

# Patient Centered Education in Radiology

A teaching tool using interactive modules to follow a patient through their disease course from an imaging perspective

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## History:

- 44 year old male with no significant past medical history had persistent headaches which lasted several weeks. The patient went to an acute care clinic and was given prednisone and antibiotics for a presumed sinus infection. The pressure associated with his headaches improved for several days while he was on the prednisone. However, after he stopped prednisone, his headaches returned. The patient presented to the emergency room because of worsening severe headaches.

• What imaging test is the appropriate next step?

Non-contrast CT Head    MRI of the head    CT angiogram of the head    Non-contrast CT of the sinuses    MR angiogram of the head

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**CORRECT!**

- Correct answer: Non-contrast CT of the head
- Explanation:
  - The first imaging test in the setting of acute severe headache is a non-contrast CT head. The results of the exam will dictate if further imaging is needed or if immediate medical or surgical treatment is needed.

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**INCORRECT**

- Correct answer: Non-contrast CT of the head
- Explanation:
  - The first imaging test in the setting of acute severe headache is a non-contrast CT head. The results of the exam will dictate if further imaging is needed or if immediate medical or surgical treatment is needed.


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Non-contrast CT of the Head

- What are the top 3 diagnoses in the differential?

Click here to see the answer

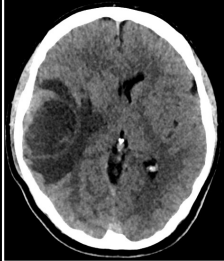


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Non-contrast CT of the Head


- What are the top 3 diagnoses in the differential?
  - Primary brain tumor (glioblastoma)
  - Brain metastasis
  - Brain abscess

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Non-contrast CT of the Head



• Which of the following is the best next imaging test?

- MR angiogram head without contrast
- MRI head without contrast
- CT angiogram of the head
- MRI head without and with contrast

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**CORRECT!**

• Correct answer: MRI head without and with contrast

• Explanation:

- For the workup of a potential mass or abscess, and MRI of the head without and with contrast is the best study. If the patient cannot get contrast, a non-contrast MRI can still be helpful. CT angiogram is best for evaluating the arteries and is not the next step in the workup of a mass lesion.

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**INCORRECT**

• Correct answer: MRI head without and with contrast

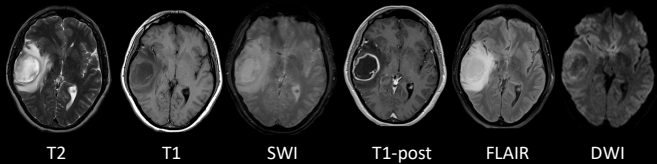
• Explanation:

- For the workup of a potential mass or abscess, and MRI of the head without and with contrast is the best study. If the patient cannot get contrast, a non-contrast MRI can still be helpful. CT angiogram is best for evaluating the arteries and is not the next step in the workup of a mass lesion.

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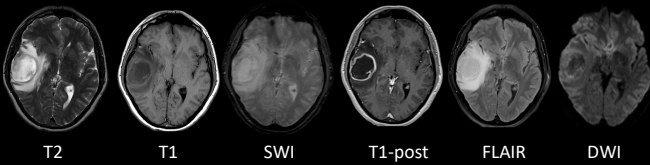


T2 T1 SWI T1-post FLAIR DWI

What feature makes abscess unlikely in this case?

Click here to see the answer

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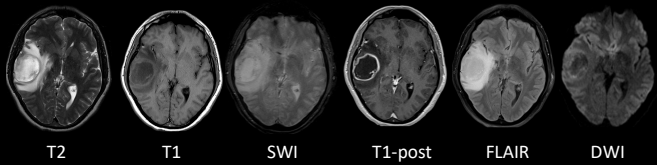
T2 T1 SWI T1-post FLAIR DWI

What feature makes abscess unlikely in this case?

Lack of restricted diffusion centrally

Click here to continue

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T2 T1 SWI T1-post FLAIR DWI

What is the most likely diagnosis?

Click here to see the answer

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T2 T1 SWI T1-post FLAIR DWI

What is the most likely diagnosis?

Glioblastoma – large solitary irregularly rim enhancing mass with surrounding FLAIR hyperintensity. Metastatic disease can look like this but often is more solid and with multiple lesions.

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T2 T1 SWI T1-post FLAIR DWI

What is the next step in the management of this patient?

[Click here to see the answer](#)

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T2 T1 SWI T1-post FLAIR DWI

What is the next step in the management of this patient?

Biopsy and/or surgical resection

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### Clinical Course

- CT of the chest, abdomen, and pelvis did not show any evidence of a primary malignancy
- The patient was taken to the OR and gross total resection of the rim enhancing mass was performed
- Pathology showed glioblastoma, IDH 1 wild type, MGMT promoter un-methylated
- An MRI was obtained 24 hours after the resection

[Click here to see the post-op MRI](#) [Click here to learn more about IDH 1 and MGMT status](#)

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### IDH1 and MGMT

- MGMT Methylation:
  - Methylated: More likely to have pseudoprogression
  - Unmethylated: Less likely to have pseudoprogression
- IDH wildtype vs mutant:
  - Wildtype: started as glioblastoma
  - Mutant: arose from a lower grade glioma

[Click here to see the post-op MRI](#)

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### 24 hour Post-operative Imaging

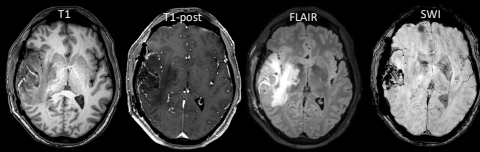
T1 T1-post FLAIR SWI

It is standard of care to do a contrast enhanced brain MRI within 72 hours of a glioblastoma resection. What is the purpose of this MRI and why does it have to be done within 72 hours?

[Click here to see the answer](#)

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## 24 hour Post-operative Imaging



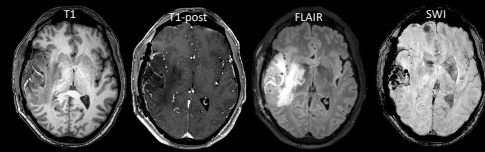
It is standard of care to do a contrast enhanced brain MRI within 72 hours of a glioblastoma resection. What is the purpose of this MRI and why does it have to be done within 72 hours?

The purpose of the immediate post operative scan is to see if there is any residual enhancing tumor. After 72 hours, granulation tissue starts to form. Granulation tissue enhances and can be indistinguishable from tumor. If scan is performed within 72 hours of surgery, any enhancement has to be residual tumor since it's too early for granulation tissue to form

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## 24 hour Post-operative Imaging

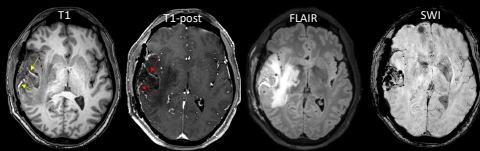


Is there any evidence of residual enhancing tumor in this case?

[Click here to see the answer](#)

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## 24 hour Post-operative Imaging



Is there any evidence of residual enhancing tumor in this case?

No. The linear areas of hyperintensity on the post contrast T1 (red arrows) are due to intrinsic T1 hyperintensity from blood products which can be seen on the T1 pre-contrast image (yellow arrows). To call true enhancement you have to see hyperintensity on the T1-post that does not have corresponding hyperintensity on the precontrast T1 images

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## Clinical Course

- The post-operative scan showed no evidence of residual enhancing tumor at the site of resection
- The patient was then treated with standard chemotherapy and radiation therapy
- What is the name of the standard first line chemotherapy used to treat glioblastoma?

[Click here to see the answer](#)

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## Clinical Course

- The post-operative scan showed no evidence of residual enhancing tumor at the site of resection
- The patient was then treated with standard chemotherapy and radiation therapy
- What is the name of the standard first line chemotherapy used to treat glioblastoma?
  - Answer: Temozolomide (also called TMZ or Temodar)

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## Clinical Course

- After completing 3 months of chemo-radiation a follow-up scan was obtained
- What are 3 reasons you may have increasing enhancement on the first post-treatment follow-up MRI in glioblastoma cases?

[Click here to see the answer](#)

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## Clinical Course

- After completing 3 months of chemo-radiation a follow-up scan was obtained
- What are 3 reasons you may have increasing enhancement on the first post-treatment follow-up MRI in glioblastoma cases?
  1. True tumor progression
  2. Pseudoprogression
  3. Enhancing subacute infarct that occurred at the time of surgery (to confirm this diagnosis you can look back at the post op MRI to see if there was restricted diffusion)

[Click here to see the post-treatment MRI](#)

[Click here to learn more about pseudoprogression](#)

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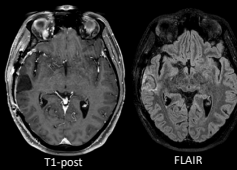
## Pseudoprogression

- Occurs in patients treated with temozolomide and radiation and also in patients on immunotherapy
- In TMZ/rad pseudoprogression occurs in a 3 month period starting at the END of radiation
  - For this reason the end date of radiation should go in the history section of every GBM report
- On imaging, pseudoprogression is increasing enhancement around the surgical cavity that mimics tumor progression.
- Some techniques such as perfusion and PET/CT can favor pseudoprogression over true progression (low perfusion, low metabolic activity on PET)
- The gold standard for making the diagnosis is a short interval (4 week) follow up MRI showing the enhancement has decreased whereas tumor will increase

[Click here to see the post-treatment MRI](#)

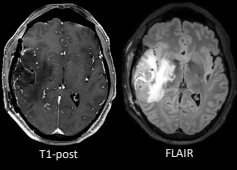
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Current Study: First post-chemo/rad MRI 3 months after resection



T1-post FLAIR

Prior Study: 24 hour post-op MRI



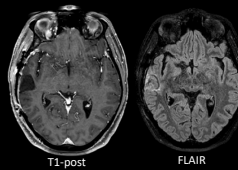
T1-post FLAIR

Is there any enhancement or new FLAIR abnormality at the surgical resection site on the current study?

[Click here to see the answer](#)

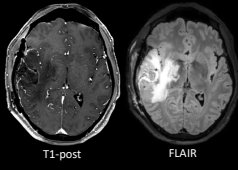
27

Current Study: First post-chemo/rad MRI 3 months after resection



T1-post FLAIR

Prior Study: 24 hour post-op MRI



T1-post FLAIR

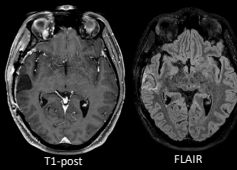
Is there any enhancement or new FLAIR abnormality at the surgical resection site on the current study?

There is no enhancement in the surgical bed. In addition, the FLAIR hyperintensity seen on the prior study has improved.

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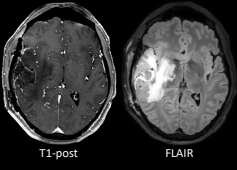
28

Current Study: First post-chemo/rad MRI 3 months after resection



T1-post FLAIR

Prior Study: 24 hour post-op MRI



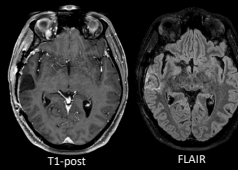
T1-post FLAIR

What criteria is used in glioblastoma cases to determine if a patient has complete response, partial response, stable disease, or disease progression?

[Click here to see the answer](#)

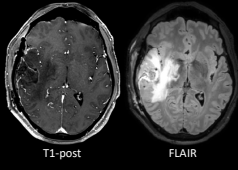
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Current Study: First post-chemo/rad MRI 3 months after resection



T1-post FLAIR

Prior Study: 24 hour post-op MRI



T1-post FLAIR

What criteria is used in glioblastoma cases to determine if a patient has complete response, partial response, stable disease, or disease progression?

Answer: The RANO criteria

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[Click here to learn more about the RANO Criteria](#)

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## RANO Criteria

Criterion	CR	PR	SD	PD
T1 gadolinium-enhancing disease	None	≤ 50% ↓	< 50% ↓, not < 25% ↓	≥ 25% ↑
T2/FLAIR	Stable or ↓	Stable or ↓	Stable or ↓	↑
New lesions	None	None	None	Present
Corticosteroids	None	Stable or ↓	Stable or ↓	N/A
Overall status	Stable or ↑	Stable or ↓	Stable or ↓	↓
Requirement for response	All	All	All	Any*

Abbreviations: RANO, Response Assessment in Neuro-Oncology; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; T1, gadolinium-enhanced magnetic resonance imaging; N/A, not applicable.

- Similar to RECIST criteria but developed specifically for glioblastoma
- RANO = Response Assessment in Neuro-Oncology
- Specifically developed for glioblastoma because:
  - FLAIR hyperintensity usually represents non-enhancing tumor and has to be taken into account
  - Changes in enhancement are more important than overall size of the lesions which are often cystic/necrotic

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Journal of Clinical Oncology 2010; 28:11, 1963-1972

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## Clinical Course

- Several follow-up MRI's were obtained at 2-3 month intervals, all showing no disease progression
- 1 year after the initial resection the patient had a new finding on his brain MRI

[Click here to see the MRI](#)

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Describe the abnormality on the new scan

[Click here to see the answer](#)

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Describe the abnormality on the new scan

There is mass like enhancement in the resection cavity and increasing surrounding FLAIR hyperintensity. The area of enhancement corresponds to an area of elevated perfusion

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Should pseudoprogession be in the differential diagnosis?

[Click here to see the answer](#)

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Should pseudoprogession be in the differential diagnosis?

No. Because this scan was performed more than 3 months after the end of radiation treatment, pseudoprogession is no longer a consideration.

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Current MRI (1 year after resection/chemo/radiation)      Prior MRI

Is the enhancing abnormality more likely to be tumor progression or radiation necrosis?

[Click here to see the answer](#)

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Current MRI (1 year after resection/chemo/radiation)      Prior MRI

Is the enhancing abnormality more likely to be tumor progression or radiation necrosis?

Tumor progression. Cerebral blood volume tends to be low in radiation necrosis. In this case the CBV is elevated favoring tumor progression.

[Click here to continue](#)      [Click here to learn more about radiation necrosis](#)

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### Radiation Necrosis

- Occurs in patients treated with radiation
- Tends to peak at around 18 months after radiation treatment (unlike pseudoprogression which occurs in the first 3 months after the end of radiation)
- Radiation necrosis causes tissue enhancement and can mimic tumor but tends to have low CBV on perfusion and low metabolic activity on PET/CT
- Over time radiation necrosis can increase, decrease, or stay the same (unlike pseudoprogression which improves over time)
- Radiation necrosis can occasionally cause symptoms and may require treatment

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### Clinical Course

- The patient underwent a re-resection of the enhancing abnormality
- Pathology showed recurrent glioblastoma
- The patient had an MRI 24 hours after the re-resection

[Click here to see the MRI](#)

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### 24 hours after re-resection of tumor

Is there any evidence of residual enhancing tumor at the resection site?

[Click here to see the answer](#)

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### 24 hours after re-resection of tumor

Is there any evidence of residual enhancing tumor at the resection site?

Yes. On the coronal images there is a small focus of enhancement with no intrinsic T1 hyperintensity on the pre-contrast images (red arrows). The linear hyperintensity at the posterior and inferior margin of the resection cavity on both T1 pre and post contrast images represents post operative blood products (yellow arrows)

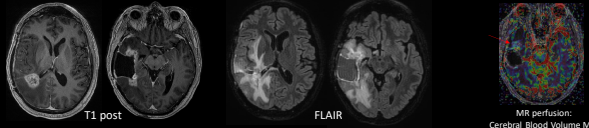
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### Clinical Course

A follow up MRI 2 months after the re-resection showed tumor progression



Findings: New mass-like enhancement around the resection cavity which corresponds to elevated CBV on perfusion MR. Increasing FLAIR hyperintensity around the resection cavity.

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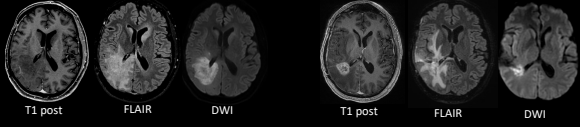
### Clinical Course

- In addition to more radiation and temozolomide the patient was started on bevacizumab (Avastin)
- After 2 months, a follow-up MRI was obtained.

[Click here to see the MRI](#)

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Current MRI (after bevacizumab + TMZ/radiation) Previous MRI

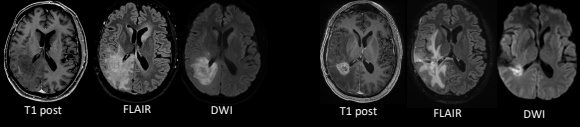


What are the findings on the new MRI?

[Click here to see the answer](#)

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Current MRI (after bevacizumab + TMZ/radiation) Previous MRI



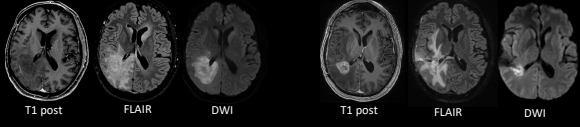
What are the findings on the new MRI?

The enhancement has nearly completely resolved but the FLAIR hyperintensity is larger. There are new FLAIR abnormalities around the frontal horn of the left lateral ventricle and right caudate. The area of diffusion restriction has increased in size.

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Current MRI (after bevacizumab + TMZ/radiation) Previous MRI

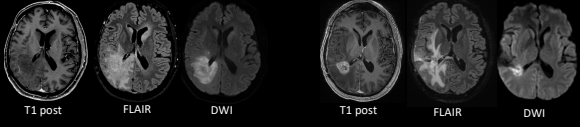


What explains the improved enhancement despite worsening appearance on FLAIR an DWI?

[Click here to see the answer](#)

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Current MRI (after bevacizumab + TMZ/radiation) Previous MRI



What explains the improved enhancement despite worsening appearance on FLAIR an DWI?

This represents "pseudoresponse" which is something that occurs in patients treated with bevacizumab (Avastin).

[Click here to learn more about pseudoresponse](#) [Click here to continue](#)

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## Pseudoresponse

- Bevacizumab is an antiangiogenic chemotherapy
- It can cause constriction of vessels leading to a decrease in enhancement despite progression of non-enhancing tumor
- The diagnosis is made when a patient being treated with bevacizumab has improved enhancement but worsening FLAIR and/or diffusion abnormalities

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## Summary

This case follows a patient with Glioblastoma. Concepts that are highlighted in this module include:

- Initial diagnosis and differential diagnosis of brain mass
- Relevant genetic markers in GBM
- What to look for on immediate post operative images
- What to look for on follow-up post treatment scans
- The typical chemotherapies used for GBM
- RANO criteria for characterization of GBM on follow-up imaging
- True progression
- Pseudoprogression
- Pseudoresponse
- Radiation necrosis

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