

Dosimetric Analysis of Intensity Modulated Radiotherapy versus 3D Conformal Radiotherapy in Adult Primary Brain Tumors: Regional Cancer Centre, India

Ravi Kiran Pothamsetty, Radha Rani Ghosh, Baby Paul Thaliath

Abstract—Radiation therapy has undergone many advancements and evolved from 2D to 3D. Recently, with rapid pace of drug discoveries, cutting edge technology, and clinical trials has made innovative advancements in computer technology and treatment planning and upgraded to intensity modulated radiotherapy (IMRT) which delivers in homogenous dose to tumor and normal tissues. The present study was a hospital-based experience comparing two different conformal radiotherapy techniques for brain tumors. This analytical study design has been conducted at Regional Cancer Centre, India from January 2014 to January 2015. Ten patients have been selected after inclusion and exclusion criteria. All the patients were treated on Artiste Siemens Linac Accelerator. The tolerance level for maximum dose was 6.0 Gy for lenses and 54.0 Gy for brain stem, optic chiasm and optical nerves as per RTOG criteria. Mean and standard deviation values of PTV98%, PTV 95% and PTV 2% in IMRT were 93.16 ± 2.9 , 95.01 ± 3.4 and 103.1 ± 1.1 respectively; for 3DCRT were 91.4 ± 4.7 , 94.17 ± 2.6 and 102.7 ± 0.39 respectively. PTV max dose (%) in IMRT and 3D-CRT were 104.7 ± 0.96 and 103.9 ± 1.0 respectively. Maximum dose to the tumor can be delivered with IMRT with acceptable toxicity limits. Variables such as expertise, location of tumor, patient condition, and TPS influence the outcome of the treatment.

Keywords—IMRT, 3D CRT, Brain, tumors, OARs, RTOG.

I. INTRODUCTION

PRIMARY malignant brain tumors are uncommon and constitutes about 2% [1]-[3]. The number of incidences and mortality cases according to SEER data, 2016, estimated to be 23,770 and 16,050 respectively in the United States [1]-[3]. The clinical symptoms of brain cancer depend on the anatomy of location of tumor and most of them presents with headache, vomiting, seizures, poor orientation to person, place and time and loss of memory etc. Contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) aid in the diagnosis of brain cancers. WHO has formulated a grading system for brain tumors viz. Grade I-IV [4]. Grade III and IV brain cancers tend to behave more aggressively with

poor prognosis citing to its tumor biology, location of tumor and general condition of the patient.

Surgical intervention is the foremost step in brain cancers to debulk the tumor to relieve the mass effect and fetch the histopathology. Radiation therapy after surgery is mandated for tumor control and improving survival of the patients. Radiation therapy plays a vital role in the management of brain tumor. The aim of the treatment should be defined either as curative or palliative based on individual cases.

Radiation therapy has undergone many advancements and evolved from 2D to 3D. Three-dimensional conformal radiation therapy (3DCRT) is a sophisticated irradiation technique which delivers a high dose to the tumor with acceptable toxicity to adjacent normal tissues. This improves cure rates and decreases chances of treatment related complications. Recently, with rapid pace of drug discoveries, cutting edge technology, and clinical trials has made innovative advancements in computer technology and treatment planning and upgraded to intensity modulated radiotherapy (IMRT) which delivers in homogenous dose to tumor and normal tissues. It improves the repeated efficacy by delivering high dose to tumor and sparing normal tissue with less treatment related toxicities.

The present study was a hospital-based experience comparing two different conformal radiotherapy techniques viz. 3DCRT versus IMRT(SS) for adult primary brain tumors.

II. OBJECTIVES

The study design has set the following objectives:

1. Comparison of PTV parameters of both the plans.
2. Evaluating the dose delivered to organs at risk (OARs) of both the plans.
3. Depicting the monitor units (MU), color wash and isodose fill of both the plans.
4. Comparing Homogeneity Index (HI) of both the plans.

III. RESEARCH METHODOLOGY

A. Study Area

This analytical study design has been conducted in the Department of Radiation Oncology, Regional Cancer Centre (RCC), Kamala Nehru Memorial Hospital, Allahabad, Uttar Pradesh. The institute is recognized by Ministry of Health and Family Welfare, Department of Science and Technology, and

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Department of Atomic Energy, Government of India as research institute.

B. Study Population

The institute being Regional Cancer Centre caters to the needs of the cancer patients from the neighboring districts of Allahabad and the adjacent states of Uttar Pradesh i.e. western parts of Bihar, Northern parts of Madhya Pradesh.

C. Study Design

The present study is a retrospective cross sectional analytical study design involving adult patients of age more than 30 years with histological proven WHO grade III & IV, who has undergone gross total resection. Adjuvant treatment in the form of radiotherapy along with telozolamide (TMZ) has been delivered. The patients were treated with conformal radiotherapy (3D CRT) on LINAC. The tumor parameters and critical structures were delineated slice by slice and the plans have been compared to IMRT-SS technique to depict the therapeutic gain and emphasize its impact in treating the patients with precision radiotherapy.

D. Study Period

A total of ten patients with primary brain cancer were enrolled in the database in the period January 2014–January 2015.

E. Sample Size

Total number of patients with brain cancer reported to RCC were 71, out of which males and females accounts for 51 and 20 cases respectively. Excluding pediatric population, palliative patients, treatment delivery by Cobalt-60, other than astrocytomas histology of both the sexes, ten cases had been selected for the study design.

F. Statistical Method

The variation between the IMRT and the 3DCRT dosimetric endpoints were examined using 't' test.

G. Patient Selection Criteria

- Inclusion Criteria
 - Operable patients
 - Age > 30 years
 - Only histological proven astrocytomas grade III&IV.
 - ECOG PS 0-3.
- Exclusion Criteria
 - Inoperable patients
 - Pediatric and adolescent population
 - Other than astrocytomas histology
 - Metastatic brain tumors
 - Midline crossing tumors.

H. Data Collection

A mandatory work up of each patient included in the study was carried out prior to the commencement of treatment. It assisted in the staging the disease, evaluation of performance status and the eligibility of the patient to undergo the proposed treatment.

I. Treatment Protocol

The study design has included post-operative either optimal or suboptimal surgery patients with WHO grade III and IV in the study design. Adjuvant treatment in the form of radiotherapy along with telozolamide (TMZ) has been delivered. The study design has certain patient eligibility criteria and as per the criteria 10 patients were selected. The patients were treated with conformal radiotherapy (3D CRT) on LINAC. The plans were remade with IMRT SS technique and compared the tumor parameters for clinical utility using Prowess Pather TPS using Siemens Linac. The treatment was illustrated in Fig. 1.

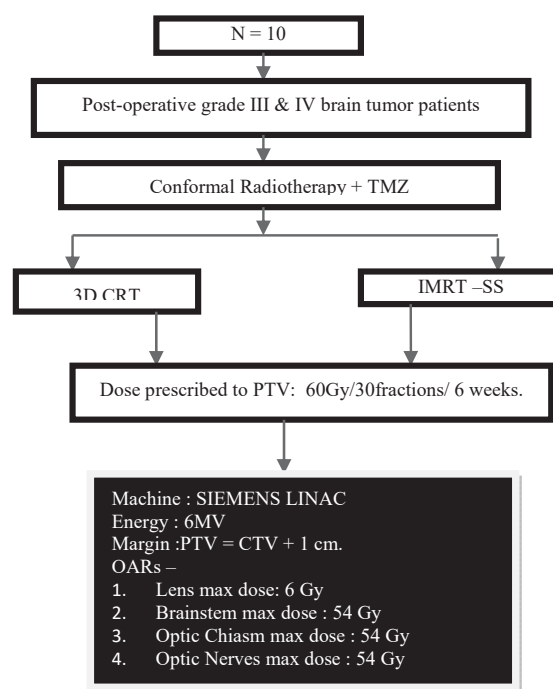


Fig. 1 Treatment Protocol

J. Treatment Procedure

All the patients were treated on Artiste Siemens Linac Accelerator. All patients underwent CT scan 3mm slice thickness and the tumor volume such as gross target volume, clinical target volume and planning target volume (GTV, CTV and PTV) had been delineated. The organ at risk (OAR) like brainstem, optic chiasm, eyes (right and left), optical nerves (right and left) and lenses (right and left) were contoured on the CT images and were transferred to treatment planning system (TPS).

Ten patients were selected with WHO grade III& IV brain tumor. Postoperative radiotherapy has been planned with IMRT and 3D CRT. 5 non-coplanar beams were created for inverse planned IMRT (IP-IMRT). The energy used was 6 MV. The dose prescription and dose constraints were followed as per institution protocol. For PTV, the parameters, D98%, D95% and D2% were used whereas for OARs, the mean and maximum dose were used for treatment plan evaluation.

IV. RESULTS

The most common age group presented with WHO grade III and grade IV was 50-59 years. as per the study. Tumor characteristics and patient profile were recorded and tabulated (as shown in Table I). Mean and standard deviation values of PTV98%, PTV 95% and PTV 2% in IMRT were 93.16 ± 2.9 , 95.01 ± 3.4 and 103.1 ± 1.1 respectively; for 3DCRT were 91.4 ± 4.7 , 94.17 ± 2.6 and 102.7 ± 0.39 respectively. PTV max dose (%) in IMRT and 3D-CRT were 104.7 ± 0.96 and 103.9 ± 1.0 respectively (as shown in Fig. 2). IMRT delivered reduced dose to optic chiasm (36.53 ± 21.70) and optic nerves (right: 23.29 ± 19.38 ; left: 21.42 ± 17.7) compared to 3D-CRT for optic chiasm (42.18 ± 22.23) and optic nerves (right: 30.85 ± 26.6 , left: 29.69 ± 26.81). But the brain stem (52.78 ± 16.92 vs 50.11 ± 15.92) and the lenses (right: 4.87 ± 1.65 vs 1.59 ± 1.77 ; left: 3.04 ± 1.86 vs 1.54 ± 1.70) were received higher dose with IMRT relative to 3D-CRT. HI of IMRT and 3DCRT were 0.084 ± 0.025 and 0.088 ± 0.035 respectively. The values were not statistically significant (as shown in Fig. 3). For 3DCRT less time consumed for treatment time compared to IMRT (p value is $0.0002 < 0.05$ for MU).

V. DISCUSSION

The patients were treated with 3DCRT and we had compared the dosimetric parameters with IMRT plan. The results depicted there is good tumor PTV coverage with IMRT technique relative to 3DCRT. The PTV coverage was acceptable if 95% of the volume were covered by 95% of the prescribed dose. PTV 98% coverage is relatively high in IMRT compared to 3DCRT. This implies maximum dose to the tumor can be delivered with IMRT technique with acceptable toxicities.

The critical structures optic nerves and optic chiasm with IMRT technique received minimal dose compared to 3DCRT. Brainstem and lenses received less dose with 3DCRT. Right lens dose received less dose with 3DCRT and showed statistical significance compared to IMRT citing the tumor location and scattered radiation by the beam lets. The HI of both the plans has depicted not quite statistically significant. For 3DCRT less time consumed for treatment time compared to IMRT (p value is $0.0002 < 0.05$ for MU).

Dose volume histograms (DVH) and color wash of both the plans were constructed using the TPS and analyzed. The DVH of IMRT plan depicted higher therapeutic ratio compared to that of 3D CRT. It indicated that maximum tumor dose can be delivered while respecting critical structures with the help of IMRT technique compared to 3D CRT (as shown in Figs. 4 and 5).

The outcome of the treatment depends on tumor location, expertise in implementing the plan, software suitable for the advanced technique and sophisticated machines. A large sample size is required to arrive at any statistical significance. Many versatile studies have thrown light on this domain and were documented regarding the significance of IMRT in brain tumors [5]-[7].

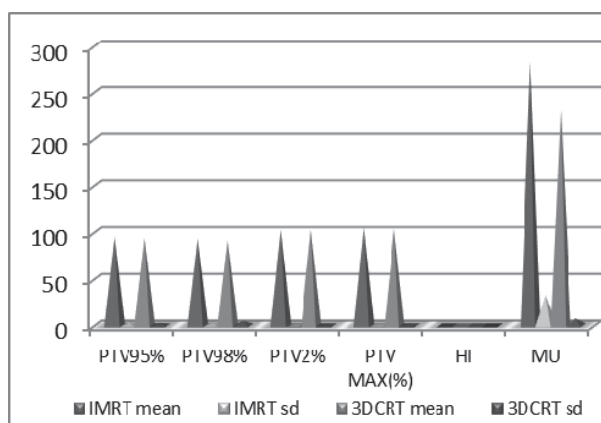


Fig. 2 IMRT vs 3D CRT PTV tumor dose parameters (n=10)

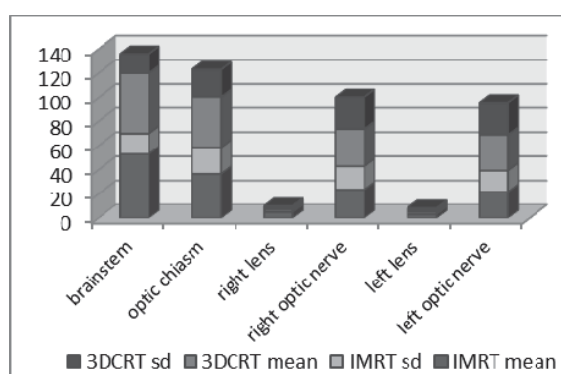


Fig. 3 OARs'. IMRT vs 3D CRT (n=10)

TABLE I
TUMOR AND PATIENT CHARACTERISTICS

S. No.	Determinants	%[N=10]
1	Age	
	30-39	20
	40-49	30
	50-59	40
2	Sex	
	60-69	10
	Male	60
	Female	40
3	Location of tumor	
	Left Temporo – Parietal Lobe	40
	Right Temporal Lobe	20
	Right Temporo- Parietal Lobe	20
	Left Frontol Lobe	10
4	Histopathology	
	Right Parietal Lobe	10
	GBM	70
	Anaplastic Astrocytoma	30
5	ECOG Scale	
	0	0
	1	20
	2	70
	3	10

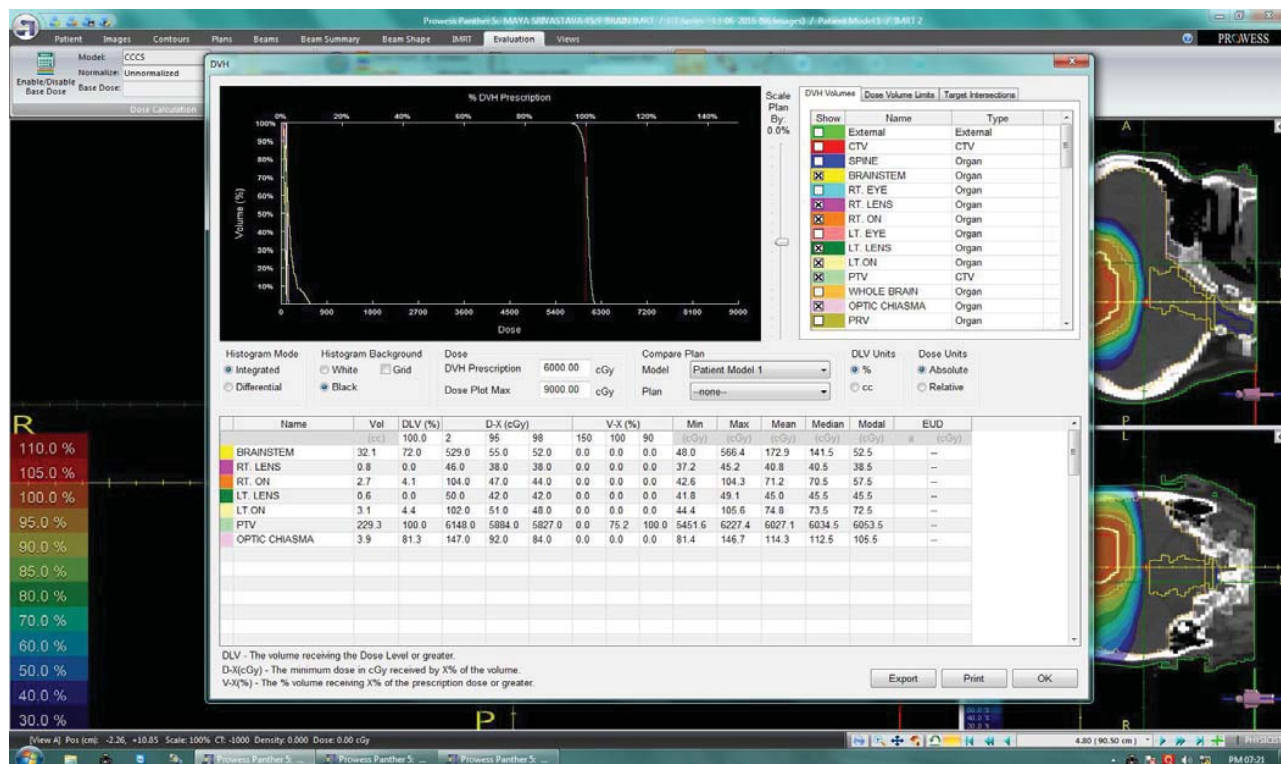


Fig. 4 (a) DVH of IMRT plan

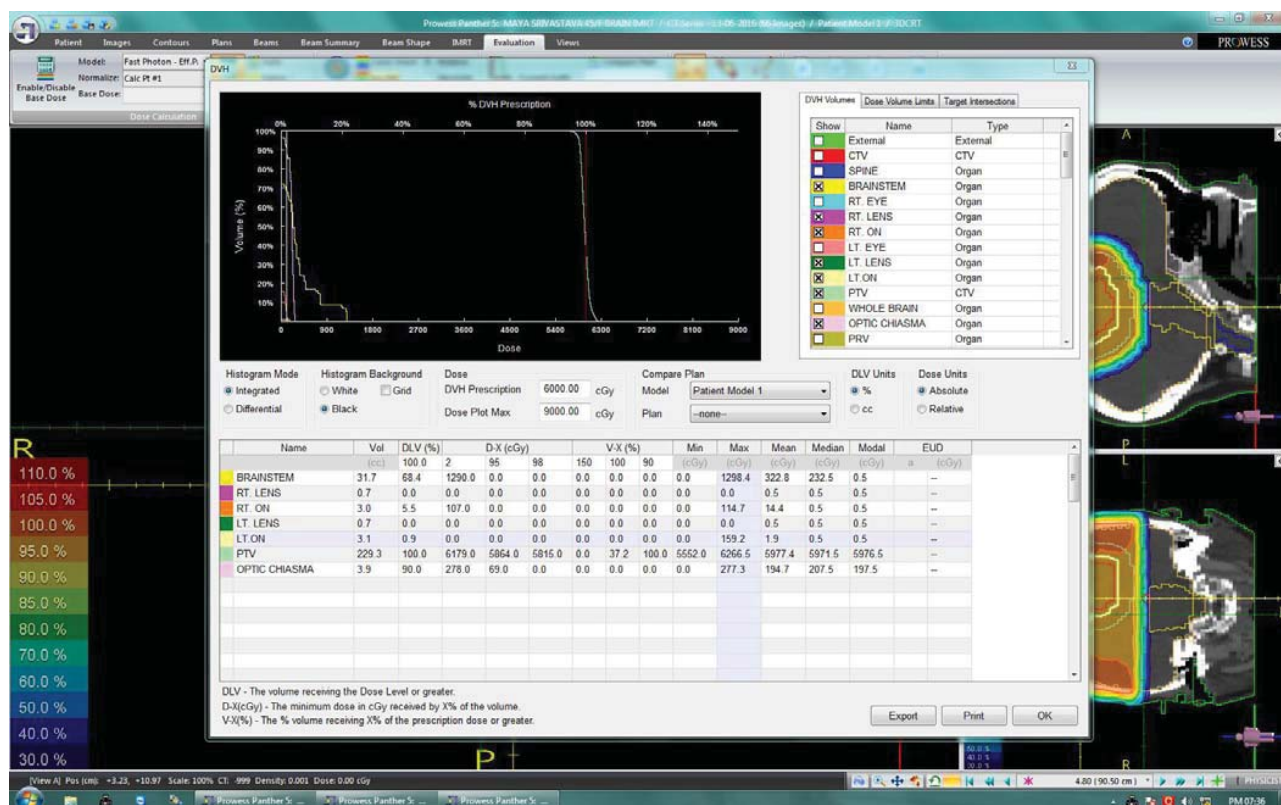


Fig. 4 (b) DVH of 3D CRT plan

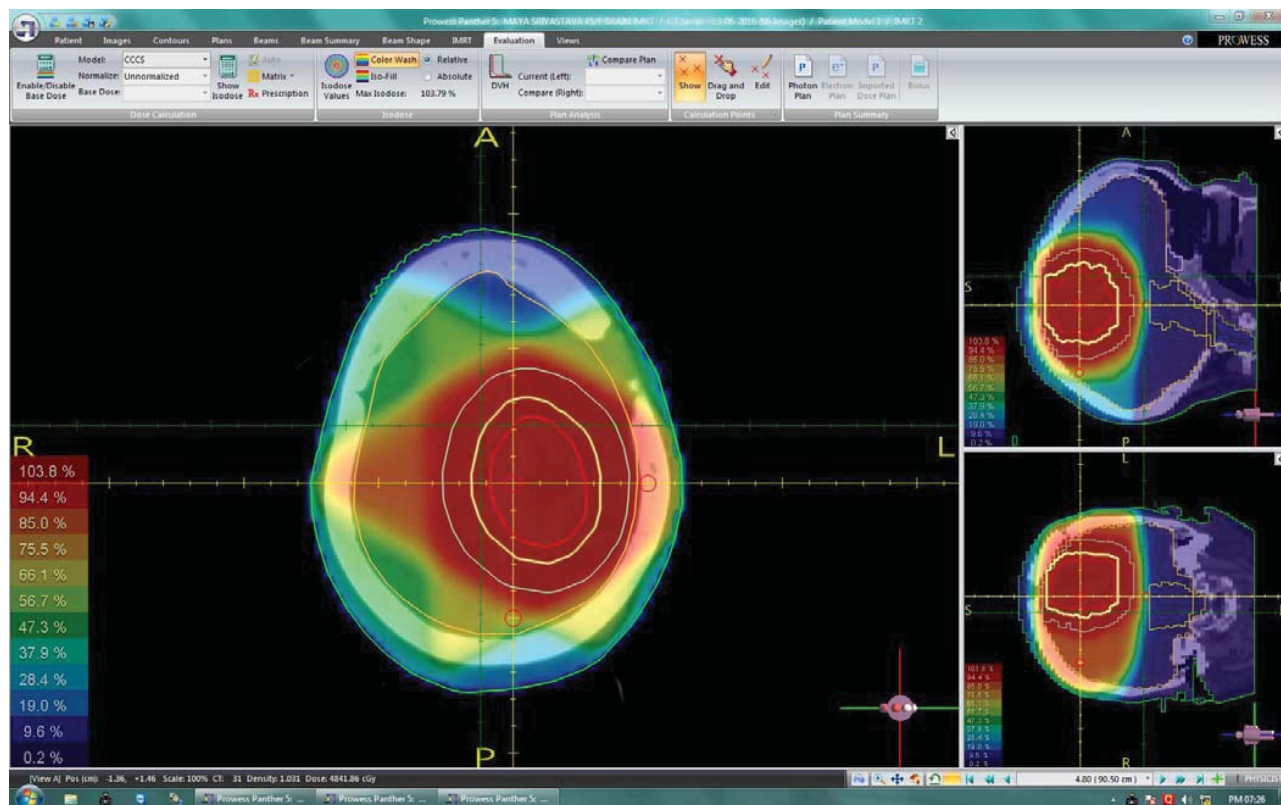


Fig. 5 (a) Color wash of IMRT plan

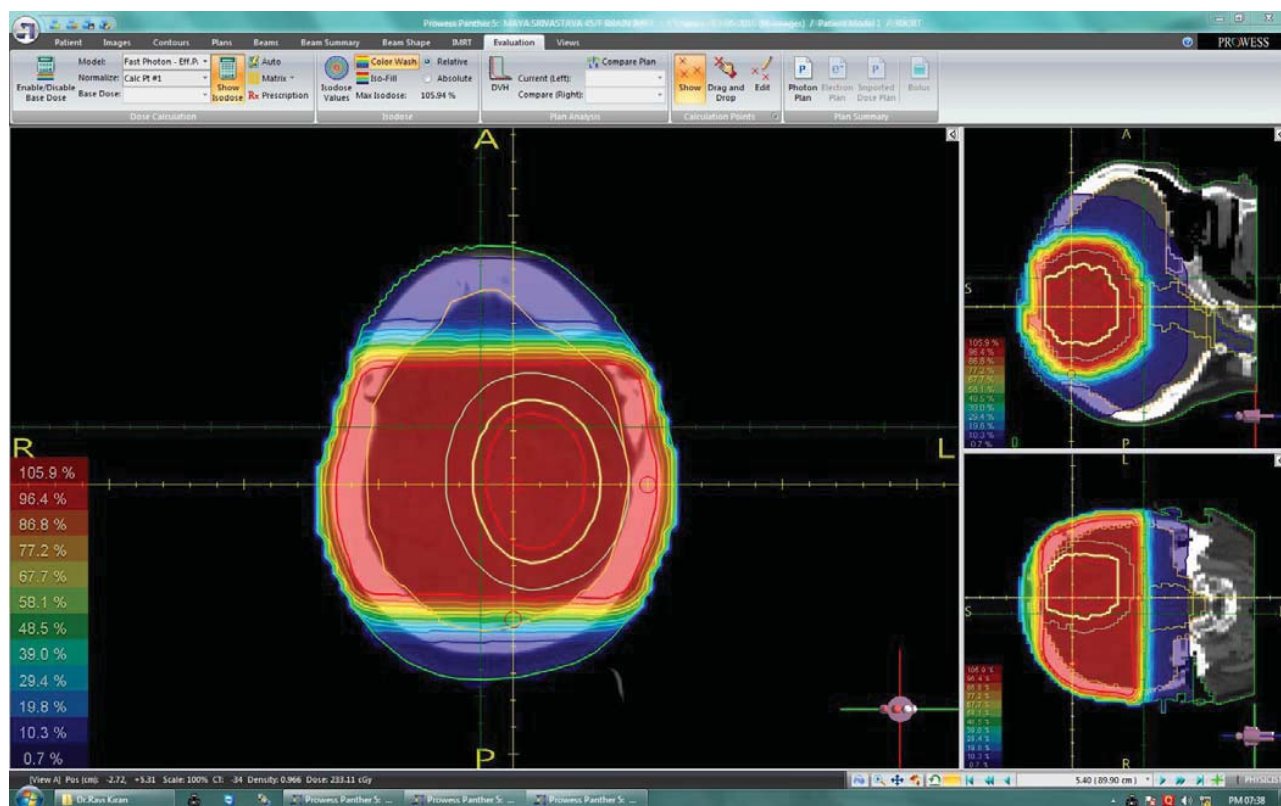


Fig. 5 (b) Color wash of 3D CRT plan

VI. CONCLUSION

Dose coverage of the planning target volume (PTV) was better with IMRT. Variables such as expertise, location of tumor, patient condition, and TPS software, and upgraded machines influence the outcome of the treatment. The dosimetric advantages can be translated into clinical outcome is uncertain and to arrive any statistical significance, larger sample size and meta-analysis is mandated in this domain.

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REFERENCES

- [1] Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. *CA Cancer J Clin* 2005;55(1):10-30.
- [2] Mehta M, Vogelbaum MA, Chang S, et al.: Neoplasms of the central nervous system. In: DeVita VT Jr, Lawrence TS, Rosenberg SA: *Cancer: Principles and Practice of Oncology*. 9th ed. Philadelphia, Pa: Lippincott Williams & Wilkins, 2011, pp 1700-49.
- [3] American Cancer Society: *Cancer Facts and Figures 2016*. Atlanta, Ga: American Cancer Society, 2016.
- [4] Kleihues P, Burger PC, Scheithauer BW: The new WHO classification of brain tumours. *Brain Pathol* 3 (3): 255-68, 1993
- [5] Lorentini S, Amelio D, Giri MG, Fellin F, Meliardo G et al., "IMRT or 3D-CRT in glioblastoma? A dosimetric criterion for patient selection", *Technol Cancer Res Treat*, 2013 Oct;12(5):411-20.
- [6] Ding M, Newman F, Chen C et al., " Dosimetric comparison between 3DCRT AND IMRT using different MLC in the treatment of brain tumors", *Med Dosim*. 2009 Spring;34(1):1-8.
- [7] Michael Back, Shaun Clifford, HELEN Wheeler et al., "Dosimetric Improvements Utilising Intensity Modulated Radiation Therapy for Patients with GlioblastomaMultiforme", *Journal of Cancer Therapy*, 2013,4,18-24.

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