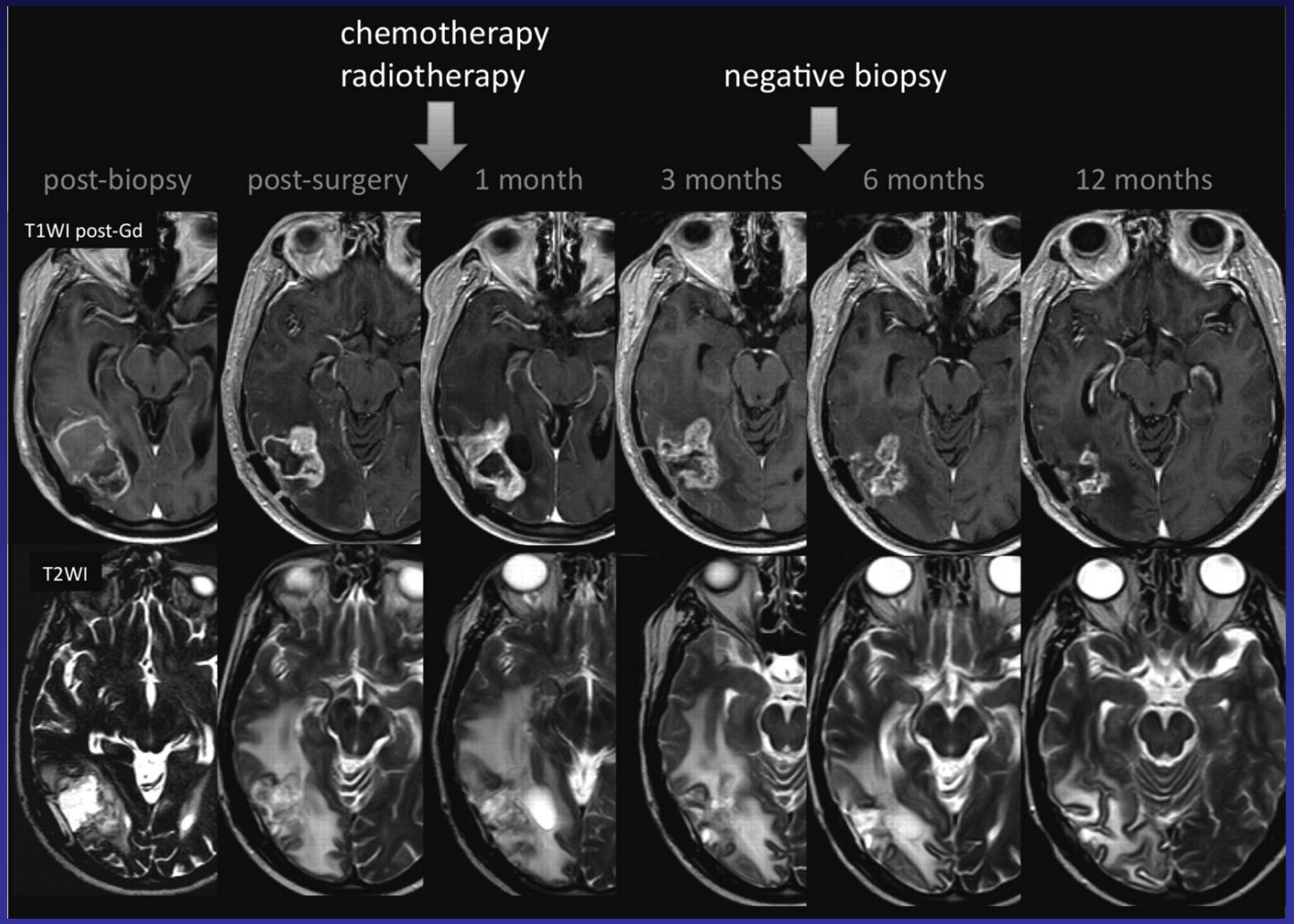
# Pseudoprogression

- Current standard of care for GBM is surgical resection followed by RT and concomitant and adjuvant temodar (temozolomide, TMZ).
- Shortly after completion of RT
  - patients with high-grade brain tumors can present with an increase in contrast-enhancing lesion size
  - followed by improvement or stabilization without any further treatment.
  - This mimics tumor progression
- Perhaps pseudoprogression represents an active "inflammatory" response against the tumor.

# Avastin

- Bevacizumab, a humanized monoclonal antibody against vascular endothelial growth factor A
- Blocks a protein called vascular endothelial growth factor, or VEGF.
- Normal cells make VEGF, but some cancer cells make too much VEGF.
- Blocking VEGF may prevent the growth of new blood vessels, including normal blood vessels and blood vessels that feed tumor.

# Example


chemotherapy
radiotherapy
negative biopsy
post-biopsy
post-surgery
1 month
3 months
6 months
12 months
T1WI post-Gd
T2WI

# MGMT

- DNA repair enzyme that contributes to temozolomide resistance.
- Methylation of the MGMT promoter, found in approximately 45% of glioblastoma multiformes.
- Results in an epigenetic silencing of the gene, decreasing the tumor cell's capacity for DNA repair and increasing susceptibility to temozolomide

# O6-Methylguanine *DNA* MGMT Promoter

- Methylation status of the MGMT promoter has been shown to be a potent prognostic factor in patients with GBM;
- Cells that are deficient in MGMT have shown an increased sensitivity to TMZ.
- Patients with low MGMT expression (due to methylation of the promoter) benefit more from adjuvant TMZ.
- Patients with methylated MGMT show pseudoprogression more frequently

# Pathophysiology

- Increased contrast enhancement and peritumoral edema following RT, with or without concomitant TMZ, may reflect tumor growth if the changes become stable.
- Increased contrast enhancement and peritumoral edema that diminish with time are characteristic of pseudoprogression.
  - Although it can occur following RT alone, pseudoprogression is widely believed to be more frequent following concomitant RT-TMZ

# Pseudoprogression

- Can be associated with other chemotherapy regimens and has even been observed in cases in which chemotherapy-infused wafers were placed in the surgical cavity
- By definition, it subsides without further treatment
  - but, in some cases, it appears to progress with time into radiation necrosis or treatment-related necrosis
- Concept of therapy-induced necrosis and its radiologic manifestations of pseudoprogression should replace the outdated term “early necrosis”

# Cont

- gliosis and reactive radiation-induced changes without evidence of viable tumor.
- may represent an exaggerated response to effective therapy, involving early changes to the vascular endothelium and the BBB,
- as well as oligodendroglial injury leading to inflammation and increased permeability

# Diagnosis

- Diagnosis should depend on follow-up scans until an improved method is established.
- It is not incorrect to say that pseudoprogression represents a mild and self-limiting variant of treatment-related necrosis.

# Example

- If increased enhancement at the first post-RT MR imaging is observed, this is some sort of radiation effect and most likely will subside.
- However, early rapid progression cannot be ruled out and is merely the less probable diagnosis, not something that imaging findings can confidently establish.

# Rad Nec vs Pseudo

## "Time frame"

- Radiation necrosis typically occurs 18–24 months post-treatment and has repeatedly been shown to be difficult to distinguish from recurrence.
- Pseudoprogression is observed only in the first few months after treatment, much earlier than radiation necrosis.
- Therapy-induced necrosis and its radiologic manifestations of pseudoprogression should replace the outdated term "early radionecrosis"; we concur

# Advanced MR imaging

- Neither DWI nor DTI provides sufficient information for differential diagnosis between pseudoprogression and true tumor progression.
- MR spectroscopy
  - In most settings, the differential diagnosis between pseudoprogression and true disease progression is highly challengeing.
- No specific imaging characteristic findings are yet able to make such a differentiation

# Bottom Line

- Clinical course, including imaging during a lengthy follow-up interval, enables the distinction of these 2 entities rather than specific imaging data.
- On some occasions, a brain biopsy may be needed.
- **DSC** dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging shows promise.