# Automated Volumetric Analysis of Postoperative Magnetic Resonance Imaging Predicts Survival in Patients with Glioblastoma

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BACKGROUND: **Glioblastomas (GBMs) are primary brain tumors that are very difficult to treat. Magnetic resonance imaging (MRI) is the reference tool for diagnosis, postoperative control, and follow-up of GBM. The MRI tumor contrast enhancement part serves as a target for surgery. However, there are controversial data about the influence of pre- and postoperative tumor volumetric MRI parameters on overall survival (OS).**

METHODS: **Data of 57 patients with GBM were analyzed retrospectively. All patients had maximum safe resection and standard adjuvant treatment. All patients underwent 1.5-T MRI with contrast in the first 24 hours postoperatively. The data of pre- and postoperative volumetric parameters were analyzed using the original software.**

RESULTS: **Correlation analysis between the postoperative volume of the tumor contrast enhancement part and the patient's OS revealed a significant level (on the Chaddock scale) of inverse correlation. Residual tumor volume associated with OS of >6 months was determined as <2.5 $cm^3$. The mortality risk in the first 6 months after tumor resection is 3.4 times higher when the tumor remnant is >2.5 $cm^3$ (risk ratio, 3.4; $P = 0.0002$).**

CONCLUSIONS: **The volume of MRI contrast-enhancing GBM remnants after surgery, automatically measured by the software, was a significant predictor for early postoperative progression and death.**

## INTRODUCTION

Glioblastoma (GBM) is the most aggressive primary malignant brain tumor with an extremely high proliferative activity, infiltrative growth, and abundance of protective mechanisms against existing treatments.

Safe maximal resection followed by chemoradiation known as Stupp protocol is the current standard for newly diagnosed malignancies. Magnetic resonance imaging (MRI) is the reference tool for GBM diagnosis, postoperative control, and follow-up. Postoperative MRI is used to assess the success of surgery and also serves as the baseline for future comparison.[1,2] Imaging should be performed within 72 hours after surgery to assess the extent of tumor resection, while avoiding false-positive contrast enhancement caused by blood–brain barrier disruption.[3] Safe resection of >98% of the GBM contrast-enhancing part is associated with improved overall survival (OS).[4-6]

At this time, there is no standard method for volumetric estimation of various tumor parameters based on MRI data. The impact of pre- and postoperative tumor volumetric MRI parameters (volumes of the contrast-enhancing part, necrosis, and hyperintense signal on T2 sequences) on OS is inconsistent in previously published data, and the results are highly specialist-dependent.[7-10] There is no standard software for estimating the volume of tumor remnant in the

**Key words**
- Glioblastoma management
- Gross total resection
- MRI evaluation
- Software for MRI
- Volumetric tumor estimation

**Abbreviations and Acronyms**
**FOV**: Field of view
**GBM**: Glioblastoma
**MRI**: Magnetic resonance imaging
**OS**: Overall survival
**TE**: The echo time
**TR**: Repetition time

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postoperative period. In this article, we used NeuroSegment (Novosibirsk, Russia), an automated image analysis software developed in our center,[11] to analyze the impact of various pre- and postoperative volumetric MRI characteristics on OS in a series of 57 patients with GBM.

## MATERIALS AND METHODS

### Patient Information

The retrospective study was conducted in accordance with ethical standards of the 1964 Helsinki Declaration of the World Medical Association. This study was approved by the local institutional review board. All experimental protocols in this article were approved by the ethical committee of Novosibirsk State Medical University. The study enrolled 57 patients with new brain GBM (grade IV), that received maximum safe resection with MRI frameless neuronavigation and δ-aminolevulinic acid guidance. Patients were followed for 45 months after surgery. Intraoperative neurophysiologic monitoring was used for resection of GBM located in proximity to eloquent areas (21/57 patients). Patients with gliomatosis cerebri and tumors involving deep brain structures such as the thalamus, basal ganglia, or brainstem were excluded. Tumor samples were morphologically assessed according to the 2016 World Health Organization classification of central nervous system tumors.[12] The immunohistochemical examination included the following markers: GFAP, p53, Olig.2, Ki-67, and IDH1 (R132H). The status of $O^6$-methylguanine-DNA methyltransferase methylation status was assessed in all patients. The average age ±SD of the patients was 51.4 ± 1.8 years (range, 22–75 years). Thirty-two of the patients were men (56.1%), and 25 were women (43.9%). All patients had standard adjuvant treatment according to Stupp protocol. All patients had a follow-up including neurologic assessment and MRI evaluation. The date of death was recorded for all but 3 patients, who are alive at the time of this article's submission. Pre- and postoperative volumetric parameters were derived from the MRI to identify their correlation with OS. The following parameters were measured by 2 radiologists and 1 neurosurgeon using a semi-automated algorithm included in Syngo.via (Siemens Healthineers, Erlangen, Germany): preoperative tumor volume, preoperative volume of contrast-enhancing part of the tumor, preoperative volume of necrosis, preoperative volume of the hyperintense signal on T2-weighted magnetic resonance images. Postoperatively, we measured the volume of the contrast-enhancing part of the tumor using an automated algorithm included in the NeuroSegment software.[11]

### MRI Study Protocol

MRI studies with contrast (infusion parameters: 2.5 mL/s; dose, 0.2 mL/kg; Gadovist Gadobuterol (1 mmol/mL) [Bayer Pharma AG, Leverkusen, Germany]) were performed prior to surgery and within the first 24 hours after tumor resection using General Electric Signa Infinity 1.5 T (Boston, Massachusetts, USA) and SIEMENS MAGNETOM Aera 1.5 T (Erlangen, Germany) MRI machines. A standard head coil was used.

The following MRI sequences were acquired: 1) localizer; 2) T2 turbo spin echo axial 4-mm slice thickness; field of view (FOV), 220 mm; matrix, 448; repetition time (TR)/the echo time (TE), 5640/91 ms; 3) fluid-attenuated inversion recovery axial 4-mm slice thickness; FOV, 220 mm; matrix, 320; TR/TE, 9000/82 ms; 4) T1 magnetization-prepared rapid gradient-echo 3-dimensional precontrast 1-mm slice thickness; FOV, 227 mm; matrix, 256; TR/TE, 2200/3.2 ms; inversion time, 900 ms; 5) diffusion weighted imaging (b = 0.50, 1000 s/mm²); slice thickness, 4 mm; FOV, 230 mm; matrix, 176; TR/TE, 7300/109 ms; 6) susceptibility weighted imaging; FOV, 230 mm; matrix, 256; 7) dynamic contrast-enhanced (T1 perfusion); slice thickness, 4 mm; FOV, 230 mm; matrix, 192; TR/TE, 4.5/1.8 ms; 8) dynamic susceptibility contrast (T2* perfusion); slice thickness, 5 mm; FOV, 230 mm; matrix, 128; TR/TE 1810/38 ms; 9) T1 magnetization-prepared rapid gradient-echo postcontrast (identical to sequence 4); and 10) T1 turbo spin echo Fat-Sat axial postcontrast slice thickness; 4 mm; FOV, 230 mm; matrix, 320; TR/TE, 582/8.9 ms.

### Data Processing and Statistical Analysis

***NeuroSegment Software.*** Earlier we reported on the performance of NeuroSegment software developed in our institution.[11] Absolute discrepancy among measurements of residual GBM volume obtained by specialists using the NeuroSegment, on the average ± SD was 0.24 ± 0.05 $cm^3$. The interval was 0.48 $cm^3$, and the agreement index was 0.97 ± 0.07. There was no statistically significant difference in the results between the specialists with <3 years of experience in neuro-oncology and those with >10 years.[11]

Here we briefly describe the software as pertinent to this investigation. In the first step, we performed the 3-dimensional rigid registration of pre- and postcontrast T1 images (3 translation and 3 rotation parameters) using the composite reverse algorithm[13,14] to compensate for patient motion. In the second step, we segmented out the whole brain by registering the head surface atlas[13] to the T1-weighted image using an affine transformation. To further refine the brain boundaries, we used the active contour algorithm[15,16] using the registered atlas brain boundary as the initial approximation. The registration result was the brain position on the image.

The implementation was based on the level set methods using the signed distance function as a level line. This level line was applied with the use of sparse field technology.[15] The evolution of the segmenting contour is described by the following equation:

$$\varphi_t(\vec{x},t) = \mu g(\nabla I(\vec{x})) \times \kappa(\varphi(\vec{x},t)) + \nu g(\nabla I(\vec{x}))|\nabla\varphi(\vec{x},t)| + \nabla g(\nabla I(\vec{x})) \times \nabla\varphi(\vec{x},t),$$

where $\varphi(\vec{x},t)$ is the signed distance function, $I(\vec{x})$ is a segmented image, $g(\nabla I(\vec{x}))$ is the edge detector function, and $\kappa(\varphi(\vec{x},t))$ is the curvature of the contour. The constants μ and ν correspond to the definition of the contribution of the regularizing term and the motion along the normal to the contour.

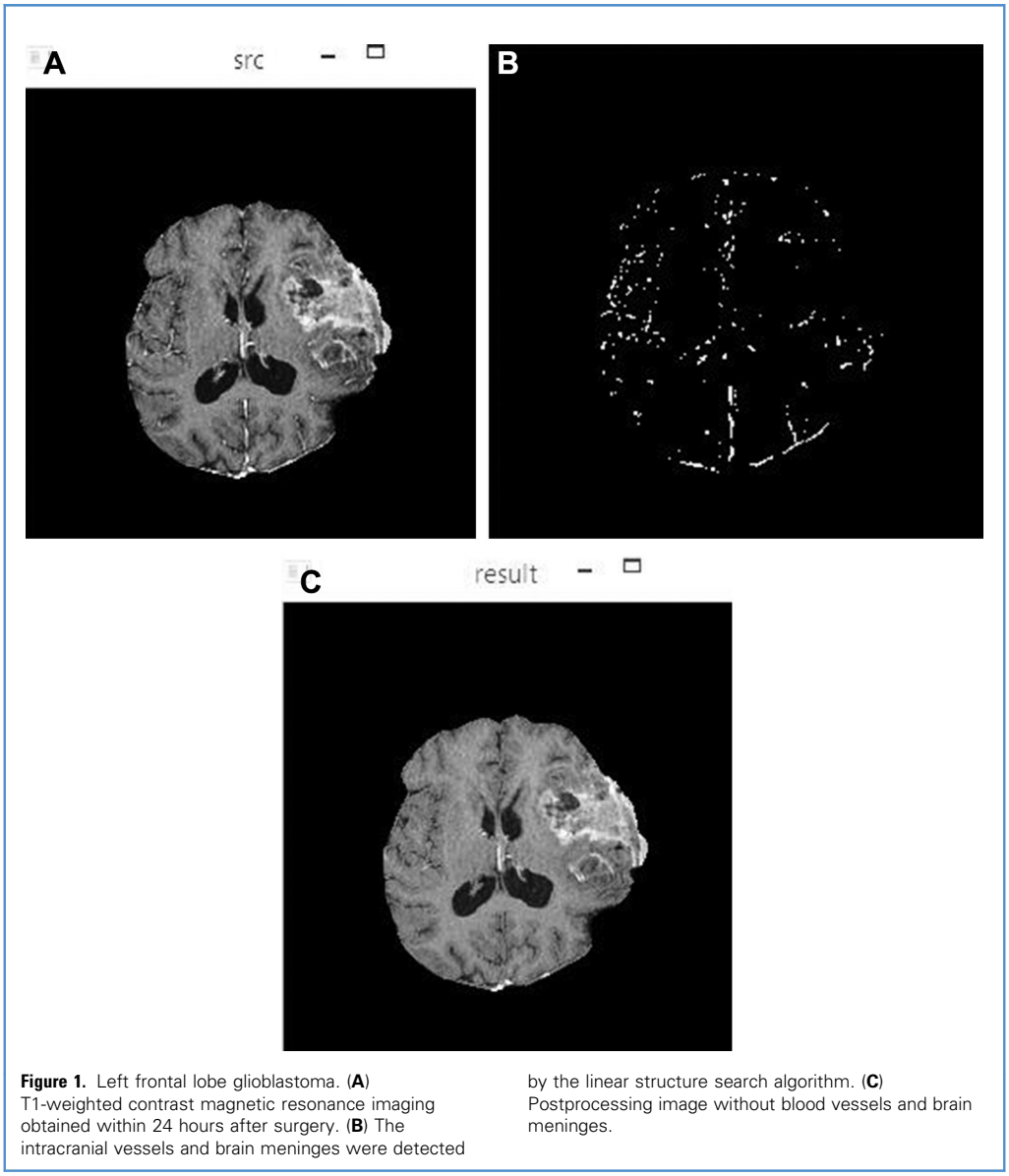


**Figure 1.** Left frontal lobe glioblastoma. (**A**) T1-weighted contrast magnetic resonance imaging obtained within 24 hours after surgery. (**B**) The intracranial vessels and brain meninges were detected by the linear structure search algorithm. (**C**) Postprocessing image without blood vessels and brain meninges.

The next step was to apply a linear structure search algorithm to the postsegmentation images for the verification and subtraction of intracranial vessels and brain meninges (Figure 1).

In the final step, a physician user contoured the target area with residual tumor on 1 axial slice (Figure 2F).

Then we determined the relationship between the overall survival of patients and the postoperative volume of the tumor contrast-enhancing part. In 100% of cases from our observation group, patients lived >6 months with a tumor remnant of <2.5 $cm^3$. Therefore, patients were divided into 2 groups. The first group included patients with residual tumor volume <2.5 $cm^3$, and the second group included all other patients. The groups were checked for homogeneity according to the following criteria: 1) patient general state prior to surgery (Karnofsky Performance Status Scale); 2) volumetric parameters of the tumor; and 3) preoperative contrast-enhancing tumor volume part.

## Statistical Analysis

The homogeneity of the groups was verified using the following methods: Kruskal-Wallis 1-way analysis of variance, Kolmogorov-Smirnov test and Student t distribution, and multivariate analysis of variance test. The influence of the volumetric indicators on the patient's OS was verified using the factor analysis based on the correlation matrix of the involved variables. OS of the patients was assessed using the Kaplan-Meier estimator (log-rank tests).

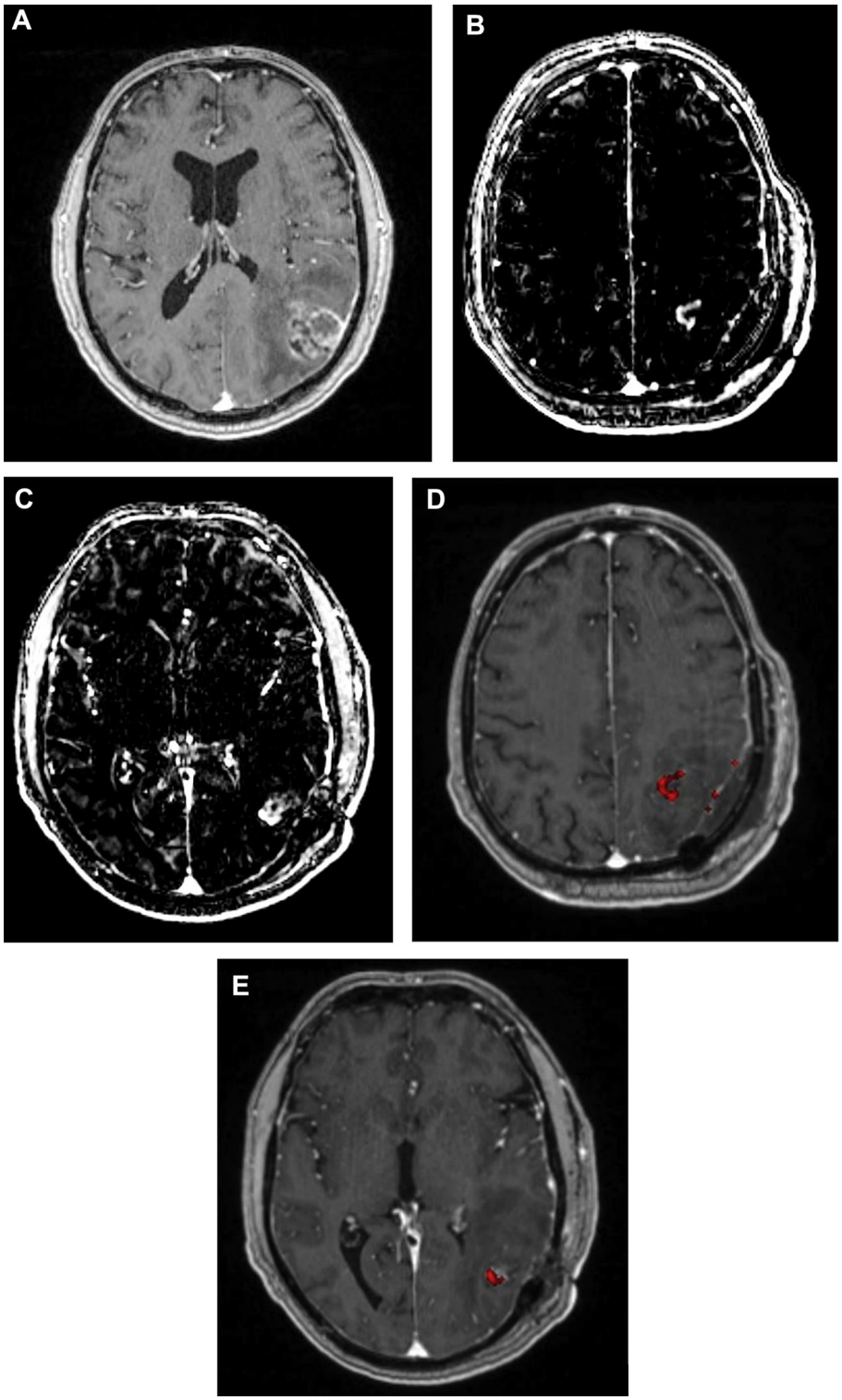


**Figure 2.** (**A**) Preoperative T1-weighted magnetic resonance imaging (MRI) with contrast of axial slice with left temporal lobe glioblastoma. (**B** and **C**) Postoperative T1-weighted MRI subtraction of axial slices. (**D** and **E**) The tumor remnants (*red color*) were indicated in the NeuroSegment software. (**F**) The target area was contoured by the user on 1 axial slice. (Continues)

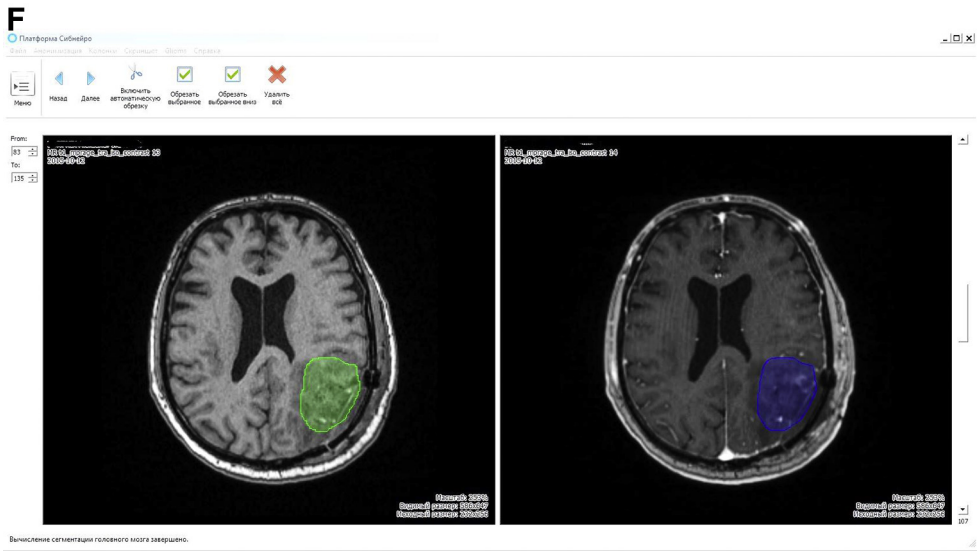


**Figure 2.** (Continued).

**Table 1.** Correlation Between Tumor Volumetric Parameters and Patient Overall Survival

| Correlation Matrix Parameter | OS | V_Flair | V_postop | V_preop |
|---|---|---|---|---|
| OS | | | | |
| Pearson correlation | 1 | −0.310 | −0.606* | −0.124 |
| Sig. (2-tailed) | | 0.131 | 0.000 | 0.446 |
| Number of patients | 57 | 25 | 57 | 40 |
| V_Flair | | | | |
| Pearson correlation | −0.310 | 1 | 0.250 | 0.322 |
| Sig. (2-tailed) | 0.131 | | 0.227 | 0.125 |
| Number of patients | 25 | 25 | 25 | 24 |
| V_postop | | | | |
| Pearson correlation | −0.606* | 0.250 | 1 | 0.235 |
| Sig. (2-tailed) | 0.000 | 0.227 | | 0.144 |
| Number of patients | 57 | 25 | 57 | 40 |
| V_preop | | | | |
| Pearson correlation | −0.124 | 0.322 | 0.235 | 1 |
| Sig. (2-tailed) | 0.446 | 0.125 | 0.144 | |
| Number of patients | 40 | 24 | 40 | 40 |

FLAIR, fluid-attenuated inversion recovery; OS, overall survival; Sig, significance; V_Flair, volume of hyperintense signal on T2-Flair; V_postop, postoperative volume; V_preop, preoperative volume.
*Correlation is significant at the 0.01 level (2-tailed).

**Table 2.** Patient Characteristics

| Patient Characteristics | First Group* | Second Group† |
|---|---|---|
| Tumor localization | | |
| Temporal lobe | 16 (45.7) | 7 (38.1) |
| Frontal lobe | 6 (17.1) | 5 (23.8) |
| Parietal lobe | 5 (14.3) | 0 (0) |
| Occipital lobe | 4 (11.4) | 6 (28.6) |
| Several lobes | 4 (11.4) | 4 (9.5) |
| Karnofsky Performance Status Scale | | |
| 100—90 | 25 (71.4) | 16 (72.7) |
| 70—80 | 8 (22.9) | 3 (13.6) |
| 50—60 | 2 (5.7) | 3 (13.6) |
| Tumor volume before surgery (preoperative volume of tumor contrast-enhanced part plus necrosis) ($cm^3$) | 338 ± 7 | 45.4 ± 6 |
| Preoperative volume of tumor contrast-enhanced part ($cm^3$) | 19.7 ± 5.3 | 17.1 ± 4.1 |
| Postsurgery contrast-enhanced tumor volume ($cm^3$) | 1.5 ± 0.13 | 10.2 ± 1.3 (range, 4—23) |
| Patient's glioma with methylated MGMT promoter | 15 (42.9) | 9 (40.9) |
| OS (months) | 19.6 ± 3.3 (median, 18) | 5.4 ± 0.8 (median, 4) |

Values are mean ± SD or number of patients (%). MGMT, $O^6$-methylguanine-DNA methyltransferase methylation status.
*Postoperative volume of the tumor contrast-enhanced part <2.5 $cm^3$.
†Postoperative volume of the tumor contrast-enhanced part >2.5 $cm^3$.

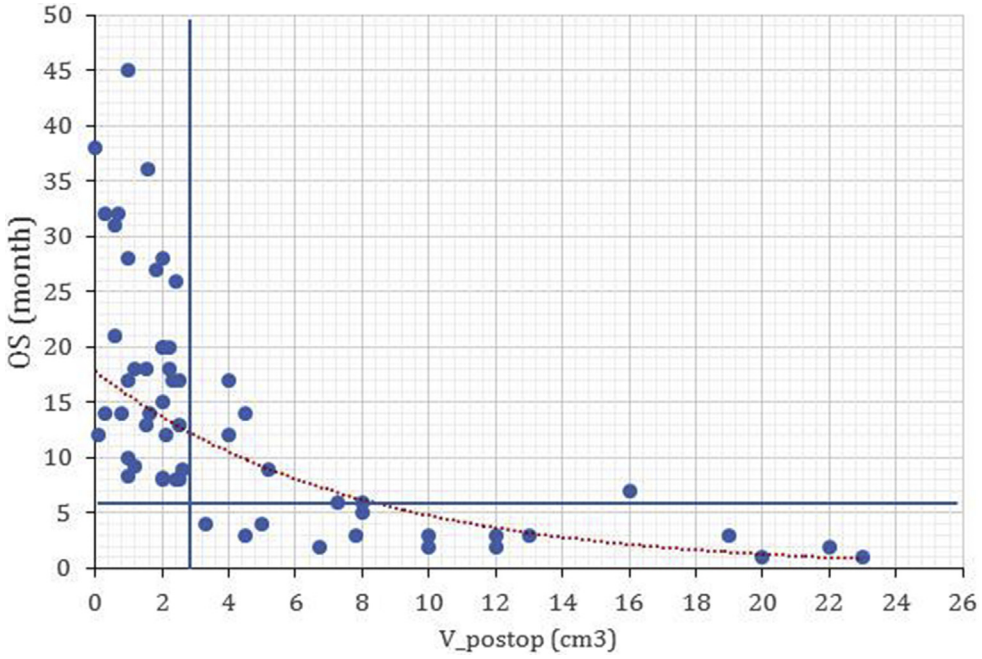


**Figure 3.** Graph of survival versus postoperative volume of the tumor contrast-enhancing part with exponential trend line ($y = 17.957e\text{-}0.132x$, $R^2 = 0.6448$, where $y$ is life expectancy and $x$ is the volume tumor contrast-enhanced part). OS, overall survival; V_postop, postoperative volume.

## RESULTS

Correlation analysis between the postoperative volume of the tumor contrast-enhancement part and the patient's OS revealed a significant level (on the Chaddock scale) of inverse correlation (Table 1 and Figure 2).

Residual tumor volume associated with OS of >6 months was determined as <2.5 $cm^3$. Therefore, 2 groups of patients were formed (Table 2).

First and second groups of patients (postoperative volume of tumor contrast-enhanced part <2.5 $cm^3$ and >2.5 $cm^3$, respectively).

In the first group, there were 3 long-term survivors (8.5%). These patients were alive at the end of the study.

Data analysis of the preoperative tumor volume, volume of necrosis, and contrast enhancing part in these groups showed the normal distribution of values and the equality of variances (Livin criterion for dispersions equality, $P > 0.05$). Analysis of variance test did not reveal statistically significant differences between groups for these parameters, therefore confirming the homogeneity of the groups. Multivariate Pillai trace = 0.247 also confirmed the absence of differences for the dependent variables between the formed groups ($P = 0.184$) and the absence of impact on OS.

OS in these groups was significantly different (log-rank test, $P < 0.01$) (Figure 3).

The mortality risk in the first 6 months after tumor resection is 3.4 times higher when the tumor remnant is >2.5 $cm^3$ (risk ratio, 3.4; $P = 0.0002$) (Figure 4).

## DISCUSSION

A recent large systematic review concluded that the extent of resection of the contrast-enhancing part of the tumor had significant impact on the final outcome,[17] even though not all surveyed publications found a statistically significant correlation. In general, gross total resection was associated with improved survival when compared with biopsy only.[4,5,18,19] Consequently, the measurements of residual tumor volume on MRI should become a part of standard postsurgical assessment. However, the methods currently accepted in neurosurgical practice, such as MacDonald criteria and Response Evaluation Criteria in Solid Tumors, are based on measurements of linear tumor parameters[20-22] and do not involve calculations of residual tumor volume.[23] At the same time, overall tumor burden is related to tumor volume rather than its linear dimensions, and volumetric characterization of residual tumor holds promise for more accurate prediction of surgical outcomes.[4,19,23-26] Better methods for volumetric assessment of tumor remnants are being developed by researchers,[19,25] but practical tools are not currently available for neurosurgeons and neuroradiologists because of several challenges, including high degree of dependence on operator experience, subjectivity of measurements, and interobserver disagreement.[23] The variability is, to a large degree, caused by hyperintensity of T1-weighted MRI signal in dura mater, choroidal plexus, cerebral vessels, blood biodegradation products, and hemostatic material, which can be confused with

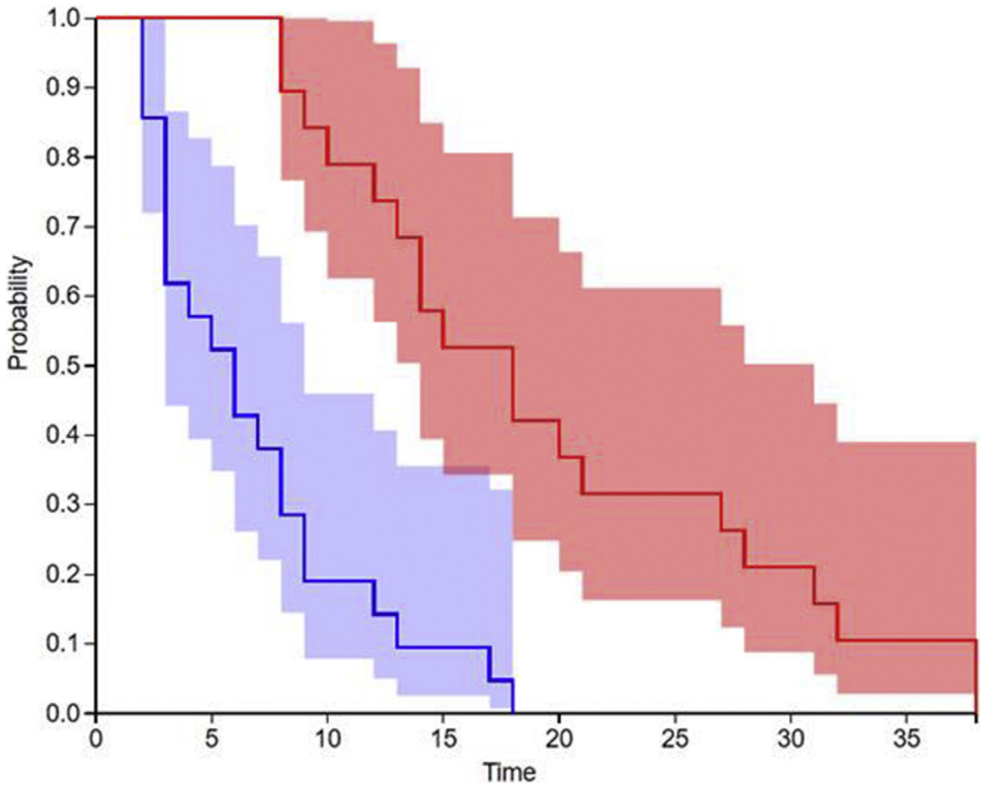


**Figure 4.** Kaplan-Meier survival analysis. The *red line* indicates the first group, and the *blue line* indicates the second group.

hyperintensity of residual tumor. Consequently, existing methods require a significant amount of manual input and are time consuming.

Earlier, we demonstrated that NeuroSegment had a high degree of consistency when used by both neurosurgeons and radiologists (agreement index improved from 0.67 to 0.97).

In this study, we used the NeuroSegment software[11] created to assess the extent of GBM resection by effective segmentation of postoperative hyperintense MRI signal.

In a series of 57 patients with brain GBMs we evaluated the influence of volumetric GBM characteristics on OS. We demonstrated that the postoperative volume of the contrast-enhancing part of the tumor was the most important volumetric predictor of OS, which is consistent with previous reports from other groups.[4,17,19,27] For example, similar conclusions were made by Lacroix et al.[4] They showed a significant increase in patient's OS when >98% of the contrast-enhancing part of the tumor was removed. Grabowski et al.[19] demonstrated the influence of volumetric parameters of the contrast-enhancing part of the tumor after surgery on OS in a group of 128 patients. The best result was achieved with the GBM remnant <2 $cm^3$. In our study, a significant difference in OS was obtained in the group of patients with a residual tumor volume <2.5 $cm^3$.

Limitations of this single-site study include limited statistical power. Therefore, these results should be interpreted with caution, and larger, prospective, multicenter trials using diverse imaging equipment should be conducted with proposed software to validate study findings.

## CONCLUSIONS

The new automated software for quantitative postoperative MRI analysis allows accurate and rapid assessment of the extent of GBM resection and is suitable for daily neurosurgical practice and research. The volume of MRI contrast-enhancing GBM remnant after surgery, automatically measured by the software, was a significant predictor for early postoperative progression and death in studied patient groups. A randomized study in a larger patient cohort is warranted.

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## REFERENCES

1. Albert FK, Forsting M, Sartor K, Adams HP, Kunze S. Early postoperative magnetic resonance imaging after resection of malignant glioma: objective evaluation of residual tumor and its influence on regrowth and prognosis. *Neurosurgery*. 1994;34:45-60.

2. Chow KL, Gobin YP, Cloughesy T, et al. Prognostic factors in recurrent glioblastoma multiforme and anaplastic astrocytoma treated with selective intra-arterial chemotherapy. *AJNR Am J Neuroradiol*. 2000;21:471-478.

3. Nabors LB, Portnow J, Ammirati M, et al. NCCN guidelines insights: central nervous system cancers, version 1.2017. *J Natl Compr Canc Netw*. 2017; 15:1331-1345.

4. Lacroix M, Abi-Said D, Fourney DR, et al. A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. *J Neurosurg*. 2001;95:190-198.

5. Laws ER, Parney IF, Huang W, et al. Survival following surgery and prognostic factors for recently diagnosed malignant glioma: data from the Glioma Outcomes Project. *J Neurosurg*. 2003; 99:467-473.

6. Schucht P, Beck J, Abu-Isa J. Gross total resection rates in contemporary glioblastoma surgery: results of an institutional protocol combining 5-aminolevulinic acid intraoperative fluorescence imaging and brain mapping. *Neurosurgery*. 2012;71: 927-935 [discussion: 935-936].

7. Keles GE, Anderson B, Berger MS. The effect of extent of resection on time to tumor progression and survival in patients with glioblastoma multiforme of the cerebral hemisphere. *Surg Neurol*. 1999;52:371-379.

8. Naeini KM, Pope WB, Cloughesy TF, et al. Identifying the mesenchymal molecular subtype of glioblastoma using quantitative volumetric analysis of anatomic magnetic resonance images. *Neuro Oncol*. 2013;15:626-634.

9. Nestler U, Lutz K, Pichlmeier U, et al. Anatomic features of glioblastoma and their potential impact on survival. *Acta Neurochir (Wien)*. 2015;157: 179-186.

10. Stummer W, Reulen HJ, Meinel T, et al. Extent of resection and survival in glioblastoma multiforme: Identification of and adjustment for bias. *Neurosurgery*. 2008;62:564-576 [discussion: 564-576].

11. Krivoshapkin AL, Sergeev GS, Gaĭtan AS, Kurbatov VP, Kal'neus LE, Tarantsev IG. New software for objective evaluation of brain glioblastoma resection degree. *Zh Vopr Neirokhir Im N N Burdenko*. 2014;78:33-40.

12. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol*. 2016;131:803-820.

13. Richard S. *Image Alignment and Stitching: A Tutorial, Vol. 2*. 2006:1-104.

14. Sinclair AG, Scoffings DJ. Imaging of the postoperative cranium. *Radiographics*. 2010;30:461-482.

15. Anthony Y, Kichenassamy S, Kumar A, Olver P, Tannenbaum A. A geometric snake model for segmentation of medical imagery. *IEEE Trans Med Imaging*. 1997;16:199-209.

16. Osher S, Fedkiw R. *Level Set Methods and Dynamic Implicit Surfaces*. New York: Springer-Verlag; 2003.

17. Brown TJ, Brennan MC, Li M, et al. Association of the extent of resection with survival in glioblastoma: a systematic review and meta-analysis. *JAMA Oncol*. 2016;2:1460-1469.

18. Buckner JC. Factors influencing survival in high-grade gliomas. *Semin Oncol*. 2003;30(6 suppl 19): 10-14.

19. Grabowski MM, Recinos PF, Nowacki AS, et al. Residual tumor volume versus extent of resection: predictors of survival after surgery for glioblastoma. *J Neurosurg*. 2014;121:1115-1123.

20. James K, Eisenhauer E, Christian M, et al. Measuring response in solid tumors: unidimensional versus bidimensional measurement. *J Natl Cancer Inst*. 1999;91:523-528.

21. Macdonald DR, Cascino TL, Schold SC Jr, Cairncross JG. Response criteria for phase II studies of supratentorial malignant glioma. *J Clin Oncol*. 1990;8:1277-1280.

22. Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. *J Natl Cancer Inst*. 2000;92:205-216.

23. Kubben PL, Postma AA, Kessels AG, van Overbeeke JJ, van Santbrink H. Intraobserver and interobserver agreement in volumetric assessment of glioblastoma multiforme resection. *Neurosurgery*. 2010;67:1329-1334.

24. Chaichana KL, Jusue-Torres I, Navarro-Ramirez R, et al. Establishing percent resection and residual volume thresholds affecting survival and recurrence for patients with newly diagnosed intracranial glioblastoma. *Neuro Oncol*. 2014;16: 113-122.

25. Meier R, Porz N, Knecht U, et al. Automatic estimation of extent of resection and residual tumor volume of patients with glioblastoma. *J Neurosurg*. 2017;127:798-806.

26. Senft C, Bink A, Franz K, Vatter H, Gasser T, Seifert V. Intraoperative MRI guidance and extent of resection in glioma surgery: a randomised, controlled trial. *Lancet Oncol*. 2011;12:997-1003.

27. Vuorinen V, Hinkka S, Farkkila M, Jaaskelainen J. Debulking or biopsy of malignant glioma in elderly people: a randomised study. *Acta Neurochir (Wien)*. 2003;145:5-10.

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