

ANSWERING REVIEWERS



March 25, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8163-edited.doc).

Title: Clinical Outcomes following Salvage Gamma Knife Radiosurgery for recurrent Glioblastoma. A review of the literature

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Name of Journal: *World Journal of Clinical Oncology*

ESPS Manuscript NO: 8163

The manuscript has been improved according to the suggestions of reviewers:

1. Reviewer # 646543: Revisions have been made according to suggestions by the reviewer

- 1) *"Too many authors for a brief review (11)".* We acknowledge that there are 11 authors on this paper, and all 11 authors provided critical review and are involved in additional studies regarding this clinical question.
- 2) *"Too many abbreviations that make the lecture of the text difficult".* Removed, and replaced with appropriate text, the following abbreviations: 'PFS', 'HBO', 'ARE', and 'WHO'. 'EBRT' and 'KPS' are common abbreviations for 'external beam radiation therapy' and 'Karnofsky Performance Status', respectively, and are frequently used in the literature.
- 3) *"Although the term "salvage therapy" is frequently used... in the case of GBM it would be dubious of GKRS could be a real "salvage therapy" due to the poor results obtained."* We have added language, and the appropriate source, to the Introduction and Discussion sections to highlight that the best prognosis for patients is 17.1 months when given the best adjuvant therapy for GBM. The results obtained in most of the reviewed studies showed overall survival times greater than expected for the historical prognostic indicators (as long as 33.2 months).
- 4) *"Other strategies like radiosensitization (P7,p4,L1-4) include chloroquine as adjuvant, this would be discussed."* Chloroquine radiosensitization added to discussion, with source.
- 5) *"The most important point in any therapeutic approach for GBM is the analysis of cost-benefit which is not even mentioned in the review".* Thank you for pointing this out. It has been added to the Introduction with the appropriate source.
- 6) *"The mean number, or frequency of rGKRS which show best results should be included in the review."* There have not been large studies assessing the number or frequency of repeated salvage GKRS for recurrent GBM, but there have been some case reports that suggest that eligible patients ought to be offered as many repeated therapies as can be tolerated/feasible. References to two such case studies have now been added to this article.

2. Reviewer # 1752498: Revisions have been made according to the suggestions of the reviewer

- 1) Thank you for your suggestions. The intention for this review was for Gamma Knife treatments only. We excluded other modalities such as linac and CyberKnife. Language has been added to emphasize that this is the scope of this review, why this was chosen, and that

Gamma Knife is only one method of delivering stereotactic radiosurgery.

- 2) *"Page 7 para 4, line 2-3 : ? If the tumor tissue can be sensitized to GK radiation ..etc ?. "GK" should be removed ,since "GK radiation" is not a physical entity ...". "GK" has now been removed.*
- 3) *"The authors should define what are the accepted selection criteria to deliver RS to their patients with rGBM: size, KPS, interval of time between the first treatment and the recurrence etc."* Thank you for this suggestion. This information has been added to the Conclusion.
- 4) *"Table 1: column 5 on MGMT status: This column is useless and should be removed, as there is no information at all on MGMT status in any of these series ("not known" or not" reported)".* This column has now been removed and a sentence was added indicating that MGMT status was not known for any of the studies.

3. Reviewer # 646241: Revisions have been made according to the suggestions of the reviewer

- 1) *"when reporting the data from Park et al., on page 6, they quote a survival of 33.2 months (95% CI, 23.7–42.7 months) in the treatment group and exactly the same survival in the control group".* Thank you for catching this error. This has been corrected to '26.7 months (95% CI, 21.8–31.6 months)'
- 2) *"if survival data are given, each time it should be mentioned whether median, average or maximum survival is given".* This has now been added to each mention of survival data
- 3) *"When quoting references, the authors always put a komma before "et al." which is unusual".* These have now been removed.
- 4) *"On Page 7, a sentence is incomplete - "reported for of these studies" - reported for how many of these studies??"* Thank you for bringing this error to light. This was reported for all nine studies and has been added to the manuscript.
- 5) *"the authors state that recurrences may occur "up to 4 cm from" original tumor margin, while on p. 8, in the section "Factors contributing to outcomes:" this number is given as 2 cm".* This has been corrected to reflect 4cm in both places

4. The manuscript has been reformatted and updated as suggested by the editor

Thank you again for publishing our manuscript in the *World Journal of Clinical Oncology*.

Thank you for your time,

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