

# Validation of Neuroradiologic Response Assessment in Adult Glioblastoma: Cross-comparison of Linear and Volumetric Methods on Post-contrast Standard Thick and High Resolution T1WI

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**Introduction:** With improvements in imaging technology and volume measurement software, volumetric methods have become practical and may be a more promising endpoint than traditional cross-sectional bidimensional measurements in evaluating tumor response status in GBM [1, 2]. In this study, the linear(cross-sectional) and volumetric measurements in adult GBM on post-contrast standard thick T1-weighted image (T1WI) and high resolution T1WI were cross-compared, and the association between tumor measurements of different methods and overall survival (OS) were also investigated.

**Patients and methods:** 390 MRI studies from 86 adult patients (mean age 56.2, range 21-78 years) with GBM formed the database for the study. Tumor diameter-based area (product of the two longest perpendicular diameters) and volume were measured and calculated with manual tracing software(Alice, Perceptive Informatics, Waltham, MA) on post-contrast 5mm thick T1WI (At and Vt) and 0.7~3.0 mm high resolution T1WI(Ah and Vh) for each MRI study(At, Vt, Ah, Vh were short for diameter-based area on thick T1WI, volume on thick T1WI, diameter-based area on high resolution T1WI, and volume on high resolution T1WI respectively). 195 pairs were made based on best response, e.g. greatest decrease in Vh from the first timepoint to the second. The four standard response categories of partial response (PR), progressive disease (PD), stable disease (SD) and complete response (CR) were used to evaluate tumor response status using different measurement techniques(Table 1) and the results were compared. The association between tumor changes across 28 days as measured with different techniques as compared with OS in 29 patients were also analyzed.

**Results and discussion:** Spearman correlation demonstrated that diameter-based areas correlated well with tumor volumes between At versus Vt ( $r = 0.84$ , 95% CI: 0.81-0.87,  $p < 0.001$ ), At versus Vh ( $r = 0.80$ , 95% CI: 0.76-0.83,  $p < 0.001$ ), and Ah versus Vh ( $r = 0.82$ , 95% CI: 0.78-0.85,  $p < 0.001$ ) at the same time point from 390 studies. There were 41 (21%), 47 (24%), and 43 (22%) discordant pairs who showed different response status according to the two methods in each comparison respectively, though the differences in tumor response status that these discordances caused did not reach statistical significance ( $p > 0.05$ ). Further analysis on the discordant pairs showed that 25/41, 36/47 and 25/43 pairs in each comparison respectively suggested that volumetric method is more sensitive and accurate than linear one in assessing tumor response (Fig 1). When comparing Vt and Vh, Vt was in average 12.88% (Q: 7.19~16.18) larger than Vh ( $Z=7.76$ ,  $p<0.001$ ) in 390 studies. There were 33 (17%) discordant pairs where applying four response categories to evaluate tumor response status, but no significant difference was demonstrated between the two methods ( $\chi^2=1.68$ ,  $p=0.64$ ); 15/33 discordant pairs suggested that Vh is more accurate than Vt in evaluating tumor changes (Fig 2), and only 7/33 pairs indicated Vt is better than Vh. We estimate our study had 80% power to detect at least a 14.6% change in tumor volume, which we interpret to be a clinically meaningful amount. Cox regression revealed that there did not appear to be a significant association between the percentile changes of tumor size from day-1 to day 28 and OS for any of the tumor measurement techniques on both post-contrast thick and high resolution T1WI ( $p>0.05$ ).

**Conclusions:** Volumetric approaches to tumor burden measurement had more sensitivity and accuracy than linear method in detecting tumor response in adult GBM, particularly Vh; with the advantage of less time-consuming in image acquisition and volume measurement, Vt may be an alternative to Vh in evaluating tumor response status.

**Table 1.** Definition of response categories for different measurement methods

Method	% CR	% PR	% SD	% PD
Area	100 ↓	>50 ↓	25 ↓ to 25 ↑	>25 ↑
Volume	100 ↓	>65 ↓	40 ↓ to 40 ↑	>40 ↑

References: 1. Sorensen AG, et al. J Clin Oncol. 2001;19(2):551-7.

2. Sorensen AG, et al. Nat Clin Pract Oncol, 2007, in press.

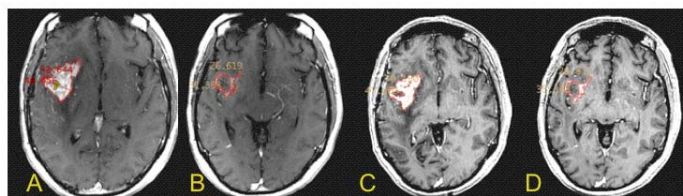


Figure 1. Comparison of linear and volumetric methods. Post-contrast thick(A-B) and high resolution (C-D) T1WI MRI of 60 years old male with recurrent GBM, prior to initiation of anti-angiogenic therapy(A, C) and 96 days later(B, D). Bidimensional measurements are shown per definition. The enhancing tumor is also outlined in red per typical volumetric analysis. If diameter measurements are used to estimate cross sectional area, the lesion has shrunk to 60% of its original size on At and 65% on Ah respectively, and both of them would be classified as stable disease. Using volume measurements(including all enhancing tissue, not only on the image shown but the entire lesion) the lesion has decreased to 24% of its original size on Vt and 31% on Vh respectively, and both of them would be classified as partial response. At: diameter-based area on post-contrast thick T1WI; Vt: volume on post-contrast thick T1WI; Ah: diameter-based area on post-contrast high resolution T1WI; Vh: volume on post-contrast high resolution T1WI.

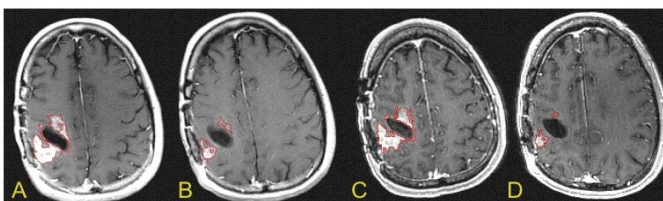


Figure 2. Comparison of Vt and Vh. Post-contrast thick(A-B) and high resolution MRI T1WI(C-D) of 55 years old female with recurrent glioblastoma, 140 days after initiation of anti-angiogenic therapy(A, C) and 35 days later(B, D). The Vt has decreased to 44% of its original size, and would be classified as stable disease; but Vh has decreased to 25%, and would be classified as a partial response.