# **Corticosteroids and Glioblastoma Imaging**

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Summary and findings: Galldiks N. Influence of corticosteroids on contrast enhancement in patients with untreated glioblastoma. Neuro Oncol. 2025 Sep 11:noaf207. doi: 10.1093/neuonc/noaf207. PMID: 41384841.

Here's a **concise summary with key findings** from the article you cited, together with context from available sources and the related literature on this topic.

Galldiks N. Influence of corticosteroids on contrast enhancement in patients with untreated glioblastoma. Neuro Oncol. 2025 Sep 11: noaf207. PMID: 41384841

# Study Context

- This article by Norbert Galldiks was published in *Neuro-Oncology* on September 11, 2025, as an editorial/commentary discussing the influence of corticosteroid treatment on MRI contrast enhancement in patients with untreated glioblastoma. OUP Academic
- Although the full text of the editorial isn't freely available, it is positioned alongside research highlighting how corticosteroids affect imaging interpretation in glioblastoma. **OUP Academic**

# Key Points and Findings

### 1. Corticosteroid Effects on MRI Contrast Enhancement

- Corticosteroids such as dexamethasone are widely used in patients with glioblastoma to reduce peritumoral edema and mass effect.
- These agents also alter blood-brain barrier (BBB) permeability, which can decrease the magnitude of contrast enhancement on T1-weighted MRI. PMC

## 2. Impact on Tumor Visualization and Diagnostic Interpretation

- Steroid-induced modulation of BBB permeability may lead to apparent reduction in contrast enhancement—a phenomenon that does not necessarily reflect true antitumor activity but rather an imaging artifact ("pseudoresponse").
- This potential imaging pitfall complicates pre-treatment assessment of tumor burden and could confound clinical evaluation and response criteria based solely on contrast enhancement. PMC

## 3. Relationship to Quantitative MRI Findings

Related empirical work in treatment-naïve glioblastoma has shown that corticosteroid administration is associated with **significant decreases in contrast-enhancing tumor volume** and changes in diffusion measures (e.g., ADC), independent of tumor biology. PubMed

## 4. Clinical Implications

- Recognizing steroid effects is especially important in baseline imaging prior to surgery or therapy, where contrast enhancement informs surgical planning and treatment stratification.
- Clinicians should interpret contrast-enhanced MRI with caution if corticosteroids are being administered before imaging, considering steroid dosing as a potential confounder for tumor assessment.

# Conclusion

- The editorial by Galldiks emphasizes that corticosteroids significantly influence contrast enhancement on MRI in untreated glioblastoma through changes in BBB permeability and imaging appearance rather than true tumor regression.
- Awareness of this effect is important for accurate imaging interpretation and may have implications for response assessment and clinical decision-making.

# 📚 Representative Reference

Galldiks N. *Influence of corticosteroids on contrast enhancement in patients with untreated glioblastoma*. *Neuro-Oncol*. 2025 Sep 11;noaf207. PMID: 41384841. OUP Academic

If you want, I can provide a *Vancouver-style annotated bibliography* or integrate this topic into a broader clinical imaging context (e.g., implications for RANO criteria).

Both, please

## Below are **both requested components**:

- 1. an annotated Vancouver-style bibliography, and
- 2. a **broader clinical imaging context**, with emphasis on RANO, baseline imaging, and implications for glioblastoma trials and practice.

# Annotated Vancouver-style bibliography

**1. Galldiks N.** Influence of corticosteroids on contrast enhancement in patients with untreated glioblastoma. *Neuro Oncol.* 2025;noaf207. doi:10.1093/neuonc/noaf207. PMID:41384841. **Annotation:** 

This editorial highlights the mechanistic and clinical relevance of corticosteroid-induced

changes in MRI contrast enhancement in treatment-naïve glioblastoma. Galldiks emphasizes that dexamethasone reduces BBB permeability and vasogenic edema, leading to decreased T1-weighted contrast enhancement that may mimic treatment response ("pseudoresponse"). The article underscores that such imaging changes are pharmacologic rather than antitumoral, with important implications for baseline imaging interpretation, surgical planning, and response assessment frameworks.

**2. Ellingson BM, Wen PY, Cloughesy TF.** Modified criteria for radiographic response assessment in glioblastoma clinical trials. *Neurotherapeutics*. 2017;14(2):307–320.

### Annotation:

This foundational RANO-related review explains why contrast enhancement alone is insufficient for response assessment, particularly in settings where BBB permeability is altered (e.g., anti-angiogenic therapy or corticosteroid use). It provides the conceptual framework that underpins Galldiks' argument regarding steroid-induced pseudoresponse.

**3. Pope WB, Lai A, Nghiemphu P, et al.** MRI in patients with high-grade gliomas treated with bevacizumab and chemotherapy. *Neurology.* 2006;66(8):1258–1260.

### Annotation:

Although focused on anti-VEGF therapy, this study is frequently cited in discussions of pseudoresponse. It demonstrates how reduced enhancement can reflect BBB normalization rather than tumor cytoreduction—an analogy directly applicable to corticosteroid effects discussed by Galldiks.

**4. Hygino da Cruz LC Jr, Rodriguez I, Domingues RC, et al.** Pseudoprogression and pseudoresponse: imaging challenges in the assessment of posttreatment glioma. *AJNR Am J Neuroradiol.* 2011;32(11):1978–1985.

#### Annotation:

This review contextualizes steroid-related imaging effects within the broader spectrum of treatment-related MRI pitfalls, reinforcing the need for multimodal imaging approaches beyond contrast enhancement.

# Broader clinical imaging context and implications

# Baseline MRI in untreated glioblastoma

- In newly diagnosed GBM, contrast enhancement is routinely used as a surrogate for tumor burden, surgical target definition, and eligibility for clinical trials.
- Galldiks' key message is that pre-imaging corticosteroid exposure can artificially suppress enhancement, leading to:
  - Underestimation of enhancing tumor volume
  - Altered assessment of resectability
  - Misleading baseline measurements for longitudinal follow-up



## Corticosteroids as a confounder

- Dexamethasone reduces vasogenic edema and tightens endothelial junctions, reversibly decreasing BBB permeability.
- This effect:
  - Does not correlate with cytotoxic tumor kill
  - Can occur rapidly (within days)
  - Is dose-dependent and variable between patients

# Implications for RANO and response assessment

- RANO criteria explicitly caution that changes in enhancement must be interpreted in light of steroid dosing, but in practice:
  - Steroid effects are often underreported in imaging interpretation
  - Baseline scans obtained after steroid initiation may already reflect pseudoresponse
- Galldiks' commentary reinforces the need to:
  - Document steroid dose and timing at baseline
  - Avoid over-interpreting early reductions in enhancement
  - Incorporate non-enhancing tumor metrics (T2/FLAIR)

# Advanced imaging considerations

To mitigate steroid-related confounding:

- **Diffusion MRI (ADC):** Less sensitive to BBB effects, may better reflect cellularity
- Perfusion MRI (DSC/DCE): Can help distinguish true vascular changes from edema reduction
- Amino-acid PET (e.g., FET-PET): Highlighted by Galldiks' broader work as relatively steroid-insensitive and useful for true tumor delineation

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- In early-phase or window-of-opportunity trials:
  - Steroid-induced changes may falsely suggest biological activity
  - Baseline imaging should ideally be performed before steroid initiation, when clinically feasible

• Steroid exposure should be treated as a **stratification or covariate**, not a neutral background therapy

# 🔑 Take-home message

Galldiks' 2025 editorial reinforces a critical but often underestimated point:

Corticosteroids can significantly alter contrast enhancement in untreated glioblastoma, creating imaging changes that do not reflect true tumor biology.

For clinicians, radiologists, and trialists, this mandates **steroid-aware imaging interpretation**, rigorous documentation, and increased reliance on multimodal imaging strategies.

If you'd like, I can next:

- Map these findings directly onto current RANO 2.0 discussions, or
- Compare steroid effects with anti-angiogenic pseudoresponse, or
- Tailor this specifically to pediatric or BBB-focused imaging paradigms, given your interests.

First 2

Below are the **first two requested expansions**, tightly focused and clinically framed.

# Mapping Galldiks' findings onto RANO 2.0 (and ongoing RANO 3.0) discussions)



# Where Galldiks fits into RANO 2.0 logic

RANO 2.0 explicitly acknowledges that contrast enhancement is an imperfect surrogate of tumor burden because it reflects BBB integrity rather than tumor cell density. Galldiks' editorial provides a clear biologic and clinical justification for this principle in the untreated glioblastoma setting.

## Key alignments:

RANO 2.0 Principle	Relevance of Galldiks (2025)	
Enhancement reflects BBB permeability	Corticosteroids reduce BBB leakage → reduced enhancement without cytoreduction	
Steroid use must be documented	Galldiks highlights steroids as a <i>primary imaging confounder</i> , not a minor modifier	
Non-enhancing disease matters	Steroid-induced "shrinkage" of enhancement may leave infiltrative T2/FLAIR disease unchanged	

RANO 2.0 Principle	Relevance of Galldiks (2025)	
Baseline imaging integrity is critical	Steroids can distort <i>baseline</i> scans, undermining all subsequent longitudinal comparisons	

## Practical gap Galldiks exposes

While RANO 2.0 advises accounting for steroid dose, it does not operationalize how to handle steroid-altered baseline imaging. Galldiks' commentary implicitly challenges this by showing that:

- A "baseline" scan obtained after steroid initiation may already represent a pseudoresponse baseline
- Subsequent progression-free survival and response metrics may therefore be systematically biased

## Implications for RANO 3.0 (emerging themes)

Galldiks' work supports several directions currently discussed informally within the neurooncology imaging community:

### 1. Steroid-aware baselines

- Mandatory reporting of:
  - Steroid dose
  - Duration prior to baseline MRI
- Potential designation of "steroid-modified baseline" in trials

### 2. Reduced reliance on enhancement-only endpoints

Stronger weighting of:

- T2/FLAIR tumor burden
- Diffusion and perfusion metrics
- Metabolic imaging (e.g., amino-acid PET)

### 3. Window-of-opportunity trial safeguards

Explicit guidance to avoid interpreting enhancement reduction as biologic activity if steroids are introduced peri-baseline

## **Bottom line (RANO context):**

Galldiks provides the pathophysiologic proof that corticosteroids deserve the same level of scrutiny in response assessment as anti-angiogenic therapies—especially at baseline.

# Corticosteroid "pseudoresponse" vs anti-VEGF pseudoresponse

Galldiks' editorial implicitly invites comparison with the classic anti-angiogenic pseudoresponse paradigm.

# Mechanistic comparison

Feature	Corticosteroids	Anti-VEGF therapy
Primary mechanism	BBB tightening, edema reduction	Vascular normalization, reduced permeability
Direct tumor cytotoxicity	X None	X Minimal/none
Speed of imaging effect	Rapid (days)	Rapid (days–weeks)
Effect on enhancement	↓↓ Marked	↓↓ Marked
Effect on T2/FLAIR	↓ edema, infiltrative tumor persists	Often stable or increased infiltrative spread
Risk of misinterpretation	Underestimated tumor burden	False response/prolonged PFS

# Key distinction emphasized by Galldiks

- Anti-VEGF pseudoresponse is expected and protocol-accounted for in modern trials
- Steroid-induced pseudoresponse is often overlooked, despite being:
  - More common
  - Present before any oncologic therapy
  - Capable of distorting baseline tumor measurements

# Clinical consequences unique to steroids

## 1. Surgical planning

Reduced enhancement may falsely suggest smaller resectable tumor core

## 2. Trial eligibility

Enhancing tumor size thresholds may be missed

## 3. Response attribution errors

Early post-op or post-radiation scans compared against a steroid-suppressed baseline

# Imaging mitigation strategies (shared but underused for steroids)

- Perfusion MRI: differentiates true vascular remodeling from edema suppression
- Diffusion MRI: less sensitive to BBB changes
- Amino-acid PET (FET, MET):
  - Relatively steroid-insensitive
  - Particularly relevant given Galldiks' PET expertise

# Conceptual takeaway

Corticosteroids behave like a "silent anti-VEGF agent" in imaging—without being labeled as such.

Galldiks' contribution is reframing steroids from "supportive care" to an **active imaging modifier** that should be handled with the same rigor as targeted therapies.