T1-Weighted Subtraction Images for Volumetric Assessment of Extent of Resection of Diffuse Low-Grade Gliomas

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Citation

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Abstract

Background: The extent of resection (EOR) of Diffuse Low Grade Gliomas (DLGG) is often challenging to assess due to post-operative hyperintensity of the resection cavity and artifacts on T2-Weighted (T2W) and Fluid-Attenuated Inversion Recovery (FLAIR) sequences. In this study we propose a novel technique using OsiriX for evaluation of the postoperative EOR of DLGG.

Methods: Twelve patients with DLGG were included in the study. All lesions were hypointense on T1-Weighted (T1W) and hyperintense on T2W and FLAIR sequences. A publicly available post-processing radiographic software “OsiriX” was used to digitally subtract postoperative T2W from T1W sequences. Volumetric analysis for EOR was calculated based on the volume calculated from the subtraction images. The volumes of tumor residual and qualitative EOR calculated by this technique were compared to the volumes based on T2W images only, which were interpreted by a neuroradiologist.

Results: Based on the two imaging techniques for residual tumor volume, 1 patient was classified as Subtotal Resection (STR) according to T2W volume and Gross Total resection (GTR) according to digital subtraction T1-T2 volume. Three patients were classified as Partial Resection (PR) according to T2W volume and STR according to T1-T2 volume. Two were classified as PR according to T2W volume and STR according to T1-T2 volume (Table 1). The mean difference between the two groups was 5.6cm3[2.3-8.9]. The two groups were statistically equivalent ($p = 0.05$).

Conclusion: Digital subtraction of postoperative T2W from T1W sequences, combined with orientation to T2W sequence proved to be easier, reliable and reproducible in assessing the extent of resection in DLGG. This technique should be helpful in the management and follow-up of this pathology after surgical resection.

INTRODUCTION

The extent of resection (EOR) of a Diffuse Low Grade Glioma (DLGG) plays a key role in determining the patient’s postoperative management. The EOR is usually subjectively assessed based on the neurosurgeon’s operative report, which seldom correlates with postoperative imaging studies. [17] In general, it is easy to distinguish high-grade glioma remnants on MRI due to contrast enhancement. However, when it comes to DLGG, distinguishing the tumor borders from the surrounding edema proves difficult. In order to overcome this limitation, we used an open-source Digital Imaging and Communications in Medicine (DICOM) viewer, OsiriX MD (Pixmeo, Geneva), to develop a specific technique able to distinguish tumor remnants from the surrounding tissue. A volume calculation method based on 3D volume rendering-assisted region-of-interest (ROI) computation has been shown to be very helpful for volume assessment. [24,33,40] The purpose of this study is to introduce a way to measure the residual volume of DLGG on post-operative MRI by utilizing the OsiriX MD DICOM viewer.

MATERIALS AND METHODS

Preoperative and Postoperative Imaging

In an attempt to validate the technique, and after obtaining approval of the local institutional review board at our university hospital, the maintained database was retrospectively reviewed for patients presenting with supratentorial DLGG who underwent surgery. Patient inclusion criteria were (1) pathology confirmed DLGG and (2) available pre- and postoperative imaging. Exclusion criteria were (1) high-grade pathologies, (2) intense contrast enhancement lesions, (3) infratentorial lesions, (4) lack of adequate imaging, (5) patients who refused surgical resection. those who had previous surgery, radiosurgery or chemotherapy.

Image Analysis

Preoperative and postoperative imaging studies of all included patients were reviewed. All volume measurements were done in cm^3. Preoperative volume was calculated based on T2-weighted (T2W) imaging. For postoperative volume, manual evaluation of T2W vs. semi-manual evaluation using T1W – T2W were compared. For the manual group, postoperative T2W were used to calculate the postoperative residual tumor (VolAresidual). For the semi-manual group, postoperative T2W were subtracted digitally from postoperative T1W images to calculate the postoperative residual tumor (VolBresidual).

Manual Contouring

Synapse 3.1.1, FUJIFILM Medical Systems USA, was used to outline and calculate the preoperative volume and the postoperative residual volume in the manual group; the areas for each slice of hyperintensity in region of interest (ROI) in T2W sequence were segmented manually with orientation to FLAIR sequence of same slice to avoid hyperintensity artifacts, like resection cavity and edema (Figure 1) then multiplied by the slice thickness to calculate each slice volume. Inter-slices volume was calculated by the median of the surface area of each two successive slices multiplied by gap thickness, and then volumes of slices and inter-slices were added together to have the final volume (VolAresidual).

Semi-automated Segmentation Method

OsiriX software was used to digitally subtract postoperative T2W from T1W sequences (Figure 2) for the semi-manual group, using the included subtraction tool (Figure 3). Resample, registration, and image fusion tools were used when needed, to readjust the two sequences together if a difference in cut thickness and orientation was found (Figure 3). Upon observation of the original T2W sequences, the isointensity signal in a region of interest (ROI) in the new subtraction sequence (Figure 4) was segmented automatically using grow region method once digitally chosen, using “Grow Region – 2D/3D segmentation” (Figure 5). An algorithm was set to (threshold) interval of the isointense signal in the subtraction image while being oriented to T2W image for the same cut. The algorithm can also be adjusted manually for more accurate segmentation of the different signal intensity resembling the residual tumor. The volume of the residual tumor “VolBresidual ” was computed based on calculating the residual volume from the above mentioned method after segmentation of the isointense signal in all the cuts in the subtraction image for ROI.

EOR percentage was calculated for both groups (T2W preoperative – VolAresidual or VolBresidual) / T2W preoperative x 100), and then sub-classified into Gross-Total Resection (GTR), Subtotal Resection (STR) and Partial Resection (PR). Gross total tumor resection was defined as 100% macroscopic removal of the tumor mass, subtotal (<100%, but ≥90%) and partial (<90%) resection. A comparison was done between the manual group versus the semi-manual group.

Statistical Methods

Statistical analysis was conducted using R 3.2.2 (Vienna, Austria).[37] The volume measurement, in cm^3, obtained from manual evaluation of post-operative imaging and measurement obtained with the studied method (T1-T2) were compared for equivalence using the R equivalence package. 29 No assumption of normality was made and the robust t-test of Yuen 42 was used to compute the robust Two once-sided test (rTOST) for the paired values obtained using the 2 different analysis modalities. The test size alpha was set at 0.1, the magnitude of the region of similarity, epsilon, was set at 10mL. The tested H0 (null) hypothesis was that the two computed volumes are not equivalent. Intraclass Correlation Coefficient Technique was used to assess the reproducibility/reliability of the results measures using a numeric outcome.

RESULTS

A total of 12 cases were accrued for validation of the aforementioned volume calculation method. Examples of postoperative ROI and segmented tumor volumes generated using subtraction method are shown in (Figure 4, 5). All studies were initially hypointense in T1W, hyperintense in T2W and hyperintense in FLAIR sequences. Postoperative T2W showed the resection cavity hyperintense, residual tumor was mild hyperintensity and vessels shown as void signals. The subtraction image showed resection cavity hypointense and residual tumor isointense. This was segmented digitally using grow region method, which was easier and more accurate. Based on subtraction imaging findings for residual tumor volume; 1 patient was classified as PR according to T2W volume and GTR according to T1-T2 volume. Three patients were classified as PR according to T2W volume and STR according to T1-T2 volume. Eight were classified as PR according to T2W volume and T1-T2 volume (Table 1).

The mean difference between the two groups was 6.9 cm3, [4.1-9.8]. The two groups were statistically equivalent (p = 0.08). Intraclass Correlation Coefficient 0.76, CI 95% (0.168- 0.931).

DISCUSSION

The importance of surgical excision on survival has led to volumetric assessment being widely used, especially in studies involving glioblastoma [10,17,20,30]. In several studies authors used T2W non-contrast and T1W contrast enhanced MRIs and measured the volume by guidance of T2W images [15,18,31,38].

Patients with brain tumors may be considered for several different treatment options during the course of their disease. EOR is usually based upon the neurosurgeon's description in the operative report, which is not quantitative and often does not correlate with postoperative imaging studies [17]. Lohle et al. reported measurement by MRI that included axial T1W-weighted images before and after contrast medium injection, as well as proton density and T2W images in malignant and benign brain lesions [23]. Lacroix et al. reported the volume assessment of glioblastoma (GBM) patients as defined by the area of increased signal intensity on contrast-enhanced T1W images. For non-enhancing tumors, volume was defined by the area of increased signal intensity on T2W images corresponding to the defined mass lesion in a computer software program [23]. There were several studies that used the same method to calculate glial tumor assessment, but most of these studies examined contrast enhancement tumors [1,2,4,6,7,9-11,13,16,17,26,27,30,32]. Hatiboglu et al. used the entire area of T2W signal abnormality and segmented on FLAIR sequences for non-enhancing tumors 10. However, it is difficult to differentiate the tumor tissue from the edematous tissue in non-enhancing tumors. Ius et al. used T1W contrast enhanced and T2W images to calculate the volume difference between preoperative and postoperative images 15. Sankar et al. used T1W contrast enhanced images to calculate the volume in oligodendroglioma cases 31. Skrap et al. and Snyder et al. used T2W magnetic resonance images (MRIs) to establish preoperative and postoperative tumor volume [34,35].

In our study, T1W sequence was used to avoid the confusion between the hyperintensity signal in T2W and FLAIR sequences in assessing the residual tumor volume. Post-processing software (OsiriX) was used to digitally subtract postoperative T2W from T1W sequences and volumetric analysis for EOR was undertaken based on the volume calculated from the subtraction image. OsiriX Medical Imaging Software is an image processing application for Mac dedicated to DICOM images produced by medical equipment (MRI, CT, PET, PET-CT, etc...) and a FDA cleared 510k class II medical device, according to US Food And Drug Regulation CFR21 part 820.

Subtraction technique was used in many applications for recurrent GBM, glomus tumor, thrombosis of vein of Galen aneurysm, evaluation of sacroiliitis and liver cirrhosis [8,14,22,25,41]. The subtraction image prepared by imaging processing software showed resection cavity as hypointense and the residual tumor isointense, which can be segmented digitally using “grow region” option in Osirix. As there was a clear difference between resection cavity and residual tumor in signal intensity after substraction, this made it more accurate to use the automated segmentation tool than the manual method of marking the whole lesion. Also, vessels were excluded in the segmented part due to different pixel values of enhancement in the subtracted images. Cordova et al. used subtraction technique to evaluate GBM resection, by creating post resection tumor volumes. Subtraction images were generated by subtracting white matter–normalized, spatially co-registered pre-contrast T1W images from post-contrast T1W images, to avoid the presence of T1 hyperintense postoperative blood products and resection cavity [3].

Accurate postsurgical residual tumor segmentation are typically difficult to determine, even using the most time-consuming manual segmentation methods, due to their complex morphology and the presence of T2 -hyperintense blood products and resection cavity. The subtraction tool in Osirix was used, which digitally subtract postoperative T2W from T1W corresponding pixels to result in the subtraction image. This subtraction image was clearer for the computer software to segment precise volume and is easier than the manual method.

Manual contouring was found to decrease the inter-rater and intra-rater variability of volume generation in multiple anatomic regions, but this required a great deal of time and effort [19,36,39]. Sorensen et al. reported that manual contouring of tumor took an average of approximately 20 minutes per tumor to complete volume calculation, which clearly limits its routine application [36].

Semi-automated segmentation techniques have been introduced in an attempt to combine the high-level visual processing and specialized knowledge exhibited by humans with the objectivity of computers. However, most of these techniques have not gained widespread acceptance and its usage is mainly adopted by the original developers [3,5,12,21,28,39.]

Automatic or semiautomatic segmentation of radiographic images relies on differences in the grey value between a region of interest and the surrounding tissue. In most linear segmentation algorithms, starting from a specific area of interest, the neighboring pixels are evaluated and are either included or excluded based on a set threshold. It is intuitive that increasing the contrast between an area of interest and the surrounding tissue would lead to a more reliable segmentation. In the specific case of low grade gliomas, these lesions are initially hypointense on T1 and hyperintense on T2, the assumption is that any residual would have similar biological behavior and therefore similar radiographic appearance. Unfortunately, post-operatively this appearance is compromised by post-operative edema and resection cavity. To overcome this limitation, subtracting post-operative T2W from T1W sequences allows diminishing the signal engendered by post-operative edema, artifacts and filling of the operative cavity with CSF. This process increases the contrast between any residual and the surrounding tissues, therefore optimizing segmentation.

The mean difference between the two groups was 6.9 cm3 [4.1-9.8]. The two groups were statistically equivalent (p = 0.08). We believe that the difference between the volumes calculated based on T2 and the subtraction image volume and the qualitative volume too, is due to two factors. First the hyperintensity signal in T2 for edema and artifacts, which was omitted using the subtraction technique then segmenting the lesion digitally based on the pixels values generated. The second factor is the method the calculation for the T2 volume was done, estimating more residual volume as the inter-slices volume was calculated based on the median between the two successive slices. Which for sure increases the estimated tumor volume; meanwhile it was calculated digitally by the software.

Figure 1

1) Preoperative FLAIR and 2) T2W showing manual segmentation of surface area of T2W hyperintensity signal in region of interest (ROI) showing surface area in mm3. 3) Postoperative FLAIR and 4) T2W showing manual segmentation of T2W hyperintensity signal in ROI with avoidance of the marked hyperintensity of a resection cavity as shown in FLAIR manually.

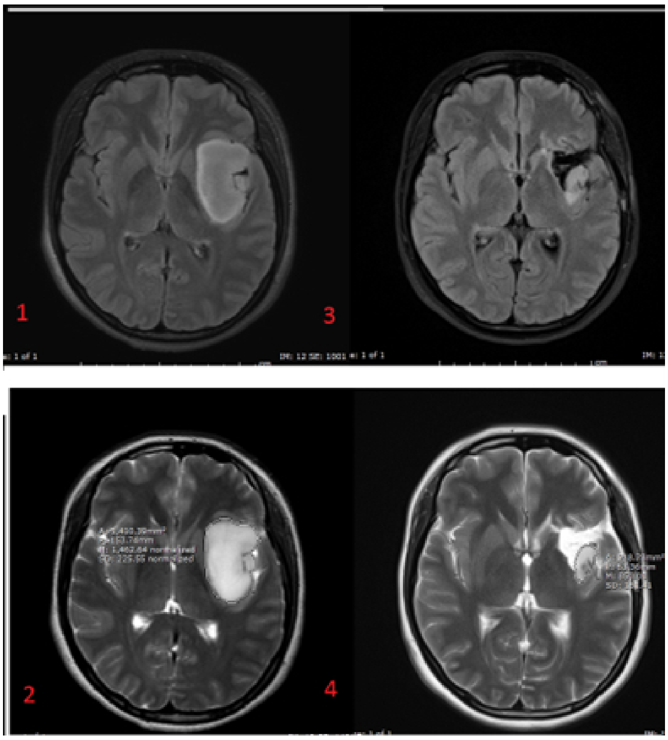

Figure 2

Postoperative T2W on left side and T1W contrasted on right side showing resection cavity hyperintense in T2W and iso to hypointese in T1W. Residual tumor showing mild hyperintensity in T2W and isointense in T1W. Vessels shown as void signals in T2W and contrast enhanced in T1W.

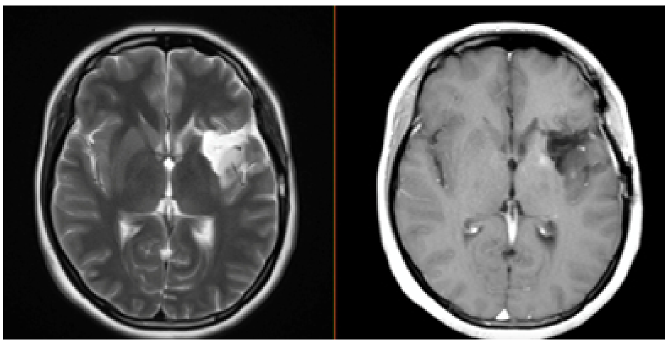

Figure 3

Subtraction tool, resample, registration, and image fusion tools were used as needed, to readjust the two sequences together if a difference in cut thickness and orientation was found.

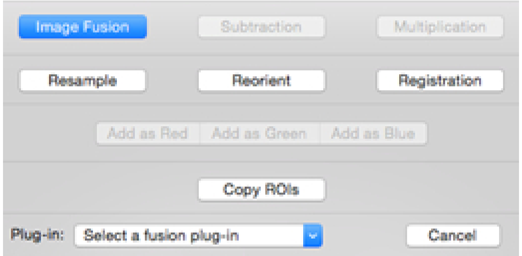

Figure 4

Postoperative T2W on left side showing resection cavity hyperintense, residual tumor showing mild hyperintensity and vessels shown as void signals. While the subtraction image on right side showing resection cavity hypointese, residual tumor isointense, and vessels contrast enhanced.

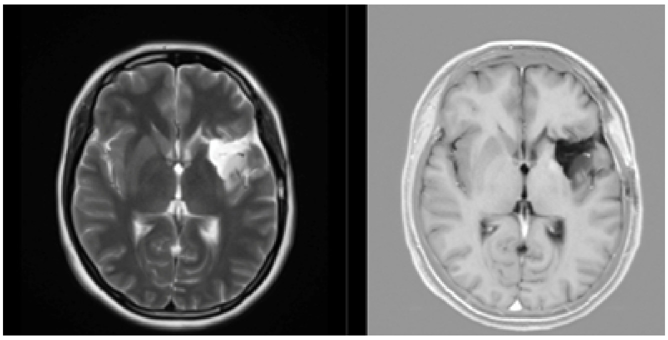

Figure 5

Postoperative T2W on left side showing resection cavity hyperintense, residual tumor showing mild hyperintensity and vessels shown as void signals. While the subtraction image on right side showing resection cavity hypointense, residual tumor isointense which was segmented automatically using grow region method once digitally chosen, which is more accurate than the manual method. Also, vessels can be seen not to be included in the segmented part due to different pixel values of enhancement.

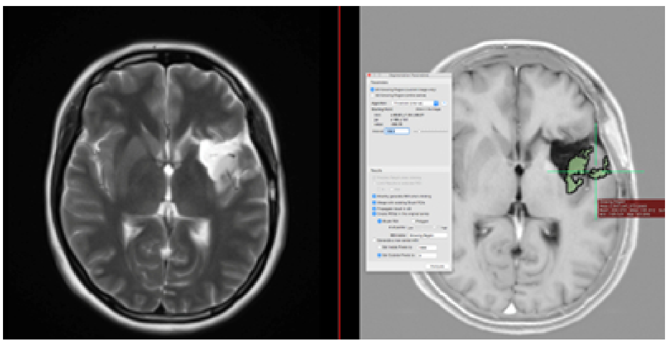

Table 1

Volume measurements based on T2 and the proposed technique:

Number	Preoperative Volume Based on T2W (cm3)	Postoperative Volume Based on T2W (cm3)	Postoperative Volume Based on T1W - T2W (cm3)	Qualitative T2	Qualitative T1 - T2	Percentage of Postop T2	Percentage of Postop T1-T2
1	36.64	6.6	4.6	PR	PR	82.0	87.4
2	65.9	21.5	16.4	PR	PR	67.4	75.1
3	49.3	19.71	14.75	PR	PR	60.0	70.1
4	108.26	20.6	14.72	PR	PR	81.0	86.4
5	117.08	60.7	47.64	PR	PR	48.2	59.3
6	46.87	39	11.34	PR	PR	16.8	75.8
7	40.86	11.9	7.7	PR	PR	70.9	81.2
8	55.36	12.4	5.07	PR	STR	77.6	90.8
9	10.32	1.2	0.54	PR	STR	88.4	94.8
10	44.66	7.3	2.63	PR	STR	83.7	94.1
11	129.64	22	16.58	PR	PR	83.0	87.2
12	18	2.3	0	PR	GTR	87.2	100.0

Abbreviations: GTR: gross total resection, STR: subtotal resection, PR: partial resection

CONCLUSION

Our proposed digital subtraction technique was easier and reliable for evaluating the extent of resection for DLGG and provides a novel digital quantitative method in comparison to the classic manual method. Digital subtraction of post-operative T2W from T1W sequences, combined with T2W orientation was helpful in assessing the extent of resection in DLGG and avoiding confusion from other hyper-intensity signals in T2W and FLAIR studies. This technique should be helpful in management and follow-up of this pathology after surgical resection.

References

1. Bloch O, Han SJ, Cha S, Sun MZ, Aghi MK, McDermott MW, et al: Impact of extent of resection for recurrent glioblastoma on overall survival: clinical article. J Neurosurg 117:1032-1038, 2012
2. Chaichana KL, Jusue-Torres I, Navarro-Ramirez R, Raza SM, Pascual-Gallego M, Ibrahim A, et al: Establishing percent resection and residual volume thresholds affecting survival and recurrence for patients with newly diagnosed intracranial glioblastoma. Neuro Oncol 16:113-122, 2014
3. Cordova JS, Schreibmann E, Hadjipanayis CG, Guo Y, Shu HK, Shim H, et al: Quantitative tumor segmentation for evaluation of extent of glioblastoma resection to facilitate multisite clinical trials. Transl Oncol 7:40-47, 2014
4. Dempsey MF, Condon BR, Hadley DM: Measurement of tumor "size" in recurrent malignant glioma: 1D, 2D, or 3D? AJNR Am J Neuroradiol 26:770-776, 2005
5. Dou WBR, S.; Chen, Y. P.; Bloyet, D.; Constans, J. M.: A framework of fuzzy information fusion for the segmentation of brain tumor tissues on MR images. Image Vis Comput 25:164- 171, 2007
6. Egger J, Kapur T, Fedorov A, Pieper S, Miller JV, Veeraraghavan H, et al: GBM volumetry using the 3D Slicer medical image computing platform. Sci Rep 3:1364, 2013
7. Ellingson BM, Cloughesy TF, Lai A, Nghiemphu PL, Mischel PS, Pope WB: Quantitative volumetric analysis of conventional MRI response in recurrent glioblastoma treated with bevacizumab. Neuro Oncol 13:401-409, 2011
8. Ellingson BM, Kim HJ, Woodworth DC, Pope WB,

Cloughesy JN, Harris RJ, et al: Recurrent glioblastoma treated with bevacizumab: contrast-enhanced T1-weighted subtraction maps improve tumor delineation and aid prediction of survival in a multicenter clinical trial. Radiology 271:200-210, 2014
9. Georgiadis P, Cavouras D, Kalatzis I, Glotsos D, Athanasiadis E, Kostopoulos S, et al: Enhancing the discrimination accuracy between metastases, gliomas and meningiomas on brain MRI by volumetric textural features and ensemble pattern recognition methods. Magn Reson Imaging 27:120-130, 2009
10. Hatiboglu MA, Weinberg JS, Suki D, Rao G, Prabhu SS, Shah K, et al: Impact of intraoperative high-field magnetic resonance imaging guidance on glioma surgery: a prospective volumetric analysis. Neurosurgery 64:1073-1081; discussion 1081, 2009
11. Huang RY, Rahman R, Hamdan A, Kane C, Chen C, Norden AD, et al: Recurrent glioblastoma: volumetric assessment and stratification of patient survival with early posttreatment magnetic resonance imaging in patients treated with bevacizumab. Cancer 119:3479-3488, 2013
12. Iftekharuddin KMZ, J.; Islam, M. A.; Ogg, R. J.: Fractal-based brain tumor detection in multimodal MRI. Appl Math Comput 207:23-41, 2009
13. Iliadis G, Selviaridis P, Kalogera-Fountzila A, Fragkoulidi A, Baltas D, Tselis N, et al: The importance of tumor volume in the prognosis of patients with glioblastoma: comparison of computerized volumetry and geometric models. Strahlenther Onkol 185:743-750, 2009
14. Irfan M, Lohman B, McKinney AM: Confirmation of T1-bright vein of Galen aneurysm spontaneous thrombosis by subtraction magnetic resonance venography: a case report. Acta Radiol 50:812-815, 2009
15. Ius T, Isola M, Budai R, Pauletto G, Tomasino B, Fadiga L, et al: Low-grade glioma surgery in eloquent areas: volumetric analysis of extent of resection and its impact on overall survival. A single-institution experience in 190 patients: clinical article. J Neurosurg 117:1039-1052, 2012
16. Kanaly CW, Ding D, Mehta AI, Waller AF, Crocker I, Desjardins A, et al: A novel method for volumetric MRI response assessment of enhancing brain tumors. PLoS One 6:e16031, 2011
17. Keles GE, Chang EF, Lamborn KR, Tihan T, Chang CJ, Chang SM, et al: Volumetric extent of resection and residual contrast enhancement on initial surgery as predictors of outcome in adult patients with hemispheric anaplastic astrocytoma. J Neurosurg 105:34-40, 2006
18. Kilday JP, Branson H, Rockel C, Laughlin S, Mabbott D, Bouffet E, et al: Tumor volumetric measurements in surgically inaccessible pediatric low-grade glioma. J Pediatr Hematol Oncol 37:e31-36, 2015
19. Kumar V, Gu Y, Basu S, Berglund A, Eschrich SA, Schabath MB, et al: Radiomics: the process and the challenges. Magn Reson Imaging 30:1234-1248, 2012
20. Lacroix M, Abi-Said D, Fourney DR, Gokaslan ZL, Shi W, DeMonte F, et al: A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. J Neurosurg 95:190-198, 2001
21. Lee CHS, M.; Murtha, A.; Bistritz, A.; Sander, M.; Greiner, R. : Segmenting brain tumors with conditional random fields and support vector machines. Berlin, Germany, 2005
22. Lloyd GA, Cheesman AD, Phelps PD, King CM: The demonstration of glomus tumours by subtraction MRI. Neuroradiology 34:470-474, 1992
23. Lohle PN, van Mameren H, Zwinderman KH, Teepen HL, Go KG, Wilmink JT: On the pathogenesis of brain tumour cysts: a volumetric study of tumour, oedema and cyst. Neuroradiology 42:639-642, 2000
24. Matsumoto T, Kanzaki M, Amiki M, Shimizu T, Maeda H, Sakamoto K, et al: Comparison of three software programs for three-dimensional graphic imaging as contrasted with operative findings. Eur J Cardiothorac Surg 41:1098-1103, 2012
25. Navallas M, Ares J, Beltran B, Lisbona MP, Maymo J, Solano A: Sacroiliitis associated with axial spondyloarthropathy: new concepts and latest trends. Radiographics 33:933-956, 2013
26. Nimsky C, Fujita A, Ganslandt O, Von Keller B, Fahlbusch R: Volumetric assessment of glioma removal by intraoperative high-field magnetic resonance imaging. Neurosurgery 55:358-370; discussion 370-351, 2004
27. Olubiyi OI, Ozdemir A, Incekara F, Tie Y, Dolati P, Hsu L, et al: Intraoperative Magnetic Resonance Imaging in Intracranial Glioma Resection: A Single-Center, Retrospective Blinded Volumetric Study. World Neurosurg 84:528-536, 2015
28. Prastawa M, Bullitt E, Ho S, Gerig G: A brain tumor segmentation framework based on outlier detection. Med Image Anal 8:275-283, 2004
29. Robinson A: R equivalence package 2016
30. Sanai N, Polley MY, McDermott MW, Parsa AT, Berger MS: An extent of resection threshold for newly diagnosed glioblastomas. J Neurosurg 115:3-8, 2011
31. Sankar T, Moore NZ, Johnson J, Ashby LS, Scheck AC, Shapiro WR, et al: Magnetic resonance imaging volumetric assessment of the extent of contrast enhancement and resection in oligodendroglial tumors. J Neurosurg 116:1172-1181, 2012
32. Shah GD, Kesari S, Xu R, Batchelor TT, O'Neill AM, Hochberg FH, et al: Comparison of linear and volumetric criteria in assessing tumor response in adult high-grade gliomas. Neuro Oncol 8:38-46, 2006
33. Shyu VB, Hsu CE, Chen CH, Chen CT: 3D-assisted quantitative assessment of orbital volume using an open-source software platform in a Taiwanese population. PLoS One 10:e0119589, 2015
34. Skrap M, Mondani M, Tomasino B, Weis L, Budai R, Pauletto G, et al: Surgery of insular nonenhancing gliomas: volumetric analysis of tumoral resection, clinical outcome, and survival in a consecutive series of 66 cases. Neurosurgery 70:1081-1093; discussion 1093-1084, 2012
35. Snyder LA, Wolf AB, Oppenlander ME, Bina R, Wilson JR, Ashby L, et al: The impact of extent of resection on malignant transformation of pure oligodendrogliomas. J Neurosurg 120:309-314, 2014
36. Sorensen AGP, S.; Harmath, C.; Bridges, S.; Synnott, J.; Sievers, A.; Yoon, Y. H.; Lee, E. J.; Yang, M. C.; Lewis, R. F.: Comparison of diameter and perimete methods for tumor volume calculation. J Clin Oncol 19:551- 557, 2001
37. Team RC: A language and environment for statistical computing. R Foundation for Statistical Computing, 2015
38. Wang Y, Liu S, Fan X, Li S, Wang R, Wang L, et al: Age-associated brain regions in gliomas: a volumetric analysis. J Neurooncol 123:299-306, 2015
39. Wang YL, Z. X.; Cao, J. G.; Li, M. Q.: Automatic MRI brain tumorsegmentation system based on localizing active contour models. Zurich,Switzerland: Trans Tech Publications LTD, 2011
40. Win Mar Salmah J, Noorfizura A, Mohd Shafie A, Helmy A, Salmi AR, Naing L: Hippocampal MR Volumetric Studies in Paediatric Patients with Epilepsy and Normal Controls. Neuroradiol J 24:503-510, 2011
41. Yu JS, Kim YH, Rofsky NM: Dynamic subtraction

magnetic resonance imaging of cirrhotic liver: assessment of high signal intensity lesions on nonenhanced T1-weighted images. J Comput Assist Tomogr 29:51-58, 2005
42. Yuen KK: The two-sample trimmed t for unequal population variances. Biometrika 61:165- 170, 1974

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