Reviewer's report

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

Version: 1 Date: 10 October 2012

Reviewer: Karl Schaller

Reviewer's report:

The authors report on a consecutive institutional series of gliomas which had been classified as inoperable previously at other institutions due to their eloquent localization. A total of n=47 out of n=51 "inoperable" supratentorial gliomas were thus scheduled for resection at the author's department, and the remaining n=4 underwent stereotactic biopsy alone. Twenty-nine of the patients presented with recurrent gliomas. All patients had complementary imaging, i.e. PET when considered necessary, and n=11 had navigated TMS prior to surgery in order to create maps for cortical representation of motor and/or language function. Patients undergoing resection of tumors within, or, within the vicinity of language-relevant areas had preoperative language testing, and at early and late follow-up dates. A standard protocol for intraoperative MEP monitoring was used in n=38 patients, and n=8 patients underwent awake craniotomy. Gross total resection was achieved in 74% of patients according to early postoperative imaging. Patients with recurrent gliomas showed higher rates of transient and permanent neurological worsening (34% and 14%) than those with primary gliomas (22% and 0%). Transient deficits were particularly high in patients with tumor extension into the subcortical white matter, and in insular and precentral gliomas, respectively. There was no statistically significant difference in the outcomes between those patients in whom resection was halted due to MEP deterioration, and those without such a deterioration. They noted n=5 postoperative rebleedings, three of which required surgical evacuation. In their Glioblastoma patients, postoperative Karnofsky scores were better than before surgery, indicating better quality of life with surgery despite lack of prolonged survival when compared with non-operated series. They conclude that such a "multimodal approach" to the treatment of cerebral gliomas may contribute to good results concerning overall survival and reasonable postoperative quality of life.

Critique

I like the concept that patients with particularly complex or eloquently located gliomas should be evaluated in all respects in a dedicated center, and be treated accordingly. Infrastructure of such centers is important and requires particular personnel (i.e. neuropsychologists, intraoperative neurophysiologists), high-end imaging (including metabolic imaging), navigation, intraoperative imaging, and particular expertise (i.e. for awake craniotomy). This has been accepted for other pathologies as well, such as for complex spinal or neurovascular disease, or for
pediatric neurosurgery, to name a few. The authors have well demonstrated that such a (desperate) cohort of patients can still be treated with acceptable and good outcomes under ideal circumstances. I would thus accept this manuscript for publication - after revision.

1. The paragraph on the correlation between postoperative deficits and primary vs. recurrent tumors needs clarification (p11): They start with the statement that postoperative worsening was more frequent in recurrent tumors, and then they continue with a long sentence with a lot of numbers - for primary tumors. Then, they return to the recurrent tumors and their respective numbers. This should be presented in the reverse order and made more understandable.

2. It is not easy to understand what the authors mean with "without the influence of IOM" (p12)? I would assume that MEPs remained unchanged during the course of surgery, but this should be explained/clarified.

3. In the same paragraph they refer to "significant MEP loss". It would be important if there was real "loss", or if there was significant deterioration (i.e. by amplitude decreases of >50%), as this is misleading in the present form.

4. How do they position themselves to the value of intraoperative monitoring as, in their study cohort, the rates of neurological deficits did not differ among the two groups, those with, and those without intraoperative MEP worsening?

5. On p15 they compare overall survival of their GBM patients with "the non-surgical series". Which series? A series from the literature? What does that have to do with table 1?

6. It seems that none of their patients who underwent resection of a recurrent tumor had combined radiochemotherapy previously (table 2). I find this highly unusual in view of the (supposed to be) rather standardized treatment regimens for adjuvant GBM therapy. Can they comment on that? Is this another argument in favour of centralization of (eloquent) glioma treatment, where patients can be discussed in pluri-disciplinary tumor boards and then treated according to dedicated (study) protocols?

7. They have not really spent much time and energy on their legends. These would merit some work in making them more explanatory.