Reviewer's report

Title: Radiotherapeutic alternatives for previously irradiated recurrent gliomas.

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Reviewer: Carolyn Freeman

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Radiotherapeutic alternatives for previously irradiated recurrent gliomas by Combs et al.

This is a review article that presents the literature on the results of radiotherapy using different techniques alone or in combination with chemotherapy or hyperthermia for the management of patients with recurrent gliomas. As an overview, it is reasonably complete and a good starting point for the development of new approaches to the management of such patients, in particular those with recurrent high-grade gliomas.

General comments

1. For comparison, it would be useful to present the expected median survival from time of progression i) without additional treatment, ii) with surgery alone and iii) with chemotherapy alone.
2. It would be helpful to add to the tables the necrosis/re-operation rates for each approach.
3. As a result of the review and in the context of the need to develop clinical trials, it would be important to discuss levels of risk that might be considered acceptable, i.e., to define “safe” in the context of treatment alternatives in this situation (page 6).
4. I think that the authors could do a better job of drawing conclusions which might be for example, based on their analysis and the data as presented in Figure 1, that certain approaches in this situation, although not necessarily associated with a longer or overall better survival, are associated with less toxicity than others, and therefore perhaps more acceptable than others.
5. The authors do not discuss tumour location as a factor, even though this may influence outcome and as well may be an important consideration with respect to choice of treatment.

Specific comments

Abstract and elsewhere in the text: “External beam” radiotherapy is more widely used in English than “percutaneous”.

Stereotactic radiosurgery:
· The higher rate of necrosis in the Hall et al. study might also relate to the higher median dose.
· Spelling of Minnesota.
· As noted, it would be helpful to define “safe”
· Define “smaller”.

Hypofractionated stereotactic radiotherapy, 2nd and 3rd lines: The side effects are not given in Table 3 but as noted should be included.

Interstitial radiotherapy / Glia-site: The results of Gabayan et al. are impressive but these may be selected patients who could undergo a subtotal if not total resection. It would be useful to at least comment on this in such an article.

Conclusion: See above


Tables 2, 3 and 5: “Median single dose” should be replaced by “median fraction size”.

Table 2: The article by Hudes et al. cited is not included.