



High Grade Asrtocytomas Whole Brain Radiotherapy (WBRT) vs Limited Volume Brain Radiotherapy (LVBRT)- A Prospective Randomized Study

Authors

Dr C.S.K. Prakash M.D (R.T)¹, Dr Manne Srinivas, M.D (R.T)²

¹Associate Professor, Department of Radiotherapy & Oncology, Kakatiya Medical College and Mahatma Gandhi Memorial Hospital, Warangal, India

²Assistant Professor, Department of Radiotherapy & Oncology, Rangaraya Medical College And Government General Hospital, Kakinada, India

Corresponding Author

Dr Chennapragada Sri Krishna Prakash M.D (R.T)

H/O Dr N. Madhavi, Plot No 44, 3rd Floor, Road No 4,
Mamatha Nagar, Old Nagole, Hyderabad-500 068.

Email: srikrishnaprakash@yahoo.co.in, csk_prakash@hotmail.com, PH: +91984800607

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Purpose: To analyze the results obtained in patients with post operative High Grade Astrocytomas treated by adjuvant Radiotherapy.

Materials and Methods: The study was carried out between 1996 and 1999 at Kasturba Medical College and Hospital, Manipal 576 119. This is a prospective randomized study of 26 patients, who were randomized to Whole Brain Radiotherapy (WBRT) and Limited Volume Brain Radiotherapy (LVBRT) groups in postoperative high grade astrocytomas. Both groups of patients received total dose of 60 Gy/30#/6 weeks with standard Radiotherapy technique based on pre and post operative CT scan reports and intraoperative findings.

The data was analysed for the prognostic factors like performance status, extent of surgery, grade of tumor. The radiation reactions (RTOG scale), survival patterns (for 6 months) were analysed.

Results: Majority (84.6%) of the patients were males. Patients with Grade III histology had better survival than patients with grade IV (90% vs 31.25%) Patients with WBRT group developed more acute reactions than LVBRT group (Grade II reactions 69 vs 23%, grade III 23% vs 0). Patients treated for tumor volume <4x4cm² had better survival than with patients with >4x4cm², up to 6x6cm² (62% vs 29%). Patients underwent near total excision had better survival than those biopsy alone (100% vs 10%). The overall survival was 61% vs 53% for WBRT vs LVBRT group. The observed test of significance was 0.546 and p values were <0.1%, which were not statistically significant.

Conclusion: Postoperative adjuvant Radiotherapy will provide better quality of life and survival benefit for the patients. The patients will not have a significant survival benefit whether treated by WBRT or by LVBRT. Hence, can be treated by LVBRT as there will be less toxicities. This study concepts were followed today with escalation of radiotherapy dose to the tumor and limiting dose to normal structures by latest and advanced techniques like Three Dimensional Conformal Therapy (3D-CRT) or Intensity Modulated Radiotherapy (IMRT).

Key words: High grade gliomas, Whole Brain Irradiation vs Limited Volume Brain Irradiation.

Introduction

The incidence of the primary intracranial and spinal axis tumors in India is 1.4 %.¹

The malignant gliomas account for 50-60 % of intracranial neoplasms, Out of which Glioblastoma multiforme is the commonest. Eighty four percent of the malignant gliomas occur in supratentorial region and the remaining ones in infratentorial region.²

The presence of either vascular endothelial proliferation or a mitotic rate > 1 per HPF is pathognomic of anaplastic changes³ but either feature is necessary for the diagnosis. Glioblastoma multiforme is distinguished from the other types by its variegated appearance; hence the term multiforme.

Svien et al⁴ and kernohan et al⁵ used a four grade system designated as grade 1 to 4 that was patterned after the histological grading system for epithelial neoplasms used at the Mayo Clinic.⁵ Necrosis was used to divide the intermediate type astrocytoma from glioblastoma.⁶ Both systems based on the histological grade on the recognition of cellular anaplasia.

With the invention of CT & MRI which drastically improved the ability to localize, diagnose and treat the patients with astrocytomas. CT & MRI became the standard diagnostic imaging techniques and PET & SPECT are used to distinguish neoplasia from radiation necrosis.^{7,8,9}

Treatment modalities consist of surgery, radiotherapy and chemotherapy. Surgery is in the form of decompression+biopsy, partial, near total and total excision

Biopsy Can be performed either free hand or image directed as with stereotactic CT^{10,11}.It is generally agreed that the tumor debulking can provide good initial palliation¹².Reoperation reserved for small symptomatic and easily accessible tumors, largely as palliative procedure.^{13,14,15}

Randomized study comparing whole brain with treatment to the whole brain followed by a local boost to identical tumor doses has not delineated a survival difference.¹⁶The optimal total dose is 55-60 Gy in doses of 1.7-2 Gy per fraction up to a dose of 60 Gy.¹⁷Radiation doses beyond 60 Gy to a

larger target volume have not demonstrated any further survival benefit. The prospective clinical trial conducted by the Brain Tumor Study Group (B T C G 69-01)¹⁷ is the first clinical trail that proved that the post operative radiotherapy significantly increases the median survival time in patients with high grade gliomas when compared with neurosurgical treatment alone

The Scandinavian glioblastoma study group (SGSG)¹⁸ also showed improvement in the median survival time as compared to those who received conservative management without radiotherapy or chemotherapy

Hochberg and Pruitt¹⁹ found that 90% of recurrence occur within 2cm of the primary site. Urtasun²⁰ and all the recurrences were within their partial brain target volumes.

Marseyand Wallnes²¹ observed that Eight out of twlve recurrences were no more than 2cm from the contrast enhancing margin of the first recurrence.

Choucair²² et al reviewed 1047 patients with supratentorial GBM and anaplastic gliomas treated from 1976-1985. All these proved that the recurrence of tumor occurred within the margins of the original tumor.

A clinical trial by Ruth G.Ramsey and William.N.²³ in a randomised study. This study concluded that a high dose delivered to a smaller volume resulted in a long survival time. Study by Hochberg and Pruitt Most of the tumor recurrences occurred within 1-2cm of their tumor location.^{24,25}

More over studies by Gasper and Fischer²⁴ found that intracranial metastasis that develop after partial brain irradiation do not affect ultimate outcome as they are nearly always accompanied by relapse of the primary tumor.

RTOG/ECOG study^{25,26} in which no significance difference could be demonstrated between patients receiving 60dy vs 70Gy to the tumor bed. A study by Miller et al" in 82 patients demonstrated no additional benefit with dosage 60Gy.

In a series reported by Leibel²⁷ proved better results with incomplete resection with EBRT than incomplete resection alone.

Several clinical observations support the use of limited radiation portals, rather than whole brain irradiation. The majority of the malignant gliomas are unifocal at the time of initial presentation', less than 5 % presented with multicentric lesions .

After initial treatment, most tumor recurrences occur at or within 1-2 cm of the original location²⁵. Furthermore, 2nd tumor recurrence after resection of the recurrent lesion also occur most commonly at the primary tumor site.

An analysis between 1983 to 1988 of 70 patients with supratentorial malignant gliomas with pre and post operative CT scan, simulator films and CT scan films documenting tumor recurrence were analyzed, who were treated at London Regional Cancer Centre (LRCC) with whole skull R.T plus boost radiation therapy with the site of recurrence to the boost dose of radiation therapy. Recurrences outside boost were most common with inadequate boost margins, small boost volumes, temporal lobe tumors and ipsilateral wedge pair technique.

Irradiation dose not effect the ultimate outcome, because they are always accompanied by the relapse of the primary tumor.

Based on the above studies, this prospective randomized study was designed to know the acute, sub acute, sub acute and delayed adverse effects and survival benefits of Limited Volume Brain Irradiation (LVBRT) vs Whole Brain Irradiation in Malignant Astrocytomas.

Materials and Methods

This is a prospective randomized clinical trial, the study group being treated with external radiotherapy localized to the tumor with an appropriate margin depending on the pre operative CT Scan and intraoperative findings. The control group will be treated with whole skull plus boost external radiotherapy depending on CT Scan findings.

Pre Treatment Evaluation: The patients with confirmed histopathological diagnosis of high grade gliomas were evaluated by physical examination and with necessary laboratory investigations

including complete hemogram, R.F.T. chest x-ray, C.T. Scan Brain (Plain & contrast) and Magnetic Resonance Imaging [optional].

Once the patient is found eligible, as per criteria, an informed consent of the patient was obtained and included in the study/control groups after randomization.

Inclusion Criteria

1. Grade 3 & 4 gliomas,
2. Karnofsky's performance status > 60. 2. Age < 70 years.
3. No previous history of radiotherapy or chemotherapy.

Exclusion Criteria

1. Multicentric foci of the disease > 3 lesions.
2. Intraventricular & brain stem gliomas.

The patients in both the groups received external radiotherapy from Tele Cobalt 60 or Linac [6MV photons] with or without electrons.

Dose and Technique of Radiotherapy:

A dose of 60 Gy in 30 # over 5-6 Weeks was used in both whole skull irradiation and limited volume irradiation. The standard radiotherapy techniques of parallel opposed lateral field, ipsilateral wedge fields depending upon the target volume as identified by clinical, per operative, and imaging evaluation were applied.

The patient is placed in supine position and the head is immobilized with mould. The treatment plan will be optimized by, computerized treatment planning system, dosimeter information was reviewed by the Senior Radiation Oncologist & physicist.

All the patients were given steroids and anti epileptics during the radiotherapy.

Treatment Volume: The patient in the limited volume Radiotherapy group was treated with a margin of 4 cm around the pre operative contrast enhancing lesion in the C T scan or hyperdense margin on T2 weighted M R I scan. The field sizes ranged from 9x9cm² to 12x12cm² and with wedge fields 8x8cm² to 11.5x 11.5²

The other group was treated by whole brain radiation up to 46 Gy and followed by boost up to

60 Gy to the lesion of 4 cm margin with lateral parallel fields or wedge fields depending on the size of the tumor. The field size for whole skull radiotherapy group was ranged from 13-14x20 cm².

Post Treatment Evaluation

1. Acute reactions during radiotherapy as per RTOG / EORT Scale.
2. Sub acute reaction are noted at 2-6 months after completion of radiotherapy.
3. Late reactions were after 6 months of radiotherapy.
4. The survival patterns at 6 months were studied.

Results

This study is conducted from February 97 to December 98 in which a total number of 26 patients were included. These patients were randomized into two groups. one group received whole skull radiation therapy while the other group received limited volume irradiation. The whole skull radiation was given as 46 grays to the whole skull later local radiation was given with a margin of 4cm to the initial pre operative tumor volume. The group receiving local radiation received 60 grays to the pre operative tumor volume with a tumor margin of 4 cm by linear accelerator or by telecobalt-60.

Out of 26 patients who were randomized male patients predominated in both groups with 11 (84.6%) in each group as against two (15.38 %) female patients in each.

The age of the patients ranged from 12 years to 61 years the mean age being 40.4 years. Out of these the maximum number of patients belonged to the age group between 30 -60 Years. 21 out of 26 patients belonged to this group.

The symptoms with which the patients presented varied widely the commonest being headache and vomiting present in as much as nineteen out of twenty six patients. This was followed by seizures in the order of frequency which was present in six patients. Other less common symptoms like paresis, memory changes, speech difficulties,

personality changes, syncope, visual and sensory changes. (table no 1).

The tumor was located commonly in frontal region in about 11 patients. In five other patients it was located in temporoparietal region. Few tumors were located in frontoparietal, frontotemporal, parieto-occipital, and temporal regions (table 2).

The size of the tumor ranged between 3x3 cm² to 7x7 cm². But most of the tumors belong to 4x4 cm²-6x6cm² group (21/26). Blood group A was predominant in both groups. 13/26 belong to this group, out of which 7(53.85%) belong to whole skull Radiotherapy group and six(46.15%) belong to Limited volume irradiation group. These patients first subjected to surgery in the form of biopsy, partial excision or near total excision. In patients who underwent WSEBRT, biopsy in four (30.77%), partial excision in three (23.08%), and near total excision in six (46.15%) patients. In patients who underwent LVRT, six (46.15%) underwent biopsy, partial excision in five(38.46%) and near total excision in two (15.38%) patients (table 2).

Histopathology was carried out by the senior pathologist at Kasturba Hospital, Manipal and also by the pathologist at NIMHANS, Bangalore. In patients who had WSEBRT, 7/13 (53.85%) were of grade III and 6/13(46.15%) were grade IV. Whereas in LVEBRT group, 3/13(23.08%) were grade III and 10/13(76.92%) were grade IV (table 2). In both groups, none of the patients experienced interruption of the treatments.

The patients were observed for reactions and haematological status as per Radiation Therapy Oncology Group (RTOG) scale for six weeks. Weekly patient review was carried out by the senior radiation oncologist and the physicist about the field size, treatment set up, dosimetric calculations, patient 's on machine set up.

a) Skin Reactions

The reactions were classified as acute and graded. In WSEBRT group, Grade 1 reactions were experienced in 7.69%, grade 2 in 69.23% and grade 3 in 23.07%. In LVRT group, 61.54%

experienced grade 1 and 38.46% in grade 2. None grade 3. In both the groups, none experienced grade 4 reactions.

b) Ear

In WSRT group, 30.77% had Grade 1 and 69.23% had grade 2 reactions. In LVRT group, 23.08% developed grade 1 and 30.77% grade 2 reactions . These reactions resolved within one month after radiotherapy with symptomatic treatment.

c) Haematological

None of the patients experienced, fall of Hb <8 gm%, Twbc <3600/mm³ and platelet count less than 1lakh during entire course of treatment.

Acute CNS reactions like changes in level of consciousness, worsening of neurological signs and generalized seizures did not occur in both groups of patients. All the patients were on prophylactic corticosteroids and anti epileptics. The corticosteroid dose was tapered after completion of EBRT.

Fifty to sixty percent of patients in both groups had nausea after radiotherapy, which was relived by anti emetics.

The head ache, occurring during treatment was relived by increasing dose of corticosteroids.

ii. **Early Delayed Effects:** The effects observed from 2-6 months of radiotherapy as follows.

Somnolence syndrome was observed during 3rd month of Radiotherapy in both groups of patients.

Ten out of thirteen (79.93%) in WSRT and 7/13 (53.85%) in LVRT group developed the same.

Patients in both groups did n't experience fatigue or exacerbation of focal neurological signs at 6 months follow up.

iii. **Late Effects:** The late effects were assed at 6mo follow up and graded according to RTOG, EORTC grading system.

In WSRT group, 2/13 (15.38%) were without head ache, lethargy or any CNS dysfunction (GRADE 0). Four out of thirteen (30.77%) had grade 1 and 7/13 had Grade 2 effects.

In LVRT group, 8/13 (61.54%) patients were without any late reactions (Grade 0), 4/13 (30.77%) had grade 1 reactions, 1/13(7.69%) had grade 2 late reactions.

None of the patients in both groups had grade 3&4 late effects.

Survival Patterns: Patients who were having better performance status were hiving better survival. patients who underwent near total or total excision had better survival than those with sub optimal surgery. Patients with grade III astrocytomas had better survival than those with grade IV astrocytomas (table 3,4,5,6) and plotted Kaplan Meyer survival curve. The observed test of significance was 0.546 and the p value for both groups was <0.1, which were not statistically significant.

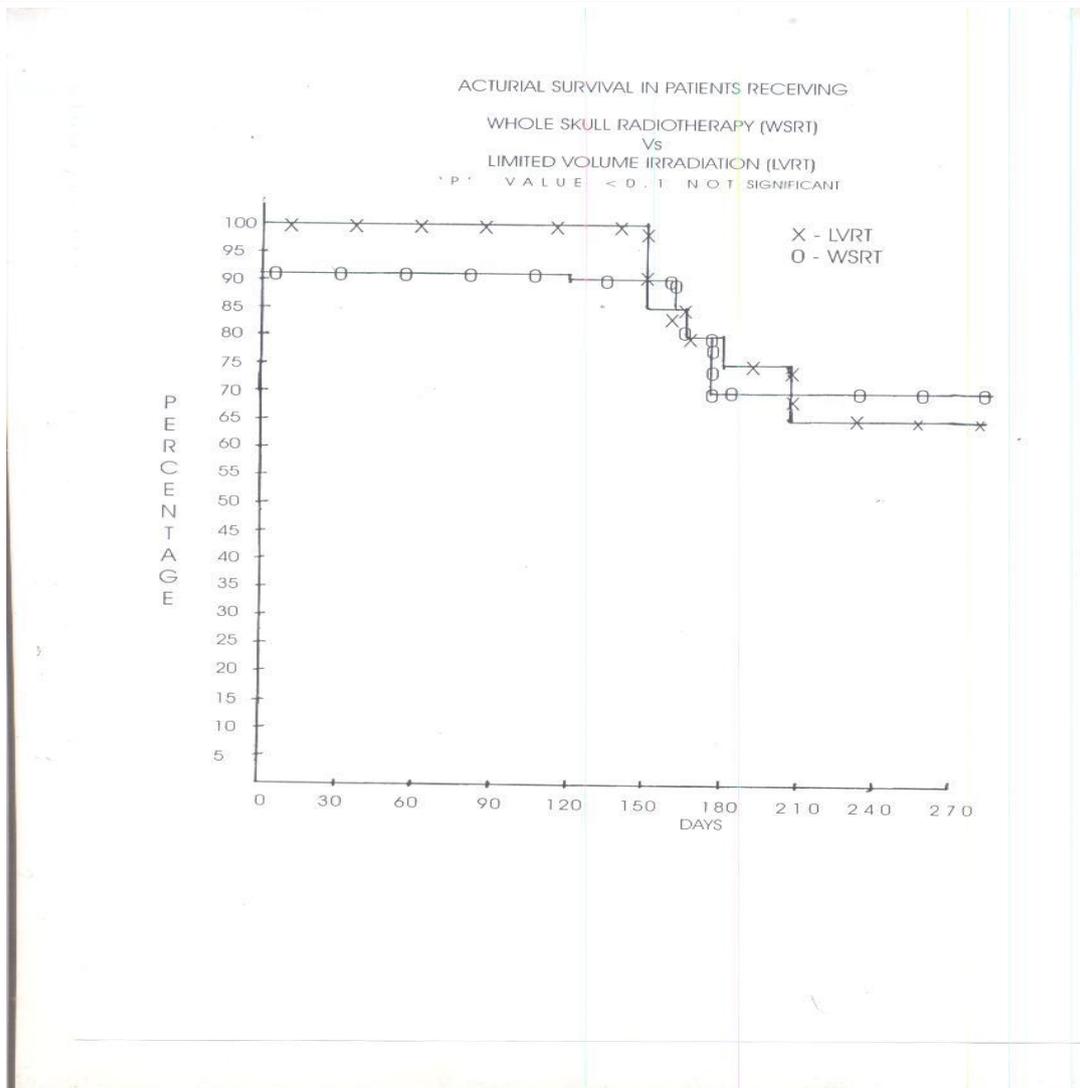


Table 1: Distribution of patients according to the sex, age, Karnofsky,s performance and symptoms at presentation of the patient

Sex of the patient	Whole Skull Radio Therapy	Limited Volume Radio Therapy
Male	11 (84.6%)	1 (84.6%)
Female	2 (15.38%)	2 (15.38%)
Age of the patient	Whole Skull Radio Therapy	Limited Volume Radio Therapy
<20 Years	-	1 (7.69%)
20-40 Years	7 (53.85%)	5 (38.46%)
40-60 Years	6 (46.15%)	6 (46.15%)
>60 Years	-	1 (7.69%)
Karnofsky's performance status	Whole Skull Radio Therapy	Limited Volume Radio Therapy
60	2 (15.38%)	5 (38.46%)
70	3 (23.07%)	1 (7.69%)
80	1 (7.69%)	1 (7.69%)
90	7 (53.85%)	6 (46.15%)
100	-	-
SYMPTOMS PRESENTATION	Whole Skull Radio Therapy	Limited Volume Radio Therapy
Headache & Vomiting	9 (69.23%)	10 (76.92%)
Other symptoms	4 (30.77%)	3 (23.08%)

Table 2: Distribution of patients according to site, size of thr tumor,blood group,and type of surgery

	Whole Skull Radio Therapy	Limited Volume Radio Therapy
Site of the tumor		
Frontal region	5(38.46%)	6(46.15%)
Other sites	8(61.54%)	7(53.85%)
Size of the tumor		
<4x4cm ²	-	1(7.69%)
>4x4cm ² -<6x6cm ²	10(76.92%)	11(84.6%)
>6x6cm ²	3(23.08%)	1(7.69%)
Blood group		
A	7(53.85%)	6(46.15%)
B	2(15.38%)	3(23.07%)
AB	1(7.69%)	2(15.38%)
O	3(23.07%)	2(15.38%)
Type of surgery		
Biopsy	4(30.77%)	6(46.15%)
Partial excision	3(23.07%)	5(38.46%)
Near total excision	6(46.15%)	2(15.38%)
Histopathology		
Grade III	7(53.85%)	3(23.07%)
Grade IV	6(46.15%)	10(76.92%)

Table 3: Relation of survival rate with site and grade of the tumor

FRONTALREGION	Whole Skull Radio Therapy	Limited Volume Radio Therapy
TOTAL NO: OF PATIENTS	5	6
GRADE III	3	1
>6 MONTHS	3 (100%)	1 (100%)
<6 MONTHS	-	-
GRADE IV	2	5
>6 MONTHS	1 (50%)	2 (40%)
<6 MONTHS	1 (50%)	3 (60%)
Location other than frontal region		
TOTAL NO: OF PATIENTS	8	7
GRADE III	4	2
>6 MONTHS	3 (75%)	2 (100%)
<6 MONTHS	1 (25%)	-
GRADE IV	4	5
>6 MONTHS	2 (50%)	-
<6 MONTHS	2 (50%)	5 (100%)

Table 4: Relation of survival rate with age and grade of the tumor

Age	Whole Skull Radio Therapy	Limited Volume Radio Therapy
<20 YEARS		
TOTAL NO: OF PATIENTS	-	1
GRADE IV	-	1
<6 MONTHS	-	1(100%)
20-40 Years		
TOTAL NO: OF PATIENTS	7	5
GRADE III	3	1
>6 MONTHS	3 (100%)	1 (100%)
<6 MONTHS	-	-
GRADE IV	4	4
>6 MONTHS	2 (50%)	2 (50%)
<6 MONTHS	2 (50%)	2 (50%)
40-60 Years		
TOTAL NO: OF PATIENTS	6	6
GRADE III	4	2
>6 MONTHS	3 (75%)	2 (100%)
<6 MONTHS	1 (25%)	-

GRADE IV	2	4
>6 MONTHS	1 (50%)	-
<6 MONTHS	1 (50%)	4 (100%)
60-70 years(grade IV)	-	1
<6 MONTHS	-	1(100%)

Table 5: Relation of survival rate with size and grade of the tumor

	Whole Skull Radio Therapy	Limited Volume Radio Therapy
<4x4cm ²		
TOTAL NO: OF PATIENTS	-	1
GRADE III		
>6 MONTHS	-	1(100%)
<6 MONTHS		
<4x4cm ² -6x6cm ²		
TOTAL NO: OF PATIENTS	10	11
GRADE III	7	2
>6 MONTHS	6 (85%)	2 (100%)
<6 MONTHS	1 (15%)	-
GRADE IV	3	9
>6 MONTHS	2 (66.66%)	3 (33.33%)
<6 MONTHS	1 (33.33%)	6 (66.66%)
>6x6cm ²		
TOTAL NO: OF PATIENTS	3	1
GRADE IV	3	1
>6 MONTHS	1 (33.33%)	-
<6 MONTHS	2 (66.66%)	1(100%)

Table 6: Relation of survival rate with type of surgery and grade of the tumor

	Whole Skull Radio Therapy	Limited Volume Radio Therapy
Biopsy alone		
TOTAL NO: OF PATIENTS	4	6
GRADE III	1	-
>6 MONTHS	1(100%)	-
<6 MONTHS	-	-
GRADE IV	3	6
>6 MONTHS	1 (33.33%)	-
<6 MONTHS	2 (66.66%)	6(100%)
Partial excision		
TOTAL NO: OF PATIENTS	3	5
GRADE III	1	2
>6 MONTHS	1(100%)	2(100%)
<6 MONTHS	-	-
GRADE IV	2	3
>6 MONTHS	1(50%)	1 (33.33%)
<6 MONTHS	1(50%)	2 (66.66%)
Near total excision		
TOTAL NO: OF PATIENTS	6	2
GRADE III	5	1
>6 MONTHS	5(100%)	1(100%)
GRADE IV	1	1
>6 MONTHS	1(100%)	1(100%)

Discussion

Brain tumor study group²⁸ showed a significant increase in the survival period for patients treated with radiotherapy and BCNU. Walker et al¹⁷ in their randomized study proved that there is significant improvement in the median survival rate with post operative radiotherapy. Kristieins et al¹⁸ also proved role of post operative radiotherapy.

Before 1982 whole brain irradiation was considered as treatment for patients with high grade astrocytomas. Several clinical observations support the use of limited volume irradiation. In the study conducted by Hochberg, Pruitt,¹⁹ it was concluded that limited volume irradiation did not influence the outcome of these patients as the recurrences occur within 1-2cm of the tumor after

limited volume irradiation and outcome is same whether treated with wholeskull irradiation or limited volume irradiation. Moreover by limiting the volume we can deliver more dose to the tumor itself and limit the radiation dose to the normal brain tissue.

Based on above studies a prospective randomized trial was designed to compare total skull irradiation vs limited volume irradiation.

In both groups male patients predominated over female patients and constituted 84.6% of the total patients. majority of the patients (80.76%) are in the age group of

30-60 years with mean age of 40.4 years. There was only one patient with age less than 20 years. The mean age group was 56 years in study by Walker et al.¹⁷

The Karnofsky's Performance Status ranging from 60-90 and almost equally distributed in Whole Skull Radiotherapy and limited volume radiotherapy groups. and survivals are comparable in both the groups.

The most common symptom was headache and vomiting in the both the groups. Sixty nine percent in whole skull Radiotherapy and 76.92% in limited volume radiotherapy presented with these symptoms. A study by Adam²⁹ and C.H.Chang et al²⁶ showed that 60.4% presented with tumors in the frontal lobe. We could not draw any correlation regarding seizures as presenting symptom and the prognosis which carries better prognosis as shown in the study by Leibel et al.²⁷

The common site of the tumor in these patients was frontal region with 42.31% in this study and 35.30% in the study by C.H.Chang et al²⁶ and 45% in study by Adam et al.²⁹

Patients with whole skull radiotherapy had more acute reactions than limited volume radiotherapy group. Sixty nine percent of patients in whole skull Radiotherapy developed grade II reactions while 46.15% in limited volume radiotherapy developed no reactions. only 30.77% of patients developed grade II reactions in limited volume radiotherapy group. These results are comparable to results in the study by Cantane et al.³⁰ It is observed that patients with temporal lobe lesions and who were randomized to local skull Radiotherapy group developed

middle ear reactions when compared to tumors at other sites.

Haematological reactions are comparable in both the groups and none of the patients developed grade II reactions.

Somnolence syndrome was observed in 79.93% of patients who received whole skull Radiotherapy when compared to 53.85% of patients who received localized skull Radiotherapy.

Fifty four percent of patients with whole skull Radiotherapy developed grade II late reactions when compared to 7.69% of patients in local skull Radiotherapy.

The survival patterns with relation to site and grade were studied. It varied with grade of the tumor. The tumor in the frontal region which were histologically grade III had better survival than grade IV tumors in both groups. Cent percent of patients having grade III tumors survived for >6 months while patients with grade IV tumors, there was fifty percent survival in whole skull radiotherapy group and forty percent in limited volume radiotherapy. Though there is subtle difference in survival in both groups with grade IV tumors, there was correlation in survival in both groups on the whole. Similar results were seen in tumors located in sites other than frontal region.

The grade of the tumor was limiting factor when the survival was studied in relation to age. there were almost equal number of patients in 20-40 years and 40-60 years. The survival for >6 months was 66.66% in patients with age between 20-40 years while the survival in the age group 40-60 years was 50%. The survival was less than 6 months in patients with age more than 60 years.

The study by Adams showed that lesser the tumor size better the survival. There was a definite relationship between survival and size of the tumor, the survival being better with tumors of smaller size. Cent percent of the patients having tumor size <4x4 cm² survived for > 6 months. There was a difference of survival in limited volume irradiation and whole skull irradiation with the tumor size ranging from > 4x4cm² -<6x6cm² which was more significant with grade IV gliomas the results being better

with whole skull radiotherapy in tumors with this grade. The overall survival for more than six months in tumors with this size was 62%. Only 25% of the patients with tumor size > 6x6cm² months survived for >6 months.

The relation of survival with surgery was evident, when more extensive surgery was done to clear the tumor, the survival was better. The survival patterns in patients receiving whole skull irradiation and limited volume irradiation postoperatively were comparable with similar results. A study by Leibel et al²⁷ showed that survival was better with more tumor clearance and radiotherapy than with biopsy and radiotherapy. In our study 10% of the patients treated with biopsy and radiotherapy survived for more than six months. The survival for the same period in patients who underwent partial resection and near total resection were 62.5% and 100% respectively.

A study by Mario Ammirati et al³¹ in patients with malignant astrocytomas showed a significant improvement in survival as well as functional status when more tumor clearance surgery was done. In this study 61 % of patients who underwent gross total resection survived for more than nine months while 39% of patients who underwent subtotal resection survived for only six months.

But a study by Adam et al²⁹ showed no correlation between the extent of surgery and survival.

Patients presented with progression of symptoms during follow-up period and recurrence of tumor was confirmed by CT scan. These patients were advised repeat surgery but refused due to financial constraints. Two of these patients received whole skull irradiation and the other two received limited volume irradiation. All of the recurrences were within the field of irradiation. These patterns of failure are compared with study by Adam et al.²⁹

The difference in the survival in the study Adam S.G. et al when compared to our study is due to re-excision of tumor after detection which was lacking in our study as the patients refused the same due to financial constraints.

Conclusion

Mean age for high grade astrocytomas is 40.4 years, predominantly seen in males. commonest blood group was A and headache and vomiting are most commonest presenting symptoms. Better prognosis was seen in grade three gliomas and small sized tumors. Patients who underwent near total excision had better prognosis. There was statistically significant difference in patients receiving whole skull radiation and LVBRT. In modern era, Limited Volume brain irradiation for high grade gliomas is the standard treatment in the form of three Dimensional Conformal Therapy (3D-CRT) or Intensity Modulated Radiotherapy (IMRT), where ever the facilities were available.

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References

1. Dastur, D. K., Lalitha, V. S. : Pathological analysis of intracranial space occupying lesion in 100 cases. J. Neuro. Sci. 6:575, 1968.
 2. Chakrabarthy D., Sankar S.K., Bagchi A.K. A study of incidence of neoplasm in Central Nervous System, Neurology India, 21:1, 32-36, 1973.
 3. Fulling, K. H., Nelson J. S. Cerebral astrocytic neoplasms in adults: Contribution of histologic examination to the assessment of prognosis. Semin Diagn Pathol 1: 152-163, 1984.
 4. Svien, H. J., Mabon. R. F., Kernohan, J. W., et al : Astrocytomas. Proc Staff Meet Mayo Clin 24 : 54-64, 1949.
- Kernohan, J. W., Mabon, R. F., Svien, H. J., et al A simplified classification of gliomas. Proc Staff Meet Mayo Clin 24: 71-75, 1949.

5. Nelson J.S., Tsukada, Y. Schoenfeld D. et al Necrosis as a prognostic criteria in the malignant supra tentorial, astrocytic gliomas. *Cancer* 52:550-554, 1983.
6. Chamberlain M.C., Murovic J.A Levin V.A Absence of contrast enhancement on CT brain scans of patients with supratentorial malignant gliomas. *Neurology* 38:1371-1374, 1988.
7. Kelly, P. J., Daumas-Duport, C. Kispert, D. D. et al Imaged based stereotactic serial biopsies in untreated intracranial glial neoplasms. *J. Neurosurg* 66:865-874, 1987.
8. Kelly P. J., Daumas – Duport C. Scheitauer b.w. et al Stereotactic histologic correlations of CT and MRI – defined abnormalities in patients with glial neoplasms. *Mayo Clin Proc* 62: 450-459, 1987.
9. Chandrasoma PT, Smith MM, Apuzzo MLJ: Stereotactic biopsy in the diagnosis of brain masses: Comparison of the results of biopsy and resected surgical specimen. *Neurosurgery* 24: 160-165, 1989.
10. Greene GM, Hitchon PW, Schelper RL, et al : Diagnostic yield in CT – guided stereotactic biopsy of gliomas. *J Neurosurg* 71: 494-497, 1989.
11. Ciric I, Ammirati M, Vick N, et al: Supratentorial gliomas: Surgical consideration of immediate post operative results. Gross total resection versus partial resection. *Neurosurgery* 21:21-26, 1987.
12. Pool JL: The management of recurrent gliomas : *Clin Neurosurg* 15 : 265-280, 1968.
13. Ray BS : Surgery for recurrent intracranial tumors. *Cli. Neurosurgery* 10 : 1-30, 1964.
14. Ray BS : Surgery for recurrent intracranial tumors. *Cli. Neurosurgery* 10 : 1-30, 1964.
15. Shapiro, W. R., Green S. B., Burger P.C. et al : Randomised trial of three chemotherapy regimens and two radiotherapy regimens in postoperative treatment of malignant gliomas. *J. Neurosurg* 71: 1-9, 1989.
16. Walker M. D., Green S.B. Byar D. P. et al : Randomised comparisons of Radiotherapy and nitrosureas for treatment of malignant gliomas after surgery. *N. Eng. J. of Med* 303 : 1323-1329, 1980.
17. Kristiansen K, Hagen S, Kollevold T, et al: Combined modality therapy for operated astrocytomas grade 3 & 4. Confirmation of value of post operative radiation and lack of potentiation of bleomycin on survival time. A prospective multicentre trial of Scandinavian Glioblastoma Study Group. *Cancer* 47: 649-652. 1981.
18. Hochberg, F. H. and Pruitt, A. A. Assumption in Radiotherapy of gliomas. *Neurology* 30: 907-911, 1980.
19. Urtasun, R., Feldstein, M. L., Partington, J., Tansichuk. H et al . Radiation and nitroimidazoles in supratentorial high grade gliomas : A second clinical trial. *Br. J. Cancer* 46 : 101-108, 1982.
20. Massey, V. and Wallner, K.E. Patterns of second recurrence of malignant astrocytomas. *Int. J. Radiat. Oncol. Biol. Phy.* 19:395-398, 1990.
21. Choucair, A. K., Levin, V. A., Gutin, P. H. et al. Development of multiple lesions during radiation therapy and chemotherapy in patients with gliomas. *J. Neurosurg.* 65:654-658, 1986.
22. Ruth G. Ramsey, and William N. Brand. Radiotherapy of glioblastoma multiforme. *J. Neurosurg.* 39: 197-202, 1973.
23. Gaspar LE, Fisher BJ, MacDonald DR et al : Supratentorial malignant treatment. *Int J Rad Oncol Biol Phy* 24: 55-57, 1992.
24. Nelson DF, Curran WJ Jr Scott C et al: Hyperfractionated radiotherapy and bis-chloro ethyl nitrosurias in the treatment of malignant gliomas-possible advantage observed at 72Gy on 1.2Gy b. i. d.

- fractionations: Report of the Radiation Therapy Oncology Group nprotocol 8302. In J Radiat. Oncol. Biol. Phys. 25: 193-207, 1993.
25. Chang CH, Horton J, Schoenfeld D, et al: Comparison of post operative radiotherapy in multidisciplinary management of malignant gliomas. A joint RTOG and ECOG group study. Cancer:52:997-1007, 1983.
26. Leibel S. A. Teletherapy methods and expectations, in Apuzzo MLJ (ed): Malignant cerebral gliomas. Park Ridge, IL. American Association of Neurological Surgeons, 1990. Pp 159-171.
27. Wallner K. E. Galicich J. H, Krol G, et al : Patterns of failure following treatment of glioblastoma multiforme and anaplastic astrocytoma. Int. J. Radiat. Oncol. Biol. Phys. 16: 1405-1409, 1989.
28. Adam S. Garden, Moshe H. Maor, W. K. Alfred Yung et al. Outcome of Patterns of failure following limited volume irradiation for malignant astrocytomas. Radiotherapy and Oncology, 20:99-110, 1991.
29. Catane R., Schwade, J.G., Yaarr, et al: Follow up neurological evaluation in patients with small cell lung carcinoma treated with: prophylactic irradiation and chemotherapy. Int. J. Radiat. Oncol. Biol. Phys. 7:105-109, 1981.
30. Mario Ammirati, Nicholas Vick, Youlian Liao, et al: Effect of the extent of surgical resection on survival and quality of life in patients with supratentorial glioblastomas and anaplastic astrocytomas. Neurosurg, 21: 201-206, 1987.