



# RANO 2.0: critical updates and practical considerations for radiological assessment in neuro-oncology

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## Abstract

Appropriate response assessment criteria are crucial for accurate evaluation of clinical trial outcomes, and numerous criteria have been proposed to address this need. With the introduction of Response Assessment in Neuro-Oncology (RANO) criteria version 2.0 (RANO 2.0) in 2023, response assessment in gliomas has evolved significantly, requiring both clinicians and radiologists to develop a comprehensive understanding of its modifications and implementation. This review first provides an overview of standard management and imaging schedule in glioma treatment. We then review the basic framework of RANO 2.0, inherited from previous response criteria, with particular emphasis on major modifications to this framework: the implementation of the Brain Tumor Imaging Protocol and the adoption of post-radiation scan as the baseline scan. Additionally, we analyze critical changes in response evaluation and interpretation, specifically focusing on the role of preliminary progressive disease assessment with confirmation scans, and the elimination of T2/FLAIR lesion measurements from enhancing tumor assessment. Through illustrative clinical cases, we demonstrate the practical application of these modifications and discuss the implementation of three distinct imaging-based categories: enhancing tumor, non-enhancing tumor, and tumors with both enhancing and non-enhancing components (in short, mixed tumor). This comprehensive narrative review provides clinicians with practical guidance for implementing RANO 2.0 in their clinical practice.

**Keywords** Glioma · MRI · Treatment response criteria · RANO 2.0 · Pseudoprogression · Pseudoresponse

## Introduction

The Response Assessment in Neuro-Oncology (RANO) criteria version 2.0 (RANO 2.0), published in 2023, were designed as comprehensive framework for treatment response assessment in clinical trials across all glioma

subtypes [1]. Here, “all” encompasses a wide range of clinical and pathological contexts, including: (1) contrast enhancement pattern, (2) newly diagnosed setting versus recurrent disease, (3) presence or absence of residual disease following initial treatment, (4) type of therapeutic intervention, (5) histological grade, and (6) molecular classification (e.g., isocitrate dehydrogenase (*IDH*) mutation status). This breadth represents an ambitious undertaking. Rather than applying a uniform assessment strategy across heterogeneous disease presentations, the effective use of RANO 2.0 requires careful consideration of these factors to appropriately identify and categorize target lesions [2].

This review begins by introducing the standard diagnostic approaches, therapeutic strategies, and imaging protocols and schedules essential for glioma management. Building upon foundational elements of previous response criteria, we explore RANO 2.0's key modifications, particularly focusing on the standardization of imaging acquisition protocols and the implementation of post-radiation baseline scans which

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allows for more accurate response assessment following initial treatment. The review also discusses critical methodological changes, including the introduction of preliminary progressive disease (PD) assessment with confirmation scans and the refinement of T2/FLAIR lesion evaluation criteria. Finally, through carefully selected clinical scenarios, we show the practical implementation of these modifications across various tumor types, providing concrete guidance for response assessment in clinical practice. This work aims to bridge the gap between updated evaluation criteria and their application in everyday clinical settings.

## Standard management and imaging protocols in glioma

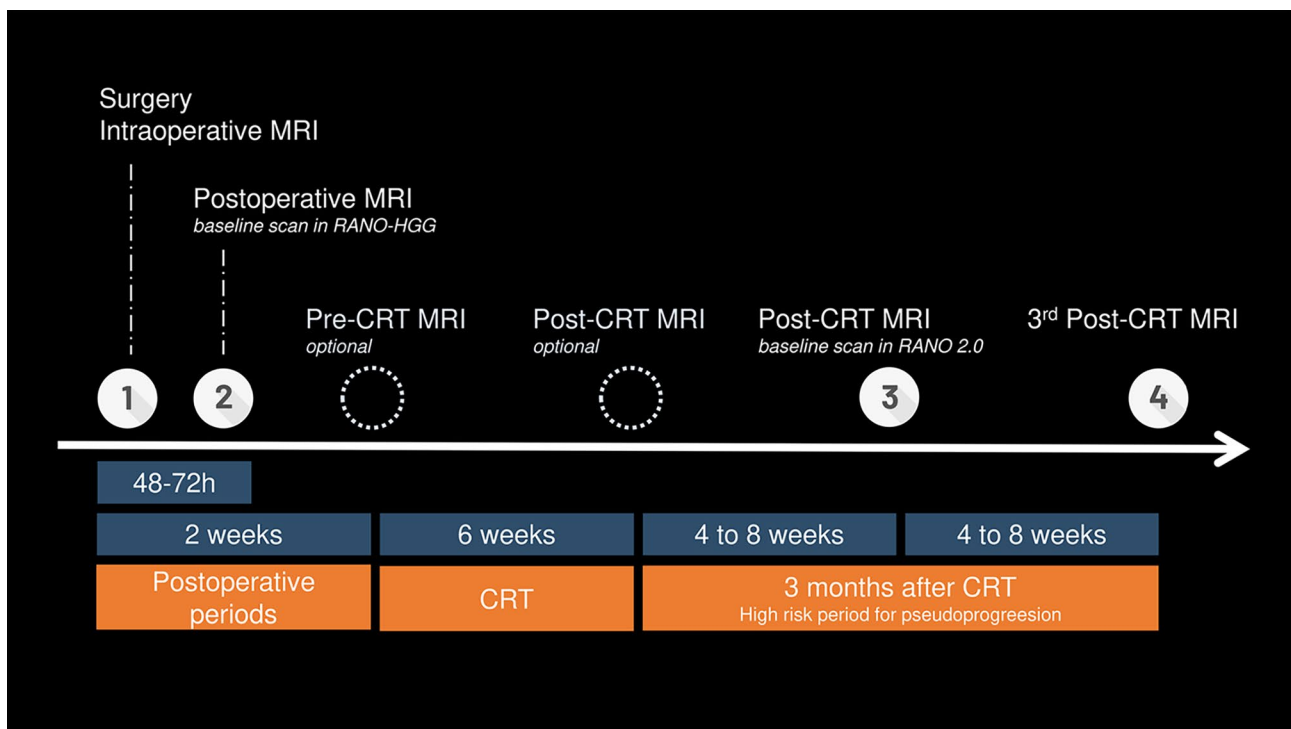
Glioma management requires a multifaceted approach that integrates histological grade and tumor subtype with other critical factors such as tumor location, molecular markers, and patient characteristics [3]. While maximal safe resection is a universal goal to reduce tumor burden, the feasibility of surgical intervention varies considerably based on tumor location and patient-specific factors, sometimes limiting procedures to partial resection or biopsy [4, 5]. Even after achieving gross total resection, adjuvant therapy remains necessary due to glioma infiltration beyond radiographically visible margins [6, 7]. For high-grade gliomas, after resection, the standard of care consists of the Stupp regimen, comprising concurrent temozolomide (TMZ) and radiotherapy followed by adjuvant TMZ chemotherapy [8, 9]. Tumor-treating fields are increasingly being incorporated into this therapeutic protocol to further improve outcomes [10, 11]. For low-grade gliomas, management decisions are more nuanced, with varying approaches to the timing and implementation of postoperative chemotherapy and radiotherapy based on molecular profiles and progression risk factors [12]. In recurrent disease settings, therapeutic options include repeat surgical intervention when feasible, alternative chemotherapy regimens, bevacizumab in selected cases, and consideration for radiation therapy if not previously administered or if re-irradiation is deemed appropriate [13].

In recent years, molecular biological characteristics, particularly *IDH* mutation status, have gained increasing significance in glioma classification [14–16]. While the fundamental treatment strategy remains largely unchanged, treatment selection for low-grade gliomas has changed based on molecular biological characteristics. A notable example involves *IDH*-mutant low-grade gliomas. *IDH* inhibitors have demonstrated improvement of progression-free survival (PFS) and delaying the time to the next intervention, and are expected to be incorporated into routine clinical practice [17]. Another example is a group termed molecular glioblastoma. A subset of *IDH*-wildtype gliomas that are

histologically classified as lower-grade are now recognized as molecular glioblastoma [18–23]. Although definitive evidence is still lacking [24], these cases are increasingly being treated more aggressively, following protocols similar to those for glioblastoma.

MRI with contrast agent has become the de facto standard for appropriate assessment of treatment response. However, to our knowledge, there are no definitive guidelines regarding imaging schedules [25–27]. While several groups have conducted excellent retrospective studies [28–30], current imaging protocols for glioma appear to be based more on pragmatic considerations rather than robust evidence. Figure 1 illustrates our institution's treatment and MRI imaging schedule for high-grade gliomas. At our institution, the extent of resection is initially verified using intraoperative MRI. The first postoperative MRI with contrast agent is performed within 48 h following surgical resection. Additional MRI examinations before initiating concurrent chemoradiotherapy (CRT) at approximately 2 weeks post-surgery and following completion of the standard 6-week radiotherapy regimen, while optional, provide valuable clinical information for treatment response evaluation. Subsequently, follow-up MRI examinations are scheduled at regular intervals of one to two months to monitor disease progression and therapeutic efficacy. This represents an observational clinical case rather than a formal clinical trial; therefore, the follow-up interval will be incrementally extended contingent upon the absence of disease recurrence. If there is a suspicion of recurrence, a further examination may be carried out after approximately one month. In low-grade gliomas, while MRI scanning intervals tend to be longer compared to high-grade gliomas, the nature of the disease necessitates long-term follow-up. Furthermore, as contrast-enhancing lesions in these cases often emerge after extended periods of post-treatment surveillance, determining how long to continue administering gadolinium-based contrast agents throughout this prolonged monitoring presents a particularly challenging clinical consideration.

Clinical trials in glioma encompass both newly diagnosed and recurrent cases. While many of these trials evaluate survival improvement through novel therapeutic agents as their primary outcome, some aim to optimize existing treatment modalities, such as radiation dose reduction in elderly patients [31, 32]. In these clinical trials, while some protocols strictly specify MRI acquisition sequences, others may accept standard institutional imaging sequences provided they meet basic requirements. The timing of imaging acquisitions is generally specified in the protocol schedules. Treatment response is evaluated by trial physicians using standardized criteria. Although response assessments are typically performed at the treating institutions, central radiologic review may be required in many trials. Discrepancies between local and central assessments can occur [33, 34],



**Fig. 1** Representative treatment and imaging schedule for high-grade gliomas in Kyoto University hospital

potentially affecting trial outcomes and patient management decisions. Hence, these response assessment criteria are generally required to demonstrate high inter-observer reproducibility regardless of the evaluating physicians, and to show strong correlation with patient outcomes, particularly PFS.

### Basic framework and technical requirements in RANO 2.0

Since Levin proposed the first response assessment criteria in 1977 [35], several criteria have been introduced for evaluating treatment response in glioma clinical trials [36–41]. Until very recently, RANO-HGG (published in 2010) [37] and RANO-LGG (published in 2011) [38] had been widely used as response assessment criteria in numerous clinical trials [17, 33, 42]. Based on the accumulated knowledge and experience over the last decade since the publication of these two criteria, RANO 2.0 was introduced in 2023 [1]. These criteria have already been adopted in several imaging research studies [43, 44] and are expected to be implemented in many upcoming brain tumor trials. Therefore, radiologists need to become familiar with these criteria.

While RANO 2.0 inherits many elements from RANO-HGG and RANO-LGG, it indeed incorporates significant modifications (Table 1). Most notably, RANO 2.0 incorporates major revisions regarding the imaging modalities,

target lesions, and timing used for response assessment. In this section, we will focus on these modifications, while addressing the remaining improvements in the latter part of this article.

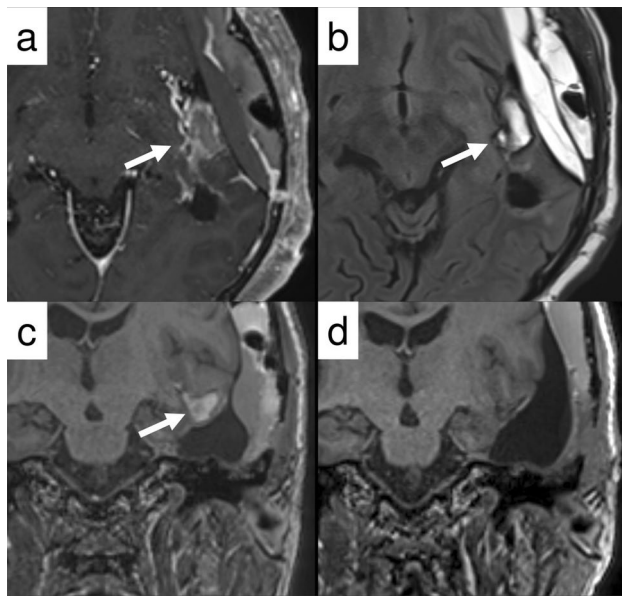
### Use of brain tumor imaging protocol

Both in RANO (RANO-HGG and RANO-LGG) and RANO 2.0, the MRI sequences utilized for glioma response assessment includes non-contrast and contrast-enhanced T1WI, T2WI, and T2-FLAIR imaging. Careful evaluation of multiple sequences is essential both for assessing target lesions and for preventing the misdiagnosis of treatment-related changes (e.g., hemorrhage, infarction) as tumor progression (Fig. 2). While multiparametric evaluation methods incorporating advanced sequences such as diffusion-weighted image (DWI), magnetic resonance spectroscopy, and perfusion-weighted image (PWI), as well as positron emission tomography (PET) imaging with different tracers, are clinically significant [45–52], these modalities are not included in these criteria [53]. (Note: A separate RANO-PET framework for amino acid PET imaging was published in 2024 [54], but lies beyond the scope of this review.)

One of the major revisions in RANO 2.0 is the recommendation to use the Brain Tumor Imaging Protocol (BTIP) [55, 56], which was not addressed in the original RANO criteria that lacked protocols or sequence details.

**Table 1** Comparison of radiographic response assessment between RANO-HGG, RANO-LGG and RANO 2.0

	RANO-HGG		RANO-LGG		RANO 2.0
	Post-operation/pre-radiation	Post-operation/pre-radiation	Post-operation/pre-radiation	Post-radiation	
Baseline scan for newly diagnosed glioma					
Measurement technique	2D	2D or 3D (optional)	2D or 3D (optional)	2D or 3D (optional)	
Tumor component evaluation					
Enhancing lesion	Required	Required	Required	Required	
Non-enhancing lesion (i.e., T2/FLAIR lesion)	Required	Required	Required	Omitted for glioblastoma; can be considered with agents that affect vascular permeability; required for non-enhancing or mixed tumor	
Confirmation scan (performed after > 4 weeks) for PD					
Within the first 12 weeks of completion of RT	Optional	Optional		Mandatory	
Beyond 12 weeks of RT					
Confirmation scan (performed after > 4 weeks) for CR/PR/MR	Mandatory	Mandatory		Optional; mandatory confirmation scan can be considered with therapy associated with high rates of pseudoprogression, or <i>IDH</i> -mt glioma	
Evaluation Glioma	High-grade glioma	Low-grade glioma		All glioma	



**Fig. 2** Postoperative imaging of a 72-year-old man with *IDH*-wildtype glioblastoma. **a** Contrast-enhanced T1WI shows a hyperintense lesion (arrow) adjacent to the resection cavity. **b** FLAIR sequence shows the same lesion as hyperintense with a smooth intersulcal contour. **c** Coronal T1WI confirms the lesion is confined between cerebral sulci. **d** Follow-up post-contrast T1WI shows complete resolution of the lesion, consistent with an intersulcal hematoma

This standardized approach is strongly recommended to reduce imaging assessment variability across clinical sites. The BTIP is summarized in Table 2. Briefly, this protocol features parameter-matched pre and post-contrast 3D T1WI with high spatial resolution ( $\leq 1.5$  mm isotropic), either

2D gapless (with  $\leq 4$  mm slice thickness) or 3D ( $\leq 1.5$  mm isotropic) T2WI and T2-FLAIR images, and DWI. More advanced sequences, such as PWI, can be added to the BTIP protocol. For optimal consistency throughout the study period, participants should undergo MRI scans using either the same machine or equipment with equivalent magnetic field strength. While not mandatory, 3D T2WI and FLAIR sequences are included as options, enabling more precise volumetric measurements and offering advantages in the evaluation of *IDH*-mutant gliomas—typically non-enhancing lesions characterized by slow progression [57]. While both 2D and 3D measurements are acceptable, the measurement approach must be predefined in accordance with sponsor preferences to maintain methodological consistency throughout the study [2].

### Measurable lesion, non-measurable disease and target lesions

Similar to the original RANO-HGG/LGG criteria, RANO 2.0 initially classifies lesions as measurable or non-measurable, from which one or more target lesions are selected. Measurable disease is fundamentally defined as clearly demarcated lesions with a minimum short-axis diameter of 10 mm, extending across at least two slices in 2D imaging. For 2D assessment, select the imaging plane that displays the greatest extent of the lesion. In the context of volumetric analysis, target lesions are defined as those measuring at least 10 mm in each of the three orthogonal dimensions. For enhancing tumors, the enhancing component is measured, while for non-enhancing tumors, the T2 hyperintense

**Table 2** Minimum standard 3 T MRI protocol

	3D-T1w Pre	Ax 2D FLAIR	3D FLAIR	Ax 2D DWI <sup>a</sup>	Ax 2D T2WI	3D-T1w Post
Sequence	IR-GRE	TSE/FSE	TSE/FSE	SS-EPI <sup>b</sup>	TSE/FSE	IR-GRE
Plane	Sagittal/axial	Axial	Sagittal/axial	Axial	Axial	Sagittal/axial
Mode	3D	2D	3D	2D	2D	3D
TR [ms]	2100	> 6000	90–140	> 5000	> 2500	2100
TE [ms]	Min	100–140	6000–10000	Min	80–120	Min
TI [ms]	1100	2000–2500 <sup>c</sup>	2000–2500 <sup>c</sup>	N/A	N/A	1100
Flip angle	10°–15°	90°/≥ 160°	Not specified	90°/180°		10°–15°
Frequency	≥ 172	≥ 256	≥ 244	≥ 128	≥ 256	≥ 172
Phase	≥ 172	≥ 256	≥ 244	≥ 128	≥ 256	≥ 172
NEX	≥ 1	≥ 1	Not specified	≥ 1	≥ 1	≥ 1
FOV	256 mm	240 mm	≤ 250 mm	240 mm	240 mm	256 mm
Slice Thickness	≤ 1.5 mm	≤ 4 mm	≤ 1.5 mm	≤ 4 mm	≤ 4 mm	≤ 1.5 mm
Gap/spacing	0	0	0	0	0	0
Parallel imaging	Up to 2×	Up to 2×	Up to 2×	Up to 2×	Up to 2×	Up to 2×

<sup>a</sup>b factor is 0, 500, 1000 s/mm<sup>2</sup> ≥ 3 direction; it is acceptable to omit the intermediate shell b = 500 s/mm<sup>2</sup>, if needed

<sup>b</sup>In the event of significant patient motion and EPI is not an option, a radial acquisition scheme may be used

<sup>c</sup>Chosen based on vendor recommendation for optimized protocol and field strength

lesion is measured. Non-measurable disease is those that do not meet the measurable lesion criteria, specifically lesions with a short-axis diameter less than 10 mm and/or ill-defined borders.

Special attention is required when measuring lesions with large cystic components, predominantly necrotic lesions, or lesions around the resection cavity [2]. For lesions predominantly composed of necrotic or cystic components, measurements should be confined to the solid portions of the tumor, excluding the dimensions of necrotic or cystic regions. When measuring lesions along the resection cavity, it is critical that the measurements exclude the cavity itself—the diameters should lie entirely within the lesion.

In cases presenting with multiple measurable lesions, target lesion selection should be limited to a minimum of two and a maximum of three lesions when assessing either enhancing or non-enhancing tumors. For tumors with both enhancing and non-enhancing components (namely mixed tumor presentation), target lesion selection may comprise up to two enhancing and two non-enhancing lesions. The primary criterion for target lesion selection should prioritize lesions demonstrating progressive enlargement, irrespective of their comparative dimensions. This selection principle applies to multiple lesion cases, where dimensional dominance is subordinate to documented growth progression in determining target status.

## Baseline scan

The immediate postoperative MRI scan, obtained within 48 h of surgery, has been used as the baseline MRI in most response criteria for newly diagnosed gliomas, including RANO-HGG [37] and immunotherapy RANO [39]. This approach was originally adopted to provide prompt assessment of residual tumor and establish an early reference point for tracking treatment effects. The surgical goal is typically to remove the enhancing portion of the tumor; however, non-specific enhancement frequently develops in the wall of the surgical cavity within 48–72 h after surgery and can persist for weeks [58]. Therefore, RANO recommended obtaining baseline scans within 24–48 h after surgery to avoid misinterpreting these postoperative changes as residual enhancing disease.

By contrast, the modified RANO (mRANO) criteria recommend using the first post-radiotherapy MRI as the baseline for newly diagnosed gliomas to reduce the impact of the increased contrast enhancement from pseudoprogression (PsP) after CRT [40], and address the challenges associated with immediate postoperative scans including the presence of postoperative changes (blood products and edema) [59], and variability in corticosteroid dosing, timing of the scans, and imaging techniques used.

Recent research has shown that even with intraoperative MRI, postoperative changes related to surgery can cause contrast enhancement in a significant proportion of patients [60]. This finding, indicating that structural changes from surgery itself can lead to contrast enhancement in the immediate postoperative period, highlights a potential limitation of the original RANO approach. In contrast, mRANO aims to minimize the impact of radiotherapy and improve the accuracy of treatment response assessment by establishing the post-radiotherapy MRI as the baseline scan. RANO 2.0 also adopts this mRANO principle, setting the baseline scan at around 4 weeks (21–35 days) after the completion of radiation therapy, primarily to minimize the influence of PsP [1]. A recent retrospective large single-center study demonstrated that post-radiation scans showed a significantly higher correlation with PFS, a reliable endpoint in clinical trials, compared to immediate post-surgical scans, supporting the validity of this change in newly diagnosed or recurrent glioblastoma [61].

With the exception of glioblastoma, radiation therapy is not necessarily used as the initial treatment for glioma. Even in such cases, Ellingson et al. suggest that it is not necessary to use the scan immediately after surgery as the baseline [2]. Instead, it is preferable to take a pretreatment scan at a time when the effects of the surgical invasion have lessened, and within 14 days of the start of treatment. For recurrent gliomas, a pretreatment scan should also be used as baseline, with a standardized time interval (no more than 14 days) before the start of treatment, which is supported by recent evidence showing that recurrent glioblastoma can grow by an average of 15% over a 20-day period, with some tumors showing  $\geq 25\%$  growth even within 17 days—potentially compromising accurate response assessment [62].

## Response evaluation and interpretation in RANO 2.0

In addition to the fundamental modifications in the baseline conditions for response assessment, RANO 2.0 introduces substantial revisions to the response evaluation criteria themselves. Notable changes include the introduction of preliminary PD as a new assessment category with its associated confirmation scan protocol, as well as the exclusion of T2/FLAIR lesion evaluation from the assessment criteria for high-grade gliomas. This section describes the major modifications to response assessment categories in RANO 2.0.

### Basic assessment structure

Tumor response in the original RANO criteria for both high-grade gliomas and low-grade gliomas was primarily assessed based on changes in the Sum of the Products of



Perpendicular Diameters (SPPD) of target lesion(s), measured from either the baseline or the nadir scan [37, 38]. The RANO-HGG response system comprised four categories—PD, stable disease (SD), partial response (PR), and complete response (CR)—whereas the RANO-LGG system included a fifth category: minor response (MR), allowing for more granular assessment in indolent tumors (Table 3). In both systems, confirmation scans were mandated for all response categories except PD, which permitted optional confirmation.

The foundational framework and structure of these systems is largely preserved in RANO 2.0, although several modifications were introduced. Specifically, the updated criteria apply RANO-HGG principles to enhancing lesions and RANO-LGG principles to non-enhancing lesions. While this structural consistency is maintained, some conceptual elements have been substantially revised. In the following subsections, we address two major modifications related to treatment response evaluation introduced in RANO 2.0:

### Evolution of progressive disease assessment

The determination of PD has undergone significant modification in RANO 2.0, primarily due to the challenges posed by PsP. PsP, occurring in up to 40% of cases within 12 weeks post-treatment [63–66], presents as temporary enhancement that reflects treatment-induced inflammation rather than disease progression. RANO-HGG criteria addressed this by not classifying new enhancement within the radiation field as PD during the initial 12 weeks post-treatment [37]. While this aimed to prevent premature treatment discontinuation due to misinterpretation of PsP

as PD, the approach complicated accurate PFS measurement in cases of early recurrence. The complexity was further amplified by RANO criteria's optional requirement for confirmation scans when evaluating disease progression, thereby introducing additional uncertainty into the progression assessment process.

To address these challenges, RANO 2.0 has implemented the following key changes to PD assessment [2, 67, 68].

- Implementation of preliminary PD, defined by either a more than 25% increase in SPPD or new enhancing lesions during 12 weeks initial treatment.
- Mandatory confirmation scans after 4 or 8 weeks for new enhancement within 12 weeks post-treatment if the patient is clinically stable.
- If the subsequent scan confirmed progression, the date of progression should be backdated to the time initial tumor progression was noted.
- If enhancing lesions emerge after the initial 12 weeks period, PD will be determined without a confirmatory scan unless specifically required by the clinical trial sponsor.
- Optional confirmation scans are warranted for new enhancement detected outside the radiation field or beyond 12 weeks post-treatment in the context of immunotherapy, given the recognized high incidence of potential immunotherapy-associated PsP [39, 69].

These changes enable earlier differentiation between PsP and true PD while facilitating more accurate PFS measurement [61].

**Table 3** Response categories in RANO 2.0

Category	CR	PR	MR	SD	PD <sup>a</sup>
Threshold to target lesion					
2D	No lesion	More than 50% reduction	Less than 50% but more than 25% reduction	Other than CR/PR/MR/PD	More than 25% increase
3D	No lesion	More than 65% reduction	Less than 65% but more than 40% reduction	Other than CR/PR/MR/PD	More than 40% increase
New measurable lesion	None	None	None	None	Any
Steroids	None	Stable or dose reduction	Stable or dose reduction	Stable or dose reduction	N/A
Clinical status	Stable or improved	Stable or improved	Stable or improved	Stable or improved	Deteriorated
Requirement	All	All	All	All	Any

CR complete response, PR partial response, MR minor response, SD stable disease, PD progressive disease

<sup>a</sup>PD can also be clearly determined by any of the following: (1) appearance of definite leptomeningeal disease, (2) clear progression of non-measurable lesions (increase in bidirectional diameters by at least 5×5 mm to >10×10 mm), or (3) unequivocal progression of existing non-target lesions (requiring ≥25% increase in sum of products of perpendicular diameters or ≥40% increase in volume)

## Elimination of T2/FLAIR lesion from enhancing tumor assessment

Pseudoresponse and non-enhancing tumor progression represent two distinct radiological phenomena in glioma patients treated with anti-angiogenic therapy (particularly bevacizumab). Pseudoresponse is characterized by rapid reduction in contrast enhancement that may not reflect true tumor response, as it primarily results from decreased vascular permeability rather than actual tumor reduction [70]. In contrast, non-enhancing tumor progression manifests as expanding T2/FLAIR abnormality despite stable or decreased contrast enhancement, indicating infiltrative tumor growth [71].

In response to these complex imaging findings, the RANO criteria have emphasized the importance of evaluating both contrast-enhanced T1WI and T2/FLAIR sequences. While T2/FLAIR evaluation is valuable for detecting pseudoresponse and identifying non-enhancing tumor progression, there remains a risk of misinterpreting treatment-related T2/FLAIR signal changes as progressive disease. Furthermore, non-enhancing tumor progression typically transitions to enhancing progression within 1–2 months, and notably, previous studies have failed to demonstrate significant correlations between non-enhancing lesion measurements and either PFS or survival outcomes [61, 72, 73].

RANO 2.0 has modified the relative weight given to T2/FLAIR imaging in glioblastoma assessment, placing greater emphasis on contrast-enhancing lesions. The modification reflects dual considerations: firstly, the limited prognostic utility of non-enhancing lesion assessment in glioblastoma, and secondly, the operational burden of complex volumetric analyses. Moreover, the omission of T2/FLAIR evaluation criteria for enhancing tumors in RANO 2.0 may mitigate the potential misclassification of transient post-treatment change as PD [74]. Nevertheless, the criteria maintain that T2/FLAIR hyperintensity should be incorporated into response evaluation during anti-angiogenic therapy, analogous to the approach used in predominantly non-enhancing tumors. This specific recommendation persists because anti-angiogenic agents can mask tumor progression through vascular normalization while infiltrative growth continues beyond contrast-enhancing regions.

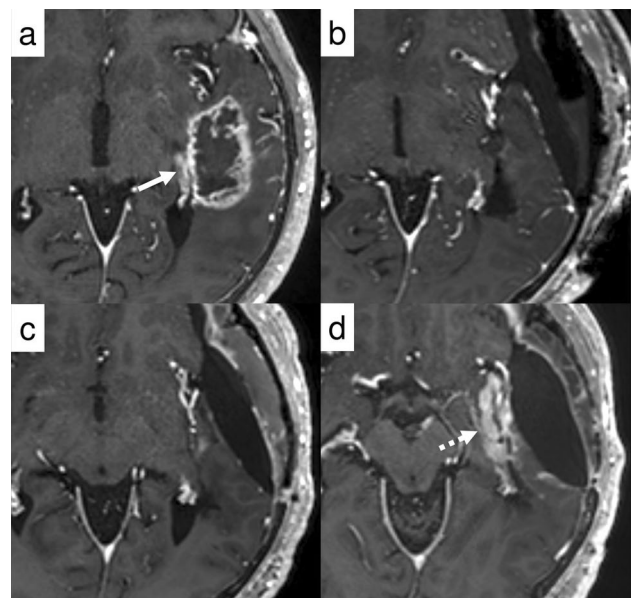
## Practical application of RANO 2.0: representative clinical scenarios

As with the major modifications discussed above, a notable feature of RANO 2.0 is the adoption of three imaging-based categories: enhancing tumor, non-enhancing tumor, and mixed tumor, which is defined by the concurrent presence of both enhancing and non-enhancing tumor components.

The major revisions outlined in preceding sections and these newly introduced imaging categories are intricately inter-related, with varying weights and frequencies depending on the clinical contexts, making uniform interpretation challenging. To facilitate clearer understanding of these concepts, the following section presents representative cases illustrating how RANO 2.0 principles can be applied in dynamic clinical scenarios. While that treatment response criteria are primarily intended for clinical trials [75–77], the types of disease progression and treatment response observed in such settings are often analogous to those encountered in routine imaging assessments. Accordingly, we interpret the following cases through the lens of RANO 2.0 to help the reader become more familiar with the updated structure and conceptual framework of RANO 2.0 through its practical application.

*Case 1 newly diagnosed, no residual enhancing tumor, new measurable lesion after 12 weeks of CRT (PD)*

Glioblastoma treatment follows a multimodal approach [78]. Case 1 (Fig. 3) demonstrates a typical treatment course for this malignancy. Most histologically classified high-grade gliomas, with glioblastoma being a prime example, are categorized as enhancing tumors according to RANO 2.0. The standard protocol involves maximal safe surgical resection of the contrast-enhancing lesion, followed by radiation



**Fig. 3** Case 1: A 72-year-old man with *IDH*-wildtype glioblastoma presented with a contrast-enhancing tumor (**a**, arrow), which was completely resected (**b**). He subsequently underwent chemoradiotherapy (CRT). Four weeks after completing CRT—corresponding to the RANO 2.0 baseline scan—no residual tumor was observed on contrast-enhanced T1WI (**c**). A new measurable lesion (12×17 mm, dotted arrow) was detected 4 months later (**d**), fulfilling the criteria for progressive disease



therapy delivered to the tumor volume with an appropriate margin.

As seen in Case 1, where complete removal of the enhancing tumor was accomplished, evaluating the treatment response presents a specific challenge. In situations where there is no measurable disease on the initial imaging, stable disease (SD) represents the best possible outcome during follow-up; without a measurable target lesion at the start, objective responses (MR/PR/CR) cannot be achieved. The assessment remains SD unless either new measurable disease develops or a pre-existing non-measurable component (limited to contrast-enhancing components in contrast-enhancing tumors) shows sufficient growth (reaching  $\geq 5 \times 5$  mm to  $\geq 10 \times 10$  mm) compared to initial size, in which case the response is classified as PD.

Under RANO 2.0, PD can be determined when new measurable enhancing lesions appear more than 12 weeks after treatment completion (Fig. 3), though specific clinical trial protocols may necessitate confirmation scans.

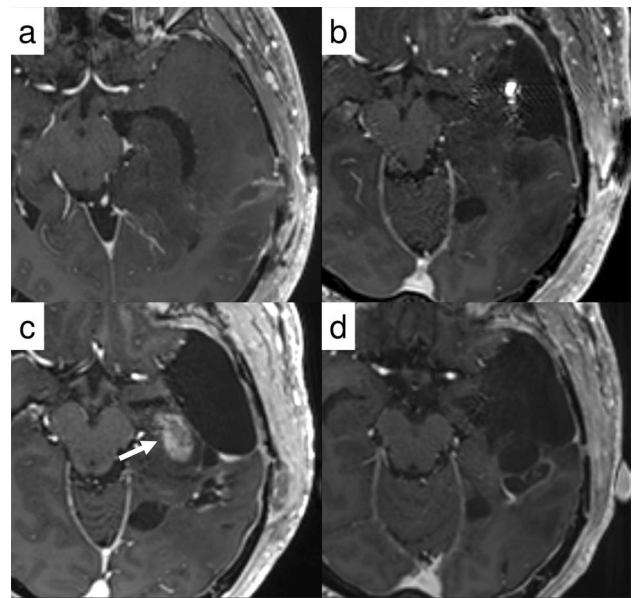
*Case 2 newly diagnosed, non-enhancing residual tumor, new measurable lesion within 12 weeks of CRT (PsP)*

Case 2 (Fig. 4) exemplifies typical PsP occurring within 12 weeks following completion of concurrent CRT, without accompanying symptoms. For such cases, while both criteria essentially avoid designating these changes as PD, their approaches differ: the original RANO criteria exclude new enhancement within three months post-treatment from PD assessment, whereas RANO 2.0 requires confirmatory scans to actively verify the absence of true progression.

Notably, in *IDH*-mutant cases, it is important to remember that PsP may occur beyond 12 weeks post-CRT [79–82]. In recognition of this characteristic, RANO 2.0 suggests that confirmation scans may be considered for new enhancement appearing after 3 months post-treatment in *IDH*-mutant cases.

*Case 3 newly diagnosed, enhancing or mixed residual tumor, new measurable lesion after 12 weeks of CRT (PD)*

While complete resection is optimal for glioma treatment, cases involving multiple lesions, as in case 3 (Fig. 5), often present challenges that preclude total removal, even with advanced techniques such as awake surgery. According to RANO 2.0, beyond 3 months after completion of radiotherapy, PD can be determined when pre-existing measurable lesions demonstrate either a  $\geq 25\%$  increase in 2D measurements or a  $\geq 40\%$  increase in 3D volume. However, some clinical trials may require confirmation scans, in which case these findings are initially classified as preliminary PD. In such trials, treatment continues while awaiting a confirmation scan performed at least 4 weeks later. PD is confirmed

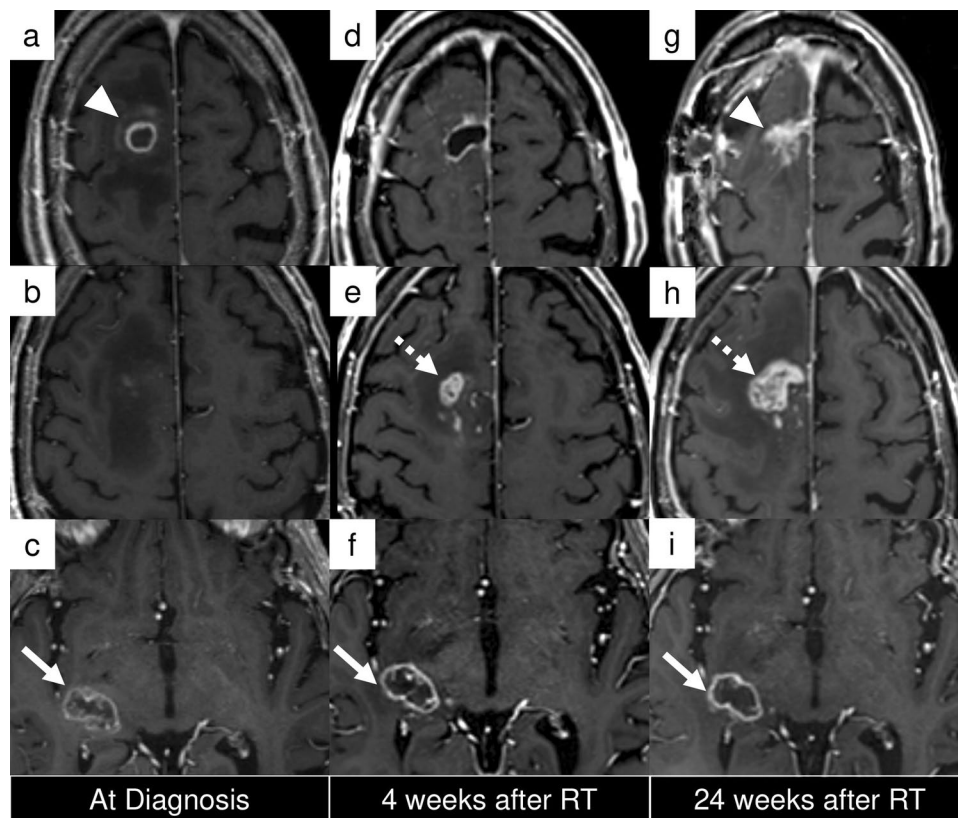


**Fig. 4** Case 2: A 37-year-old man presented with a non-enhancing tumor in the left temporal lobe (a). Maximal safe resection was performed, and histopathology confirmed an *IDH*-mutant astrocytoma, WHO grade 3 (b). The patient underwent concurrent chemoradiotherapy (CRT). One month after completing CRT, baseline post-treatment imaging showed nodular contrast enhancement (arrow) along the margin of the resection cavity (c). The first confirmation scan (not shown) demonstrated spontaneous regression of the enhancement, and complete resolution was observed on the 3-month follow-up (d). Based on this clinical and radiological course, a diagnosis of pseudo-progression (PsP) was made

if there is a further 25% increase in SPPD or 40% increase in volume, with the date of progression backdated to the preliminary PD date. If these criteria are not met, the case is classified as PsP, and the clinical trial continues. Although the emergence of new measurable lesions in this case was sufficient to establish PD, it is important to note that PD assessment in cases with multiple measurable lesions generally requires calculation of the sum of SPPDs (in 2D imaging) or volumetric measurements (in 3D imaging). This principle is especially relevant when evaluating progression of non-target lesions, which requires  $\geq 25\%$  increase in sum of products of perpendicular diameters or  $\geq 40\%$  increase in volume of the lesion(s), with these measurements being added to the sum of target lesions to determine overall disease status.

*Case 4 newly diagnosed, residual enhancing tumor, new measurable lesion within 12 weeks of CRT (PD)*

Case 4 (Fig. 6) warrants systematic evaluation following RANO 2.0, as it presents a complex clinical course with multiple findings requiring careful interpretation. First, there is a measurable lesion in the medial temporal lobe that maintains SD. A contrast-enhancing lesion



**Fig. 5** Case 3: A 79-year-old man with glioblastoma, *IDH*-wildtype presented with multiple enhancing and non-enhancing lesions, including a dominant right frontal lesion (**a**, arrowhead). Partial resection of the right frontal lesion was performed (**d**), and concurrent chemoradiotherapy (CRT) was administered, including coverage of a non-resected right temporal lesion (**c**, arrow). At 4 weeks post-CRT, new non-measurable enhancing lesions appeared around the resection cavity (**e**, dashed arrow), and remained stable through

12 weeks post-CRT (not shown), without evidence of progression. At 24 weeks (**h**), the lesions (dashed arrow) had enlarged and met the criteria for progressive disease (PD). Irregular contrast enhancement was also noted around the surgical cavity (**g**, arrowhead). In contrast, the right temporal lesion, designated as a target lesion, showed no measurable change over time (**f**, **i**, arrows). Panels **a–c**, **d–f**, and **g–i** represent equivalent axial, sagittal, and coronal levels, respectively, at diagnosis, early, and late follow-up

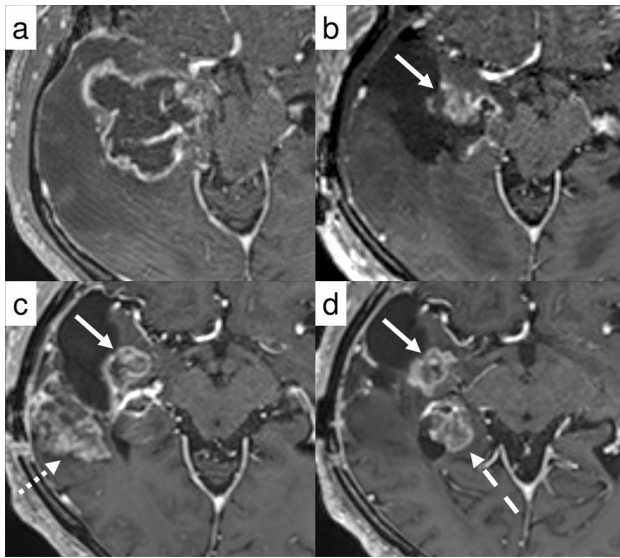
dorsal to the resection cavity transiently enlarged within 3 months after CRT, but subsequently decreased in size, consistent with PsP. However, the appearance of new measurable lesions beyond the 3-month window led to an overall assessment of PD[68].

#### *Case 5 newly diagnosed, non-enhancing tumor (MR)*

In RANO 2.0, non-enhancing tumors typically include lower-grade *IDH*-mutant gliomas, though on rare occasions, *IDH*-wildtype gliomas may also fall into this category when they lack contrast enhancement. For these tumors that present without measurable contrast-enhancing lesions, measurable disease is defined as a clearly demarcated T2/FLAIR hyperintense lesion with a minimum short-axis diameter of 10 mm. Unlike their *IDH*-wildtype counterparts, *IDH*-mutant low-grade gliomas are characterized by slow growth and gradual treatment responses in both clinical trials and routine practice. To better capture modest but meaningful responses, RANO-LGG introduced a “minor response”

category, which RANO 2.0 has retained for non-enhancing tumors [57, 83].

Treatment response must be evaluated in comparison to pretreatment baseline scans, with particular attention to temporal changes, as lesion reduction typically occurs gradually over years, as demonstrated in case 5 (Fig. 7). Ellingson et al. addressed this challenge of temporal assessment through two innovative approaches. First, they identified “yo-yoing”—inconsistency in measurements—as a significant limitation of 2D assessment, advocating for volumetric measurement using 3D scans [57]. Additionally, they proposed the “digital flipbook” method to facilitate visual detection of temporal changes in imaging [84]. While radiologists have traditionally performed such temporal comparisons, implementation of these advanced tools in clinical viewers could enhance detection of subtle changes [85, 86]. However, given the current challenges in establishing standardized segmentation workflows and the associated labor intensity, RANO 2.0 maintains volumetric analysis as an optional approach.



**Fig. 6** Case 4: A 73-year-old man with right temporal glioblastoma, *IDH*-wildtype, underwent maximal safe resection followed by adjuvant chemoradiotherapy (CRT). Postoperative contrast-enhanced T1WI demonstrated a small residual lesion in the medial margin of the surgical cavity (**b**, solid arrow), which remained stable in size throughout the observation period (**c**, **d**). At 8 weeks following CRT completion, a new contrast-enhancing lesion emerged along the posterior resection margin (**c**, dotted arrow), meeting RANO 2.0 for preliminary progressive disease (preliminary PD). However, this lesion spontaneously resolved on the 12-week follow-up scan (**d**), supporting a diagnosis of PsP. Concurrently, a new contrast-enhancing lesion appeared in the right hippocampus (**d**, dashed arrow). Progressive disease was subsequently confirmed based on follow-up imaging performed 4 months after treatment completion (not shown)

*Case 6 recurrent, residual non-measurable enhancing tumor (pseudoresponse and non-enhancing tumor progression)*

Anti-angiogenic therapy such as bevacizumab can cause reduction in enhancement within 1–2 days after administration, with a radiographic response in 25–60% of patients. As previously mentioned, RANO 2.0 excludes T2/FLAIR assessment in treatment response evaluation for enhancing tumors. Case 6 (Fig. 8) exemplifies why modified response criteria may be necessary in clinical trials of anti-angiogenic agents, as conventional contrast enhancement patterns can be misleading and may not accurately reflect actual disease status.

While this article does not detail RANO 2.0 regarding steroid use and clinical deterioration, it is important to note that some cases with diffusely infiltrative patterns may be classified as PD based on clinical deterioration despite minimal imaging changes. This underscores that radiologists, like their colleagues in neuro-oncology, should remain mindful that imaging findings, while

providing objective metrics, may not fully capture the complete spectrum of disease progression.

*Case 7 recurrent, residual mixed tumor, with measurable enhancing lesion (PD)*

*Case 8 recurrent, residual mixed tumor, with non-measurable enhancing lesion (SD)*

As previously mentioned, RANO 2.0 has adopted an “imaging-based” classification system that categorizes gliomas into enhancing tumors, non-enhancing tumors, and mixed tumors, implementing a unified response assessment approach. Regarding enhancing and non-enhancing tumors, this classification system parallels the original RANO criteria, which employed two distinct assessment systems based on histological classification (high-grade versus low-grade), as in practice, enhancing tumors typically correspond to glioblastoma, *IDH*-wildtype, while non-enhancing tumors generally align with *IDH1/2*-mutant low-grade gliomas [87, 88].

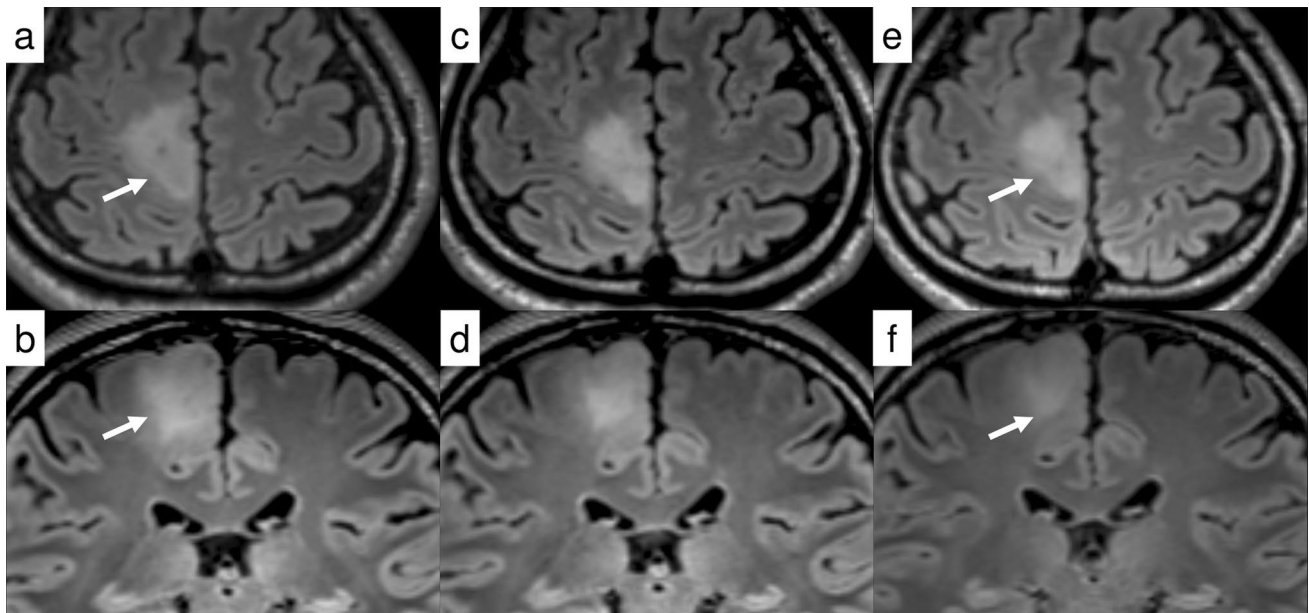
The newly introduced category of mixed tumors appears less intuitive and is characterized by measurable contrast-enhancing lesions within relatively extensive non-enhancing regions. This category appears to correspond to an imaging pattern historically described as secondary glioblastoma or gliomatosis cerebri (with enhancing foci), though it should be noted that these historical terms are no longer recommended under current molecular-based classification schemes.

The imaging pattern characteristic of mixed tumors may be observed in several tumor types described in WHO CNS5:

- *IDH*-mutant high-grade glioma (Fig. 9) [89, 90].
- Certain *IDH*-wildtype tumors (Fig. 10), predominantly those diagnosed as molecular glioblastoma [20, 91, 92].
- Some pediatric-type high-grade gliomas, including those with H3K27a and H3G34m [93–95].

Three important caveats should be noted regarding this classification: First, while these tumor types may present as mixed tumors, their classification should be determined on a case-by-case basis, as these categorical distinctions may be significantly influenced by clinical trial design considerations. Second, while most histological glioblastomas also present with T2 hyperintense lesions accompanying contrast enhancement, cases where contrast-enhancing lesions are considered representative of disease activity (i.e., cases with relatively limited non-enhancing disease) should be classified as enhancing tumors. Notably, there are no clear definitions regarding what proportion of total tumor volume should be considered “representative” enhancing disease, suggesting

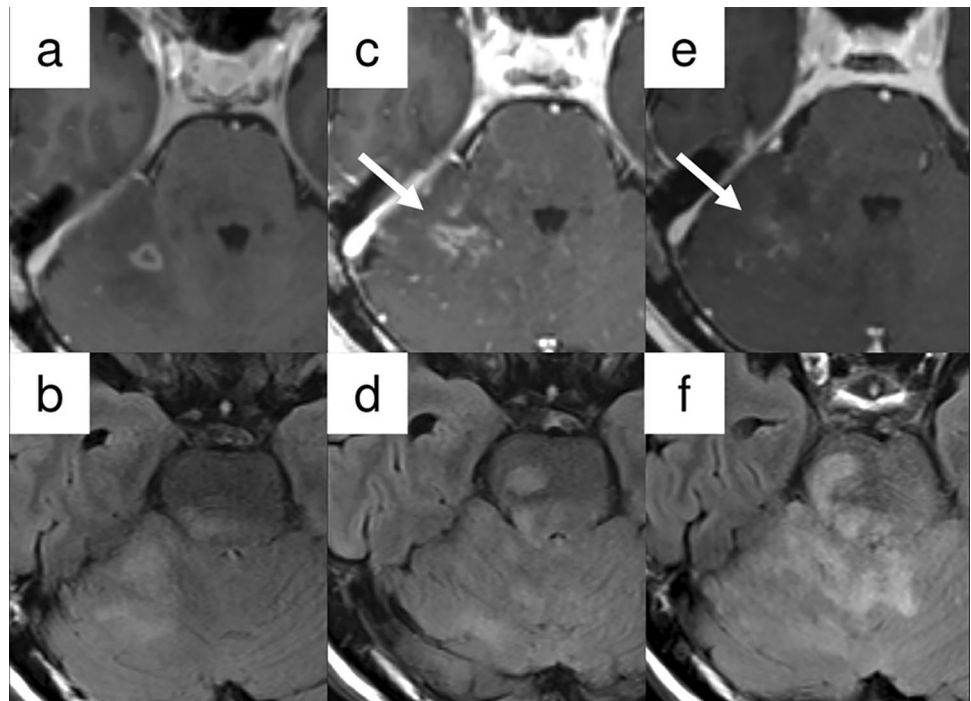




**Fig. 7** Case 5: A man in his 20 s presented with a right frontal lobe tumor. Biopsy revealed an *IDH*-mutant diffuse glioma, histologically classified as WHO Grade 2 (**a**, **b**). The tumor gradually enlarged during follow-up, and the patient was subsequently enrolled in a clinical trial involving a novel therapeutic agent. After initiation of treatment, the lesion demonstrated a slow but continuous reduction in size over

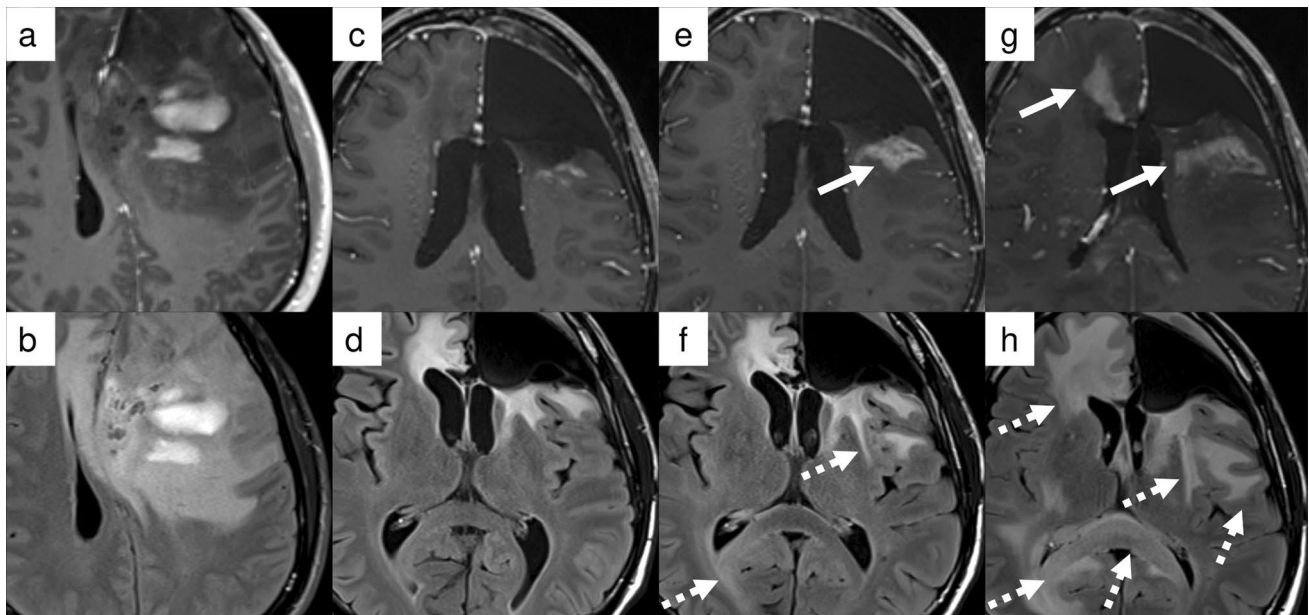
time (**c**, **d**: 1 year after treatment initiation; **e**, **f**: 2 years after treatment initiation). All images are 3D FLAIR sequences. The top row shows axial reconstructions; the bottom row shows coronal reconstructions. Arrows indicate the lesion of interest at the initial and latest timepoints

**Fig. 8** Case 6: A 75-year-old man presented with a tumor involving the cerebellum and pons. Stereotactic biopsy suggested diffuse midline glioma with H3K27-altered status (**a** and **b**). Eight months following completion of concurrent CRT, surveillance imaging revealed increased contrast-enhancing foci (arrow), raising concern for disease progression (**c** and **d**). The patient was subsequently initiated on second-line chemotherapy including bevacizumab. Follow-up imaging at one month demonstrated rapid resolution of contrast enhancement (arrow) (**e**) as well as progression of T2-FLAIR lesion (**f**); consistent with pseudoresponse and non-enhancing tumor progression, a characteristic imaging pattern associated with anti-angiogenic therapy



this threshold may need to be specified in individual trial protocols. Lastly, the mixed tumors are relatively rare entities. For instance, *IDH*-mutant, WHO grade 4 gliomas constitute merely 2% of all gliomas [96], and

H3-altered tumors occur at similarly low frequencies [95]. Furthermore, considering that maximal safe resection—whether of contrast-enhancing lesions with or without FLAIR-evident abnormalities (supramarginal resection



**Fig. 9** Case 7: A 33-year-old male presented with a large left frontal lobe tumor demonstrating focal enhancement (**a** and **b**). Surgical resection was performed, and histopathological analysis revealed WHO grade 3 oligodendroglioma (**c** and **d**). The patient received adjuvant chemoradiotherapy. At 18 months post-treatment, surveillance imaging demonstrated enlargement of residual enhancement

focus (arrow, **e**) concurrent with equivocal non-enhancing progression (dotted arrow, **f**). Based on these radiological findings, progressive disease was diagnosed. Despite initiation of salvage chemotherapy, both the enhancing (arrow, **g**) and non-enhancing components (dotted arrow, **h**) showed continued progression

[97–99])—represents the standard of care, there are relatively few cases that warrant monitoring as mixed tumor components following appropriate surgical intervention. Although this perspective may include some subjective assessment, it suggests that the primary candidates for such monitoring might be limited to cases where complete resection is deemed challenging, such as tumors involving multiple lobes with unresectable enhancing components, or recurrent *IDH*-mutant gliomas.

In the assessment of mixed tumors, up to two target lesions can be designated for both enhancing and non-enhancing components, as noted previously. These components must be monitored separately with dedicated target lesions. The overall response classification follows specific criteria (Table 4): PD is determined if either component demonstrates PD; when one component shows MR/PR/CR while the other shows SD, the overall response is classified as MR/PR. A CR classification requires both components to demonstrate CR, and similarly, SD is only assigned when both components exhibit SD. Importantly, the assessment of non-enhancing components should exclude vasogenic edema, though this distinction becomes particularly challenging in cases with significant blood–brain barrier disruption, despite being relatively straightforward in typical mixed tumors.

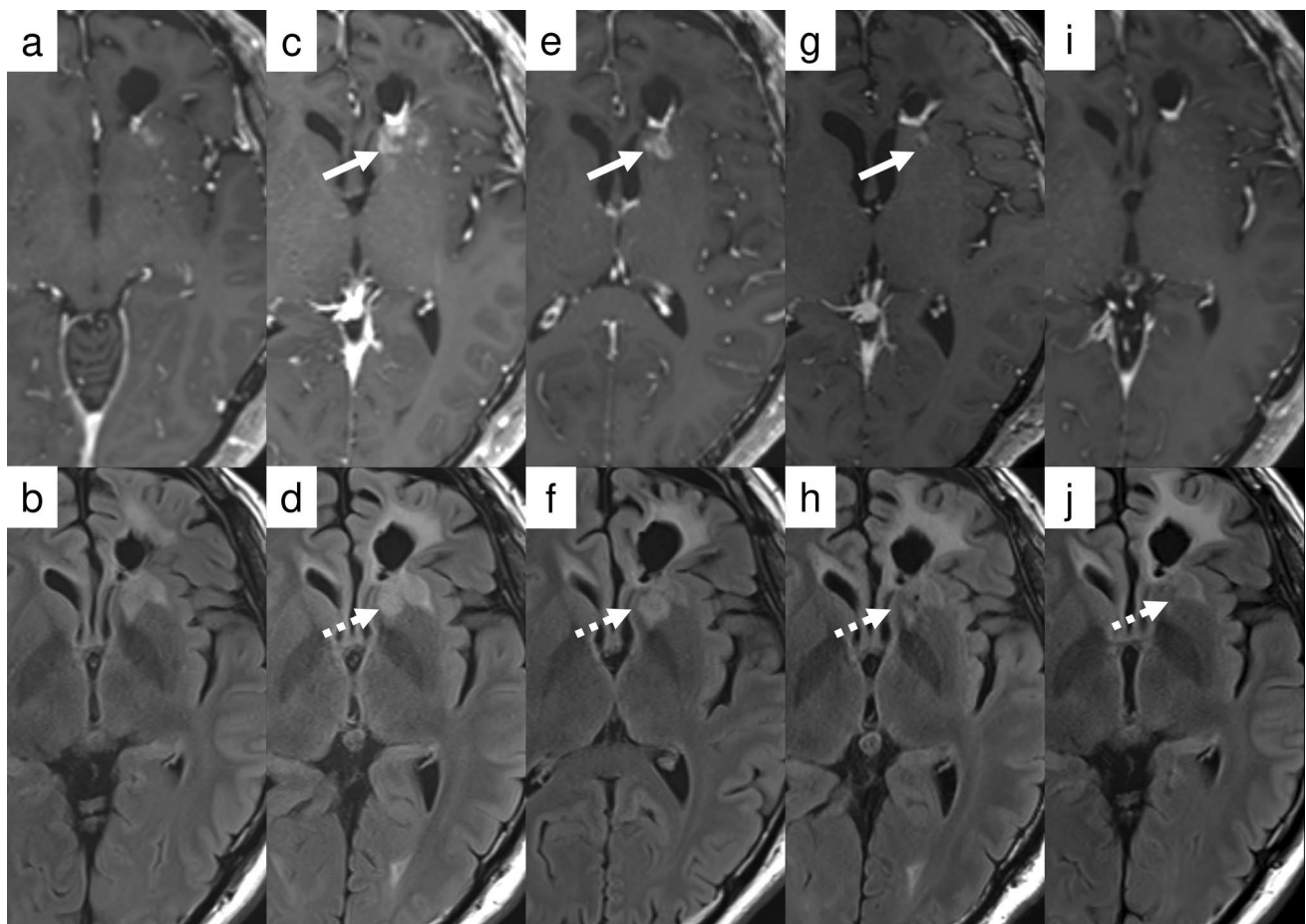
## Future perspectives

Where will RANO go from here? Just as the decade between RANO and RANO 2.0 brought significant knowledge and advancements, will RANO 2.0 continue to evolve through upcoming clinical trials and the introduction of novel therapeutic agents?

It should be noted that this past decade has also witnessed the widespread introduction of artificial intelligence (AI) into clinical medicine, fundamentally transforming the landscape of medical practice [100–106]. Within this context, the AI-RANO initiative represents a pivotal development, aiming to standardize and clinically implement AI technologies in brain tumor management [107, 108]. The convergence of clinical insights with advanced AI capabilities promises to enhance the objectivity and precision of response assessment through automated tumor segmentation [109], volumetric analysis [110], and identification of subtle imaging biomarkers that may escape conventional evaluation [111].

As we stand at this crossroads of accumulated clinical experience and emerging AI technologies, the future evolution of response assessment criteria in neuro-oncology will likely be shaped by both the lessons learned from





**Fig. 10** Case 8: A 35-year-old male underwent biopsy that revealed a histologically low-grade glioma. Molecular biological examination identified *IDH*-wildtype status with *TERT* promoter and *BRAF* V600E mutations (**a** and **b**). Despite these molecular findings, the patient was initially placed under careful observation. At 27 months after biopsy, newly developed enhancing foci appeared, raising concern for tumor progression (arrow, **c**). Targeted combination therapy with dabrafenib and trametinib was initiated. Follow-up scans at

3 months (**e**, **f**), 7 months (**g**, **h**), and 9 months (**i**, **j**) demonstrated near-complete disappearance of the enhancing lesions (white arrows, **c** and **e**) and gradual reduction of the non-enhancing T2/FLAIR abnormalities (dotted arrows, **d**, **f**, **h**, **j**). Although both components showed radiographic improvement, they were classified as non-measurable under RANO 2.0. The response was thus formally categorized as stable disease, though the clinical and radiologic course was consistent with a minor response or near-partial response

**Table 4** Response category when mixed glioma is treated

	Enhancing lesion	Non-enhancing lesion	Overall response
Response category	PD	Any	PD
	Any	PD	
	SD	SD	SD
	PR	SD	PR <sup>a</sup> /MR
	SD	PR/MR <sup>b</sup>	
	PR	PR/MR <sup>b</sup>	
	CR	CR	CR

<sup>a</sup>If PR is determined based on reduction in tumor size of enhancing disease, non-enhancing disease must be at least stable and vice versa

<sup>b</sup>MR applies to non-enhancing disease: MR can only be determined if the enhancing disease is at least stable

novel therapeutic approaches and the transformative potential of artificial intelligence-driven methodologies. Throughout this evolution, we fervently hope that radiologists will remain at the forefront, guiding and interpreting these advancements.

## Conclusions

RANO 2.0 represents the most current response assessment criteria for gliomas. While designed primarily for clinical trials—aiming to standardize imaging interpretation and optimize PFS measurements to better correlate with patients' overall survival—strict application of these criteria may present challenges in routine clinical practice.

However, as radiologists and members of the neuro-oncology team involved in brain tumor patient care, understanding these assessment principles is crucial, even when modifications may be necessary for day-to-day practice. This understanding enhances our ability to contribute meaningfully to treatment monitoring and decision-making.

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## Declarations

**Conflict of interest** The authors declare no competing interests that are relevant to the content of this article.

**Ethics approval** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** This study is based on previously published studies and does not contain any studies with human participants performed by any of the authors. The use of clinical images in this study was approved by the ethics committee (Ethics Committee Number: R2088).

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## References

- Wen PY, van den Bent M, Youssef G, Cloughesy TF, Ellingson BM, Weller M, et al. RANO 2.0: update to the response assessment in neuro-oncology criteria for high- and low-grade gliomas in adults. *J Clin Oncol*. 2023;41:5187–99.
- Ellingson BM, Sanvito F, Cloughesy TF, Huang RY, Villanueva-Meyer JE, Pope WB, et al. A neuroradiologist's guide to operationalizing the response assessment in neuro-oncology (RANO) criteria version 2.0 for gliomas in adults. *AJNR Am J Neuroradiol*. 2024;45:1846–56.
- Weller M, van den Bent M, Preusser M, Le Rhun E, Tonn JC, Minniti G, et al. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. *Nat Rev Clin Oncol*. 2021;18:170–86.
- Jiang B, Chaichana K, Veeravagu A, Chang SD, Black KL, Patil CG. Biopsy versus resection for the management of low-grade gliomas. *Cochrane Database Syst Rev*. 2017;4: CD009319.
- Hart MG, Grant GR, Solyom EF, Grant R. Biopsy versus resection for high-grade glioma. *Cochrane Database Syst Rev*. 2019;6: CD002034.
- Price SJ, Gillard JH. Imaging biomarkers of brain tumour margin and tumour invasion. *Br J Radiol*. 2011;84(Spec No 2):S159–67.
- Kim YZ, Kim CY, Lim DH. The overview of practical guidelines for gliomas by KSNO, NCCN, and EANO. *Brain Tumor Res Treat*. 2022;10:83–93.
- Stupp R, Mason WP, van den Bent MJ, Weller M, Fisher B, Taphoorn MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med*. 2005;352:987–96.
- Nishioka K, Takahashi S, Mori T, Uchinami Y, Yamaguchi S, Kinoshita M, et al. The need of radiotherapy optimization for glioblastomas considering immune responses. *Jpn J Radiol*. 2023;41:1062–71.
- Stupp R, Taillibert S, Kanner AA, Kesari S, Steinberg DM, Toms SA, et al. Maintenance therapy with tumor-treating fields plus temozolomide vs temozolomide alone for glioblastoma: a randomized clinical trial. *JAMA*. 2015;314:2535–43.
- Kanamori M, Tsuzuki S, Shibahara I, Saito K, Shimoda Y, Tanaka K, et al. Impact of tumor-treating fields on the survival of Japanese patients with newly diagnosed glioblastoma: a multicenter, retrospective cohort study. *Neurooncol Adv*. 2024;6: vdae176.
- Mohamed AA, Alshaibi R, Faragalla S, Mohamed Y, Lucke-Wold B. Updates on management of gliomas in the molecular age. *World J Clin Oncol*. 2024;15:178–94.
- Birzu C, French P, Caccese M, Cerretti G, Idhah A, Zagonel V, et al. Recurrent glioblastoma: from molecular landscape to new treatment perspectives. *Cancers (Basel)*. 2020. <https://doi.org/10.3390/cancers13010047>.
- Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO classification of tumors of the central nervous system: a summary. *Neuro Oncol*. 2021;23:1231–51.
- Kurokawa R, Kurokawa M, Baba A, Ota Y, Pinarbasi E, Camelo-Piragua S, et al. Major changes in 2021 World Health Organization classification of central nervous system tumors. *Radiographics*. 2022;42:1474–93.
- Park YW, Vollmuth P, Foltyn-Dumitru M, Sahm F, Ahn SS, Chang JH, et al. The 2021 WHO classification for gliomas and implications on imaging diagnosis: part 1—key points of the fifth edition and summary of imaging findings on adult-type diffuse gliomas. *J Magn Reson Imaging*. 2023;58:677–89.
- Mellinghoff IK, van den Bent MJ, Blumenthal DT, Touat M, Peters KB, Clarke J, et al. Vorasidenib in IDH1- or IDH2-mutant low-grade glioma. *N Engl J Med*. 2023;389:589–601.
- Fares J, Wan Y, Mair R, Price SJ. Molecular diversity in isocitrate dehydrogenase-wild-type glioblastoma. *Brain Commun*. 2024;6: fcae108.
- Makino Y, Arakawa Y, Yoshioka E, Shofuda T, Kawauchi T, Terada Y, et al. Prognostic stratification for IDH-wild-type lower-grade astrocytoma by Sanger sequencing and copy-number alteration analysis with MLPA. *Sci Rep*. 2021;11:14408.
- Ikedo S, Sakata A, Fushimi Y, Okuchi S, Arakawa Y, Makino Y, et al. Telomerase reverse transcriptase promoter mutation and histologic grade in IDH wild-type histological lower-grade gliomas: the value of perfusion-weighted image, diffusion-weighted image, and (18)F-FDG-PET. *Eur J Radiol*. 2023;159: 110658.
- Komori T. Update of the 2021 WHO classification of tumors of the central nervous system: adult diffuse gliomas. *Brain Tumor Pathol*. 2023;40:1–3.
- Brat DJ, Aldape K, Colman H, Holland EC, Louis DN, Jenkins RB, et al. cIMPACT-NOW update 3: recommended diagnostic criteria for “Diffuse astrocytic glioma, IDH-wildtype, with molecular features of glioblastoma, WHO grade IV.” *Acta Neuropathol*. 2018;136:805–10.

23. Vollmuth P, Karschnia P, Sahm F, Park YW, Ahn SS, Jain R. A radiologist's guide to IDH-wildtype glioblastoma for efficient communication with clinicians: part I-essential information on preoperative and immediate postoperative imaging. *Korean J Radiol.* 2025;26:246–68.
24. Keric N, Krenzlin H, Kalasauskas D, Freyschlag CF, Schnell O, Misch M, et al. Treatment outcome of IDH1/2 wildtype CNS WHO grade 4 glioma histologically diagnosed as WHO grade II or III astrocytomas. *J Neurooncol.* 2024;167:133–44.
25. van Dijken BRJ, Doff AR, Enting RH, van Laar PJ, Jeltrema HR, Dierckx R, et al. Influence of MRI follow-up on treatment decisions during standard concomitant and adjuvant chemotherapy in patients with glioblastoma: is less more? *Cancers (Basel).* 2023;15:4973.
26. Rykkje AM, Larsen VA, Skjoth-Rasmussen J, Nielsen MB, Carlsen JF, Hansen AE. Timing of early postoperative MRI following primary glioblastoma surgery—a retrospective study of contrast enhancements in 311 patients. *Diagnostics (Basel).* 2023;13:795.
27. Jo J, van den Bent MJ, Nabors B, Wen PY, Schiff D. Surveillance imaging frequency in adult patients with lower-grade (WHO Grade 2 and 3) gliomas. *Neuro Oncol.* 2022;24:1035–47.
28. Ji SY, Lee J, Lee JH, Lee ST, Won JK, Kim JW, et al. Radiological assessment schedule for high-grade glioma patients during the surveillance period using parametric modeling. *Neuro Oncol.* 2021;23:837–47.
29. Collaborative I-G, Neurology, Neurosurgery Interest G, British Neurosurgical Trainee Research C. Imaging timing after surgery for glioblastoma: an evaluation of practice in Great Britain and Ireland (INTERVAL-GB)—a multi-centre, cohort study. *J Neurooncol.* 2024;169:517–29.
30. Kang H, Lee J, Ji SY, Choi SW, Kim KM, Lee JH, et al. Radiological assessment schedule for 1p/19q-codeleted gliomas during the surveillance period using parametric modeling. *Neurooncol Adv.* 2021;3: vdab069.
31. Arakawa Y, Sasaki K, Mineharu Y, Uto M, Mizuwaki T, Mizusawa J, et al. A randomized phase III study of short-course radiotherapy combined with Temozolomide in elderly patients with newly diagnosed glioblastoma; Japan clinical oncology group study JCOG1910 (AgedGlio-PIII). *BMC Cancer.* 2021;21:1105.
32. Ono T, Uto M, Mineharu Y, Arakawa Y, Nakamura M, Nishio T, et al. Dummy run study for outlining and plan quality of intensity-modulated radiotherapy in elderly patients with newly diagnosed glioblastoma: the Japan clinical oncology group study JCOG1910 (AgedGlio-PIII). *Radiat Oncol.* 2025;20:32.
33. Kinoshita M, Fushimi Y, Masumoto T, Sasaki K, Sekita T, Natsume A, et al. Image-based re-evaluation of the JCOG0911 study focusing on tumor volume and survival, disease progression diagnosis, and radiomic prognostication for newly diagnosed glioblastoma. *Magn Reson Med Sci.* 2024. <https://doi.org/10.2463/mrms.mp.2024-0103>.
34. Field KM, Fitt G, Rosenthal MA, Simes J, Nowak AK, Barnes EH, et al. Comparison between site and central radiological assessments for patients with recurrent glioblastoma on a clinical trial. *Asia Pac J Clin Oncol.* 2018;14:e359–65.
35. Levin VA, Crafts DC, Norman DM, Hoffer PB, Spire JP, Wilson CB. Criteria for evaluating patients undergoing chemotherapy for malignant brain tumors. *J Neurosurg.* 1977;47:329–35.
36. Macdonald DR, Cascino TL, Schold SC Jr, Cairncross JG. Response criteria for phase II studies of supratentorial malignant glioma. *J Clin Oncol.* 1990;8:1277–80.
37. Wen PY, Macdonald DR, Reardon DA, Cloughesy TF, Sorensen AG, Galanis E, et al. Updated response assessment criteria for high-grade gliomas: response assessment in neuro-oncology working group. *J Clin Oncol.* 2010;28:1963–72.
38. van den Bent MJ, Wefel JS, Schiff D, Taphoorn MJ, Jaecle K, Junck L, et al. Response assessment in neuro-oncology (a report of the RANO group): assessment of outcome in trials of diffuse low-grade gliomas. *Lancet Oncol.* 2011;12:583–93.
39. Okada H, Weller M, Huang R, Finocchiaro G, Gilbert MR, Wick W, et al. Immunotherapy response assessment in neuro-oncology: a report of the RANO working group. *Lancet Oncol.* 2015;16:e534–42.
40. Ellingson BM, Wen PY, Cloughesy TF. Modified criteria for radiographic response assessment in glioblastoma clinical trials. *Neurotherapeutics.* 2017;14:307–20.
41. Youssef G, Wen PY. Updated response assessment in neuro-oncology (RANO) for gliomas. *Curr Neurol Neurosci Rep.* 2024;24:17–25.
42. Nysom K, Kilburn LB, Leary SES, Landi DB, de Vos-Kerkhof E, Perreault S, et al. Radiographic and visual response to the type II RAF inhibitor tovorafenib in children with relapsed/refractory optic pathway glioma in the FIREFLY-1 trial. *Neuro Oncol.* 2025. <https://doi.org/10.1093/neuonc/noae274>.
43. De Luca F, Suneson A, Kits A, Palmer E, Skare S, Delgado AF. Diagnostic performance of fast brain MRI compared with routine clinical MRI in patients with glioma grades 3 and 4: a pilot study. *AJNR Am J Neuroradiol.* 2025;46:983–9.
44. Henriksen OM, Maarup S, Hasselbalch B, Poulsen HS, Christensen IJ, Madsen K, et al. Magnetic resonance imaging and O-(2-[(18F)fluoroethyl]-l-tyrosine positron emission tomography for early response assessment of nivolumab and bevacizumab in patients with recurrent high-grade astrocytic glioma. *Neurooncol Adv.* 2024;6: vdae178.
45. Kim D, Lee SH, Hwang HS, Kim SJ, Yun M. Recent update on PET/CT radiotracers for imaging cerebral glioma. *Nucl Med Mol Imaging.* 2024;58:237–45.
46. Lawrence LSP, Maralani PJ, Das S, Sahgal A, Stanisz GJ, Lau AZ. Magnetic resonance imaging techniques for monitoring glioma response to chemoradiotherapy. *J Neurooncol.* 2025;171:255–64.
47. Hangel G, Schmitz-Abecassis B, Sollmann N, Pinto J, Arzanforoosh F, Barkhof F, et al. Advanced MR techniques for preoperative glioma characterization: part 2. *J Magn Reson Imaging.* 2023;57:1676–95.
48. Hirschler L, Sollmann N, Schmitz-Abecassis B, Pinto J, Arzanforoosh F, Barkhof F, et al. Advanced MR techniques for preoperative glioma characterization: part 1. *J Magn Reson Imaging.* 2023;57:1655–75.
49. Wang Y, Fushimi Y, Arakawa Y, Shimizu Y, Sano K, Sakata A, et al. Evaluation of isocitrate dehydrogenase mutation in 2021 World Health Organization classification grade 3 and 4 glioma adult-type diffuse gliomas with 18F-fluoromisonidazole PET. *Jpn J Radiol.* 2023;41:1255–64.
50. Hu LS, Smits M, Kaufmann TJ, Knutsson L, Rapalino O, Galldiks N, et al. Advanced imaging in the diagnosis and response assessment of high-grade glioma: AJR expert panel narrative review. *AJR Am J Roentgenol.* 2025;224: e2330612.
51. Chaban A, Waschulzik B, Bernhardt D, Delbridge C, Schmidt-Graf F, Wagner A, et al. Amino acid PET vs. RANO MRI for prediction of overall survival in patients with recurrent high grade glioma under bevacizumab therapy. *Eur J Nucl Med Mol Imaging.* 2024;51(6):1698–702.
52. Miyake K, Suzuki K, Ogawa T, Ogawa D, Hatakeyama T, Shinomiya A, et al. Multiple positron emission tomography tracers for use in the classification of gliomas according to the 2016 World Health Organization criteria. *Neurooncol Adv.* 2021;3: vdaa172.
53. Galldiks N, Kaufmann TJ, Vollmuth P, Lohmann P, Smits M, Veronesi MC, et al. Challenges, limitations, and pitfalls of PET

- and advanced MRI in patients with brain tumors: a report of the PET/RANO group. *Neuro Oncol.* 2024;26:1181–94.
54. Albert NL, Galldiks N, Ellingson BM, van den Bent MJ, Chang SM, Cicone F, et al. PET-based response assessment criteria for diffuse gliomas (PET RANO 1.0): a report of the RANO group. *Lancet Oncol.* 2024;25:e29–41.
  55. Ellingson BM, Bendszus M, Boxerman J, Barboriak D, Erickson BJ, Smits M, et al. Consensus recommendations for a standardized Brain Tumor Imaging Protocol in clinical trials. *Neuro Oncol.* 2015;17:1188–98.
  56. Sanvito F, Kaufmann TJ, Cloughesy TF, Wen PY, Ellingson BM. Standardized brain tumor imaging protocols for clinical trials: current recommendations and tips for integration. *Front Radiol.* 2023;3:1267615.
  57. Ellingson BM, Kim GHJ, Brown M, Lee J, Salamon N, Steelman L, et al. Volumetric measurements are preferred in the evaluation of mutant IDH inhibition in non-enhancing diffuse gliomas: evidence from a phase I trial of ivosidenib. *Neuro Oncol.* 2022;24:770–8.
  58. Bette S, Gempt J, Huber T, Boeckh-Behrens T, Ringel F, Meyer B, et al. Patterns and time dependence of unspecific enhancement in postoperative magnetic resonance imaging after glioblastoma resection. *World Neurosurg.* 2016;90:440–7.
  59. Miyamoto S, Sugii N, Tsurubuchi T, Ishikawa E. Acute cerebral hemorrhage mimicking glioblastoma on intraoperative magnetic resonance imaging: a case report. *Radiol Case Rep.* 2023;18:3243–7.
  60. Masuda Y, Akutsu H, Ishikawa E, Matsuda M, Masumoto T, Hiyama T, et al. Evaluation of the extent of resection and detection of ischemic lesions with intraoperative MRI in glioma surgery: is intraoperative MRI superior to early postoperative MRI? *J Neurosurg.* 2019;131:209–16.
  61. Youssef G, Rahman R, Bay C, Wang W, Lim-Fat MJ, Arnaout O, et al. Evaluation of standard response assessment in neuro-oncology, modified response assessment in neuro-oncology, and immunotherapy response assessment in neuro-oncology in newly diagnosed and recurrent glioblastoma. *J Clin Oncol.* 2023;41:3160–71.
  62. Dobber L, Geurts M, van den Bent MJ. Tumor growth in recurrent glioblastoma-RANO: when to plan the baseline scan? *Neuro Oncol.* 2024;26:1536–7.
  63. Blakstad H, Mendoza Mireles EE, Heggebo LC, Magelssen H, Sprauten M, Johannesen TB, et al. Incidence and outcome of pseudoprogression after radiation therapy in glioblastoma patients: a cohort study. *Neurooncol Pract.* 2024;11:36–45.
  64. Young JS, Al-Adli N, Scotford K, Cha S, Berger MS. Pseudoprogression versus true progression in glioblastoma: what neurosurgeons need to know. *J Neurosurg.* 2023;139:748–59.
  65. Abbasi AW, Westerlaan HE, Holtman GA, Aden KM, van Laar PJ, van der Hoorn A. Incidence of tumour progression and pseudoprogression in high-grade gliomas: a systematic review and meta-analysis. *Clin Neuroradiol.* 2018;28:401–11.
  66. Kucharczyk MJ, Parpia S, Whitton A, Greenspoon JN. Evaluation of pseudoprogression in patients with glioblastoma. *Neurooncol Pract.* 2017;4:120–34.
  67. Wen PY, Van Den Bent MJ, Youssef G, Cloughesy TF, Ellingson BM, Weller M, et al. RANO 2.0: proposal for an update to the response assessment in neuro-oncology (RANO) criteria for high- and low-grade gliomas in adults. *J Clin Oncol.* 2023. [https://doi.org/10.1200/JCO.2023.41.16\\_suppl.2017](https://doi.org/10.1200/JCO.2023.41.16_suppl.2017).
  68. Park JE, Park YW, Kim YH, Song SW, Hong CK, Kim JH, et al. Determining progressive disease using RANO 2.0-further clarifications and explanations. *Korean J Radiol.* 2024;25:859–64.
  69. Ranjan S, Quezado M, Garren N, Boris L, Siegel C, Lopes Abath Neto O, et al. Clinical decision making in the era of immunotherapy for high grade-glioma: report of four cases. *BMC Cancer.* 2018;18:239.
  70. Hygino da Cruz LC Jr, Rodriguez I, Domingues RC, Gasparotto EL, Sorensen AG. Pseudoprogression and pseudoresponse: imaging challenges in the assessment of posttreatment glioma. *AJNR Am J Neuroradiol.* 2011;32:1978–85.
  71. Gerstner ER, Frosch MP, Batchelor TT. Diffusion magnetic resonance imaging detects pathologically confirmed, nonenhancing tumor progression in a patient with recurrent glioblastoma receiving bevacizumab. *J Clin Oncol.* 2010;28:e91–3.
  72. Huang RY, Rahman R, Ballman KV, Felten SJ, Anderson SK, Ellingson BM, et al. The impact of T2/FLAIR evaluation per RANO criteria on response assessment of recurrent glioblastoma patients treated with bevacizumab. *Clin Cancer Res.* 2016;22:575–81.
  73. Gallego Perez-Larraya J, Lahutte M, Petrirena G, Reyes-Botero G, Gonzalez-Aguilar A, Houillier C, et al. Response assessment in recurrent glioblastoma treated with irinotecan-bevacizumab: comparative analysis of the Macdonald, RECIST, RANO, and RECIST + F criteria. *Neuro Oncol.* 2012;14:667–73.
  74. Hidano A, Sugii N, Ishikawa E. Newly emerged T2 high-signal intensity area mimicking oligodendroglioma expansion on intraoperative magnetic resonance imaging: a case report. *Radiol Case Rep.* 2024;19:5038–43.
  75. Meira T. Considerations on the application of RANO 2.0 criteria in clinical practice. *AJNR Am J Neuroradiol.* 2025;46:220.
  76. Ellingson BM, Sanvito F, Pope WB, Cloughesy TF, Huang RY, Villanueva-Meyer JE, et al. Is personality pathology associated with physical diseases? A systematic review and meta-analysis. *AJNR Am J Neuroradiol.* 2025;46:221–2.
  77. Sanvito F, Castellano A, Cloughesy TF, Wen PY, Ellingson BM. RANO 2.0 criteria: concepts applicable to the neuroradiologist's clinical practice. *Curr Opin Oncol.* 2024;36:536–44.
  78. Vollmuth P, Karschnia P, Sahn F, Park YW, Ahn SS, Jain R. A radiologist's guide to IDH-wildtype glioblastoma for efficient communication with clinicians: part II-essential information on post-treatment imaging. *Korean J Radiol.* 2025;26:368–89.
  79. Dworkin M, Mehan W, Niemierko A, Kamran SC, Lamba N, Dietrich J, et al. Increase of pseudoprogression and other treatment related effects in low-grade glioma patients treated with proton radiation and temozolomide. *J Neurooncol.* 2019;142:69–77.
  80. Seyve A, Dehais C, Chinot O, Djelad A, Cohen-Moyal E, Bronnimann C, et al. Incidence and characteristics of pseudoprogression in IDH-mutant high-grade gliomas: a POLA network study. *Neuro Oncol.* 2023;25:495–507.
  81. Wetzel EA, Farrell MJ, Eldred BSC, Liu V, Saha I, Zapanta Rinonos S, et al. Retrospective examination of pseudoprogression in IDH mutant gliomas. *Neurooncol Adv.* 2023;5: vdad028.
  82. van West SE, de Bruin HG, van de Langerijt B, Swaak-Kragten AT, van den Bent MJ, Taal W. Incidence of pseudoprogression in low-grade gliomas treated with radiotherapy. *Neuro Oncol.* 2017;19:719–25.
  83. Huang RY, Young RJ, Ellingson BM, Veeraraghavan H, Wang W, Tixier F, et al. Volumetric analysis of IDH-mutant lower-grade glioma: a natural history study of tumor growth rates before and after treatment. *Neuro Oncol.* 2020;22:1822–30.
  84. Cho NS, Le VL, Sanvito F, Oshima S, Harper J, Chun S, et al. Digital “flipbooks” for enhanced visual assessment of simple and complex brain tumors. *Neuro Oncol.* 2024;26:1823–36.
  85. Gui C, Lau JC, Kosteniuk SE, Lee DH, Megyesi JF. Radiology reporting of low-grade glioma growth underestimates tumor expansion. *Acta Neurochir (Wien).* 2019;161:569–76.
  86. Fathallah-Shaykh HM, DeAtkine A, Coffee E, Khayat E, Bag AK, Han X, et al. Diagnosing growth in low-grade gliomas with



- and without longitudinal volume measurements: a retrospective observational study. *PLoS Med.* 2019;16: e1002810.
87. Ikeda S, Sakata A, Arakawa Y, Mineharu Y, Makino Y, Takeuchi Y, et al. Clinical and imaging characteristics of supratentorial glioma with IDH2 mutation. *Neuroradiology.* 2024;66:973–81.
  88. Maynard J, Okuchi S, Wastling S, Busaidi AA, Almossawi O, Mbatha W, et al. World Health Organization grade II/III glioma molecular status: prediction by MRI morphologic features and apparent diffusion coefficient. *Radiology.* 2021;298:E61.
  89. Lee MD, Patel SH, Mohan S, Akbari H, Bakas S, Nasrallah MP, et al. Association of partial T2-FLAIR mismatch sign and isocitrate dehydrogenase mutation in WHO grade 4 gliomas: results from the respond consortium. *Neuroradiology.* 2023;65:1343–52.
  90. Uetani H, Azuma M, Khant ZA, Watanabe Y, Kudo K, Kadota Y, et al. Importance of age and noncontrast-enhancing tumor as biomarkers for isocitrate dehydrogenase-mutant glioblastoma: a multicenter study. *J Comput Assist Tomogr.* 2023;47:659–65.
  91. Izquierdo C, Barrिताult M, Poncet D, Cartalat S, Joubert B, Bruna J, et al. Radiological characteristics and natural history of adult IDH-wildtype astrocytomas with TERT promoter mutations. *Neurosurgery.* 2019;85:E448–56.
  92. Muench A, Teichmann D, Spille D, Kuzman P, Perez E, May SA, et al. A novel type of IDH-wildtype glioma characterized by gliomatosis cerebri-like growth pattern, TERT promoter mutation, and distinct epigenetic profile. *Am J Surg Pathol.* 2023;47:1364–75.
  93. Kurokawa R, Baba A, Kurokawa M, Pinarbasi ES, Makise N, Ota Y, et al. Neuroimaging features of diffuse hemispheric glioma, H3 G34-mutant: a case series and systematic review. *J Neuroimaging.* 2022;32:17–27.
  94. Kurokawa R, Kurokawa M, Baba A, Ota Y, Kim J, Capizzano A, et al. Dynamic susceptibility contrast-MRI parameters, ADC values, and the T2-FLAIR mismatch sign are useful to differentiate between H3-mutant and H3-wild-type high-grade midline glioma. *Eur Radiol.* 2022;32:3672–82.
  95. Yoshimoto K, Hatae R, Sangatsuda Y, Suzuki SO, Hata N, Akagi Y, et al. Prevalence and clinicopathological features of H3.3 G34-mutant high-grade gliomas: a retrospective study of 411 consecutive glioma cases in a single institution. *Brain Tumor Pathol.* 2017;34:103–12.
  96. Price M, Ballard C, Benedetti J, Neff C, Cioffi G, Waite KA, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2017–2021. *Neuro Oncol.* 2024;26:vi1–85.
  97. Goethe E, Rao G. Supramarginal resection of glioblastoma: a review. *Neurosurg Clin N Am.* 2025;36:83–9.
  98. Li YM, Suki D, Hess K, Sawaya R. The influence of maximum safe resection of glioblastoma on survival in 1229 patients: can we do better than gross-total resection? *J Neurosurg.* 2016;124:977–88.
  99. Molinaro AM, Hervey-Jumper S, Morshed RA, Young J, Han SJ, Chunduru P, et al. Association of maximal extent of resection of contrast-enhanced and non-contrast-enhanced tumor with survival within molecular subgroups of patients with newly diagnosed glioblastoma. *JAMA Oncol.* 2020;6:495–503.
  100. Fujita S, Fushimi Y, Ito R, Matsui Y, Tatsugami F, Fujioka T, et al. Advancing clinical MRI exams with artificial intelligence: Japan's contributions and future prospects. *Jpn J Radiol.* 2025;43:355–64.
  101. Ueda D, Kakinuma T, Fujita S, Kamagata K, Fushimi Y, Ito R, et al. Fairness of artificial intelligence in healthcare: review and recommendations. *Jpn J Radiol.* 2024;42:3–15.
  102. Laukamp KR, Terzis RA, Werner JM, Galldiks N, Lennartz S, Maintz D, et al. Monitoring patients with glioblastoma by using a large language model: accurate summarization of radiology reports with GPT-4. *Radiology.* 2024;312: e232640.
  103. Nakaura T, Ito R, Ueda D, Nozaki T, Fushimi Y, Matsui Y, et al. The impact of large language models on radiology: a guide for radiologists on the latest innovations in AI. *Jpn J Radiol.* 2024;42:685–96.
  104. Akbari H, Bakas S, Sako C, Fathi Kazerooni A, Villanueva-Meyer J, Garcia JA, et al. Machine learning-based prognostic subgrouping of glioblastoma: a multicenter study. *Neuro Oncol.* 2025;27:1102–15.
  105. Kurokawa R, Ohizumi Y, Kanzawa J, Kurokawa M, Sonoda Y, Nakamura Y, et al. Diagnostic performances of Claude 3 Opus and Claude 3.5 Sonnet from patient history and key images in Radiology's "Diagnosis Please" cases. *Jpn J Radiol.* 2024;42:1399–402.
  106. Rastogi A, Brugnara G, Foltyn-Dumitru M, Mahmutoglu MA, Preetha CJ, Kobler E, et al. Deep-learning-based reconstruction of undersampled MRI to reduce scan times: a multicentre, retrospective, cohort study. *Lancet Oncol.* 2024;25:400–10.
  107. Villanueva-Meyer JE, Bakas S, Tiwari P, Lupo JM, Calabrese E, Davatzikos C, et al. Artificial intelligence for response assessment in neuro oncology (AI-RANO), part 1: review of current advancements. *Lancet Oncol.* 2024;25:e581–8.
  108. Bakas S, Vollmuth P, Galldiks N, Booth TC, Aerts H, Bi WL, et al. Artificial Intelligence for Response Assessment in Neuro Oncology (AI-RANO), part 2: recommendations for standardisation, validation, and good clinical practice. *Lancet Oncol.* 2024;25:e589–601.
  109. Cepeda S, Romero R, Luque L, Garcia-Perez D, Blasco G, Lupino LT, et al. Deep learning-based postoperative glioblastoma segmentation and extent of resection evaluation: development, external validation, and model comparison. *Neurooncol Adv.* 2024;6: vdae199.
  110. Zhang J, LaBella D, Zhang D, Houk JL, Rudie JD, Zou H, et al. Development and evaluation of automated artificial intelligence-based brain tumor response assessment in patients with glioblastoma. *AJNR Am J Neuroradiol.* 2025;46:990–8.
  111. Fares J, Wan Y, Mayrand R, Li Y, Mair R, Price SJ. Decoding glioblastoma heterogeneity: neuroimaging meets machine learning. *Neurosurgery.* 2025;96:1181–92.

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