# Evaluation of Different Radiotherapy Schedules In Brain Metastases

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**Abstract: Purpose:** We evaluated different fractionation schedules of radiotherapy in brain metastases ; Comparing 20 Gy/5 fractions, 12 Gy/2 fractions and 10 Gy in a single fraction with a dose of 30 Gy/10 fractions whole cranial irradiation (WCI), as regard subjective response and treatment morbidities with quality of life (QOL) assessment**. Patients and methods:** 200 patients with brain metastases (93 males& 107 females, median age 50 years, range 30-76 years), Karnofsky performance score (KPS) of ≤ 70, were assigned to 4 arms each arm included 50 patients; (group **A**) who have received 30 Gy/10 fractions; (23 males& 27 females, median age 47 years), (group **B**) who have received 20 Gy/5 fractions; (20 males& 30 females, median age 49 years), (group **C** ) who have received 12 Gy/2 fractions; (26 males & 24 females, median age 54 years), (group **D**) who have received 10 Gy in single fraction; (23 males& 27 females, median age 51 years). **Results:** All patients were evaluated weekly during treatment and monthly thereafter, for subjective response, survival, related toxicity and QOL assessment; whereas 18 patients (36%) in group A, 17 (34%) in group B, 15 (30%) in group C and 13 patients (26%) who complained from moderate to extremely severe symptoms before treatment had changed to mild or no symptoms after treatment, without statistical significance between groups, The overall survival was significantly affected by 4 factors; age, KPS, primary tumor control and presence of extracranial metastases (Log rank *P*- value < 0.001) but without significant difference between groups. Overall toxicity was acceptable in all groups. About 50% of patients had maintained their good QOL after treatment and 10 - 20% of patients with bad QOL changed to good QOL after treatment, (*P*- value >0.05). **Conclusion**: Different schedules of short course WCI were quite similar to long course WCI regarding subjective response, survival, toxicity and effect on quality of life for patients with brain metastases.
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**Key words:** Brain metastases; Radiotherapy; Hypofractionation; Quality of Life.

## 1. Introduction

**B**rain metastases occur much more frequently than primary brain tumors in adults as represented about 10% to 30% of all adult cancer during the course of their disease, WCI is the most frequently treatment option for patients with brain metastases, the optimal dose fractionation that used as a palliation is still controversial [1]**.** The median survival of untreated patients with multiple lesions is approximately one month [2]. Brain metastases has direct effect on quality of life as regard neurocognitive functions as the patients may suffer from motor, sensory affection, headache, aphasia and seizures [3]**.**

A variety of total doses and dose per fraction have been used without prove that any schedule has better outcome in terms of subjective response and quality of life improvement, meanwhile the schedule of 30 Gy in ten fractions represent the most frequent used pattern.[4]**.** Dose escalation beyond 30 Gy doesn't increase the survival or local control but may increase the neurotoxicity [1]**.**The most common primary sites that give brain metastases are small cell lung cancer (29.7%), breast cancer (20%), non-small cell lung cancer (12.6%), melanoma (10%) especially head and neck type [5] then colorectal carcinoma and sarcoma, meanwhile the unknown primary still account for more than quarter of the cases [6]**.**

The radiobiological aspect of different hypofractionation schedules mainly depends on the theory of use of large fraction size in late responding tissue that characterized by low α/β ratio had greater capacity for sublethal damage repair and relatively steeper decline in the survival rate of target cells, so larger doses per fraction are more harmful for late responding tissue and this theory was confirmed by linear quadratic response model and isoeffect curve especially for doses ranged 2-8 Gy per fraction, the only disadvantage was increase the late sequelae in relation to early sequelae but in patients with brain metastases who had short life expectancy ( 3 - 6 months), the late radiation complications may be of no importance in this situation due to short survival [1].

QOL assessment was considered standard component to understand the patient experience of the impact of disease and therapy, the FACT scale covered the physical, social, emotional and functional wellbeing; that easily completed in 5 minutes in form of multi-item questionnaire [7]**.**

## 2. Patients and Methods

**Eligibility:**

We entered 200 patients with brain metastases who met the following eligible criteria: informed consent; histologically or cytologically proven original malignancy, brain metastases; (single or multiple) confirmed by CT or MRI, excluding patients received prior brain irradiation; Karnofsky performance score (KPS) of 70 or less. Adequate bone marrow (absolute neutrophil count 1,500/µL, platelets 100,000/µL, and hemoglobin 10 g/dL at least), renal function (serum creatinine 2 mg/dL), and hepatic function (bilirubin less than 1.5 mg/dL and AST/ALT less than twice the upper limit of normal, life expectancy more than one month.

**Patient assessment:**

All patients had pretreatment evaluation including complete medical history and detailed neurological and physical examination, assessment of Karnofsky performance status (KPS), complete blood count (CBC), liver functions test (LFT) and kidney function test (KFT). Radiological studies were routinely done including chest roentgenography, brain CT or MRI, pelvi-abdominal ultrasonography, and QOL assessment using FACT scale [7].

**Treatment Schedule:**

All patients were allocated into four groups; ***Group A:*** Included 50patients who received 30 Gy over two weeks (3Gy per fraction), five days per week; ***Group B:*** Included 50patients who received 20 Gy over five days (4Gy per fraction); ***Group C:*** Included 50patients who received 12Gy over two consecutive days (6Gy per fraction); ***Group D:*** Included 50patients who received 10 Gy over one day per one fraction.

**Radiotherapy plan:**

Patient was simulated, lying supine, fixation was done using a thermoplastic mask and a headrest was applied for each patient to be comfortable and reducible. Whole-brain irradiation was administered through parallel opposed lateral portals with the total dose calculated at midplane. The inferior field border was placed inferior to the cribriform plate, the middle cranial fossa, and the foramen magnum, all of which should be distinguishable on simulation or portal localization radiographs. The anterior border of the field was about 3 cm posterior to the ipsilateral eyelid for diverging beam to exclude the contralateral lens. This supplies the posterior ocular bulbs about 40% of the prescribed dose. To correct this, the beam was angled 5 degrees to 7 degrees against the frontal plane so that the anterior beam border traverses the head in a frontal plane about 0.5 cm posterior to the lenses (about 2 cm posterior to eyelid markers). This arrangement provides a full dose to posterior parts of ocular bulbs. The radiation course was implemented using Cobalt 60 machine. Corticosteroids such as dexamethasone in dose of 16-32 mg daily intravenous and anticonvulsant medication were given to all patients during radiotherapy according to severity of symptoms.

**Response and toxicity criteria**

Patients were evaluated weekly during treatment and monthly after treatment for treatment subjective response, treatment morbidities and QOL assessment.

**Treatment Subjective response:**

Was scaled according to Union International Contra le Cancer (UICC) into: *Grade 0:* No symptoms; *Grade 1:* Mild; *Grade 2:* Moderate; *Grade 3:* Severe; *Grade 4:* Extremely severe life-threatening.

Neurological status improvement was assessed on neurological examination of the intellectual function. Clinical assessment of neurological symptoms, performance status and response evaluation were carried out monthly after the end of radiotherapy until death. Subjective response was defined as improvement in at least one neurological symptom without deterioration of any other neurological symptoms or signs, or development of new neurological deficit. This response had to last for a minimum of 4 weeks.

**Treatment morbidities:**

Was evaluated according to RTOG; ***Russell et al.*** [8]. The morbidity associated with radiotherapy was documented with assessment of any side effects thought to be attributable for irradiation 4 weeks after completion of treatment.

**Assessment of quality of life (QOL):**

Was evaluated according to FACT scale (Functional assessment of cancer therapy scale); ***Cella et al.*** [7].

**Statistical methods**

SPSS package (version 13) was used for data analysis. Mean and standard deviation were estimates of quantitative data and median for non-normally distributed data.

## 3. Results

**Patient characteristics:**

This study included 200 patients with brain metastases presented to Clinical Oncology department, Zagazig University between November 2009 and February 2011. 72% of patients in groups A & B and 52% in groups C&D were aged >50 years with range (30-76 years), 106 patients were females representing 53% of all patients, with female to male ratio of 1.1:1, the most common primary site was lung in 37% of all patients followed by breast in 34%, then colon in 10%, 8% for melanoma, 4.5% for hepatocellular carcinoma, 4% for urinary bladder and 2.5% for unknown primary. Symptoms of increased intracranial pressure were the most common presenting symptoms in about

70-90% in all patients especially headache, while motor weakness was presented in 31% in all patients, epileptic fits was in about 23 %.( Table1).

**Treatment response:**

As regard subjective response; before treatment, patients with grades 3&4 (severe and extremely severe symptoms) were representing 38% in group A, 32% in group B, 36% in group C and 40% in group D; while after treatment these percentages were changed to 12% in groups A and B, 16% in group C and 30% in group D. Sixteen percent of Patients in groups A&B had no symptoms after treatment and also 14%, 8% in groups C&D (Table 2). As regard performance status; there were much improvement in all patients, as Sixteen percent of Patients in groups A&B had KPS more than 70% after treatment and also 14%, 8% in groups C&D, for whose KPS of 50-60, the percentage of patients changed in all groups as follow; from 40% to 20% in group A, from 40% to 22% in group B ,from 38% to 22% in group C and from 38% to 28% in group D, but no improvement in patients with KPS of less than 50, with no statistically significant difference between groups (*P*-value=0.9). (Table3).

**Survival:**

After 6 months of follow up, there were only four alive patients (8%) in group A and two in groups B&C while none of group D. Median survival time in days was 90±55, 60±47, 60±52 and 60±53 in groups A&B&C and D respectively, patients lived more than 60 days were representing 60%, 52%, 46% and 40% in groups A&B&C and D respectively, but with no statistically significant difference (*P*= 0.7).(Table4).

**Treatment related toxicity:**

Alopecia, scalp redness, headache, nausea and vomiting were the common treatment related toxicity, but all were tolerated and accepted; Grade 3 alopecia was recorded in 14 patients in group D versus 7 in groups A&B and 9 in group C with no statistically significant difference (*P*=0.2). Deterioration of consciousness and development of coma were observed in six patients in group D (12%) and three in group C (6%), two in group B (4%) and only one patient (2%) in group A. (Table 5).

**Prognostic factors:**

Age more than 60 years, presence of extra-cranial metastases, KPS less than 60 and loss of control of primary tumor had significant negative independent prognostic factor on overall survival, but with no statistically significant difference between groups (*P*= >0.05).(Table 6).

**Quality of Life Assessment:**

QOL of 10 patients (20%) in group A, nine (18%) in group B, eight (16%) in group C and another five (10%) in group D was changed from bad before treatment to good QOL after treatment, about 50% of patients in all groups maintained their good QOL after treatment, 32%, 30%, 34% and 44% of patients in groups A, B, C and D respectively still had bad QOL after treatment. These changes were statistically insignificant between studied groups. (Table7).

**Table 1: Patient characteristics**

| Characteristics | Group A 30 Gy in 10 F(s). N=50 | | Group B 20 Gy in 5 F(s). N=50 | | Group C 12 Gy in 2 F(s). N=50 | | Group D 10 Gy in single F. N=50 | | *P*- value |
|---|---|---|---|---|---|---|---|---|---|
| | No | % | No | % | No | % | No | % | |
| **Age** | | | | | | | | | |
| **≤50 years** | 14 | 28 | 14 | 28 | 24 | 48 | 24 | 48 | |
| **51->60 years** | 36 | 72 | 36 | 72 | 26 | 52 | 26 | 52 | 0.8 |
| **Age range in years** | 30 - 70 | | 30 - 73 | | 30 – 70 | | 30 - 76 | | |
| **Sex** | | | | | | | | | |
| **Male** | 24 | 48 | 20 | 40 | 26 | 52 | 24 | 48 | 0.9 |
| **Female** | 26 | 52 | 30 | 60 | 24 | 48 | 26 | 52 | |
| **Clinical presentation** | | | | | | | | | |
| **Increased ICP** | | | | | | | | | |
| **Headache** | 47 | 94 | 44 | 88 | 40 | 80 | 44 | 88 | |
| **Vomiting** | 30 | 60 | 34 | 68 | 36 | 72 | 40 | 80 | 0.9 |
| **Blurring vision** | 34 | 68 | 36 | 72 | 36 | 72 | 34 | 68 | |
| **Motor weakness** | 20 | 40 | 11 | 22 | 17 | 34 | 14 | 28 | |
| **seizure** | 14 | 28 | 8 | 16 | 10 | 20 | 14 | 28 | |
| **Primary tumor site** | | | | | | | | | |
| **Lung** | 20 | 40 | 22 | 44 | 17 | 34 | 15 | 30 | |
| **Breast** | 17 | 34 | 16 | 32 | 20 | 40 | 15 | 30 | |
| **Colon** | 5 | 10 | 6 | 12 | 4 | 8 | 5 | 10 | |
| **Melanoma** | 4 | 8 | 4 | 8 | 3 | 6 | 5 | 10 | |
| **Other sites:** | 4 | 12 | 2 | 6 | 6 | 14 | 10 | 20 | 0.68 |
| **HCC** | 2 | 4 | 1 | 2 | 2 | 4 | 4 | 8 | |
| **Urinary bladder** | 1 | 2 | 1 | 2 | 2 | 4 | 4 | 8 | |
| **Unknown primary** | 1 | 2 | 0 | 0 | 2 | 4 | 2 | 4 | |
| **Abbreviations** | F(s): fraction(s); Gy: Gray; HCC: hepatocellular carcinoma | | | | | | | | |

**Table 2: Subjective response after treatment**

| | Group A | | | | Group B | | | | Group C | | | | Group D | | | | *P*- value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Before | | After | | Before | | After | | Before | | After | | Before | | After | | |
| | No | % | No | % | No | % | No | % | No | % | No | % | No | % | No | % | |
| No symptoms | 0 | 0 | 8 | 16 | 0 | 0 | 8 | 16 | 0 | 0 | 7 | 14 | 0 | 0 | 4 | 8 | 0.18 |
| Mild | 11 | 22 | 21 | 42 | 12 | 24 | 21 | 42 | 11 | 22 | 19 | 38 | 8 | 16 | 17 | 34 | |
| Moderate | 20 | 40 | 15 | 30 | 22 | 44 | 15 | 30 | 21 | 42 | 16 | 32 | 22 | 44 | 14 | 28 | |
| Severe | 13 | 26 | 4 | 8 | 12 | 24 | 4 | 8 | 12 | 24 | 5 | 10 | 13 | 26 | 8 | 16 | |
| Extremely severe | 6 | 12 | 2 | 4 | 4 | 8 | 2 | 4 | 6 | 12 | 3 | 6 | 7 | 14 | 7 | 14 | |

**Table 3: Performance status before and after treatment**

| | Group A | | | | Group B | | | | Group C | | | | Group D | | | | P- value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Before | | After | | Before | | After | | Before | | After | | Before | | After | | |
| | No | % | No | % | No | % | No | % | No | % | No | % | No | % | No | % | |
| KPS > 70 | 0 | 0 | 8 | 16 | 0 | 0 | 8 | 16 | 0 | 0 | 7 | 14 | 0 | 0 | 4 | 8 | 0.9 |
| KPS 60-70 | 24 | 48 | 26 | 52 | 26 | 52 | 27 | 54 | 25 | 50 | 26 | 52 | 23 | 46 | 24 | 48 | |
| KPS 50-60 | 20 | 40 | 10 | 20 | 20 | 40 | 11 | 22 | 19 | 38 | 11 | 22 | 19 | 38 | 14 | 28 | |
| KPS < 50 | 6 | 12 | 6 | 12 | 4 | 8 | 4 | 8 | 6 | 12 | 6 | 12 | 8 | 16 | 8 | 16 | |

**Table 4: Survival time in days**

| | Group A | Group B | Group C | Group D | P- value |
|---|---|---|---|---|---|
| MST± SD | 90 ± 55 | 60 ± 47 | 60 ± 52 | 60 ± 53 | 0.7 |
| Survival time range in days | 17 - 180 | 25 - 180 | 16– 180 | 14 - 150 | |
| Abbreviation; MST: Median survival time; SD: standard deviation | | | | | |

**Table (5) Treatment toxicity**

| Toxicity | Group A | | Group B | | Group C | | Group D | | *P*-value |
|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | |
| Alopecia | | | | | | | | | 0.2 |
| Grade 1 | 23 | 46 | 27 | 54 | 7 | 14 | 7 | 14 | |
| Grade 2 | 7 | 14 | 7 | 14 | 30 | 60 | 14 | 28 | |
| Grade 3 | 7 | 14 | 7 | 14 | 9 | 18 | 14 | 28 | |
| Scalp redness | 17 | 34 | 24 | 48 | 7 | 14 | 14 | 28 | |
| Scalp soreness | 7 | 14 | 0 | 0 | 7 | 14 | 4 | 8 | |
| Headaches | 34 | 68 | 20 | 40 | 26 | 52 | 37 | 74 | |
| Nausea and vomiting | 30 | 60 | 30 | 60 | 26 | 52 | 37 | 74 | |
| Fits | 7 | 14 | 10 | 20 | 10 | 20 | 10 | 20 | |
| Coma | 1 | 2 | 2 | 4 | 3 | 6 | 6 | 12 | |

**Table (6) Prognostic factors**

| Prognostic factors | Patients number & median survival time (MST) in days | | | | | | | | Log-rank *P*- value |
|---|---|---|---|---|---|---|---|---|---|
| | Group A | | Group B | | Group C | | Group D | | |
| | N0. | MST | N0. | MST | N0. | MST | N0. | MST | |
| Age in years | | | | | | | | | <0.001 |
| ≤ 60 | 34 | 85 | 30 | 60 | 40 | 60 | 44 | 60 | |
| > 60 | 16 | 90 | 20 | 50 | 10 | 45 | 6 | 40 | |
| Extra-cranial metastases | | | | | | | | | <0.001 |
| Yes | 17 | 77 | 14 | 50 | 30 | 60 | 20 | 35 | |
| No | 33 | 90 | 36 | 60 | 20 | 40 | 30 | 60 | |
| KPS | | | | | | | | | <0.001 |
| 60-70 | 30 | 90 | 34 | 60 | 37 | 60 | 34 | 60 | |
| 50-60 | 14 | 40 | 14 | 35 | 7 | 30 | 10 | 27 | |
| < 50 | 6 | 20 | 2 | 30 | 6 | 16 | 6 | 14 | |
| Primary tumor control | | | | | | | | | |
| Yes | 34 | 90 | 30 | 60 | 27 | 60 | 25 | 60 | |
| No | 16 | 25 | 20 | 20 | 23 | 30 | 25 | 40 | <0.001 |

**Table (7) Quality of Life Assessment before and after treatment**

| | | Group A | | Group B | | Group C | | Group D | |
|---|---|---|---|---|---|---|---|---|---|
| | | After Treatment | | | | | | | |
| | | Good | Bad | Good | Bad | Good | Bad | Good | Bad |
| Before treatment | Good | 24 | 0 | 26 | 0 | 25 | 0 | 23 | 0 |
| | Bad | 10 | 16 | 9 | 15 | 8 | 17 | 5 | 22 |
| P- Value | | 0.372 | | 0.429 | | 0.531 | | 0.893 | |

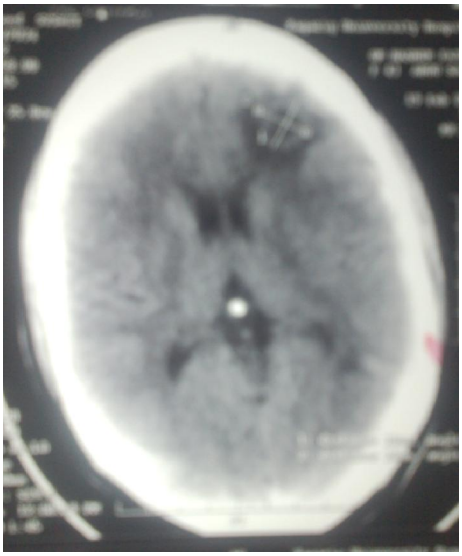

**Figure 1: Axial CT brain of male patient 55 years old smoker with metastatic cancer lung before receiving 12GY in two fractions**

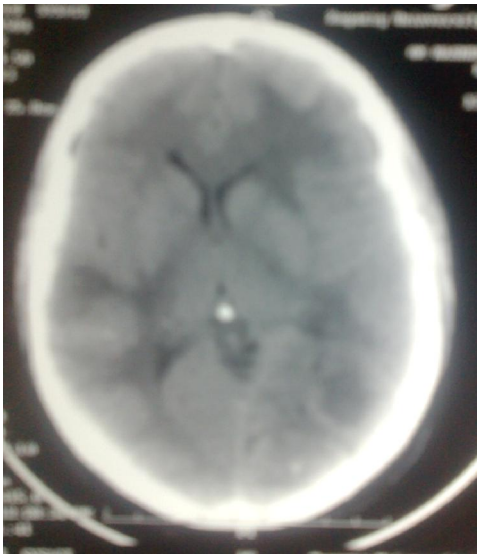

**Figure 2: Axial CT brain of the same patient 4 months after end of treatment**

## 4. Discussion

Brain metastases are the most common form of intracranial cancer. The majority of patients with brain metastases receive whole cranial irradiation (WCI), but the optimal dose-fractionation schedule remains controversial [1]. Most patients with brain metastases had very poor survival. The median survival of untreated patients with multiple lesions is about 1 month, even with treatment, median life expectancy of only 90-150 days [2]. As the biological effectiveness of irradiation depends on the dose per fraction, the biological effectiveness of radiation schedules of short course WCI with 4 Gy × 5 was similar to long course WCI programs with 3 Gy × 10 and 2 Gy × 20, so WCI over a short time is preferable to longer programs, as it is more convenient for these often debilitated patients [1]. Furthermore longer palliative radiation programs increase the cost of therapy [9]. Short course WCI can be recommended only if it provides similar survival to longer programs. In an attempt to find out the appropriate fractionation schedules of WCI. We carried out this study which included 200 patients with brain metastases presented to clinical oncology department from November 2009 to February 2011.

In our study the median age is 47 years and the range is between 30-70 in group A while the median age is 49 years and the range is between 30-73 years in group B & median age is 54 years and the range is between 30-70 years in group C and the median age is 51 years and the range is between 30-76years in group D. This differs from study reported by ***Rades et al.*** [1] which included 404 patients with NSCLC and compared 4Gy × 5 vs. 3Gy × 10 fractions where male percentage was higher, nearly 61% for both groups; this difference may be due to presence of different primaries in our study rather than lung cancer.

Our results were supported by study conducted by ***Chatani et al.*** [10]***;*** where whole brain dose fractionation radiotherapy schedules were investigated in seven trials as regard subjective response assessment. None of the seven trials detected a difference in symptom control with altered dose fractionation schedules compared to conventionally fractionated schedules (30Gy in10 fractions).

In our study, toxicity of WCI was tolerable and greatly similar between all fractionation groups, grade 3 alopecia was observed in 14 patients in group D, 7 patients in groups A & B and 9 patients in group C, with no statistically significant difference between groups and didn't interfere with daily life functioning

and this was confirmed by ***Pottgen and Stuschke***[12]. Scalp redness was frequent ; 24 patients (48%) in group B& 17patients (34%) in group A& 14 patients (28%) in group D and 7 patients (14%) in group C, which is nearly similar to the findings of ***Pottgen and Stuschke*** [11] **and** ***Russell et al.*** [8].

Our results were supported by the report of ***Sneed et al.*** [12] who found that acute sequelae of WCI include mild fatigue, epilation, and mild to moderate skin erythema and hyperpigmentation, early delayed radiation reactions may develop 3 to 10 weeks after treatment and can result in the somnolence syndrome (somnolence, anorexia, and irritability) or transient neurologic deterioration that resolves within 6 weeks .Radiation-induced progressive mental disturbances and neurologic abnormalities including dementia, ataxia, and death in the absence of tumor recurrence These late side effects, however, are seldom noted because most patients with brain metastases have a short life expectancy as a result of progressing systemic disease and this is correlated with our study. So in our study most treatment toxicity shows no statistical significant difference between all groups. Long term toxicity remains poorly defined because of short survival time.

Treatment groups were well balanced with respect to potential prognostic factors, improved 6 months survival in all groups was associated with age < 60 years, KPS ≤ 70, primary tumor control and lack of extra-cranial metastases. This is very similar to that obtained by ***Rades et al.*** [1]**,** who found the same result. There is a Meta-analysis that summarized data from published 9 trials that compared 30 Gy in 10 fractions to altered fractionation schedules and found no difference in survival among different WCI regimens as reported by ***Tsao et al.*** [13]**.** The data from the current study are in agreement with the findings of other studies that compared short course and long course WCI programs with regard to survival in the treatment of brain metastases. As ***Harwood and Simpson*** [14]***;*** compared 30Gy in ten fractions with single fraction of 10 Gy in a series of 101 patients and found no significant difference in median survival between both groups. In our study patients with a KPS <70, have a median survival time of 2 months this was similar to median survival time of 2,3 months in the study conducted by ***Gaspar et al.*** [15]. A variety of total doses and doses per fraction have been used in prospective randomized phase III clinical trials, primarily in patients with multiple brain metastases; These regimens include 10 Gy in 1 fraction, 12 Gy in 2 fractions, 18 Gy in 3 fractions, 20 Gy in 5 fractions, 30 Gy in 10 fractions, 40 Gy in 20 fractions, 50 Gy in 20 fractions, and 54.4 Gy in 34 fractions (160 cGy bid); None of these regimens could not prove any difference in terms of survival or efficacy for each than another and about half of patients have an improvement in their neurologic symptoms [4]**.**

In our study, after 6 months of follow up, there were only 4 alive patients (8%) in group A and 2 in groups B&C (4%), while none of group D. Although group A & B patients survive more than group C& D, this is may be attributed to number of patients with extra-cranial metastases were more in groups C & D than groups A& B. No statistically significant difference was found between groups as regard survival, which was similar to the results of three trials Compared lower dose radiation (10 Gy in a single fraction, 12 Gy in 2 fractions, or 20 Gy in 5 fractions) with a traditional dose of WCI of 30 Gy in 10 fractions. The six-month mortality out come for those trials showed no statistical significant difference in overall mortality at 6 months [14, 16]. ***Borgelt et al.*** [17] reported on the RTOG trials 6901 and 7361 that the median survival after 20 Gy in five fractions (n = 447), 30 Gy in ten fractions (n = 228), were 4.0 months and 3.7 months respectively ($p > 0.05$). In a second report, ***Borgelt et al.*** [18] observed no significant differences in median survival with 10 Gy in one fraction compared to 30 Gy in ten fractions (3.5vs.4.8 months; $p$- value> 0.05). ***Rades et al.*** [19] reported that active extra-cranial metastases, KPS and uncontrolled primary were negative independent prognostic factors that proved in our study.

**Conclusion**

Short course WCI with 20 Gy in 5 fractions &12 Gy in 2 fractions and 10 Gy as single fraction are similar to long course WCI 30 Gy in 10 fractions, regarding response rate, survival, and effect on quality of life. So short course WCI may be preferable to longer programs for palliation of brain metastases. These patients are often debilitated and would benefit by spending less time receiving therapy, moreover decreasing the cost of therapy.

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