

FRACTIONATED RADIOSURGERY FOR LOW GRADE ASTROCYTOMAS

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Plathow

Radiosurgery is having more and more impact on the treatment of benign and malignant tumors.

The appeal of stereotactic fractionated radiosurgery is that it is a very precise method of set-up. In the past, treatment using standard radiation by definition gives radiation dose to healthy normal tissue. In general, the more healthy normal tissue that is treated, the more potential adverse effects. Also, without guidance systems it is possible to even miss the tumor.

Yes, there is appeal for stereotactic radiosurgery including accurate targeting of the tumor as well as decreasing radiation doses to the healthy normal tissue.

A recent article by Plathow et al, published in the prestigious International Journal of Radiation Oncology, Biology and Physics evaluated long-term outcome in the use of fractionated stereotactic radiation for low-grade astrocytomas.

There are many types of low-grade gliomas. Gliomas in general are tumors that start within the central nervous system- most commonly in the brain. With time they can infiltrate and evolve into higher-grade faster growing cancers. While sometimes surgery is used but often surgery cannot be attempted because of the extent of the tumor and the fact that the tumor is a diffuse process.

The role of radiation is often important but sometimes controversial. Some people propose holding off on radiation probably because of adverse side effects.

Grade II astrocytomas, as defined by the World Health Organization, have been treated and these authors have reported findings.

One hundred forty three patients were treated with Grade III astrocytomas. Sixty-one percent were men and 39% were women. The median age was 40.5 years with a range of 18 to 86. There were some patients who were excluded because they had Gemistocytic astrocytomas or brainstem gliomas.

Who received radiation? Those patients who had inoperable or incompletely removed tumor or showed evidence of progression of their disease.

After complete excision radiation was not routinely used. So patients had measurable disease or disease that could be evaluated before and after radiation. There are two groups of radiation, those having 5500 rad (a measurement of radiation dose) or less and the second group having more than 5500 rad.

Sixty percent underwent stereotactic radiation after biopsy or surgery and 39% underwent radiation at the time of relapse or progression after primary surgery. Location included 74% in the parietal, 62% in temporal lobe and 58% in frontal lobe. Most common symptoms were seizures in 36%. There were generalized and focal seizures in 34%. Headaches were seen in 29%, difficulty with movement in 23% and sensation in 9%. In 39% of patients, their first symptom was a seizure and 51% showed contrast-enhancement on CT scan or MRI. Contrast-enhancement means that an injection of contrast material is given through the vein and the tumor lights up when imaged.

Patients were treated on a dedicated linear accelerator with median target dose of 57Gy (a measurement of radiation dose) daily fractionation of 1.8 to 2Gy. Forty percent of the patients received a total dose of 54Gy. Boost techniques were used when there was suspicious of high-grade elements which were seen in 25 patients or 17%. The mean size of target volume was 257cc (cubic centimeter) with a range of 23 to 675. Patients had follow-up MRI's six weeks after radiation and every three to six months thereafter. Tumor progression was said to be a 25% increase in tumor size as measured by perpendicular measurements. The researchers looked at

prognostic factors including age, gender, Karnofsky performance or function, enhancement by scanning, extent of surgery and radiation dose.

Follow-up was 44 months with a range of 11 to 146. Of 143 eligible patients, 87% were monitored for at least three years. All patients completed the intended radiation. The median interval from initial symptoms to radiation was eleven months with a median interval from histologic confirmation to radiation of eight months. Overall survival was 58% at five years and 50% at eight years. Sixty percent had a relapse and in 90% of those, relapse was located in high dose area. About 8% of relapses occurred in the border area and one patient had a relapse more than 2cm (centimeter) beyond the low dose area.

It was said the toxicity was mild. 2.8% of the patients had Grade III toxicity including one patient from the moderate dose and three patients from the high dose groups. Fewer side effects were seen in the low dose group than with the high dose group.

Before radiation the Karnofsky score was 80, 90 or 100%, which would be the best three categories, and existed in 54% of patients and 31% and 1.3% respectively. After stereotactic radiation Karnofsky was 80 in 20%, 90 in 55% and 100 in 18% meaning there was an average improvement in function after stereotactic fractionated radiation. Karnofsky waiting or functional waiting improved in 51% and decreased in 3.5% of patients.

Motor deficits diminished from 23% to 14.7% after radiation and headache decreased from 29% to 16% after radiation. Forty-four percent of patients had anti-seizure medication before radiation and 28% after radiation.

The only relevant factor for outcome was enhancement before stereotactic radiation. Patients without contrast enhancement had a longer survival than those with contrast. The extent of

surgery, age and gender were not prognostic indicators. Tumor dose that was greater than 55Gy was not a significant prognosticator.

Thus this paper is important as a record of results after fractionated radiosurgery. It allows target volume radiation with precision and reduces dose to healthy tissue.

The authors concluded, "Fractionated stereotactic radiation is feasible and effective in the treatment of progressive World Health Organization Grade II astrocytomas. Compared with conventional conformal radiation it might be possible to reduce safety margins without enhancing the risk of out of field recurrences or marginal failure. Furthermore, the reduction in the target volume will lead to minimization of radiation-induced side effects. The quality of life as determined by Karnofsky performance status improves in most of our patients and got worse in only 3.5% at first presentation after fractionated stereotactic radiation. Pretherapeutic contrast enhancement proved to be the only significant prognosticator for disease free survival and overall survival and must be interpreted as a sign of higher grade elements."

This important article looks at patients who have been treated with fractionated radiosurgery for low-grade gliomas and makes an important point about dose and also about where tumors recur, which is usually in the same place the tumor commenced.

Our group of physicians certainly has great experience in performing fractionated stereotactic radiosurgery for gliomas both in low and high-grade group. We have data even using radiation again in a hypofractionated technique often with concurrent Taxol. Our data has been presented at national meetings and seems to show better survival than what would be otherwise expected.

It is critical to continue to track patients and report information both to future patients, their families and medical meetings.