Clinical Neurology and Neurosurgery 196 (2020) 105972

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Glioblastoma survival is better analyzed on preradiotherapy MRI than on postoperative MRI residual volumes: A retrospective observational study

Amaury De Barros[a,b,*], Justine Attal[b,c], Margaux Roques[b,d], Julien Nicolau[a,b], Jean-Christophe Sol[a,b], Saloua Charni[b,f], Elizabeth Cohen-Jonathan-Moyal[b,c,e], Franck-Emmanuel Roux[a,b,f]

[a] Pôle Neuroscience (Neurochirurgie), Toulouse University Hospital, Toulouse, France
[b] Université Paul Sabatier, Toulouse III, 118 route de Narbonne, Toulouse, 31062, France
[c] Department of Radiation Oncology, Institut Universitaire du Cancer de Toulouse-Oncopôle, 1 Avenue Irène Joliot-Curie, 31059, Toulouse, France
[d] Neuroradiology Department, Toulouse University Hospital, Toulouse, France
[e] INSERM U1037, Centre de Recherche contre le Cancer de Toulouse, 1 avenue Irène Joliot-Curie, Toulouse Cedex, 31059, France
[f] CNRS UMR5549 Brain and Cognition (Cerco), Hôpital Purpan, Toulouse, France

ARTICLE INFO

Keywords:
Glioblastoma
Radiotherapy
Extent of resection
Residual volume
Volumetry

ABSTRACT

Objectives: Establishing an overall survival prognosis for resected glioblastoma during routine postoperative management remains a challenge. The aim of our single-center study was to assess the usefulness of basing survival analyses on preradiotherapy MRI (PRMR) rather than on postoperative MRI (POMR).

Patients and methods: A retrospective review was undertaken of 75 patients with glioblastoma treated at our institute. We collected overall survival and MRI volumetric data. We analyzed two types of volumetric data: residual tumor volume and extent of resection. Overall survival rates were compared according to these two types of volumetric data, calculated on either POMR or PRMR and according to the presence or absence of residual enhancement.

Results: Analysis of volumetric data revealed progression of some residual tumors between POMR and PRMR. Kaplan-Meier analysis of the correlations between extent of resection, residual tumor volume, and overall survival revealed significant differences between POMR and PRMR data. Both MRI scans indicated a difference between the complete resection subgroup and the incomplete resection subgroup, as median overall survival was longer in patients with complete resection. However, differences were significant for PRMR (25.3 vs. 15.5, $p = 0.012$), but not for POMR (21.3 vs. 15.8 months, $p = 0.145$). With a residual tumor volume cut-off value of 3 cm^3, Kaplan-Meier survival analysis revealed non-significant differences on POMR ($p = 0.323$) compared with PRMR ($p = 0.007$).

Conclusion: Survival in patients with resected glioblastoma was more accurately predicted by volumetric data acquired with PRMR. Differences in predicted survival between the POMR and PRMR groups can be attributed to changes in tumor behavior before adjuvant therapy.

1. Introduction

Glioblastoma (GBM) is the most common malignant primary brain tumor in adults, with an incidence rate of 25 per 100,000 population [1–3]. Performing maximum safe resection is now standard practice in the neurosurgical community. Surgical techniques such as awake surgery, intraoperative MRI, intraoperative ultrasound, and fluorescence-guided microsurgery have been developed in order to achieve full resection wherever surgically possible [4].

Extent of resection and residual volume are the classic metrics used in the postoperative period to quantify tumor resection and estimate patient survival. *Extent of resection* allows data to be discretized as complete resection (or gross total resection), near total resection, subtotal resection, or partial resection, and has been extensively correlated with overall survival (OS). However, *residual volume* seems to be a more accurate predictor of survival [5,6]. For example, a recent analysis based on 1511 patients showed a strong log-linear relationship between OS and residual volumes ranging from 0 to 20 cm^3 [7]. Several authors have proposed cut-off values below which the usefulness of resective surgery is debatable. These values range from 70 to 98 % for extent of

* Corresponding author at: Service Neurochirurgie Hôpital Pierre-Paul Riquet Purpan, 1 place du Dr Baylac, 31300, Toulouse, France.
E-mail address: debarros.a@chu-toulouse.fr (A. De Barros).

https://doi.org/10.1016/j.clineuro.2020.105972
Received 20 January 2020; Received in revised form 9 April 2020; Accepted 26 May 2020
Available online 29 May 2020

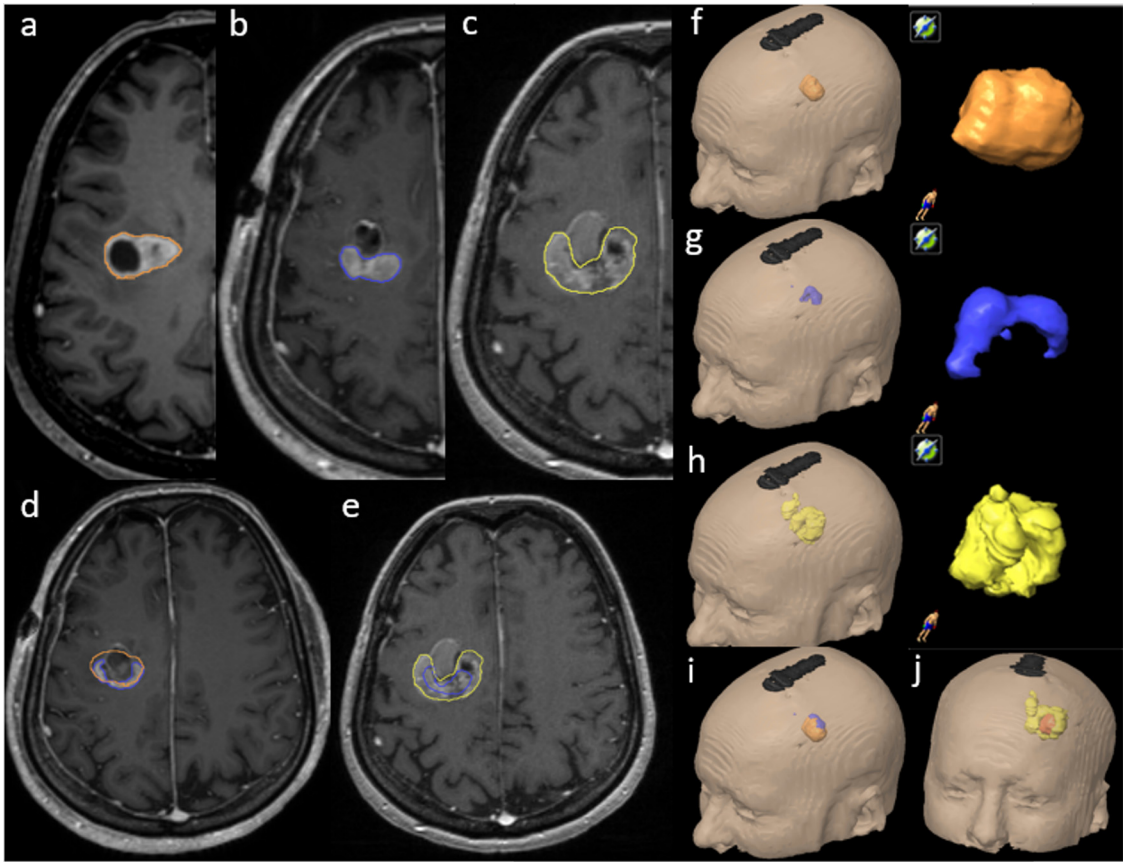

Fig. 1. Volumetric analyses performed on pre-operative, post-operative (POMR) and pre-radiotherapy (PRMR) MRI in a 67 years-old female patient with a right precentral glioblastoma in eloquent region.
a: Pre-operative T1-Gado MRI with orange initial tumoral volume contouring.
b: Post-operative T1-Gado MRI (POMR) with blue residual tumoral volume contouring.
c: Pre-radiotherapy T1-Gado MRI (PRMR) with yellow tumoral volume contouring.
d: POMR with initial (orange) and residual (blue) tumoral volume contouring.
e: PRMR with residual (blue) and pre-radiotherapy tumoral volume contouring.
f: 3D volume rendering from Pre-operative T1-Gado MRI (4.795 cm^3).
g: 3D volume rendering from POMR (1.568 cm^3).
h: 3D volume rendering from PRMR (11.729 cm^3).
i: Combined 3D volume rendering from Pre-operative T1-Gado MRI and POMR.
j: Combined 3D volume rendering from Pre-operative T1-Gado MRI and PRMR.
The delay between POMR and PRMR was 27 days. The POMR extent of resection was 67.3 %. The vicinity of the primary motor cortex and the cortico-spinal tractus explained the suboptimal resection. An "explosive" early regrowth occurred with a PRMR residual extent of resection estimated at −144.6 %. She died 4 months after surgery.

resection, and from 2 to 5 cm^3 for residual volume [5,6,8–11]. There have been numerous meta-analyses and literature reviews dealing with volume metrics and OS in GBM [12–16].

Guidelines recommend performing an MR examination within 72 h of surgery to evaluate the extent of surgical resection, 2–6 weeks after chemoradiotherapy to evaluate response, and then every 3–4 months for follow up [17]. A preradiotherapy MRI scan (PRMR) can help neurooncologists diagnose and manage true or pseudoprogression of GBM, by indicating which patients have early progression before the start of chemoradiotherapy. Furthermore, PRMR can be used to identify different patterns of growth correlated with different OS rates [1821], early progression being correlated with a poorer prognosis [21]. Although some authors claim that preradiotherapy tumor volume is an independent prognostic factor associated with a poorer OS [19,20], no study has yet compared OS rates in relation to postoperative MRI (POMR) versus PRMR residual volumes.

The aim of our study was to establish which MRI (POMR or PRMR) examination based on residual volumes is more predictive of OS values for resected GBM.

2. Material and methods

2.1. Patients

This retrospective study formed the second part of a research project (for the patient selection flowchart, see [21]). Briefly, we included 75 patients with newly diagnosed IDH-wildtype supratentorial GBM (WHO 2016 classification) [22] treated at our institute between 2007 and 2018. All these patients underwent surgical resection first, followed by chemoradiotherapy, in accordance with STUPP et al.'s protocol [23].

For each patient, we collected OS, postoperative tumor volume and extent of resection, and preradiotherapy tumor volume and residual extent of resection.

We studied times between surgery, POMR, and PRMR, and times between surgery and the start of radiotherapy. Based on POMR, extent of tumor resection was classified as incomplete resection, if there was residual enhancing tissue, or complete resection if the tumor's enhancing component total resection had been achieved [19,24].

Readers should be aware that patients treated rapidly after surgery

Table 1
Summary of the patient characteristics used for this study.

Characteristics	
Number of patients:	75
Age (years):	62 (25 – 84)
Median (range)	
Gender/Sex ratio:	1.21
Male/Female	41(55 %)/34(45 %)
Days between POMR and PRMR:	27 (10–64)
Median (range)	
Days between surgery and radiotherapy:	43 (34–79)
Median (range)	
Initial tumoral volume (cm3):	24.20 (0.09–114.65)
Median (range)	
POMR tumoral volume (cm3):	0.77 (0.00–31.65)
Median (range)	
POMR extent of resection (%):	98 % (44–100)
Median (range)	
POMR:	27 (36 %) / 49 (64 %)
Complete resection / Incomplete resection	
PRMR tumoral volume (cm3):	2.22 (0.00–74.48)
Median (range)	
PRMR residual resection (%):	89 % (−505 to 100)
Median (range):	
PRMR:	19 (25 %) / 56 (75 %)
No residual tumor / Residual tumor	
Overall survival (Months):	18.9 (15.8–23.5)
Median (range)	
Number of patients alive:	18/75 (24 %)
Number of tumor regrowth:	54/75 (72 %)

Abbreviations: POMR: Postoperative MRI; PRMR: Preradiotherapy MRI.

did not undergo a PRMR in our institution so they could not be included.

All data were anonymized and, as required under French law, the French Data Protection Authority was informed.

2.2. Image acquisition

Preoperative and immediate POMR were performed on 1.5 (Philips Ingenia; Philips, Best, The Netherlands; or Siemens Avanto; Siemens, Munich, Germany) or 3 T (Philips Intera Achieva; Philips, Best, The Netherlands) MR scanners. All sequences included at least the acquisition of a 1-mm thick 3D T1-weighted sequence before and after injection of a gadolinium-based contrast agent. Diffusion-weighted images (DWI) were obtained, and we calculated the apparent diffusion coefficient (ADC) map. All PRMR images were acquired with another 1.5 T scanner in the radiotherapy department. All sequences included at least 1-mm thick T1 gradient-echo pre- and post-contrast enhancement.

2.3. Image analyses

As described elsewhere in greater detail [21], visual assessment was performed by the first author (ADB) on iPlan Net Server (BrainLab, Munich, Germany). Complicated cases were reviewed with a neuroradiologist (MR). An image fusion tool was used to compare two different images (T1/T1 post-contrast or T1 post-contrast/ADC). Next, volumetric measurements were made using semi-automatic segmentation (smartbrush) or the manual segmentation option proposed by the software. We performed segmentation on gadolinium contrast enhancement on initial MRI, then POMR and PRMR. An example of volumetry is provided in Fig. 1. Regions of new contrast enhancement on the PRMR were visually compared with the extent of reduced diffusion seen on postsurgical ADC, to differentiate tumor growth from postsurgical injury. We assumed that necrotic tumor with peripheral enhancement was considered in its entirety, in terms of volume on presurgical images. Regarding the postoperative MRI scans, a thin contrast enhancement rim was not considered for volumetry. Thick linear enhancement was considered abnormal and was delineated without the resection cavity for volumetry [25].

2.4. Volumetric analyses

All previous studies based on volumetry used postsurgical MRI to calculate residual contrast-enhancing tumor volume and its correlate (extent of resection). We performed similar calculations, but using PRMR in addition to POMR, to obtain *PRMR residual tumor volume* and *PRMR residual extent of resection* for comparison with *POMR residual tumor volume* and *POMR extent of resection*. POMR extent of resection was calculated as follows: (preoperative tumor volume - postoperative tumor volume)/preoperative tumor volume). The same procedure was followed to calculate *residual extent of resection* on PRMR, replacing postoperative volume with preradiotherapy volume. We introduced the term *residual extent of resection* for PRMR compare to *extent of resection* which is a dedicated term for POMR volumetric measurements. It is important to note that *residual extent of resection* on PRMR could have a negative value if the residual tumor volume was greater than the initial one, as a result of *explosive* regrowth between POMR and PRMR. For example, one patient with an initial tumor volume of 21.01 cm^3 had an estimated 93.5 % extent of resection on POMR (residual volume: 1.37 mL). However, 6 weeks later on PRMR, tumor volume was 36.11 cm^3, with a *residual extent of resection* of $\frac{21.01 - 36.11}{21.01} = -0.72$

2.5. Statistical analysis

Survival was calculated by our statistician (SC) as the time between the date of surgery and date of death or date last known alive, and censored accordingly. Kaplan-Meier curves were plotted to compare survival in the complete resection and incomplete resection groups. For all graphs, we performed a log-rank test to evaluate statistical significance. *P* values less than or equal to 0.05 were considered statistically significant. Statistical analyses were performed with the help of an experienced statistician from the neurological department of our institution, using commercially available software (XLSTAT 2017; Addinsoft, Paris, France).

3. Results

Volumetric data and different times are summarized in Table 1. Patients' median age was 62 years, and 55 % were male. Median overall survival was 18.9 months (range: 15.823.5). At the time of the final assessment (May 2018), 18 of the 75 patients we had initially studied were still alive. As explained in a previous study [21], 54 patients experienced regrowth between POMR and PRMR that could be either fairly moderate or explosive, and eight of these patients belonged to the POMR complete resection subgroup ($n = 27$). Fig. 2 illustrates changes in extent of resection and tumor volume between POMR and PRMR, showing some cases of residual tumor progression. Because of these cases, we postulated that the data acquired with PRMR are more sensitive than POMR data when it comes to predicting patients' OS. Table 2 confirms this hypothesis, showing median OS values with associated *p* values according to complete resection versus incomplete resection, extent of resection, and residual tumor volume. Fig. 3 shows the Kaplan-Meier OS curves for complete resection versus incomplete resection. A log-rank test showed that the difference in OS became significant when OS was calculated on PRMR ($p = 0.012$) instead of POMR ($p = 0.145$). Fig. 4 shows that PRMR predicted OS significantly better than POMR, regarding the evaluation of residual tumor volumes. We defined an arbitrary cut-off volume of 3 cm^3 for residual tumor in accordance with the literature described above. (our study was not built to define a precise reliable cut-off and it was only defined for the illustration of our purpose). In the POMR group, median survival was 15.8 months (95 % CI [14.8, 25.5]) for residual tumor > 3cm^3, and 14.9 months (95 % CI [8.2, 20.9]) for residual tumor < 3cm^3 ($p =$

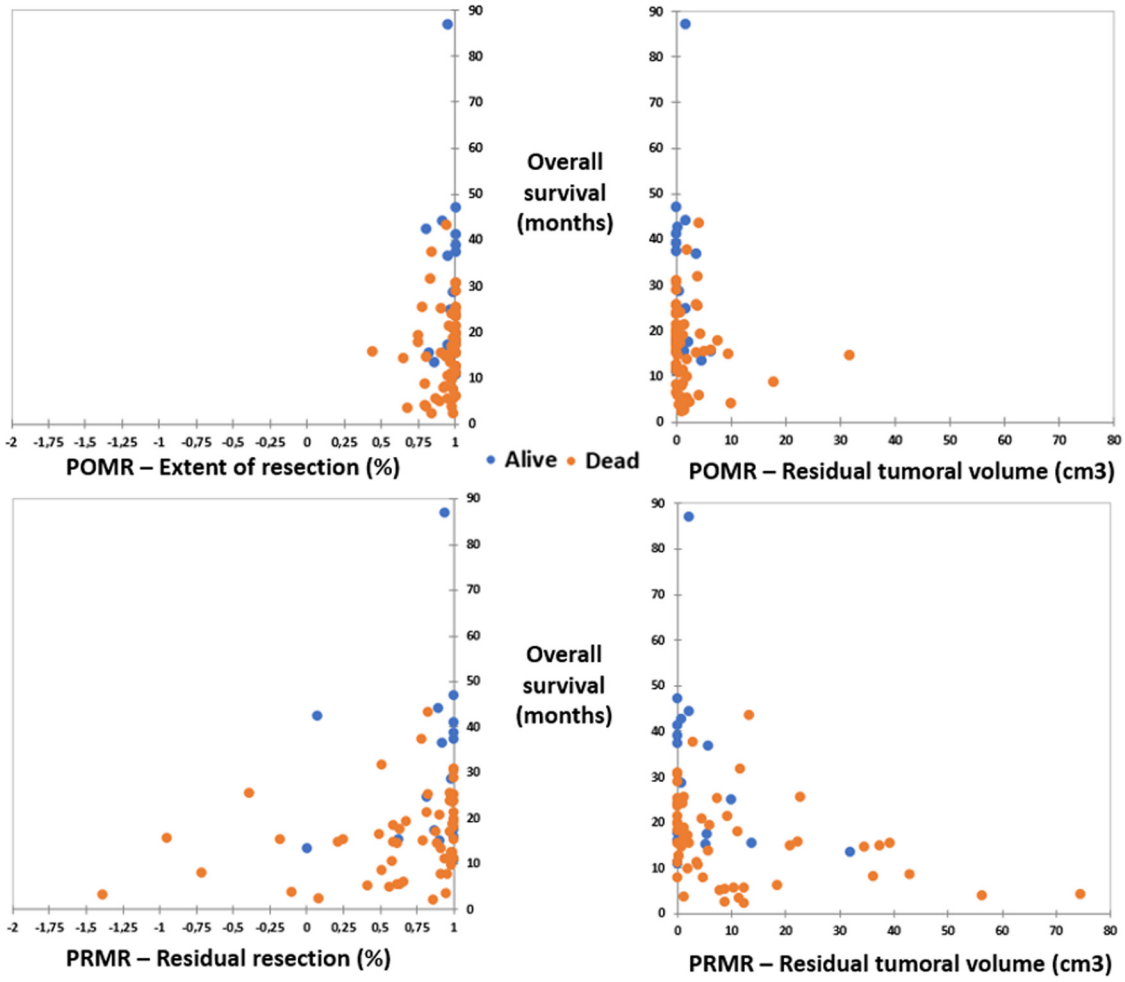

Fig. 2. Scatterplots of extent of resection according to POMR (top) and PRMR (bottom) on the left and scatterplots of tumor volume according to POMR (top) and PRMR (bottom) on the right.
Both residual tumor volume and extent of resection values were more scattered, owing to some early regrowth between surgery and radiotherapy. Median extent of resection was 98 % for all patients, and 75 % of patients had > 90 % resection on POMR. PRMR indicated a median extent of resection of 89 %, and only 49 % of patients had > 90 % resection. Regarding residual volume, we found a median residual volume of 0.77 cm^3 (77 % of patients with a residue < $3cm^3$) on POMR, and a median residual volume of 2.22 cm^3 (only 53 % of patients with a residue < $3cm^3$) on PRMRC.
Abbreviations: POMR: postoperative MRI; PRMR: preradiotherapy MRI.

0.231). By comparison, OS for the PRMR group appeared more contrasted, as median survival was 17.2 months (95 % CI [15.2, 24.0]) for a tumor volume < $3cm^3$, and 14.8 months (95 % CI [8.2, 19.4]) for a tumor volume > $3cm^3$ ($p = 0.007$).

In summary, PRMR was a significantly better predictor of OS than POMR was, according to the notions of extent of resection and residual tumor volume.

Table 2
of the patient characteristics used for.

	POMR Median (range) in months	*p* value	PRMR Median (range) in months)	*p* value
Complete resection:	21.29 (18.20 – 28.88)	→	25.30 (20.01 – 30.85)	
Number of patients (%)	*27/75 (36 %)*	***Early regrowth***	*19/75 (25 %)*	
Incomplete resection:	15.77 (13.63 – 19.35)	0.145	15.47 (13.63 – 18.89)	**0.012**
Number of patients (%)	*48/75 (64 %)*		*56/75 (75 %)*	
Extent of resection:			**Residual extent of resection:**	
100 %	21.29 (18.20 – 28.88)		25.30 (20.01 – 30.85)	
90 – 99%	16.56 (13.63 – 21.36)		17.05 (12.55 – 24.02)	
< 90 %	14.82 (5.75 – 25.53)	0.231	15.47 (14.52 – 18.56)	**0.031**
Residual tumoral volume:				
0 cm3	21.29 (18.20 – 28.88)		25.30 (20.01 – 30.85)	
0 – 3 cm3	14.90 (8.25 – 20.90)		17.22 (15.21 – 24.02)	
> 3cm3	15.77 (14.82 – 25.53)	0.323	14.82 (8.25 – 19.35)	**0.007**

Abbreviations: POMR: postoperative MRI; PRMR: preradiotherapy MRI.

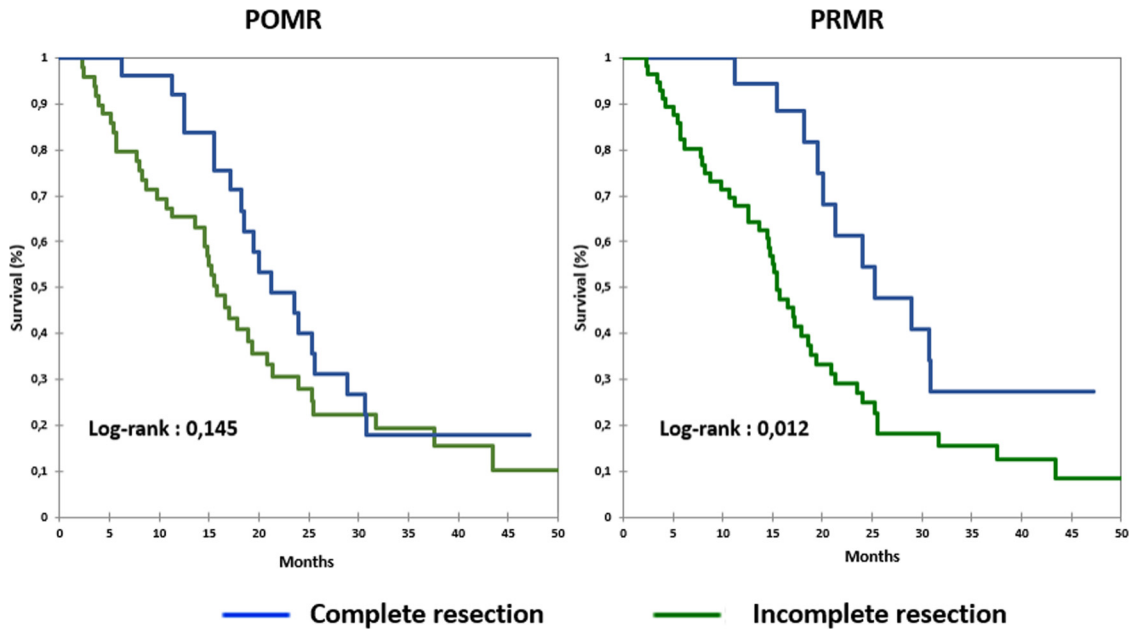

Fig. 3. Kaplan-Meier survival curves based on complete resection versus incomplete resection. Left: POMR-based curves; right: PRMR-based curves.
POMR classified 27 patients as complete resection, with a median survival of 21.3 months (95 % CI [18.2, 28.9]). PRMR classified 19 patients as complete resection, with a median survival of 25.3 months (95 % [20.0, 30.9]). For comparison, median survival decreased to 15.8 months (95 % CI [14.5, 20.9]) on POMR and 15.5 months (95 % CI [13.6, 18.9]) on PRMR for patients classified as incomplete resection.
Abbreviations: POMR: postoperative MRI; PRMR: preradiotherapy MRI.

4. Discussion

Extent of resection and residual tumor volume are acknowledged to be strong outcome factors for resected GBM [7,13], but to our knowledge, this is the first time that these factors have been evaluated by comparing data from POMR versus PRMR. The latter is now widely used in oncology centers, even though there are no clear recommendations to do so in current guidelines [17]. PRMR can result in modifications to radiation therapy planning, if it shows that the patient has an early tumor regrowth, and serve as a reference for imaging follow up. It can help clinicians distinguish between pseudo- and true progression at the first post-radiation MRI scan. In a previous paper, we showed that incomplete resection and longer delays between surgery and adjuvant treatment increase the risk of GBM regrowth and are factors for poorer outcomes [21]. In the current study, we demonstrated the importance of PRMR for evaluating survival in GBM. Differences between POMR and PRMR can be attributed to several factors still not completely understood. One of them could be the different patterns of GBM progression during the interval between surgery and radiotherapy, as shown by Majós et al. [18], who stratified patients according to the pattern of tumor regrowth on PRMR and found a steady and significant decrease in survival according to various regrowth patterns of resected GBM. Although they did not stratify their cohort according to residual tumor volume or extent of resection, their results

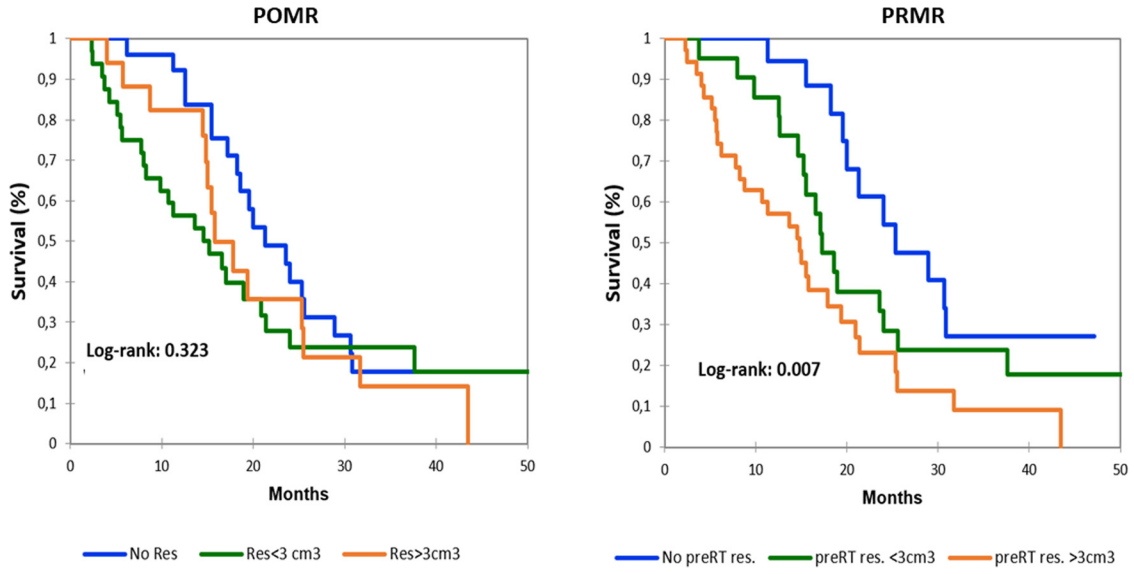

Fig. 4. Kaplan-Meier survival curves based on residual tumor volume (3-cm^3 cutoff). Left: POMR-based curves; right: PRMR-based curves.
This figure illustrates the differences between POMR and PRMR for stratified residual tumor volumes.
Abbreviations: POMR: postoperative MRI; PRMR: preradiotherapy MRI.

were similar to ours. These results need to be confirmed with larger prospective cohorts. Unfortunately, data based on volumetry can still be very time-consuming to acquire.

There are different GBM subtypes, and each behaves differently [26]. Many potential spectroscopic, diffusion, perfusion and molecular markers of early tumor regrowth before radiotherapy have been identified, with the debate focusing on which tumor profile is particularly at risk of rapid growth [19,21,24].

4.1. Limitations

Some points can limit the impact of this study. It was a retrospective study in a single center. This cohort did not reflect our real practices because of the exclusion of patients treated rapidly after surgery because of the absence of PRMR. It could, in part, explain why we failed to define OS statistical differences in the POMR group and why our delays could be judged by certain as too long. Another limit is the low statistical power of our limited sample. But, the aim of this study was not to establish the precise OS of the patients treated in our institution but to compare the utility of PRMR volumetric measures with POMR measures. Regarding the cut-off we used, it served solely to illustrate our purpose, as our study was not designed to define a precise and reliable cut-off. Furthermore, in the literature, cut-offs vary, bringing into question their medical relevance. We assume, like Ellingson and colleagues [7], that a linear relationship between OS and residual volumes is a more accurate indicator. However, the use of Kaplan-Meier curves always requires a cluster approach when comparing several groups. As one person performed all the volumetric measurements, this may have led to a measurement bias.

4.2. Conclusion

Volumetric data acquired with PRMR are more predictive of survival in patients with resected GBM. Differences in predicted survival between POMR and PRMR can be attributed to differences in tumor behavior prior to adjuvant therapy. Regarding the results of the current study and those in the literature, we urge physicians to systematically perform MRI before radiochemotherapy.

Funding

There was no funding for this study.

Ethical approval

All procedures performed in studies involving human participants complied with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

In accordance with the French Data Protection Act of 6 January 1978, the French Data Protection Authority (CNIL) was informed of this retrospective study.

CRediT authorship contribution statement

Amaury De Barros: Conceptualization, Data curation, Methodology, Writing - original draft, Writing - review & editing. **Justine Attal:** Conceptualization, Methodology, Investigation. **Margaux Roques:** Investigation. **Julien Nicolau:** Investigation. **Jean-Christophe Sol:** Project administration, Supervision. **Saloua Charni:** Methodology. **Elizabeth Cohen-Jonathan-Moyal:** Supervision. **Franck-Emmanuel Roux:** Conceptualization, Methodology, Project administration.

Declaration of Competing Interest

The authors declare they have no conflicts of interest.

References

[1] S. Larjavaara, R. Mäntylä, T. Salminen, H. Haapasalo, J. Raitanen, J. Jääskeläinen, et al., Incidence of gliomas by anatomic location, Neuro Oncol. 9 (3) (2007) 319–325, https://doi.org/10.1215/15228517-2007-016.

[2] I. Baldi, A. Gruber, A. Alioum, E. Berteaud, P. Lebailly, A. Huchet, et al., Descriptive epidemiology of CNS tumors in France: results from the Gironde Registry for the period 2000–2007, Neuro Oncol. 13 (12) (2011) 1370–1378, https://doi.org/10.1093/neuonc/nor120.

[3] Q.T. Ostrom, H. Gittleman, P. Liao, T. Vecchione-Koval, Y. Wolinsky, C. Kruchko, et al., CBTRUS Statistical Report: primary brain and other central nervous system tumors diagnosed in the United States in 2010–2014, Neurooncology 19 (suppl_5) (2017) v1–88, https://doi.org/10.1093/neuonc/nox158.

[4] T. Garzon-Muvdi, C. Kut, X. Li, K.L. Chaichana, Intraoperative imaging techniques for glioma surgery, Future Oncol. 13 (19) (2017) 1731–1745, https://doi.org/10.2217/fon-2017-0092.

[5] M.M. Grabowski, P.F. Recinos, A.S. Nowacki, J.L. Schroeder, L. Angelov, G.H. Barnett, et al., Residual tumor volume versus extent of resection: predictors of survival after surgery for glioblastoma, J. Neurosurg. 121 (5) (2014) 1115–1123, https://doi.org/10.3171/2014.7.JNS132449.

[6] P.Y.M. Woo, J.M.K. Ho, T.P.K. Tse, S.W. Lam, C.H.K. Mak, D.T.M. Chan, et al., Determining a cut-off residual tumor volume threshold for patients with newly diagnosed glioblastoma treated with temozolomide chemoradiotherapy: a multicenter cohort study, J. Clin. Neurosci. 63 (2019) 134–141, https://doi.org/10.1016/j.jocn.2019.01.022.

[7] B.M. Ellingson, L.E. Abrey, S.J. Nelson, T.J. Kaufmann, J. Garcia, O. Chinot, et al., Validation of post-operative residual contrast enhancing tumor volume as an independent prognostic factor for overall survival in newly diagnosed glioblastoma, Neuro-Oncology 20 (9) (2018) 1240–1250, https://doi.org/10.1093/neuonc/noy053.

[8] N. Sanai, M.-Y. Polley, M.W. McDermott, A.T. Parsa, M.S. Berger, An extent of resection threshold for newly diagnosed glioblastomas, J. Neurosurg. 115 (1) (2011) 3–8, https://doi.org/10.3171/2011.2.JNS10998.

[9] M.E. Oppenlander, A.B. Wolf, L.A. Snyder, R. Bina, J.R. Wilson, S.W. Coons, et al., An extent of resection threshold for recurrent glioblastoma and its risk for neurological morbidity, J. Neurosurg. 120 (4) (2014) 846–853, https://doi.org/10.3171/2013.12.JNS13184.

[10] K.L. Chaichana, I. Jusue-Torres, R. Navarro-Ramirez, S.M. Raza, M. Pascual-Gallego, A. Ibrahim, et al., Establishing percent resection and residual volume thresholds affecting survival and recurrence for patients with newly diagnosed intracranial glioblastoma, Neuro-Oncology 16 (1) (2014) 113–122, https://doi.org/10.1093/neuonc/not137.

[11] W. Stummer, H.-J. Reulen, T. Meinel, U. Pichlmeier, W. Schumacher, J.-C. Tonn, et al., Extent of resection and survival in glioblastoma multiforme: identification of and adjustment for bias, Neurosurgery 62 (3) (2008) 564–576, https://doi.org/10.1227/01.neu.0000317304.31579.17.

[12] T.J. Brown, M.C. Brennan, M. Li, E.W. Church, N.J. Brandmeir, K.L. Rakszawski, et al., Association of the extent of resection with survival in glioblastoma: a systematic review and meta-analysis, JAMA Oncol. 2 (11) (2016) 1460–1469, https://doi.org/10.1001/jamaoncol.2016.1373.

[13] D.A. Hardesty, N. Sanai, The value of glioma extent of resection in the modern neurosurgical era, Front. Neurol. [Internet] (2012), https://doi.org/10.3389/fneur.2012.00140 Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3474933/.

[14] S.L. Hervey-Jumper, M.S. Berger, Maximizing safe resection of low- and high-grade glioma, J. Neurooncol. 130 (2) (2016) 269–282, https://doi.org/10.1007/s11060-016-2110-4.

[15] J.P. Almeida, K.L. Chaichana, J. Rincon-Torroella, A. Quinones-Hinojosa, The value of extent of resection of glioblastomas: clinical evidence and current approach, Curr. Neurol. Neurosci. Rep. 15 (2) (2015) 517, https://doi.org/10.1007/s11910-014-0517-x.

[16] R.S. D'Amico, Z.K. Englander, P. Canoll, J.N. Bruce, Extent of resection in glioma-a review of the cutting edge, World Neurosurg. 103 (2017) 538–549, https://doi.org/10.1016/j.wneu.2017.04.041.

[17] M. Weller, M. van den Bent, K. Hopkins, J.C. Tonn, R. Stupp, A. Falini, et al., EANO guideline for the diagnosis and treatment of anaplastic gliomas and glioblastoma, Lancet Oncol. 15 (9) (2014) e395–403, https://doi.org/10.1016/S1470-2045(14)70011-7.

[18] C. Majós, M. Cos, S. Castañer, A. Pons, M. Gil, A. Fernández-Coello, et al., Preradiotherapy MR imaging: a prospective pilot study of the usefulness of performing an MR examination shortly before radiation therapy in patients with glioblastoma, AJNR Am. J. Neuroradiol. 37 (12) (2016) 2224–2230, https://doi.org/10.3174/ajnr.A4917.

[19] A. Pirzkall, C. McGue, S. Saraswathy, S. Cha, R. Liu, S. Vandenberg, et al., Tumor regrowth between surgery and initiation of adjuvant therapy in patients with newly diagnosed glioblastoma, Neuro Oncol. 11 (6) (2009) 842–852, https://doi.org/10.1215/15228517-2009-005.

[20] S. Saraswathy, F.W. Crawford, K.R. Lamborn, A. Pirzkall, S. Chang, S. Cha, et al., Evaluation of MR markers that predict survival in patients with newly diagnosed GBM prior to adjuvant therapy, J. Neurooncol. 91 (1) (2009) 69–81, https://doi.

org/10.1007/s11060-008-9685-3.
[21] A. De Barros, J. Attal, M. Roques, J. Nicolau, J.-C. Sol, E. Cohen-Jonathan-Moyal, et al., Impact on survival of early tumor growth between surgery and radiotherapy in patients with de novo glioblastoma, J. Neurooncol. 142 (3) (2019) 489–497, https://doi.org/10.1007/s11060-019-03120-3.
[22] D.N. Louis, A. Perry, G. Reifenberger, A. von Deimling, D. Figarella-Branger, W.K. Cavenee, et al., The 2016 world health organization classification of tumors of the central nervous system: a summary, Acta Neuropathol. 131 (6) (2016) 803–820, https://doi.org/10.1007/s00401-016-1545-1.
[23] R. Stupp, W.P. Mason, M.J. van den Bent, M. Weller, B. Fisher, M.J.B. Taphoorn, et al., Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma, N. Engl. J. Med. 352 (10) (2005) 987–996, https://doi.org/10.1056/NEJMoa043330.
[24] J.E. Villanueva-Meyer, S.J. Han, S. Cha, N.A. Butowski, Early tumor growth between initial resection and radiotherapy of glioblastoma: incidence and impact on clinical outcomes, J. Neurooncol. 134 (1) (2017) 213–219, https://doi.org/10.1007/s11060-017-2511-z.
[25] G. Ekinci, I.N. Akpinar, F. Baltacioğlu, C. Erzen, T. Kiliç, I. Elmaci, et al., Early-postoperative magnetic resonance imaging in glial tumors: prediction of tumor regrowth and recurrence, Eur. J. Radiol. 45 (2) (2003) 99–107, https://doi.org/10.1016/s0720-048x(02)00027-x.
[26] S. Rathore, H. Akbari, M. Rozycki, K.G. Abdullah, M.P. Nasrallah, Z.A. Binder, et al., Radiomic MRI signature reveals three distinct subtypes of glioblastoma with different clinical and molecular characteristics, offering prognostic value beyond IDH1, Sci. Rep. [Internet] (2018), https://doi.org/10.1038/s41598-018-22739-2 Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5865162/.