular testing includes IDH, 1p19q codeletion, BRAF





Radiopaedia



Staging

Most glial neoplasms in adults are WHO grade 4

- Primary CNS tumors are graded, not staged

Tumor	WHO Grade
Pilocytic astrocytoma (and others)	1
Diffuse low-grade glioma	2
Anaplastic glioma	3
Glioblastoma Multiforme	4

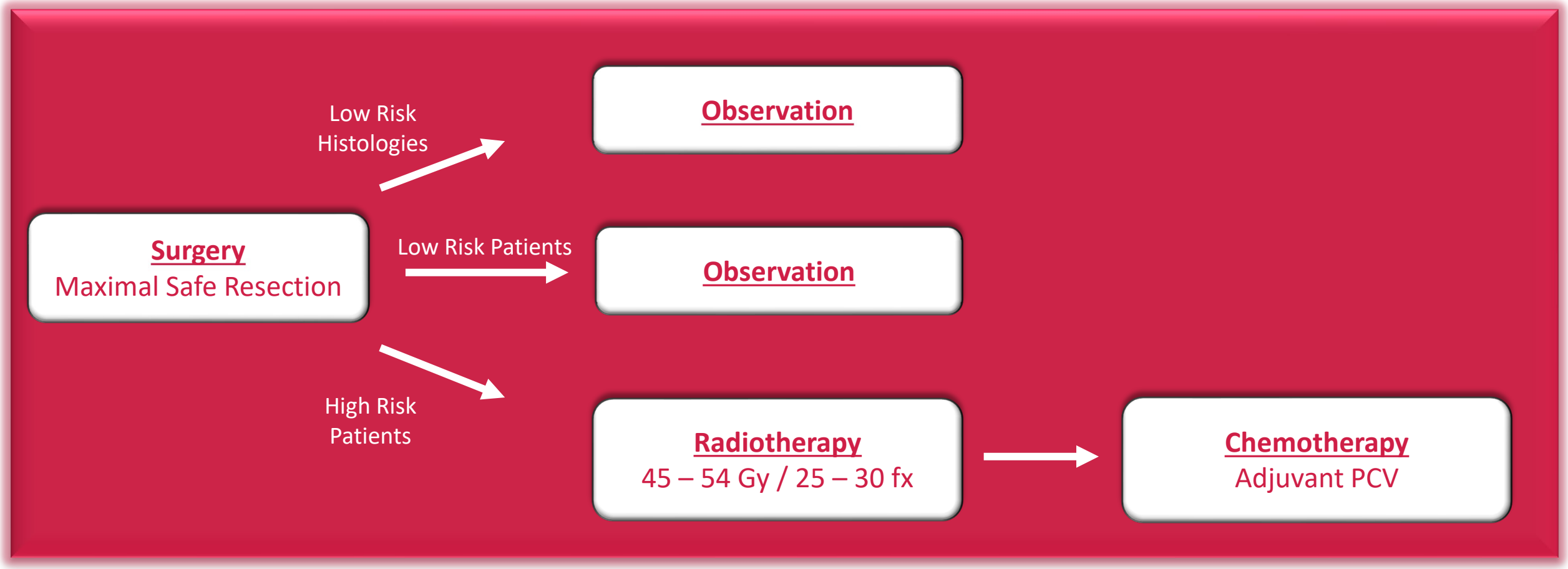
Pathology

Historical trials did not use modern molecular classification (notably IDH status)

- Low grade gliomas are a heterogenous group of tumors
- They are broadly classified into:
  - WHO grade 1 (noninfiltrative tumors)
  - WHO grade 2 (infiltrative/diffuse tumors)

- Traditionally, histology and MEAN criteria were used to characterize these tumors
  - Mitotic index, endothelial proliferation, nuclear atypia, and necrosis
- Now, we are moving towards an era of incorporating molecular classification into WHO grading (see 2021 update)
  - Astrocytomas: 1p19q intact
  - Oligodendrogliomas: 1p19q co-deleted

Treatment Summary: Low Grade Gliomas



Risk Stratification

NCCN utilizes the RTOG risk factors

RTOG Risk Factors: either one of these risk factors leads to a categorization of high risk

- Age greater than 40
- Subtotal resection

EORTC (Pignatti Risk Factors): need three of these risk factors for a categorization of high risk

- Age greater than 40
- Tumor that crosses midline
- Tumor size greater than 6 cm
- Astrocytoma histology
- Neurologic compromise prior to surgery

Per NCCN, there are certain low risk histologies which can be observed (even after an incomplete resection)

- Pilocytic Astrocytomas
- Pleomorphic Xanthoastrocytomas
- Subependymal Giant Cell Astrocytomas
- Gangliogliomas

Surgery

As these patients have a long natural history, doing no harm is of utmost importance!

As with other gliomas, a maximal safe resection is indicated

- A gross total resection is prognostic for survival
- A simple biopsy has a high risk of underrating tumor grade, as gliomas tend to be quite heterogenous

Chemotherapy

TMZ is better tolerated than PCV

- **Procarbazine, Lomustine (CCNU), and Vincristine (PCV): NCCN Category 1**
  - Schedule:
    - PCV is given as adjuvant treatment alone

Chemotherapeutic Agent	Route of Administration	Side Effects
Procarbazine	Oral	Nausea and Skin Reactions
Lomustine	Oral	Marrow Suppression
Vincristine	Intravenous	Neurotoxicity

- **Temozolomide (TMZ):**
  - Schedules:
    - TMZ can be given as adjuvant treatment alone
    - It can also be given concurrently with radiation and adjuvantly
  - It is administered orally
  - Side Effects:
    - Thrombocytopenia, development of a rash, diarrhea/constipation, nausea, mouth sores, edema, and hair thinning

Radiation

Most centers utilize a single volume; some prefer an SIB

Simulation

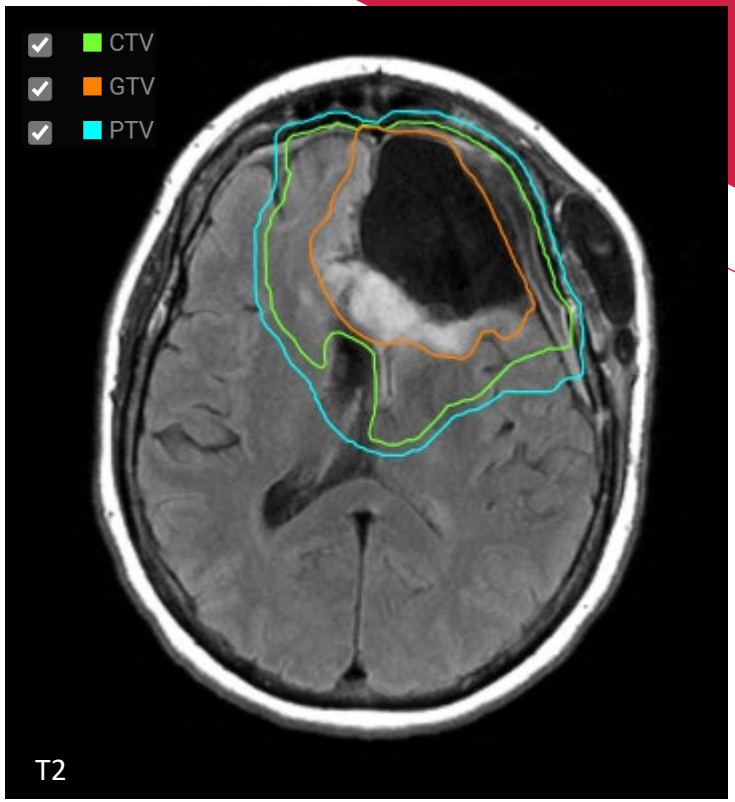
- CT head non-contrast
- Brain MRI with and without contrast
- Face mask

Volumes

- **GTV** = surgical bed + any T2 abnormality (include enhancement on the T1c MRI)
- **CTV** = standard expansion is 1 – 2 cm, cropped from natural barriers
- **PTV** = 3 – 5 mm

Doses

- There are a variety of dosing schedules based on EORTC and RTOG trials
  - 45 Gy / 25 fx
  - 50.4 Gy / 28 fx
  - 54 Gy / 30 fx



eContour

Selected CNS Dose Constraints

PMID: 25701297

Organ at Risk (OAR)	Dose Constraint (Gy)
Optic Nerves and Chiasm	Max < 54 – 60
Brainstem	Max < 54 - 60
Cochlea	Mean < 45
Pituitary	Mean < 45
Hippocampus	Max < 16, $D_{100\%}$ < 9

Radiation Toxicities

Modern radiation techniques (i.e., IMRT, VMAT, and protons) are often utilized to minimize toxicities

- Acute:
  - Fatigue
  - Alopecia
  - Nausea
  - Skin erythema

- Chronic:
  - Swelling
  - Radionecrosis
  - **Location-Dependent:** for example, if tumor is near the cochlea, radiation can possibly lead to sensorineural hearing loss (see dose constraints on previous slide)

Prognosis

At progression, nearly 70% of tumors undergo malignant transformation

- Most LGGs have a prolonged natural history
  - However, some can progress and malignantly transform
  - The rate of malignant transformation is unaffected by receipt of radiation

- Per historical data, the median overall survival range is 10 - 15 years
  - Given that these studies did not incorporate modern molecular classifications, the median survival of patients with LGGs (particularly those with 1p/19q-codeleted tumors) may be around 20 years

Review

Review #1: The Correct MRI

This sequence differs from the one best used to visualize GBMs

What of the following MRI sequences allows for the best visualization of most low-grade gliomas?

(A) T1

(B) T1 + Contrast

(C) T2

Review #2: Risk Stratification

Think NCCN/RTOG risk factors!

Which patient with a WHO grade 2 astrocytoma would radiation followed by adjuvant chemotherapy most strongly be recommended?

(A) 50-year-old with subtotal resection

(B) 4-year-old with subtotal resection

(C) 23-year-old with gross total resection

(D) 37-year-old with gross total resection

Review #3: Systemic Therapy

There is an OS benefit to this regimen (PMID: 27050206)

Which chemotherapy regimen is an NCCN Category 1 recommendation for patients with low-grade gliomas?

(A) Procarbazine, Irinotecan, and Carboplatin

(B) Procarbazine, Lomustine, and Vincristine

(C) Concurrent Temozolomide

(D) Concurrent and Adjuvant Temozolomide

Review #4: Radiation Dosing

Dose escalation has not been shown to improve outcomes (PMID: 8948338)

Which of the following doses is appropriate for adjuvant treatment following a subtotal resection of a WHO grade 2 oligodendroglioma?

(A) 30.6 Gy

(B) 50.4 Gy

(C) 59.4 Gy

(D) 64.8 Gy

Review #5: Dose Constraints

The risk of necrosis is less than 5% at this dose

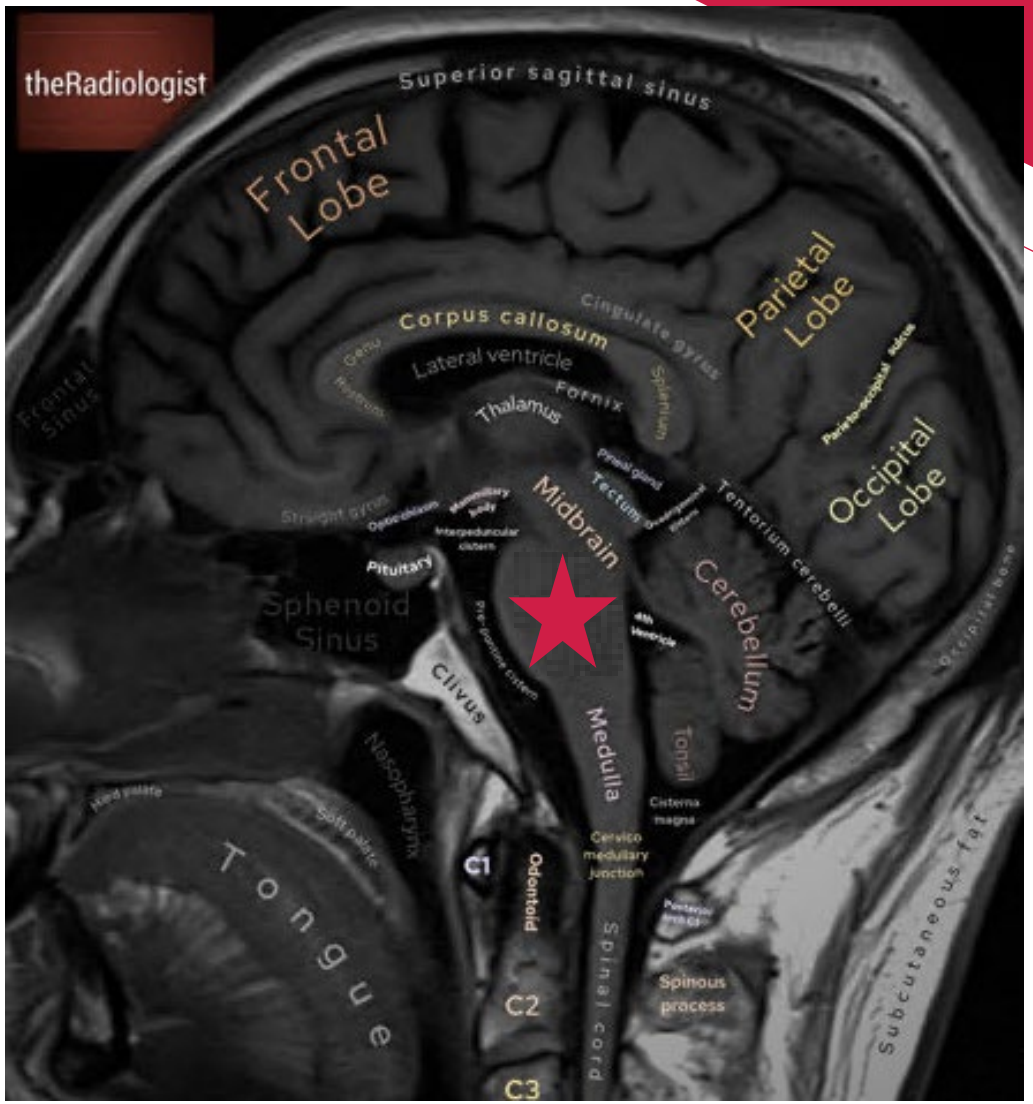
Which of the following is a reasonable dose constraint to the highlighted structure (red star)?

(A) Mean < 45 Gy

(B) Max < 54 Gy

(C) V_{20} < 37%

(D) Max < 70 Gy



Answer Key

1. C
2. A
3. B
4. B
5. B

NRG-BN005 is comparing cognitive preservation for gliomas treated with protons vs. photons