Concordance and Prognostic Value of AI-Assisted Volumetric versus Bidimensional RANO 2.0 Assessment in Glioblastoma

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BACKGROUND

Can the way a glioblastoma is measured change when we say it has progressed? In our earlier 8-patient pilot, 5 patients (62.5%) had a different pseudoprogression or progression call depending on whether 2D or 3D RANO 2.0 measurements were used (SNO 2025).GBM is a hard target. Its irregular shape is poorly captured by 2D diameters, which also leads to inter-reader variability, and pseudoprogression can mimic true tumor growth. RANO 2.0 keeps 2D area as the primary measurement and lists volumetrics as an option. Manual 3D segmentation is time-intensive, which limits its use in clinical trials.

AI can make volumetric assessment rapid, reproducible and scalable, but which method better predicts survival remains unclear. Settling this is essential before volumetric RANO 2.0 can be broadly implemented in clinical trials. AI-enabled imaging endpoints are drawing growing trial interest, but standards for validating them are still being set. We compared both methods in the same patients to ask how often they agree and which better tracks survival.

OBJECTIVES

- Evaluate concordance between AI-assisted volumetric (3D) and bidimensional (2D) RANO 2.0 assessment in GBM.
- Assess timing agreement between 2D- and 3D-detected progression.
- Compare the prognostic value of 2D versus 3D RANO 2.0 assessments for progression-free survival (PFS) and overall survival (OS).

METHODS

Cohort: Twenty GBM patients from a blinded, pooled trial cohort.

Imaging: Serial contrast-enhanced T1-weighted MRI at 8-week intervals.

Segmentation: AI-assisted segmentation performed to delineate tumor volumes.

Progression criteria (RANO 2.0): 2D defined as ≥25% increase in sum of perpendicular diameter products relative to nadir; 3D defined as ≥40% volume increase relative to nadir.

Concordance analysis: McNemar's test for agreement between methods.

Timing agreement: Bland-Altman analysis.

PFS analysis: Kaplan-Meier curves with log-rank test.

OS analysis: Time-dependent Cox regression, in the subset with available mortality data (n=9, 6 deaths).

CONCORDANCE

- Overall concordance between 2D and 3D methods: 80% (McNemar's p=0.62).
- 2D detected progression in 12/20 subjects (60%); 3D detected progression in 10/20 subjects (50%).
- Discordance rate: 20%.

PROGRESSION-FREE SURVIVAL

- Median PFS: 45.9 weeks by 2D versus 56.1 weeks by 3D (log-rank p=0.54).
- Among the 10 subjects who progressed by both methods, timing agreement was high: mean difference of -0.9 weeks (95% limits of agreement: -6.1 to 4.3 weeks).

RESULTS

Figure 1. Subject cases.

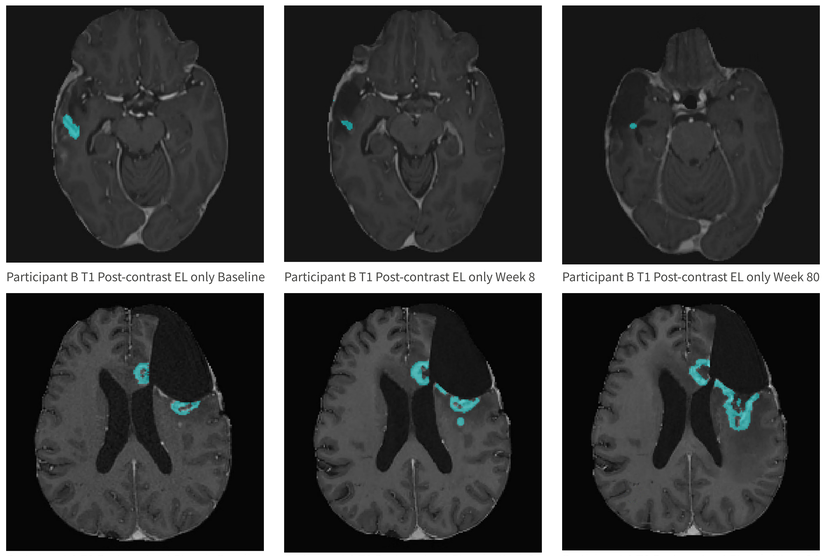
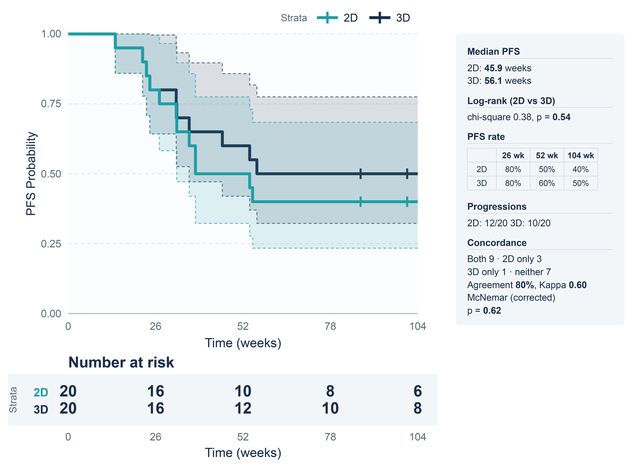
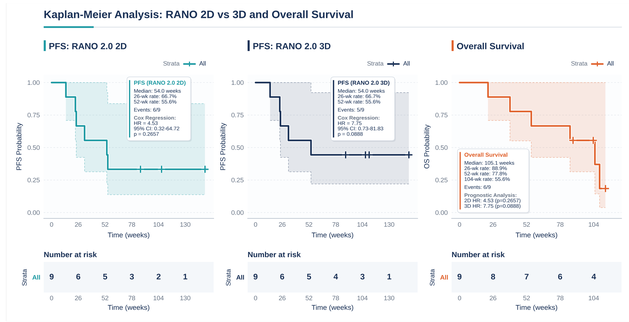


Figure 2. PFS RANO 2.0 2D vs 3D (n=20).



Overall Survival (OS subset, n=9)

- 3D assessment: HR = 7.75 (95% CI: 0.73-81.83, p=0.089).
- 2D assessment: HR = 4.53 (95% CI: 0.32-64.72, p=0.27).
- Neither hazard ratio reached statistical significance, attributed to limited sample size.



CONCLUSIONS

RANO 2.0 bidimensional and volumetric assessments demonstrated concordance (80%) with agreement in progression timing. 2D assessment showed higher sensitivity in detecting progression (60% vs 50%), while 3D demonstrated a numerically stronger association with OS.

- **Shape:** a round lesion and an irregular lesion with the same diameters can occupy different volumes, because the irregular one can fill less space. Should irregular lesions follow the same size and percent-change thresholds as round ones?
- **2D tool and reference:** RANO 2.0 keeps 2D primary and volumetrics optional. When methods disagree (insert %), which anchors PFS?
- **Pseudoprogression:** RANO 2.0 requires confirmation within 12 weeks after radiotherapy . Could 2D and 3D differ in when confirmation is triggered?
- **Role of AI:** could AI volumetrics act as one reader, with adjudication when readers disagree?

DISCLOSURES

The authors have no financial conflicts of interest to disclose.

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