

AGGRESSIVE NEW APPROACHES FOR THE TREATMENT OF AGGRESSIVE BRAIN TUMORS

by Gil Lederman

High-grade primary brain tumors such as anaplastic astrocytomas and glioblastomas are feared because of their aggressive course. People once healthy may be hit with a variety of symptoms including headaches, change in memory or speech as well as possible weakness and altered gait.

These neurologic changes are not specific to primary brain tumors and therefore a thorough evaluation should be carried out by one's physician. If a question persists, the brain is best imaged using CT scan with contrast or better yet, MRI (magnetic resonance imaging) with gadolinium. Gadolinium is a contrast agent which helps define structures with high resolution.

If an abnormality is indeed seen and is suspected to be a high grade brain tumor, then a biopsy or surgical intervention can be undertaken. Any intervention within the brain can have potential adverse effects. Needle biopsies are usually well tolerated and reveal the diagnosis. Certain brain tumors are best resected while others located in more sensitive areas of the brain may be best just biopsied.

It should be noted, however, that not all brain tumors need biopsy for diagnosis and in certain situations, biopsy may be detrimental. For benign tumors such as meningiomas and acoustic neuromas, the diagnosis is often easily made by review of CT and MRI scans.

Standard therapy for brain tumors such as glioblastoma multiforme and anaplastic astrocytoma remains external beam radiation therapy. This is given daily to relatively large areas of the brain and in retrospective analysis has shown benefit in improving the length and quality of life. Ongoing studies are looking at certain chemotherapeutic agents also aimed at achieving this goal.

Because these tumors are so devastating, innovative new techniques are being developed for sophisticated treatment rather than the routine which has had only modest results over decades.

Since radiation remains the proven standard of care, higher than standard dose radiation has been given to the brain with a variety of techniques including external beam radiation therapy, seed implantation as well as stereotactic radiosurgery with the expectation of improved outcome. The disadvantage of standard-style external beam radiation therapy to higher doses is that large areas of normal brain must be irradiated to attack the brain tumor. It is not selective specifically to the area of brain tumor.

Radioactive seed implantations also escalate radiation dose but require surgical intervention to place the seeds. There are significant risks inherent to this invasive procedure. Also, this technique cannot be used in inaccessible or sensitive areas of the brain.

In marked contrast is stereotactic radiosurgery. This is high-tech radiation and has no similarity to surgery. There is no cutting, no bleeding and no pins in the head with fractionated stereotactic radiosurgery.

Using stereotactic radiosurgery, large doses of radiation can be given to the tumor volume while sparing the normal surrounding tissues to a high degree.

Stereotactic radiosurgery can be administered to patients with gliomas both at the time of recurrence as well as part of the initial management.

In our hands, stereotactic radiosurgery is unusual in that it is non-invasive and can be fractionated. By fractionating or dividing the dose of radiation in stereotactic radiosurgery, a large dose of radiation is given with greater than expected normal tissue tolerance.

The potential advantage of this approach is that the surrounding brain is relatively further protected at the intersection between the tumor and the normal brain. We have seen a diminishment in the need for subsequent neurosurgical intervention after this technique. That is appealing for patients already with a brain tumor who, in general, seek to avoid further invasive treatment.

Combining this innovative technique with chemotherapy has a further potential advantage of radiosurgery in our hands. Chemotherapy has action of its own against certain tumors and can, as well, sensitize the tumor to the x-rays of radiosurgery.

Two new treatment protocols have been developed taking advantage of Taxol, a potentially beneficial chemotherapeutic drug in treating patients with these diseases of the brain. Other existing protocols here are also available that deliver stereotactic radiosurgery alone or in combination with Cis-Platin.

There are a number of studies indicating that Taxol compounds are radiosensitizing. Researcher Tischler et al noted results suggesting that "appropriate combinations of Taxol have a more than additive interaction in human tissue culture and may have a role in clinical protocols when studied with human astrocytoma cells." Similarly that group noted, "Taxol could function as a cell cycle selective radiosensitizer."

They noted results "with cycling aerated radioresistant brain tumor cells indicate that significant advantage may derive from appropriate time concentration dependent interaction in combined modality protocols." Those authors also noted "a role for radiation therapy and Taxol particularly in those tumors where Taxol alone showed some promise is thereby worthy of consideration. The combination may also be useful in the treatment of refractory brain tumors since normal tissue is quiescent. This difference in cellular behavior should result in a therapeutic gain for combined treatment."

The rationale of two new approaches here is to take advantage of Taxol's potential lethal effects on brain tumor cells as well as its sensitization of brain tumor to radiation.

The two new protocols are for two different groups of patients. The first is for those who have newly diagnosed high grade primary brain tumors and seek to receive Taxol weekly during external beam radiation therapy and stereotactic radiosurgery. All ten weeks of radiation are accompanied by the once-a-week Taxol intravenous therapy.

For those who have received external beam radiation therapy elsewhere, candidates accepted into the program will receive Taxol and weekly stereotactic radiosurgery concurrently for four weeks. This latter approach will be administered for selected patients whose disease has progressed after traditional therapy. Obviously, prior to any entrance into these protocols, patients are fully informed as to the risks, benefits and alternatives with all questions being answered.

The potential advantages may be great with synergistic therapy of two innovative treatments - non-invasive fractionated stereotactic radiosurgery and Taxol.

Developing such protocols has as a goal to extend the length and expand the quality of life. If these studies confirm expectations, future studies will build on that base. Subsequently randomized studies will compare this innovative treatment to standard therapy to determine the exact therapeutic advantage.

These new programs hopefully will lead to new and better outcomes for people with high grade primary brain tumors.

As this data matures, we find that the group receiving Taxol plus radiosurgery live about one-third longer than those with recurrent glioblastoma have no – or other – chemotherapy with fractionated radiosurgery. The fractionated radiosurgery group also do better than those who received single fraction radiosurgery.

Our multidisciplinary group at Radiosurgery New York offers the appeal of experts to discuss the best treatment options for you. Our experts have a long history with radiosurgery being one of the first in the nation to develop and practice fractionated stereotactic radiosurgery. We have established a hot line at 212-CHOICES and e-mail address: gil.lederman@rsny.org. We also will ask that you send in copies of films, reports, pathology for review by our panel of experts.