

Dosimetric Comparison: Volumetric Modulated Arc Therapy (VMAT) and 3D Conformal Radiotherapy (3D-CRT) in High Grade Glioma Cancer—Experience of Casablanca Cancer Center at the Cheikh Khalifa International University Hospital

Imane Benali^{1,2*#}, Othmane Kaanouch^{3*}, Asmaa Naim^{1,2*}, Hanae El Gouach^{3*}, Zineb Dahbi^{1,2*}, Fadila Kouhen^{1,2*}

¹Mohammed VI University of Health Sciences (UM6SS), Casablanca, Morocco

²Department of Radiotherapy, Casablanca Cancer Center, Cheikh Khalifa International Hospital, Casablanca, Morocco

³Medical Physics Unit of Casablanca Cancer Center, Cheikh Khalifa International Hospital, Casablanca, Morocco

Email: *imanebenali88@gmail.com

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Abstract

Background: Intensity Modulated Radiation Therapy (IMRT) is currently employed as a major arm of treatment in multiforme glioblastoma (GBM). The present study aimed to compare 3D-CRT with IMRT to assess tumor volume coverage and OAR sparing for the treatment of malignant gliomas.

Materials and methods: We assessed 22 anonymized patients datasets with High Grade Glioblastoma who had undergone post-operative Intensity Modulated Radiotherapy (IMRT) and 3D Conformal Radiotherapy (3D-CRT). This study will compare and contrast treatment plans Rapidarc and 3D-CRT to determine which technology improves significantly dosimetric parameters.

Results: Plans will be assessed by reviewing the coverage of the PTV using mean, maximum and minimum doses while the OAR doses will be compared using the maximal doses for each, as set out in the QUANTEC dose limits.

Conclusion: The use of IMRT seems a superior technique as compared to 3D-CRT for the treatment of malignant gliomas having the potential to increase the dose to the PTV while sparing OARs optimally.

Keywords

HGG, IMRT, 3D-CRT, Dosimetric Study

*Authors have equally contributed to this article.

*Corresponding author.

1. Introduction

Intensity Modulated Radiation Therapy (IMRT) and Three Dimensional Conformal Radiation Therapy (3D-CRT) are both very promising techniques for the treatment of brain tumors. The standard of care for patients with multiforme glioblastoma is represented by a combination of surgical resection, adjuvant radiation therapy (RT), and chemotherapy, despite this aggressive multimodal strategy the prognosis remains poor.

Radiotherapy is usually delivered with Three Dimensional Conformal Radiation Therapy (3D-CRT) in 1.8 - 2 Gy per fraction to a total dose of 59.4 - 60 Gy. However, considering that GBM may lie in close proximity to several organs at risk, radiation treatment planning may lead to sub-optimal target coverage. In the attempt to improve clinical outcomes, Intensity Modulated Radiation Therapy (IMRT) has been increasingly evaluated and exploited for the treatment of GBM. Overall, from the dosimetric standpoint, Three Dimensional Conformal Radiation Therapy (3D-CRT) and IMRT seem to provide similar results in terms of target coverage, while IMRT, regardless of the employed technique, is better in terms of dose conformity, in reducing the maximum dose to the organs at risk (OARs) and in healthy brain sparing.

Purpose: We aimed to evaluate the dosimetric interest of Volumetric Modulated Arc Therapy (VMAT) using Rapidarc® the varian solution for the treatment of patients with multiforme glioblastoma near to organs at risk. We report the results of a retrospective study of 22 patients treated at the Casablanca Cancer Center of Cheikh Khalifa International University Hospital.

2. Materials and Methods

Through a retrospective study, we assessed 22 patients with High Grade Glioblastoma who had undergone post-operative Intensity Modulated Radiotherapy (IMRT) and 3D Conformal Radiotherapy (3D-CRT). The patients' characteristics are summarized in **Table 1**. We included patients with tumors in a variety of locations. The cases were selected to be representative of four dosimetric scenarios, there were no overlaps between OARs and the PTV, the second, the third and the last scenarios were characterized by the superposition with the PTV of 1, 2 and 3 OARs respectively. To improve delineation of target volumes and normal tissues, planning computed tomography (CT) and post-surgical magnetic resonance imaging (MRI) were automatically co-registered by using the dedicated treatment planning system (TPS). A visual check was performed at the end of the registration process: in case the results were not satisfactory, the radiation oncologist manually edited the co-registration. MRI were acquired for diagnostic purposes without the immobilization device. Gross tumor volume (GTV) was defined as the resection cavity plus any contrast-enhancing area on a post-gadolinium T1-weighted MRI. The clinical target volume (CTV) was obtained by adding a three-dimensional 2 cm expansion to the GTV.

The physicians manually edited the CTV to respect natural anatomical barriers (bone, tentorium, falx). The CTV was then expanded by 0.5 cm to create

Table 1. Patients characteristics.

Cases	Surgical resection	PTV volume (cc)	Lesion site
1	GTR	332	R TL
2	GTR	143	R PL
3	STR	151	R PL
4	STR	645	L FL
5	STR	252	R OL
6	GTR	330	R TL
7	STR	240	L FL
8	STR	297	R TL
9	GTR	301	R TL
10	STR	215	R TL
11	STR	621	L FL
12	GTR	470	L FL
13	GTR	398	R TL
14	STR	211	R PL
15	GTR	145	R OL
16	STR	148	L FL
17	STR	558	L FL
18	STR	249	R TL

PTV: Planning target volume; OARs: Organs at risk; CC: Cubic centimeters; GTR: Gross total resection; STR: Subtotal resection; TL: Temporal lobe; FL: Frontal lobe; OL: Occipital lobe; PL: Parietal lobe; R: Right; L: Left.

the PTV. Contoured OARs were brainstem, optic nerve, optic chiasm, lenses, ocular globes and healthy brain. The prescription dose to the PTV was 60 Gy in 2 Gy per fraction with the following priorities: firstly, compliance of dose constraints for OARs; secondly, adequate target coverage. With this regard, plans were acceptable when 95% of prescription dose covered 99% or more of the PTV. After planning, both IMRT and 3D-CRT dose distributions and CT datasets were exported from treatment planning systems in DICOM format the dosimetric values suitable for analysis were gathered then the PTV dose was scored via: Conformity index (CI) (defined as the ratio V_{98}/V_{PTV}). Homogeneity index (HI) (defined as the ratio $D_5-D_{95}/D_{prescription}$). V_{95} (percentage of PTV volume receiving at least 95% of the prescription dose) used as a surrogate of minimum dose; V_{107} (percentage of PTV volume receiving at least 107% of the prescription dose) used as a surrogate of maximum dose.

3. Results

Were Based on the coverage of the predicted target volume (PTV), the conformity index (CI), the homogeneity index (HI) and on the dose-volume histogram

(HDV) of the organs at risk both plans were compared. The dosimetric coverage of the predicted target volume (D95) generated by the two techniques was almost fixed for each patient with an average compliance index for the VMAT of 0.9884 ± 0.010 and of 0.9894 ± 0.011 for the 3D-CRT in order to have a significant comparison for other dosimetric parameters. The average homogeneity index for the VMAT was 0.071 ± 0.021 and of 0.103 ± 0.023 for the 3D-CRT. VMAT showed significant reductions in mean dose delivered to the Brainstem, Optic chiasma and to the Optic Nerve (close to PTV) compared to 3D-CRT with maximum average doses of $51.46 \text{ Gy} \pm 5.91 \text{ Gy}$ respectively. against $56.24 \pm 5.63 \text{ Gy}$, $36.39 \text{ Gy} \pm 7.97 \text{ Gy}$ against $51.84 \text{ Gy} \pm 5.77 \text{ Gy}$ and $38.16 \pm 18.50 \text{ Gy}$ against $40.68 \text{ Gy} \pm 21.49 \text{ Gy}$. A statistically significant dose reduction to the healthy brain in favor of IMRT (**Figure 1**) was scored for normal brain, the mean volume receiving 60 Gy was greater in the 3D-CRT (**Figure 2**) plan compared to VMAT: 3.13% for 3D-CRT against 0.28% for VMAT.

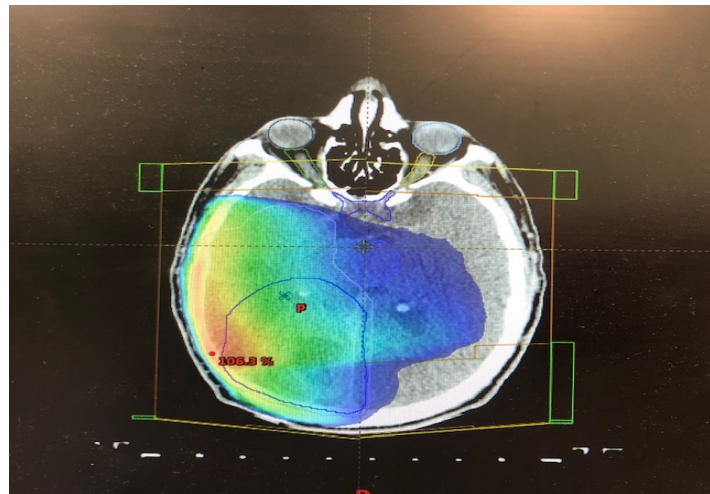


Figure 1. Isodose distribution of PTV with 3D-CRT.

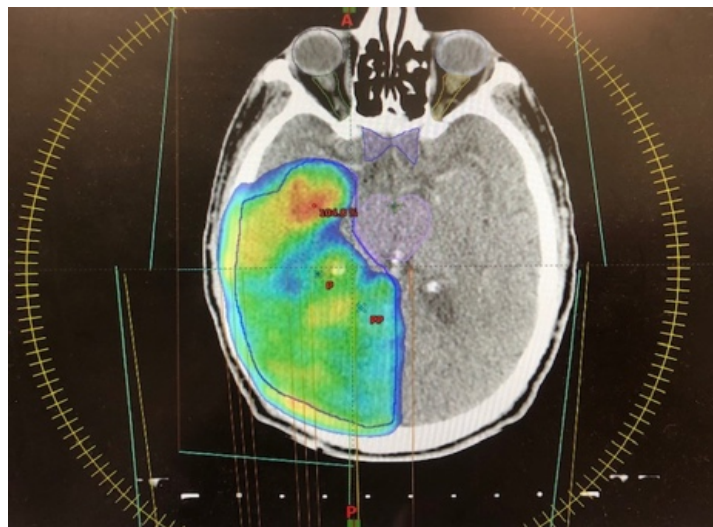


Figure 2. Isodose distribution of PTV with IMRT.

4. Discussion

Postoperative Radiotherapy with chemotherapy has been standard treatment for newly diagnosed glioblastoma as it had shown significant survival benefits after surgery.

Unfortunately HGG can develop in different sites of the brain, some lésions can be very proximal to several critical organs at risk (e.g. optical nerves, brainstem, chiasma and retina), that can cause late radiation toxicity including neuro-cognitive deficits and necrosis.

Therefore the potential for using the best technique to insure maximal coverage of the predicted target volume and simultaneously reducing radiation dose to OAR is discussed.

Our results indicate that, as compared with 3D-CRT, IMRT showed significant reductions in mean dose delivered to the brainstem, optic chiasma, normal brain and to the optic nerve, moreover IMRT also improved predicted target volume coverage and dose homogeneity over 3D-CRT.

Studying a group of 5 patients, Chan *et al.* demonstrated that, as compared with 3D-CRT, IMRT delivered higher doses (in excess of 10 Gy) to the gross tumor while respecting the same normal-tissue constraints [1]. In the Narayana study fifty-eight consecutive high-grade gliomas were treated with dynamic MLC IMRT [2] glioblastoma accounted for 70% of the cases, and anaplastic oligodendroglioma histology (pure or mixed) was seen in 15% of the cases. Surgery consisted of biopsy only in 26% of the patients, and 80% received adjuvant chemotherapy. IMRT did not significantly improve target coverage compared with Three-dimensional planning. However, IMRT resulted in a decreased maximum dose to the spinal cord, optic nerves, and eye by 16%, 7%, and 15%, respectively, owing to its improved dose conformality. The mean brainstem dose also has decreased by 7%.

Several comparison studies [3] [4] have been performed over the last years and nearly all, with few exceptions [4], suggest that IMRT techniques (static, volumetric, rotational) lead to a reduction of doses to OAR and to the healthy brain tissue [5] surrounding PTV, while maintaining target coverage without significant variations. MacDonald *et al.* [6] and Zach *et al.* [7] highlighted no differences in terms of PTV V95%. At the same time, in their comparative dosimetric study Wagner *et al.* [8] and Thilmann *et al.* [3] pointed out that IMRT achieved better target coverage with respect to 3D-CRT, scoring a V95% improvement of 13.5% and 13.1% respectively. This advantage was much more significant when PTV was in proximity of OAR [8].

MacDonald *et al.* [6] compared the dosimetry of Intensity Modulated Radiation Therapy and Three Dimensional Conformal Radiation Therapy techniques in patients treated for high-grade glioma. A total of 20 patients underwent computed tomography treatment planning in conjunction with magnetic resonance imaging fusion. Prescription dose and normal-tissue constraints were identical for the 3D-CRT and IMRT plans. As compared with 3D-CRT, IMRT

significantly increased the tumor control probability ($p < \text{or} = 0.005$) and lowered the normal-tissue complication probability for the brain and brainstem ($p < 0.033$).

Intensity Modulated Radiation Therapy improved target coverage and reduced radiation dose to the brain, brainstem, and optic chiasma. With the availability of new cancer imaging tools and more effective systemic agents, IMRT may be used to intensify tumor doses while minimizing toxicity, therefore potentially improving outcomes in patients with high grade glioma. At the same time, in their comparative dosimetric study, Wagner *et al.* [8] and Thilmann *et al.* [3] pointed out that IMRT achieved better target coverage with respect to 3D-CRT, scoring a V95% improvement of 13.5% and 13.1%, respectively.

Recently most Radiotherapy technical platforms offer a choice among these different techniques, it is important to define the parameters which will guide the final decision adopted for the treatment, following a comparative dosimetric study. IMRT planning has demonstrated its superiority over Three Dimensional Conformal Radiotherapy with regard to the preservation of organs at risk.

5. Conclusions

IMRT seems a superior technique as compared to 3D-CRT, in our study it allows for a better target dose coverage and improves the homogeneity of the dose received by the predicted target volume while maintaining equivalent OARs sparing and reducing healthy brain irradiation.

What is already known on this topic:

- The standard of care in GBM is represented by multimodal strategy consisting of surgical resection, adjuvant radiation therapy (RT), and chemotherapy.
- Radiotherapy can be challenging as the target volume is surrounded by critical organs at risk.

What this study adds:

- The goal of this study was to compare 3D-CRT and IMRT in GBM patients according to the dosimetric impact of the different scenarios on the critical structures irradiation.

Conflicts of Interest

The authors declare no conflict of interest.

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Abbreviations

IMRT: Intensity Modulated Radiation Therapy; 3D-CRT: Three-Dimensional Conformal Radiation Therapy; VMAT: Volumetric Modulated Arc Therapy; PTV: Planning Target Volume, OAR: Organs at Risk; PTV: Predicted Target Volume; HDV: Histogram Dose Volume; ID: Integral Dose; HI: Homogeneity Index; IC: inhomogeneity coefficient; HGG: High Grade Glioma; MLC: Multi Leaf Collimator.