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315-321 Lockhart Road, Wan Chai, Hong Kong, China

## ESPS Peer-review Report

**Name of Journal:** World Journal of Clinical Oncology

**ESPS Manuscript NO:** 8163

**Title:** Review: Gamma Knife radiosurgery for recurrent Glioblastoma.

**Reviewer code:** 00646241

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-12-18 16:38

**Date reviewed:** 2013-12-19 08:54

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

In their work, "Review: Gamma Knife radiosurgery for recurrent Glioblastoma.", Larson et al., give a very detailed and diligently written overview of the published data on glioblastoma therapy in general, and particularly, regarding gamma knife therapy in relapsed GBM, with particular focus on survival data. The paper is well written and full of details. I am not aware of study missing. Some errors however have to be mentioned: 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, which probably is a mistake. Further, if survival data are given, each time it should be mentioned whether median, average or maximum survival is given. When quoting references, the authors always put a komma before "et al." which is unusual. On Page 7, a sentence is incomplete - "reported for of these studies" - reported for how many of these studies?? While in the abstract, 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. In the discussion, the collected data are interpreted carefully, and the conclusions drawn are convincing. Probably, randomized clinical studies will be of high benefit in the future, thus the paper contributes significantly to future strategy planning. The literature references are impressive. The tables are clear and evidently connected with the text. Finally, the paper should receive some substantial corrections, but then might be published.



ESPS Peer-review Report

Name of Journal: World Journal of Clinical Oncology

ESPS Manuscript NO: 8163

Title: Review: Gamma Knife radiosurgery for recurrent Glioblastoma.

Reviewer code: 01752498

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-12-18 16:38

Date reviewed: 2014-02-19 17:32

Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, RECOMMENDATION, CONCLUSION. It lists various grades (A-E) and their corresponding evaluation and recommendation options.

COMMENTS TO AUTHORS

General comments This paper by Larson et al. is a review on Gamma Knife radiosurgery (GKRS) for recurrent glioblastoma (rGBM) in which 9 series are displayed, looking at overall survival, progression-free survival, local control and toxicity. These series, as expected, are heterogenous as regards previous treatments, radiosurgery (RS) dose, fractionation (in one), concomitant external beam radiotherapy, chemotherapy or other treatments for recurrence (HBO, new surgery etc). Not surprisingly overall results are rather poor, underscoring the limits of salvage GKRS (or RS as a whole, see below). At first reading this review seems to be reasonably well made (see also my specific comments). However, I have a problem with the objective of this paper. Is it a review on the role of RS overall, and in that case several important papers are missing (see below), or is it a review on Gamma-Knife RS only. In that case, authors should justify why they have excluded other RS papers, typically papers on linac-based or Cyberknife-based RS (see below). The non-expert readers should not be confused: GK, linear accelerators (linacs)- or Cyberknife are only techniques (or trade marks) to perform RS, whereas RS is defined as a general method to deliver a single high-dose, high precision radiotherapy, generally (but not always) in stereotactic conditions. In this regard, the paragraph on page 3, lines 3-11 is misleading, especially for a non-expert reader: this paragraph includes a whole discussion on "stereotactic radiosurgery" (SRS), and since the article's title is "GKRS for rGBM," non expert readers could understand that SRS and GKRS are synonymous, which is wrong. So I would suggest the following options 1) The authors are willing to make a limited review on GKRS only. In this case they should clearly state that GKRS is only one of the several methods to deliver RS, and explain why they chose to exclude the other techniques. They



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should mention that there are several other studies on RS using linac-based techniques or the Cyberknife, with similar overall results, and therefore state that their review is not a comprehensive review on RS. 2) The alternative (which I think would be better) is to complete this review with the most important linac-based RS (LRS) and Cyberknife studies, and rename this review : "Radiosurgery for rGBM". The main results of other papers (see below) could be included in the existing tables, with a brief discussion about the differences between the RS techniques. To help: here are some of the most important papers on LRS for rGBM: Cabrera et al. Int Journal of Radiation Oncol Biol Phys (IJROBP) 2013, on 15 pts Shapiro et al. IJROBP 2012, on 24 patients Torok et al. Tech Cancer Res Treat 2011, on 14 patients Cuneo et al. IJROBP 2012, on 49 patients Biswas et al. Radiat Oncol 2009, on 18 patients Combs et al., Cancer 2005, on 32 patients Papers on Cyberknife for rGBM Conti et al. Acta Neurochir 2012 , on 23 patients Villavicencio et al. Neurosurg Rev 2009, on 26 patients Specific comments : 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 . It doesn't make any more sense than a term like "Varian" radiation, "Cyberknife" radiation, "Tomotherapy" radiation etc. They are all high energy radiation, regardless of the company that produces these machines. Page 9, conclusion. 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. 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").Perhaps a short sentence should be added, saying that MGMT status was not reported in any of these studies.



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## ESPS Peer-review Report

**Name of Journal:** World Journal of Clinical Oncology

**ESPS Manuscript NO:** 8163

**Title:** Review: Gamma Knife radiosurgery for recurrent Glioblastoma.

**Reviewer code:** 00646543

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-12-18 16:38

**Date reviewed:** 2014-02-25 04:53

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The Review by Larson et al seems interesting; however various issues are not included. 1. Too many authors for a brief review (11). 2. Too many abbreviations that make the lecture of the text difficult (e.g. PFS, KPS, HBO, ARE, EBRT, WHO seem unnecessary) 3. Although the term "salvage therapy" is frequently used ("therapeutic measures taken after other measures have failed" according to Dorland's ) its idiomatic meaning (synonym of "save" according to Webster's), in the case of GBM it would be dubious of GKRS could be a real "salvage therapy" due to the poor results obtained. I suggest that this time is used less frequently along the text. 4. Other strategies like radiosensitization (P7,p4,L1-4) include chloroquine as adjuvant, this would be discussed. 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; I think that this issue should be included in the Discussion. 6. The mean number, or frequency of rGKRS which show best results should be included in the review.