

The RANO Criteria



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Medical Imaging

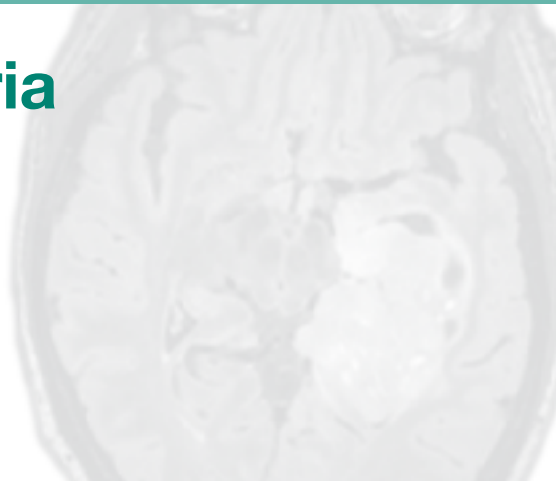


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RANO Basics

- The Revised Assessment in Neuro-Oncology (RANO) criteria was published in 2010, as an update to the existing MacDonald criteria (see references at end)
- Used for assessing disease progression and treatment response in glioblastoma multiforme (GBM)

References

Print Version:

“Updated Response Assessment Criteria for High-Grade Gliomas: Response Assessment in Neuro-Oncology Working Group.” *Journal of Clinical Oncology*. 2010 Apr 10; 28(11):1963-72.

Online Version: <http://jco.ascopubs.org/content/28/11/1963.abstract>



Image Acquisition

- MRI is the only modality used to assess response and progression
- Minimum sequences required:
 - Pre-contrast T1, T2/FLAIR
 - Post-contrast T1, with two orthogonal planes (or a volume acquisition) recommended
- Recommended slice thickness ≤ 5 mm with no gap
- Additional imaging that may be helpful:
 - Diffusion (DWI, ADC)

Definitions

- Measurable lesions
 - Contrast enhancing lesions
 - Minimum size: two perpendicular diameters ≥ 10 mm
 - If slice + gap thickness > 5 mm, minimum size is 2 times the total
 - Do not include cavity, cyst, or necrosis in the measurement
- Non-measurable lesions
 - Lesions that are too small (e.g. 12 x 8 mm)
 - Lesions that do not enhance (seen only on T2/FLAIR)
 - Lesions with a poorly defined margin

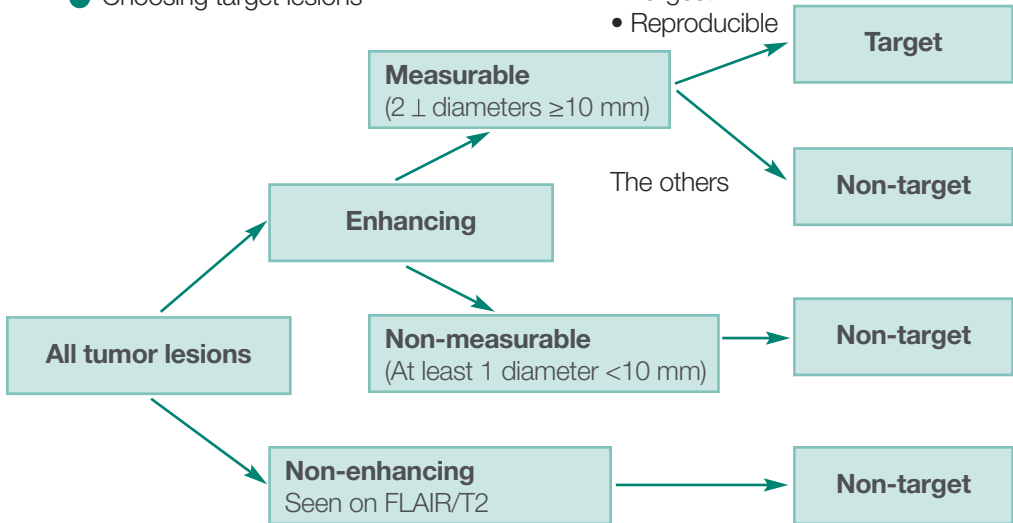
Definitions

- From measurable lesions, select target lesions:
 - 5 lesions maximum
 - Largest lesions preferred
 - Suitable for reproducible measurements

Baseline Algorithm

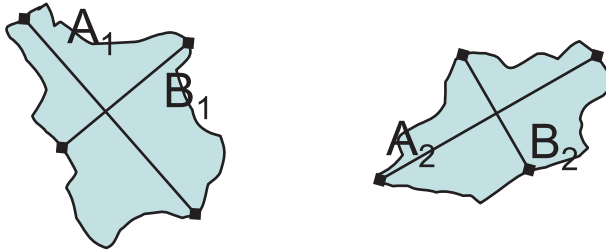
- Choosing target lesions

- Up to 5
- Largest
 - Reproducible



Target Lesions

- Calculate products of maximal diameters and add them together to yield the sum of products of diameters (SPD)



$$A_1 \times B_1 + A_2 \times B_2 + \dots = \text{SPD}$$



Follow-Up Visits



Follow-Up Visit Algorithm

1. Measure the previously defined target lesions and calculate the SPD as before
2. Qualitatively assess non-target lesions
 - Enhancing non-target lesions
 - Lesions seen only on T2/FLAIR
3. Search carefully for new lesions
4. Combine lesion assessments with neurological and steroid dose information to yield an overall timepoint response

Target Lesion Response Definitions

Response	Definition
Complete Response (CR)	All target lesions have disappeared (look out for pseudoresponse†)
Partial Response (PR)	SPD decreased by $\geq 50\%$ from baseline value (look out for pseudoresponse†)
Stable Disease (SD)	SPD $< 50\%$ decrease to $< 25\%$ increase
Progressive Disease (PD)	SPD increased by $\geq 25\%$ from nadir value (look out for pseudoprogression‡)
Unable to Assess (UA)	Some target lesions cannot be evaluated because of technical factors

† - CR and PR have to be confirmed ≥ 4 wks later. If not confirmed, response is SD.

‡ - Apparent PD within 12 weeks of radiation

Non-Target Lesions

- There are two types of non-target lesions
 - Enhancing (T1 with contrast)
 - Non-enhancing (T2/FLAIR)
- These are assessed subjectively
 - Some rules are recommended for objective assessment of progression
 - e.g. if a non-measurable enhancing lesion becomes measurable, AND either has absolute increase of >5mm OR >25% in SPD
 - However, ultimately the decision of when progression is evident is a judgment call by an expert reader.

Enhancing Non-Target Lesion Response

Response	Definition
Complete Response (CR)	All enhancing non-target lesions have disappeared completely
Incomplete Response/Stable Disease (IR/SD)	Enhancing lesions present; stable or decreased in size
Progressive Disease (PD)	Unequivocal progression
Unable to Assess (UA)	Unable to evaluate enhancing lesions because of technical factors

T2/FLAIR Lesion Response

Response	Definition
Improved	Signal abnormality decreased
Unchanged	Unchanged compared to prior imaging
Worse	Unequivocal worsening/progression of signal abnormality *
Unable to Assess (UA)	Unable to evaluate non-enhancing lesions because of technical factors

* There are many potential causes for increased T2/FLAIR signal, including infarction, infection, demyelination, radiation effects, etc. Expert reader judgment is required.

Pseudoresponse

- Pseudoresponse
 - Antiangiogenic drug effects can look like response
 - Occurs within 4 weeks of therapy
 - Confirm CR and PR at least 4 weeks later

Pseudoproggression

- Pseudoproggression
 - Enhancement that simulates tumor growth, most often caused by radiation (whole brain or focal).
 - Growth of existing lesions or appearance of new lesions within 12 weeks of completion of radiation therapy may be the result of treatment effects rather than growth of tumor.
 - Continued follow-up imaging can determine whether initial lesion growth was true progression or pseudoproggression.
 - If lesion continues to enlarge, the initial growth is called true progression
 - If lesion stabilizes or shrinks, the initial growth is confirmed as pseudoproggression
 - In such cases, the baseline SPD is no longer included when choosing the nadir value for the purposes of determining when progression occurs
 - Diffusion weighted imaging can help distinguish pseudoproggression from true tumor growth, but its use is still experimental. The use of MR perfusion and spectroscopy is also being explored.

From Lesions to Timepoint

	CR	PR	SD	PD
T1-Gd+	None	≥50%	<50%↓- <25%↑	≥25%↑*
T2/FLAIR	Stable or ↓	Stable or ↓	Stable or ↓	↑*
New Lesion	None	None	None	Present*
Corticosteroids	None	Stable or ↓	Stable or ↓	NA
Clinical Status	Stable or ↑	Stable or ↑	Stable or ↑	↓*
Requirement for Response	All	All	All	Any*

CR = Complete Response, PR = Partial Response, SD = Stable Disease, PD = Progressive Disease

* Progression occurs when any of these criteria are met present.

NA: An increase in steroid dose alone will not cause a determination of progression in the absence of clinical deterioration or radiographically documented lesion growth.



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