

Editorial

## Does gross total removal of a brain tumor produce greater longevity?

This question is an old controversy in neurosurgery, but it is also the basis of image-guided resection for brain tumors. New technology, such as intraoperative magnetic resonance (MR)-guided resections, is becoming popular in the developed world and in some places in the developing world. The technology is costly. Is it necessary? *Surgical Neurology* has stated in the past that the evidence that proves that total resection provided by image-guided surgery produces greater patient longevity does not exist. Although, intuitively, we believe that the more tumor resected the better for the patient and the slower the recurrence.

In *Lancet Oncology* (2007;7:392-401), Stummer and the Aminolevulinic Acid (ALA)-Glioma Group reported their results using 5 ALA as a nonfluorescent prodrug that accumulates in the glioma cells and will fluoresce under special light from the microscope, defining the tumor cells. The authors selected patients who had tumors "...with a distinct ring-like pattern of contrast-enhancement with thick irregular walls on magnetic resonance imaging [MRI] and a core area of reduced signal suggestive of tumor necrosis as assessed at the study centre by the study surgeon." Tumors excluded included "...tumours of the midline, basal ganglia, cerebellum, or brain stem as assessed by MRI more than one contrast-enhancing lesion; substantial, non-contrast-enhancing tumour areas suggesting low-grade glioma with malignant transformation..." or tumors that could not be resected because of location and some other criteria. Only those with histologically confirmed malignant gliomas were included in the final analysis.

The tumors fluoresced apparently at the tumor margin or the area of ring enhancement. After surgery, the authors documented the amount of resection of the tumors using contrast enhanced MR. They performed a randomized study comparing the resection in patients who received the 5 ALA drug and those who did not, as controls with conventional surgery.

What they found was that those with the ALA-aided resection had complete removal in 65% of the patients, whereas those who underwent standard resection had total removal in 36% of the cases. The progression-free survival (those without radiologic evidence of progression at

6 months) was twice as long in the 5 ALA-resected group compared with the standard resection patients. However, the survival of the patients was the same in both groups at the end.

So, this is a study showing that in these selected patients with ring enhancing borders and histologically proven malignant gliomas, 5 ALA-aided resection produced a greater removal of tumor cells and a longer (6 months, radiologically progression-free) survival than those without the fluorescence marker.

Several questions arise. Do these results apply to patients with all tumors or even to all patients with malignant gliomas? The answer is no. The study did not ask that question and only followed a selected sample of the patients. How many malignant gliomas or even slower growing gliomas have a defined border on contrast enhanced MR? To me, it would not be a large number.

Also, the overall survival of the patients from their tumors was the same regardless of the completeness of the resection. This observation says that the 5 ALA did not reveal all of the tumor cells in the patient but only allowed more tumor removal. Thus, as with all surgical resections, the full extent of the tumor cannot be appreciated by the surgeon or the imaging system at present.

5-Aminolevulinic acid may not appear in a high enough concentration in the tumor cells to be seen under the special fluorescent light at surgery. Also, as we have stated many times, the solution to primary malignant gliomas is not surgical.

Nevertheless, this is a well-done study that does provide some evidence to support a more complete resection in a defined set of patients. For those with tumors that are not as well defined on contrast MR, these results do not apply.

Does this study provide the proof necessary for intraoperative MR resection? The answer is no because the resection here is guided by the 5 ALA fluorescence; so, in reality, the intraoperative MR is unnecessary in tumors as operated in this study.

Jaimes I. Ausman MD, PhD  
Editor

*E-mail address:* [surgicalneurology@dc.rr.com](mailto:surgicalneurology@dc.rr.com)