Reviewer's report

Title: Surgery of highly eloquent gliomas primarily assessed as non-resectable: risks and benefits in a cohort study

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Reviewer: Johan Pallud

Reviewer's report:

In this retrospective study, the authors report the surgical management and outcomes of 47 patients harboring a supratentorial diffuse glioma treated in their institution between 2006 and 2012 that were judged ineligible for surgery in a previous institution. They conclude that most diffuse gliomas located in highly eloquent brain are eligible for surgical resection with an acceptable morbidity and suggest that such tumors should be referred to specialized centers.

The main idea of this study is that tumor resectability must be decided in conference by neurosurgeons experienced in brain tumor surgery, ideally during dedicated neuro-oncological staff meetings including non-surgeons specialists, but not by individuals. This is not stressed enough in the manuscript in its present form, to my opinion.

Major compulsory revisions:

1. The manuscript does not specifically address the “specialization” of the different neurosurgical departments. There is no detail regarding outside institutions that primarily concluded to the non-resectability. Regarding their own institution, the authors report 51 cases during a 6 to 7-year-long period (2006 to 2012). During the same period, how many diffuse gliomas were operated on and managed? How the tumor respectability was decided? More generally, how one can define the neuro-oncological “specialization” of a neurosurgical department? This is the hot point the authors concluded with in the last sentence of the Conclusions Part: “Moreover, neurosurgical centers with limited expertise on surgery of such highly eloquent lesions should strongly refer their patients for a second opinion to a specialized center”.

2. Page 4, Method part, lines 4-7: the definition of the tumor location is not detailed enough and is inaccurate as a “perisylvian” location encompasses the other “insular”, “precentral” and “parietal” locations. The authors should use the cerebral sulci to describe the tumor location and should add the tumor volume and the MRI sequence used for the assessment of the tumor location.

3. The main findings (clinical, imaging, pathological, treatments, outcomes) for each patient should be summarized in a Table.

4. Regarding the clarity of the manuscript:
   - Several redundancies exist between the Method, the Result and the Discussion parts. They should be avoided (for example, see the statistical significance level
in each of these parts: “when considering p<0.05 as significant”).
- The Results part is hard to follow. In addition, several data are already presented in the Method part.
- The statistical analyses performed are particularly unclear: they lack for several results and some points are discussed without the ad hoc tests.
5. The non-functional surgical morbidity must be addressed in detail: also the authors report 3 cases (6.3%) of postoperative hematomas requiring surgical evacuation, their description is unclear and minimized “However, only 3 out of these 5 cases were rated as significant hemorrhage and underwent revision surgery at the same day”. In addition, the absence of healing problems and of infections must be mentioned.

Minor essential revisions:
1. Page 3, Background part, line 5: when detailing diffuse gliomas within eloquent regions, the “peri-sylvian cortex of the dominant hemisphere” should be preferred to the “left-sided peri-sylvian cortex”.
2. Pilocytic astrocytoma is a very specific glioma. Hence, the unique case reported here should be removed from this series to obtain a homogeneous series dedicated to “diffuse gliomas” in adults.
3. Page 8, Postoperative evaluation part, line 6: How was defined the “extent of the resection”? Using a quantitative method? Which one?
4. The authors report a large panel of preoperative and intraoperative techniques to assess the location of eloquent brain areas and to achieve tumor resection. As these techniques are not used systematically, the authors should explain clearly the reasons of their preferential use and combination. For example, why language cortical and subcortical preoperative mapping under awake condition was performed only in 8 cases (17%), although these tumors were located in eloquent areas and in the dominant hemisphere in 59% of cases?
5. The term “significant” should be limited to the description of the statistical analyses that reach statistical significance in the Results part. Most of results are overstated in the Discussion part and qualified as “significant” although the statistical significance was not reached. In addition, sentences such as “cases were rated as significant hemorrhage” should be avoided for a better clarity.
6. Regarding postoperative deficits:
   - The detailed assessment of postoperative language deficit is lacking.
   - Page 17, Recurrent gliomas part, line 4: the statement that “this high rate of GTR resulted in a higher rate of very relevant postoperatively new permanent deficits” is not correct if the authors actually performed functional-based resection.
   - Page 13, Postoperative MRI scans, line 8: the statement “2 (cases) showed resection within motor eloquent regions” is strange. Do the authors explain the postoperative deficit by a partial removal of the primary motor cortex? How the authors explain this at the light of the use of pre and intraoperative functional
mapping?

- Page 16, Correlation of tumor type and location to postoperative motor deficit, lines 9-11: the authors should discuss that adjuvant oncological treatments (chemotherapy and radiotherapy) may alter brain and vessels and may reduce postoperative plasticity. This may participate to a higher risk of postoperative deficit after surgical resection of a recurrent glioma.

8. Page 19, Authors’ contributions: who performed the statistical analyses?

Discretionary revisions:
1. All along the manuscript: the authors should prefer “WHO grade X” than “WHO°X”.

2. Page 7, Awake monitoring part: the operative position of the patient should be mentioned.

3. Page 4, Tumor resection part, lines 2-3: The statement “Upon any amplitude loss or decline of more than 50%” should be referred to the monitoring technique parameter.

4. All along the manuscript: the authors should prefer “chemotherapy” than “chemo”.

5. In the Results part: regarding statistical analyses, the exact p-value should be preferred to a standard “p<0.05”.

6. Table 1:
   - The case of pilocytic astrocytoma should be removed.
   - Why the estimation of the overall survival was limited to the population of deceased patients?

7. Table 3: this table is not necessary and should be converted in a simple sentence.

8. Regarding Figures:
   - The histogram layouts should be changed to simple greyscale colors such as white/grey/black.
   - The authors should reduce the thickness of the drawing lines.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that have I no competing interests