



ACRODeck

# **Glioblastoma Multiforme**

Qateeb Khan, M.D.

# Introduction to 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: [acroresident@acro.org](mailto:acroresident@acro.org)

# Table of Contents

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

# Clinical Presentation and Differential Diagnosis

Presentation with seizures can be a positive prognostic factor

- As with any CNS lesion, the location of the lesion will determine the clinical presentation
  - Symptoms may include neurologic deficits, headaches, altered mental status, seizures, motor and sensory deficits, nausea and vomiting
- Differential Diagnosis:
  - Glioma
  - Ependymoma
  - Lymphoma
  - Brain metastasis
  - Intracranial abscess
  - Empyema
  - Multiple sclerosis

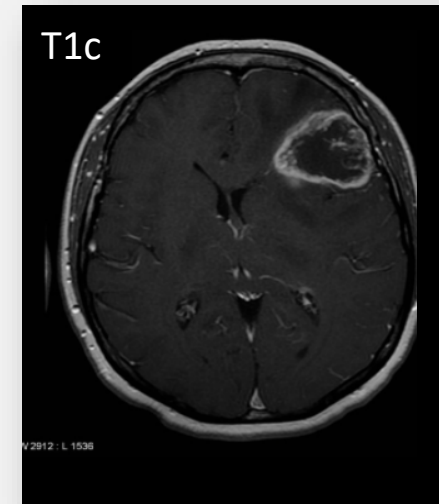
# Initial Workup

- H/P
- CBC and CMP
- MRI brain with and without contrast (obtain one within 24-48 hours of resection as well)
  - Classic findings: heterogeneous enhancement, central necrosis with surrounding edema

MRI Sequence	Appearance	Visualization of ...
T1	Hypointense	Anatomy
T1c	Ring-Enhancing Lesion	Tumor
T2 / FLAIR	Hyperintense	Edema

- Consider steroids and anti-epileptics
- Maximal safe resection
  - Test for IDH and MGMT methylation status

Per CNS WHO 2021, all GBMs are IDH-WT



Radiopaedia



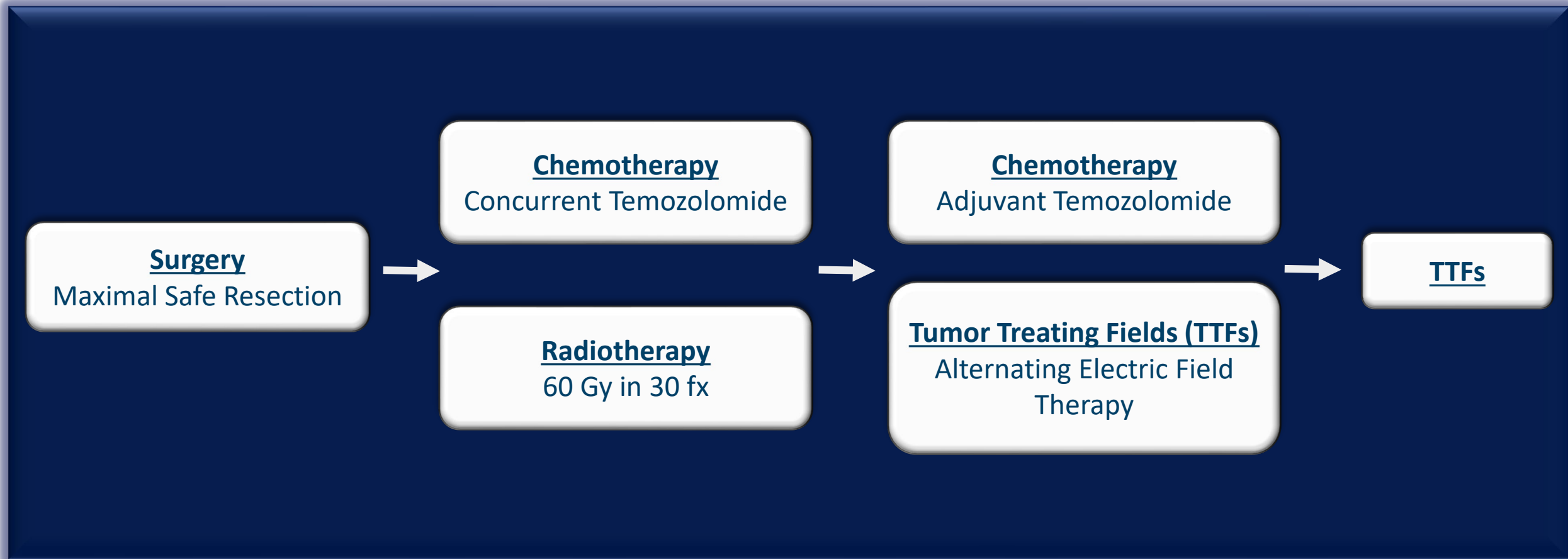
# Staging

GBM = WHO grade 4

- Primary CNS tumors are graded, not staged

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

# Treatment Summary: Glioblastoma Multiforme



# Surgery

Surgery  
Maximal Safe Resection

As with other gliomas, a maximal safe resection is indicated

- A gross total resection is prognostic



# Chemotherapy

Must give TMP-SMZ  
(Bactrim) with TMZ, as  
PCP prophylaxis

- Temozolomide (TMZ):
  - Concurrent TMZ
    - 75 mg/m<sup>2</sup> daily including weekends
  - Adjuvant TMZ
    - 6 cycles, each for 28 days
    - Dosed between 150 – 200 mg/m<sup>2</sup> daily
- Side effects of TMZ include diarrhea/constipation, development of a rash, mouth sores, edema, hair thinning, nausea, and thrombocytopenia
  - Ondansetron (Zofran) is often prescribed
  - Weekly CBC and CMP are obtained
  - Pregnant and nursing women should not use TMZ

# Radiation

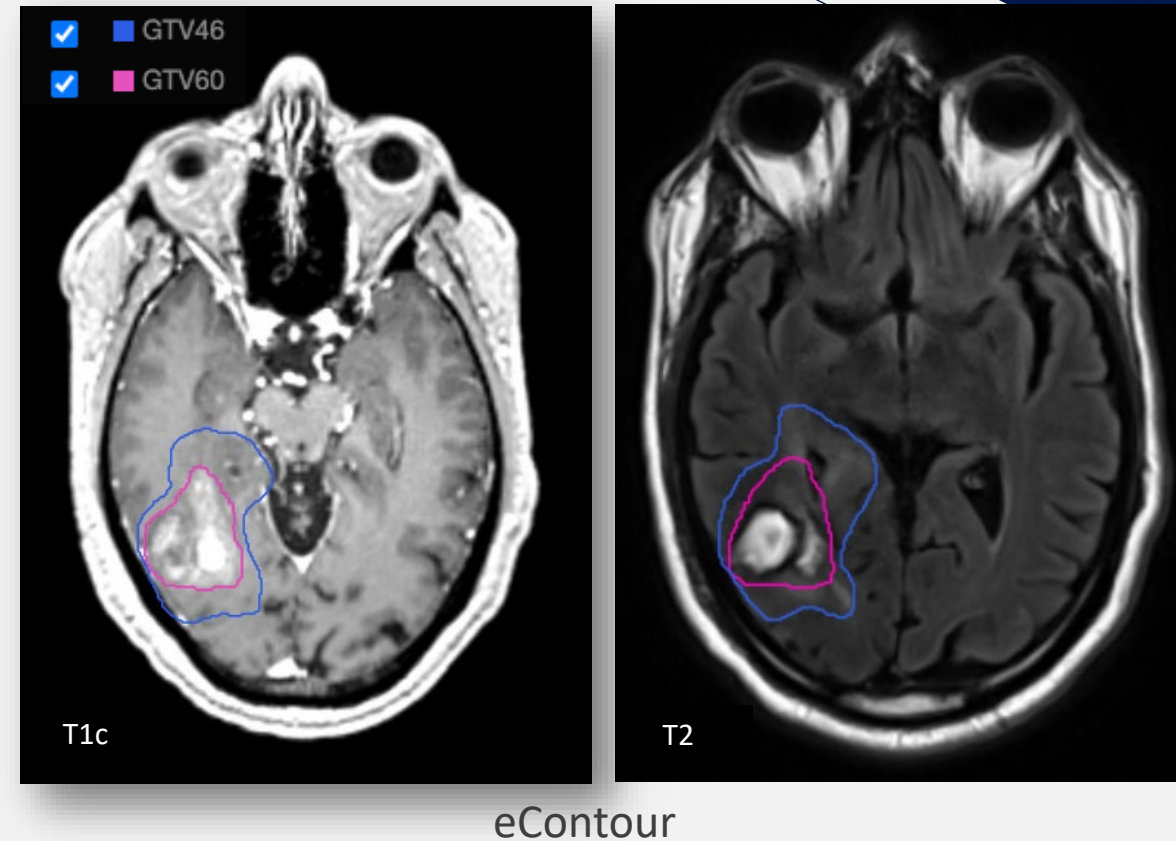
Radiotherapy  
60 Gy in 30 fx

## Simulation

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

## Treatment

- 60 Gy in 30 fx is standard per Stupp regimen
  - PMID: 29260225
- For elderly patients with poor performance status, hypofractionated regimens can be considered:
  - 40 Gy in 15 fx, 34 Gy in 10 fx, 25 Gy in 5 fx
  - Can be administered with or without chemotherapy, based on the performance status of the patient



# Radiation Treatment and Volumes: EORTC and RTOG

Please note there is considerable variation between institutions

**Table 1**  
Guidelines for target delineation of glioblastoma, according to the European Organisation for Research and Treatment of Cancer (EORTC) and the Radiation Therapy Oncology Group (RTOG).

EORTC treatment volumes (EORTC 22981/22961, 26071/22072 (Centric), 26981–22981, and AVAglio trials)	RTOG treatment volumes (RTOG 0525, 0825, 0913, and AVAglio trials)
Phase 1 (to 60 Gy in 30 fractions) GTV = surgical resection cavity plus any residual enhancing tumour (postcontrast T1 weighted MRI scans). CTV = GTV plus a margin of 2 cm*  PTV = CTV plus a margin of 3–5 mm	Phase 1 (to 46 Gy in 23 fractions) GTV1 = surgical resection cavity plus any residual enhancing tumour (postcontrast T1 weighted MRI scans) plus surrounding oedema (hyperintensity on T2 or FLAIR MRI scans). CTV1 = GTV1 plus a margin of 2 cm (if no surrounding oedema is present, the CTV is the contrast enhancing tumour plus 2.5 cm). PTV1 = CTV1 plus a margin of 3–5 mm Phase 2 (14 Gy boost in 7 fractions) GTV2 = surgical resection cavity plus any residual enhancing tumour (postcontrast T1 weighted MRI scans) CTV2 = GTV2 plus a margin of 2 cm PTV2 = CTV2 plus a margin of 3–5 mm

GTV = gross tumour volume; CTV = clinical target volumes; PTV = planning target volume.  
MRI = magnetic resonance imaging.

\* Margins up to 3 cm were allowed in 22981/22961 trial, and 1.5 cm in 26981–22981 trial.

# Selected CNS Dose Constraints

Tumor coverage may sometimes be prioritized over OAR sparing

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 <sub>100</sub> < 9

# Radiation Toxicities

- Acute:
  - Fatigue
  - Nausea
  - Alopecia
  - Skin erythema
- Chronic:
  - Swelling
  - Radionecrosis
  - **Location-Dependent:** for example, if tumor is near the hippocampus, radiation can lead to memory issues

# Tumor Treating Fields (TTFs)

- TTFs are alternating electric fields that function as a regional anti-mitotic treatment
- They are used after chemoradiation, starting with adjuvant TMZ and are used indefinitely afterwards



# Prognosis

- Median survival ranges from 1.5 to 2 years
- The tumor will almost invariably recur; salvage options include:
  - Re-resection
  - Re-irradiation
    - 35 Gy in 10 fx (per RTOG 1205)
    - Stereotactic radiosurgery
  - Temozolomide, Nitrosoureas, Avastin



Review



In the 1920s,  
hemispherectomies were  
performed for GBMs

# Review #1: The Correct Surgery

What is the correct oncologic surgery for a GBM?

- (A) Gross total resection
- (B) Stereotactic needle biopsy
- (C) Maximal safe resection
- (D) There is no role for surgery in GBM given the intensive chemoradiation treatments

# Review #2: The Stupp Regimen

Which of the following treatment regimens is considered the standard of care for a newly diagnosed glioblastoma, with residual disease after surgery?

- (A) RT to 60 Gy with concurrent and adjuvant temozolomide + tumor-treating fields
- (B) RT to 60 Gy with concurrent and adjuvant temozolomide + bevacizumab
- (C) RT with a boost to 74 Gy with concurrent and adjuvant temozolomide + tumor-treating fields
- (D) RT with a boost to 74 Gy with concurrent and adjuvant temozolomide + bevacizumab

# Review #3: Doses, Volumes, and Expansions

In 1978, WBRT to 60 Gy was found to double OS

Which of the following volumes and doses is correct for the treatment of a GBM, per the RTOG Guidelines?

- (A) A total of 46 Gy to the edema volume, seen best on the T2 MRI
- (B) A total of 60 Gy to the edema volume, seen best on the T2 MRI
- (C) A total of 46 Gy to the contrast enhancing volume, seen best on the T1c MRI
- (D) A total of 74 Gy to the contrast enhancing volume, seen best on the T1c MRI

There is less than 3% risk  
of optic neuritis at this  
dose

# Review #4: Dose Constraints

Which of the following is a reasonable dose constraint to the highlighted structure (blue arrow)?

- (A) Mean < 45 Gy
- (B) Max < 54 Gy
- (C)  $V_{20} < 37\%$
- (D) Max < 45 Gy



# Review #5: Follow-up

Note: Pseudoprogression  
can be seen on post-  
treatment imaging!

Per NCCN, which of the following is a correct follow-up timeline after treatment for a GBM?

- (A) Brain MRI q2 months indefinitely
- (B) Brain MRI q3 months indefinitely
- (C) Brain MRI at 1 month, and then q3 months indefinitely
- (D) Brain MRI at 1 month, and then q6 months indefinitely

# Answer Key

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

NRG-BN007 is comparing  
TMZ vs. Ipi/Nivo for  
unmethylated tumors