Postoperative Radiation Therapy of Astrocytoma and Glioblastoma Multiforme

Moon Baik Park, M.D. and Seong Eon Hong, M.D.

Department of Therapeutic Radiology, College of Medicine, Kyung Hee University, Seoul, Korea

Forty-four patients with brain astrocytoma and glioblastoma were treated with surgical resection and postoperative radiation from January 1980 through May 1987. Four patients were lost to follow up, and in 40 patients survival time was evaluable. Three year actuarial survival rate was 66.7% in Grade I and II astrocytoma, 30% in Grade III, and 20.4% in glioblastoma multiforme patients. The prognostic factors affecting survival rate were histologic grade in all cases, age, and total radiation dose in Grade III and glioblastoma.

Key Words: Postoperative radiation therapy, Astrocytoma, Glioblastoma multiforme

INTRODUCTION

Postoperative radiation therapy has been found to be highly efficient in prolonging median survival of patients of astrocytoma and glioblastoma. According to recent study, prognosis of astrocytoma is affected by the factors of histologic grade, age, radiation dose, tumor location, post-resection residual tumor and primary tumor size.

For glioblastoma, postoperative BCNU combination treatment with radiation therapy was reported to increase the number of long-term survivors, although not to increase median survival.

In this presentation, survival and prognostic factors were evaluated for the patients with astrocytoma and glioblastoma of brain treated with postoperative irradiation between January 1980 and May 1987 at our department.

MATERIALS AND METHODS

From Jan. 1980 through May 1987, total 44 patients of brain astrocytoma and glioblastoma were treated with surgical resection and postoperative adjuvant radiation therapy at the Department of Therapeutic Radiology in Kyung Hee University Hospital. All patients except four were followed until analysis time (March 1989). Four patient were lost to follow up at 3, 4, 6 and 8 months, respectively. Male to female ratio was 1.7:1, and the range of age was between 11 and 72 years (Table 1). All were confirmed histopathologically, and 44 patients were classified into 4 Grade I, 4 Grade II, 10 Grade III, 26 glioblastoma multiforme (Table 2). Partial resection was done in 30 cases, gross total

Table 1. Patient Characteristics

Age	Male	Female	Total
10 – 19	2	1	3
20 – 29	2	3	5
30 – 39	6	4	10
40 – 49	6	2	8
50 – 59	6	6	12
60 – 69	4	0	4
above 70	1	1	2
Total	27	17	44

Table 2. Classification of Astrocytoma by Histologic Grade

Histology	Number (Percent)
Astrocytoma	
Grade I	4 (9.1)
Grade II	4 (9.1)
Grade III	10 (22.7)
Glioblastoma Multiforme	26 (59.1)
Total	44 (100)

Table 3. Extent of Operation

	Grade				
	I	II	III	GM	Total (%)
Total Resection	0	0	1	5	6 (13.6)
Partial Resection	2	3	8	17	30 (68.2)
Biopsy	2	1	1	4	8 (18.2)

resection in 6 cases, and only biopsy in 8 cases (Table 3). Patients with Grade I and Grade II astrocytoma were treated with generous margin of involving tumor, and patients with Grade III astrocytoma and glioblastoma were treated whole brain up to 4000~4500 cGy followed by 1500 ~2000 cGy boost irradiation to primary tumor site (Table 4).

Eight out of 33 Grade III and glioblastoma patients were treated with chemotherapy and postoperative irradiation (Table 5).

Survival was analysed from the starting day of radiation therapy. Life table method was used to calculate survival rate and logrank test[1] was used for evaluation of survival data statistically.

Table 4. Radiation Dose According to Histology

	Grade				
	I	II	III	GM	Total
Below 5000cGy	1	1	0	9	11
5000–5999cGy	2	3	6	6	17
Above 6000cGy	1	0	4	11	16

Table 5. The Number of Chemotherapy (BCNU) with Postoperative Radiotherapy

	Grade III	GM	Total
Ghemotherapy Group	2	6	8
Non-Chemotherapy Group	8	17	25

RESULTS

1. Survival Rate

Three year survival rates were 66.7% for Grade I and II astrocytoma, 30% for grade III, 20.4% for glioblastoma (Fig. 1). Survival for total astrocytoma patients was 44.9% and it is statistically different significantly from glioblastoma ($p<0.05$).

2. Prognostic Factors

Survival rate was improved by increasing radiation dose above 5000 cGy significantly ($p<0.01$) especially Grade III and glioblastoma patients (Fig. 2).

Regarding age, survival rate was influenced in Grade III and glioblastoma around 50 years ($p=0.025$) (Fig. 3).

Regarding the extent of resection, survival rate was improved in totally resected group, but the cases were too small to evaluate any statistical significance ($p<0.1$) (Fig. 4).

In the chemotherapy group, survival was not improved compared to non-chemotherapy group (Fig. 5). But in only glioblastoma patients, 1 year and 2 year survival rates were 83.3% and 50% respectively in chemotherapy group, and median

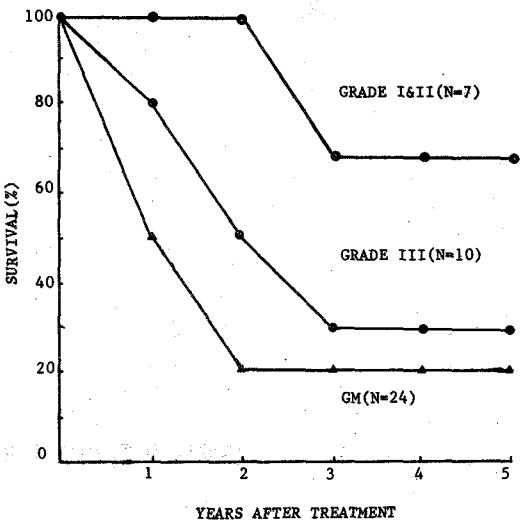

Fig. 1. Survival Rate by Histologic Grade.

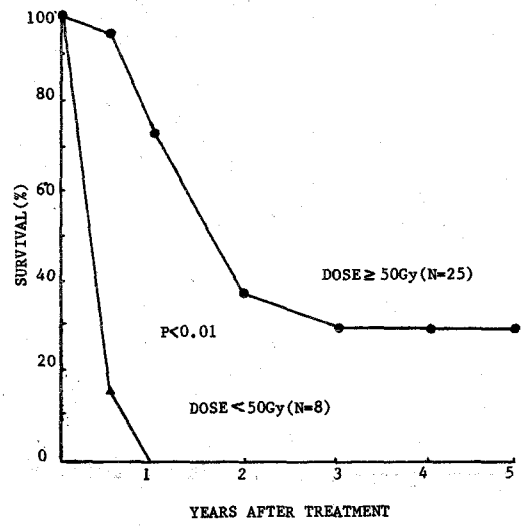

Fig. 2. Survival Rate by Dose.

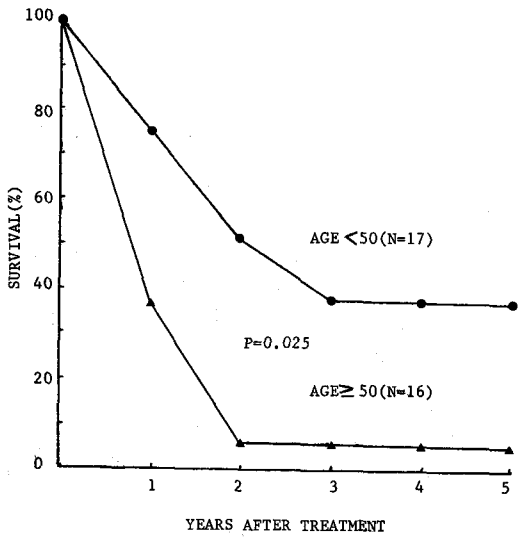

Fig. 3. Survival Rate by Age in Grade III Astrocytoma and Glioblastoma.

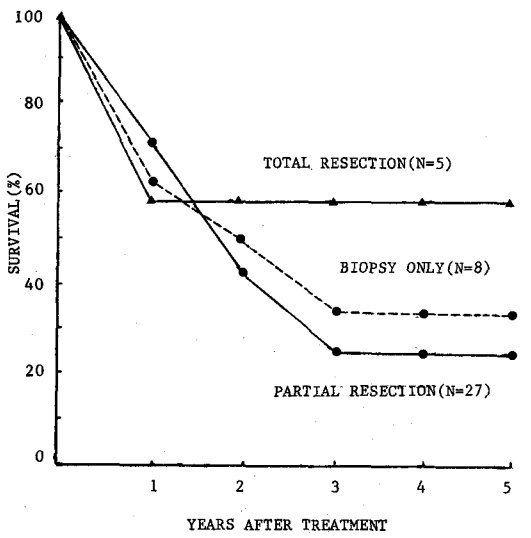

Fig. 4. Survival Rate by Extent of Operation.

survival was 25 months. In non-chemotherapy group, 1 year and 2year survival were 66.7% and 11.1% respectively. Median survival was 19.8 months. These differences were statistically significant (p=0.01).

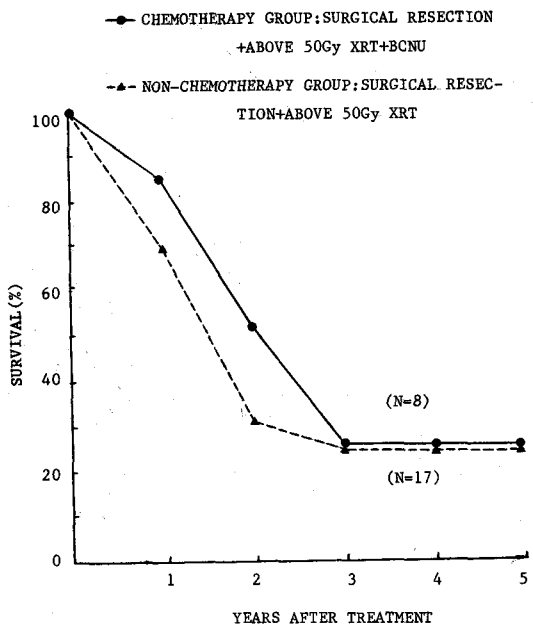

Fig. 5. Survival Rate of Chemotherapy and Non-Chemotherapy Group.

DISCUSSION

Brain astrocytoma and glioblastoma multiforme consist major portion of adult cerebral gliomas, and survival rate was increased by surgical resection and postoperative radiation therapy in recent several decades[2~7]. Leibel et al.[2] reported the 5 year survival rate was 19% in incomplete resection alone group, and 46% in postoperative irradiation group in the review of 147 cases of Grade I and II astrocytoma patients. Also, Garcia et al.[4] reported 5 year survival rates as 50% and 21% in postoperative irradiation and surgery alone group, respectively. Posttreatment neurologic function was superior to surgery alone group, too.

In the series of Mudbery et al.,[6] overall actuarial 5 year survival was 45% in low grade astrocytoma patients who received postresection radiation therapy. In our result, the acturial survival at 5 years was 66.7% in Grade I and II astrocytoma, 30.4% in Grade III astrocytoma. The results of Grade II and III were similar to other reports, but that of Grade I was low because 1 out of three patients expired at 25 months after radiation therapy.

Glioblastoma is the most malignant intracranial neoplasm, and frequently surgically inaccessible due to its anatomic sites and infiltrative character, and frequently recurs. For that reasons, radiotherapy after surgical resection was widely used. Onoyama et al.[7] reported that in a series of 127 patients of glioblastoma who were irradiated after surgical resection, overall survival rates were 52% at one year, 19% at three years, and 12% at 5 years. In our case acturial 1 year survival was 52.2%, and 20.4% at 3 and 5years. These are slightly higher than others at 5 year survival.

Survival was improved as radiation dose increased. Walker et al.[5] reported the elongation of median survival from 28 weeks to 42 weeks as dose increasing from 5,000 cGy to 6,000 cGy. And Salazar et al.[9] reported improved result of 55% 1 year survival in Grade III and IV patients by 6,000~8,000 cGy high dose irradiation.

The prognostic factors of astrocytoma were known to be histologic grade, age, extent of operation, and tumor location. In our result, the grade of cell differentiation had a strong association with survival especially Grade III and glioblastoma, but in low grade astrocytoma the case numbers were too small to evaluate statistical significance.

The survival rate was higher in younger age groups less than 50 years of age in Grade III and glioblastoma. This result was different from other reports [4,7,10,13] and is probably due to the higher proportion of glioblastoma which is the older age disease than astrocytoma in our report.

When treatment groups were examined according to extent of the surgical resection, the superior result was obtained in the group of total resection compared to partial resection or biopsy group, but that was not statiscally significant due to small number of cases. Leibel et al.[2] also reported the consistent trend of higher survival rate in totally resected tumor group.

There are several reports about the effect of BCNU chemotherapy after surgical resection combined with radiotherapy in malignant glioma. Salazar et al.[11] used the method of high dose irradiation combined with low dose pulsed BCNU chemotherapy. The median survival was 80 weeks and the result was not different from what achieved by high dose radiation alone. Walker et al. also[12] reported that there were no significant differences between BCNU plus radiotherapy and radiotherapy alone group. In our case, also the survival was not improved in all patients received chemotherapy. But in glioblastoma patients, chemotherapy group and non-chemotherapy group showed different survival with statistical significance. Improved survival in chemotherapy group might be partially due to younger age and higher performance status of chemotherapy group than non-chemotherapy group, but the case number was small and more long term follow up is needed for further evaluation.

CONCLUSION

The result of 44 cases of postoperative radiotherapy of brain astrocytoma and glioma is as follows;

1. 3 year actuarial survival rate was 66.7% for Grade I and II, 30% for Grade III, 20.4% for glioblastoma respectively. 3 year survival rate of total astrocytoma was 44.9%.

2. The prognostic factors with significance were histologic grade, age, and total radiation dose. Chemotherapy may improve the survival rate.

REFERENCES

1. **Peto R, Pike MC, Armitrage P et al:** Design and analysis of randomized trial requiring prolonged observation of each patient. II. Analysis and examples. British J Cancer 35:1-39, 1977
2. **Leibel SA, Shelein GE, Wara WM, et al:** The role of radiotherapy in the treatment of astrocytoma. Cancer 35:1551-1557, 1975
3. **Ruthen EHJM, Kazen I, Sloof JL, et al:** Radiotherapy in the management of brain astrocytoma-Retrospective study of 142 patients. Int J Radiat Oncol Biol Phys 7:191-195, 1981
4. **Garcia DM, Fulling KH, Marls JE, et al:** Ther value of radiation therapy in addition to surgery for astrocytomas of the adult cerebrum. Cancer 55: 919-927, 1985
5. **Walker MD, Strike TA, Sheline GE:** Analysis of dose effect relationship in the treatment of malignant gliomas. Int J Radiat Oncol Biol Phys 5:1725-1731, 1979
6. **Mudbery III CA, Straus KL, steinberg SM et al:** Low grade astrocytomas: Treatment results and prognostic variables. Int J Radiat Oncol Biol Phys 15: 837-841, 1988
7. **Onoyama Y, Abe M, Yabumoto E et al:** Radiation therapy in the treatment of glioblastoma. American J Roentgenology 126:481-492, 1976
8. **Scanlon PW, Taylor WF:** Radiotherapy of intracranial astrocytomas: Analysis of 417 cases treated from 1960 through 1969. J Neurosurg 5:301

-308, 1979
9. **Salazar OM, Rubin P, McDonald JV, et al:** High dose radiation therapy in the management of glioblastoma multiforme: A preliminary report. Int J Radiat Oncol Biol Phys 1:717-727, 1976
10. **Choi DH, Kim IH, Ha SW:** Radiotherapy result of brain astrocytoma and glioblastoma multiforme. J Korean Soc Ther Radiol 6:163-168, 1988
11. **Salazar OM, Vanttoutte PJ, Bennett JM, et al:** High dose radiation therapy with low dose (pulsed) BCNU in malignant gliomas. An Eastern Cooperative Onclogy Group (ECOG) report. Int J Radiat Oncol Biol Phys 8:915-919, 1982
12. **Walker MD, Alexander J, Hunt WE, et al:** Evaluation of BCNU and/or radiotherapy in the treatment of anaplastic gliomas. J Neurosurg 49:333-343, 1978
13. **Suh CO, Kim GE, Suh JH:** Radiotherapy results of brain astrocytoma. J Korean Soc Ther Radiol 2: 177-184, 1984

=국문초록=

성상세포종과 교아세포종의 수술후 방사선치료

경희대학교 의과대학 치료방사선과학교실

박 문 백·홍 성 언

1980년 1월부터 1987년 5월까지 경희대학 부속병원 치료방사선과에서 수술후 방사선 치료받은 뇌의 성상세포종과 교아세포종 환자에 대해 후향적 분석을 실시하였다.

총 44예중 40예에서 추적관찰이 가능하였고 3년 생존률은 Grand I. II 성상세포종은 각각 66.7%, Grand III 성상세포종 은 30.0%, 교아세포종은 20.4% 이었다.

Grade I과 II 성장세포종에서는 환자수가 적어 예후인자를 평가할 수 없었고, Grade III 성상세포종과 교아세포종에서는 조직학적 분화도, 환자의 나이, 총 조사선량 등이 예후에 영향을 미치는 인자로 나타났다. BCNU 항암약물 요법은 교아세포종 환자에서 생존율을 증가시키는 효과가 있었다.