Unbiased, Semi-Automated Method for Glioblastoma Extent of Resection After 5-ALA Fluorescent-Guided Surgery

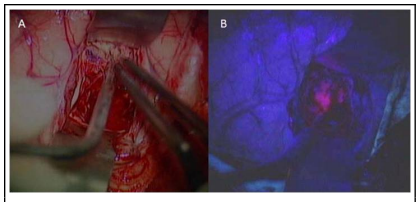
Costas George Hadjipanayis MD PhD; J. Scott Cordova; Eduard Schreibmann PhD; Chad A. Holder MD; Ying Guo PhD; Hyunsuk Shim PhD

Dept. of Neurosurgery, Medical Scientist Training Program, Dept. of Radiology, Dept of Biostatistics,

EMORY UNIVERSITY SCHOOL OF MEDICINE

Learning Objectives

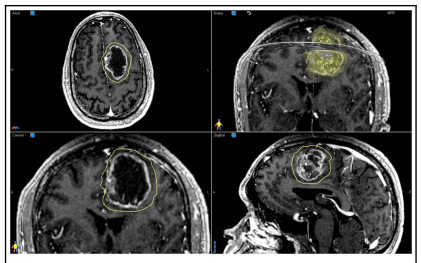
1. Residual GBM tumor volume measurements after resection are difficult to consistently measure in a precise manner.
2. A greater EOR was achieved in patients who undergent resection of their GBM with FGS in comparison to those without.
3. The standardization of this method will permit quantitative analysis of GBM EOR, offering a highly precise tool for the longitudinal monitoring of patients in clinical trials.



Left: Intraoperative white light microscopic image. Right) 375–440 nm blue light microscopic image after ALA administration (1)

Introduction

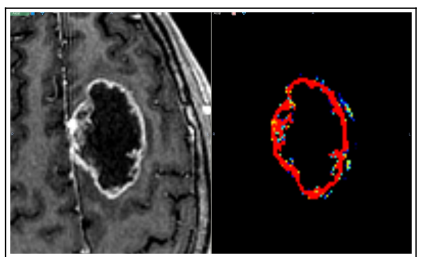
Glioblastoma (GBM) extent of tumor resection (EOR) is difficult to measure due to the nonconformal shapes of residual tumors as well as postoperative blood product infiltration. (2, 3) An MRI signal-based approach for tumor segmentation was performed using an FDA 510k-approved software package. Our volume determination method was used to compare GBM EOR in newly diagnosed patients undergoing fluorescent-guided surgery (FGS) in a Phase II trial to patients who underwent standard resection without FGS.



Coarsely contoured ROI on contrast-enhanced T1WI.

Methods

Datasets consisted of high-resolution pre- and post-operative MR images (T1-weighted images pre- and post-gadolinium) from sixteen patients enrolled in a Phase II 5-ALA study and controls matched for tumor location and size. A coarse region-of-interest (ROI) was drawn around the contrast-enhancing tumor and the software was used to segment volumes of hyper- and hypo-intensity on T1-weighted MR images within the ROI in an semi-automated fashion.



Algorithm outputs a 3D color map stratifying voxels based on intensity and degree of residence. The map pictured is the "strongly enhancing" cluster with degree of residence encoded as color (red>yellow>blue).

To estimate residual tumor after surgery, image difference maps were produced by subtracting white matter-normalized, spatially co-registered, pre- and post-gadolinium T1-weighted MR images correcting for blood accumulation.

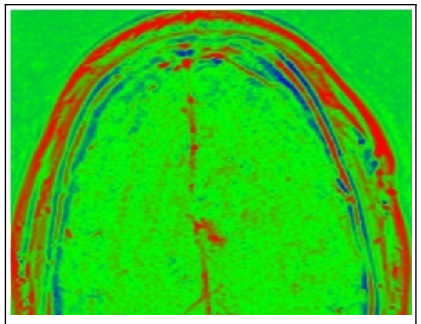
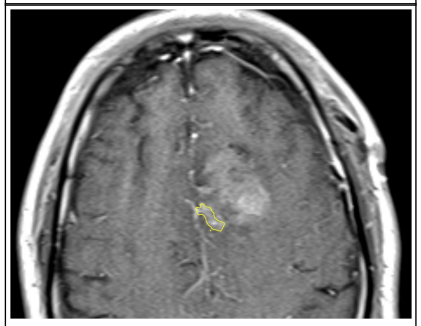


Image difference map with degree of enhancement encoded as color (red>green>blue).

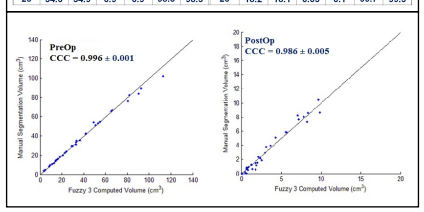


Application of our algorithm to the difference map results in residual tumor volume corrected for blood product infiltration.

Results

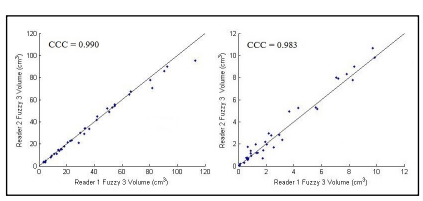
The average tumor EOR for patients without FGS was 88.1 ± 10.0%, while those patients who underwent FGS was

Ctrl	PreOp volume (cm^3)		PostOp volume (cm^3)		EOR (%)		ALA	PreOp volume (cm^3)		PostOp volume (cm^3)		EOR (%)	
	Man	Auto	Man	Auto	Man	Auto		Man	Auto	Man	Auto	Man	Auto
04	14.0	14.0	1.3	1.3	90.8	91.0	04	3.6	3.6	0.2	0.4	93.7	88.0
05	54.1	49.3	8.1	7.8	85.1	84.1	05	84.0	90.4	8.3	7.1	90.2	92.2
07	10.9	10.9	1.2	1.3	89.0	88.2	07	22.4	22.5	1.5	1.8	93.3	92.1
08	20.1	20.8	2.4	2.2	88.2	89.6	08	41.8	41.8	0.8	0.7	98.0	98.4
09	30.9	32.8	1.6	2.0	94.9	93.8	09	8.4	8.5	0.6	0.6	92.5	92.6
10	35.7	36.4	10.4	9.7	70.8	73.3	10	42.7	42.1	5.1	4.3	88.1	89.7
11	54.4	54.9	8.6	8.4	84.2	84.8	11	11.9	12.7	0	0.1	100	99.5
14	89.4	92.6	1.9	2.6	97.9	97.2	14	51.2	50.8	0.06	0.7	99.9	98.7
15	3.9	3.6	0.6	1.4	83.6	61.5	15	4.2	4.4	0	0.1	100	97.4
17	16.2	16.4	0.03	0.6	99.8	96.6	17	16.0	15.7	0.7	0.7	95.6	95.9
18	29.7	30.0	2.1	2.4	92.9	92.1	18	4.8	4.9	0.04	0.1	99.1	98.6
20	101.8	113.0	7.3	8.3	92.8	92.7	20	76.2	80.6	5.9	5.6	92.3	93.1
21	65.6	65.1	5.8	5.7	91.2	91.2	21	66.8	66.3	3.9	3.7	94.1	94.5
23	23.9	23.8	8.6	9.8	63.9	58.7	23	4.1	4.2	0.6	0.7	84.3	82.7
25	33.4	33.1	3.0	2.9	91.1	91.1	25	53.3	52.9	0.5	0.9	99.0	98.4
26	54.6	54.9	0.9	0.9	98.3	98.3	26	18.2	18.1	0.05	0.1	99.7	99.5



Concordance correlation coefficient (CCC), a measure of agreement, approached unity when volumes manually contoured by a board-certified neuroradiologist were compared (above) to those produced by the algorithm pre- (CCC = 0.996 ± 0.001) and post-operatively (CCC = 0.986 ± 0.005). Two separate readers applying the algorithm to pre- and postoperative tumors (below) also produced volumes with high agreement, thus low inter-rater variability, as well (0.990 ± 0.003 and 0.983 ± 0.006, respectively).

94.9 ± 5.0% (significantly different at p=0.0021 using the nonparametric Wilcoxon Rank-Sum Test).



Conclusions

The average EOR of newly diagnosed GBMs using 5-ALA FGS was significantly higher than the average EOR in the control group. These results corroborate with a randomized, case-controlled, multicenter phase III trial (4). The high agreement of our semi-automated segmentation method with manual contouring, along with its high inter-rater agreement, supports its use for the unbiased generation of tumor volumes in newly diagnosed GBMs pre- and post-surgery at multiple centers. As such, the standardized volumetric segmentation procedure used in this study should be further evaluated in the field of neuroradiology.

References

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