THE TREATMENT OF GLIOBLASTOMAS
WITH RADIUM

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(Received for publication May 5, 1953)

Between the years 1911 and 1946, 789 gliomas of various types were treated in my clinic. They were subdivided into the following groups:

- 256 Astrocytomas, some solid and some cystic
- 92 Medulloblastomas
- 32 Cysts with no microscopic verification
- 52 Ependymomas
- 39 Oligodendrogliaomas
- 57 Various rarer types
- 261 Glioblastomas

I think I am expressing the opinion of most neurosurgeons that all gliomas other than the glioblastomas should be operated upon and removed as radically as possible. As many grow slowly repeated operations may be undertaken to prolong the patient’s life. Views about medulloblastomas vary in that some surgeons content themselves with a biopsy and then use intensive X-ray therapy, while others remove the tumor as completely as possible and then give X-ray therapy. Whether radiation should be used following operation for other types of tumors is a question about which there still is a difference of opinion. With a slowly growing tumor that has been radically removed it is extremely difficult to determine what effect radiation has had on the course of the disease.

Our greatest problem, however, still remains the care of patients with glioblastomas and I shall limit my remarks to this group. Let me say in the first place what I have repeatedly said before, that I believe every patient with a brain tumor is entitled to an exploration to determine what can be accomplished by surgery. I am not convinced that by angiography one can positively diagnose a glioblastoma though I realize that the claim has been made. Nor can the preoperative diagnosis be definitely made on the history and course of the disease, though it may frequently be suspected.

Of the 261 cases of glioblastomas in this series it has been possible to review only 154 at this time. The histories of the others are still in St. Louis. However, the 154 cases that have been reviewed are enough to enable one to draw some conclusions.

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The majority of the patients with glioblastomas died in less than 12 months but there were 14 who lived for over a year and these have been studied particularly to determine what factor or factors were responsible for their longer survival. Of this pitifully small number, 8 lived more than 2 years and 4 for more than 3 years.

The first question to resolve was the histological character of the tumors in these cases of longer survival. The sections were therefore re-examined. From their microscopical appearance all of the tumors were malignant. They contained numerous mitoses, showed endothelial and adventitial proliferation of the blood vessels, and in some there was necrosis with pseudo-palisading. We may conclude therefore that they were histologically as malignant as in those cases in which the patients died much more quickly. The location of the tumors was of no apparent significance; some were frontal, some parietal, some temporal, and one was occipital.

Then the treatment was considered. What, if anything, was different in the handling of these tumors as compared to the others in the series?

The longest survival was in those cases in which a very large amount of radiation was given. In 1937 and 1939 three papers on the radiation of gliomas were published from my clinic. One was a study of the effect of X-ray on tumors, reported in 1937. 4 That same year a technique was described 2 by which one could give one massive dose of X-ray into an open wound at the time of operation. The largest dose we gave in this way was 6000 r. But the method was cumbersome and technically awkward. The skin wounds, of course, had to be very carefully protected so that they healed well and were not injured by this large amount of radiation. In 1939 3 119 gliomas were reviewed and the conclusion was reached that heavier doses of radiation than we had been giving would have to be employed to get any effect. At that time the usual dosage was 1500 to 2500 r.

We then began treating a series of patients by implantation of gold radon seeds into the raw surface of the brain from which all vestiges of tumor had been removed. The seeds were placed within 1 cm. of each other. In the first cases 10 to 12 seeds were used, but subsequently the number was increased to 40 seeds. The amount of radiation that the patient received by this method in a localized area is much greater than it is possible to give with X-ray, as calculated by Dr. Shapiro of the Department of Radiology at Yale University School of Medicine.

In the following brief reports, Cases 1 and 2 illustrate the advantages of using radon seeds instead of X-ray radiation, and Case 3 demonstrates that the size of the radiation dose plays an important role.

Case 1 (51203). A female, aged 26, was admitted with Jacksonian convulsions of her arm. She was operated upon but no tumor was found, so a subpial resection of her arm center was performed. Three months later she returned with the typical picture of an intracranial tumor. A radical operation was performed and she was given 2500 r of X-ray. She returned in 2 months with symptoms of a recurrence. Reoperation was performed and 30 radon seeds were implanted. The radiation amounted to 8500 r. Following this treatment she lived for 2½ years.

Case 2 (47539). A male, aged 26, had had a radical removal of a temporal tumor
and was readmitted 3 months later for a recurrence. After a second removal 40 radon seeds were implanted, representing a dosage of 11200 r. He went along for 2 years and 2 months and then returned with another recurrence. He was again operated upon but this time a dosage of 3500 r of X-ray was administered through the open wound. He died of a recurrence 5 months later.

Case 3 (57301). A female, aged 40, after removal of a temporal lobe tumor received 6000 r through the open wound. She lived for 2½ years.

These patients and some of the others who survived well beyond the average time demonstrate quite clearly that large amounts of radiation are tolerated and have a beneficial effect. The great advantages of using radon seeds are that the radiation is concentrated in the region in which it is most needed and that the rest of the brain is not affected by the radiation. Placing the radon seeds in a flat surface, as when a frontal lobe has been amputated, is much more satisfactory than if one has a cavity left after a tumor has been removed. It is difficult to place seeds into such a cavity so that the entire area receives intensive radiation without any gaps, and this I believe may be the reason why some patients in whom we put seeds did not survive so long a time. It is most important to place the seeds close together, as the radiation from seeds extends only a short distance, not more than 1 cm. in every direction.

If one has no emanation plant at hand, and we had none nearer than Chicago, it is cumbersome to make arrangements for getting seeds but we were able to obtain them 24 hours after they had been prepared and each seed amounted to 1 millicurie. We had no experience in applying radium externally but in Stanford Cade’s book\(^1\) on the treatment of malignant disease by radium, there is a record of 4 patients with glioblastomas who were operated upon by Hugh Cairns and treated for him by Cade. They lived 9, 6, 5, and 5 years respectively. In all of these cases the dosage was around 8000 r. He reported no cases of brain tumors that were treated with radon seeds but mentioned the possibility.

Our cases and those of Cairns, it seems to me, indicate quite definitely that we must make a more determined effort to treat glioblastomas with radium since it is possible to give much bigger quantities of radiation than with X-ray.

With this evidence I feel we are not justified in considering the glioblastomas a hopeless problem but rather one that needs more intensive effort to effect a cure. It would be most interesting if some clinic would undertake to treat two series of glioblastomas, one with radon seeds and another with radium or cobalt, in the form of a helmet, as described by Cade.

REFERENCES