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EVALUATION OF DOSIMETRIC PLAN QUALITY FOR GLIOBLASTOMA TREATED WITH 3D CONFORMAL RADIOTHERAPY

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Abstract. *Glioblastoma is classified as grade- IV glioma of primary brain tumors, and is faced more often in adult patients. The standard approach to therapy in the newly diagnosed glioblastoma, includes surgery followed by concurrent radiotherapy with chemotherapy. The aim of this study is retrospectively to analyze dosimetric treatment plan quality for patients treated for glioblastoma in our clinic using 3D-conformal radiotherapy. Radiotherapy treatment plans are realized by combining 3 to 6 coplanar and non- coplanar fields, open or wedged, achieving dose coverage, dose homogeneity to tumor within recommendations, while minimizing dose at organs at risk.*

Keywords: *3D conformal radiotherapy, dose, treatment plan, glioblastoma*

1. INTRODUCTION

Primary brain tumours are rare and account only 1.6 per cent of cancers.

Glioblastoma (GBM) is the commonest primary CNS tumour in adults. The major problems with high-grade gliomas are that cause significant damage to neurological function; they diffuse infiltration through the brain.

The standard approach to therapy in the newly diagnosed glioblastoma, includes surgery followed by concurrent radiotherapy with chemotherapy. The proximity of normal critical structures to the target volume, such as the optic chiasm, optic nerve and brain stem, is the main reason that limits delivery of an adequate dose of radiation to the tumor tissue while sparing the Organs at risk OAR [1].

3D- Conformal radiotherapy (3D-CRT), Intensity Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) can be used as modality for treatment of glioblastoma. Despite improved dosimetry to the advanced techniques of VMAT, IMRT, a comparison of clinical outcomes to 3D-CRT for glioblastoma has not been reported. [2,3,4].

3D-CRT modality links 3D CT visualization of the tumour with the capability of the linear accelerator to shape the beam geometrically. This encloses the target volume as closely as possible while reducing dose to adjacent normal tissues. The field shaping can be accomplished with a multileaf collimator (MLC).

The prescription of radiation treatment includes a definition of the aim of the therapy, volumes to be considered, also a prescription of dose and fractionation. Preparation of treatment plans and evaluation were based on ICRU50, 62 and 83. For a better outcome of patients that undergone radiotherapy, the dose coverage, dose homogeneity and dose conformity within PTV and sparing OAR-s were analyzed.

This is a retrospective study of postoperative cases of GBM treated with surgery followed by concurrent chemoradiation and 3D-CRT at our hospital from January 2016 to May 2017.

2. MATERIALS AND METHODS

2.1. The treatment planning process

Patient immobilization. Planning CT simulation scans were taken with patients in supine position. To ensure accurate re-positioning, the patient's head had been immobilized using an individually adapted 3-point single layer thermoplastic mask system.

Imaging acquisition protocol required was with a slice thickness of 3 mm in a multislice CT scanner (Somatom Siemens) with contrast. The images were then transferred to the Eclipse™ treatment planning system (v.11, Varian Medical Systems, CA, USA) and co-registered with postoperative enhanced magnetic resonance (MR) images.

Contouring of gross tumour volume (GTV), clinical target volume (CTV) and organs at risk (OAR) were performed on CT scanner images per patient by radiation oncologist. The GTV was defined as the resection cavity plus any residual enhancing tumour on contrast enhanced T1-weighted MRI. The clinical target volume (CTV) is delineated as a volumetric GTV expansion of 2 cm. This margin was applied to encompass areas of potential microscopic tumour

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infiltration, and was adjusted to respect anatomical borders, as reported in glioblastoma target delineation guideline [5,6]. The planning target volume (PTV) consisted of a uniform expansion around the CTV of 3 to 5 mm.

The prescription of radiation treatment includes a definition of the aim of the therapy, volumes to be considered also a prescription of dose and fractionation. Dose prescription on PTV was 60 Gy delivered in 30 fractions of 2 Gy per fraction.

Treatment beams used were photons of 6MV energy, produced by the linear accelerator Siemens Oncor.

Radiation dose prescription and planning has been performed according to ICRU guidelines (ICRU50, 62 and 83 reports). Prescription dose to the reference point should ensure that at least 95% of the PTV is encompassed by the 95% isodose surface, that the median dose to the PTV is close to the prescription dose, and that the D2% should be less than 107%. Meeting hard constraints for critical OARs (e.g. brainstem and chiasm) necessitates compromise of the PTV dose coverage. Dose constrains for OAR-s in brain have been maintained under their restrictions according to QUANTEC and Emami.

Treatment plans were realized using a 6 MV, Flattened Filter beam, and in general combining 3 to 6 coplanar and non-coplanar wedged fields. After beam optimizations, the dose calculations were performed by using AAA algorithm. Optimal plans were achieved by optimizing the dose coverage on tumour while sparing OARs. Dose–Volume Histograms (DVH) were evaluated for the planning target volume (PTV) and OARs.

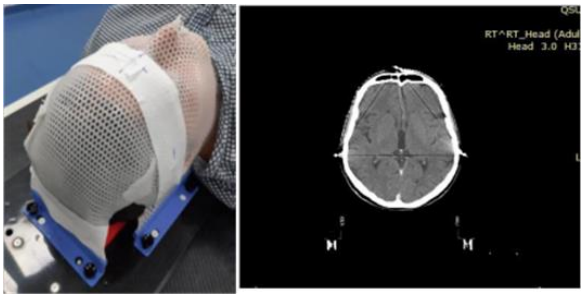

Figure 1. Patient immobilization in supine position. Axial scan slice of patient.

2.2. Patient selection and plan evaluation

This is a retrospective study of postoperative cases of GBM treated with surgery followed by concurrent chemoradiation and 3D-CRT at our hospital, from January 2016 to May 2017-en. Patients included in the analysis were classified for radical treatment and were given a total dose of 60 Gy in 30 fractions over 6 weeks.

Dose–volume histograms were evaluated for the planning target volume (PTV) and OARs. Dose constraints for OARs were according to Table 1.

Dosimetric parameters in terms of PTV coverage, conformity index (CI) and homogeneity index (HI), are estimated based on the data dose/volume extracted by Dose- Volume Histograms (DVH) for each treatment plan of patients.

Dose homogeneity and dose conformity are independent parameters of the quality of the absorbed dose distribution. Dose homogeneity characterizes the uniformity of the absorbed-dose distribution within the target volume while dose conformity characterizes the degree to which the high-dose region conforms to the target volume, usually the PTV [9].

Table1. Dose constraints for OARs.

OAR	Dose/volume constraints)
Brainstem	D100 ≤ 54 Gy V59 Gy < 10 cc
Optic nerves & Chiasm	D_{max} < 55 D_{max} < 55-60 Dmean< 50Gy
Eyes	D_{max} ≤ 50
Lens	D_{max} < 7 Gy
Cochlea	D_{mean} (Gy) ≤ 45 Gy
Dx: minimum dose received by the x% of the organ; Vx = volume of OAR receiving the dose 59Gy; D_{max}: maximum radiation dose; D_{mean}: mean dose received by the organ.	

Conformity index (CI) and homogeneity index (HI), are calculated by using the van't Reit formula [11], (CI: range 0-1, with 1 being highly conformal), and ICRU 83 formula [9], (HI: range 0-1, with 1 being highly heterogenous and values of zero indicates that the absorbed-dose distribution is almost homogeneous). The mathematical expressions for CI and HI are as follow:

$$CI = \frac{(V_{95\%}^{PTV})^2}{V^{PTV}\, x\, V_{95\%}} \qquad (1)$$

$$HI_{ICRU} = \frac{D_{2\%} - D_{98\,\%}}{D_{50\,\%}} \qquad (2)$$

In the formula:

$V_{95\%}^{PTV}$ presents the volume receiving at least 95 % of prescribed dose; $D_{x\,\%}$ the dose received by x% of the volume of PTV.

D98% and D2% gives the idea of near-minimum and near-maximum doze within PTV. D98% indicate is the dose received by at least 98% of PTV volume and D2% is maximal dose received by at least 2% of PTV volume.

-V107% gives information for "hot spot areas" within PTV. It is the PTV volume in percentage that receives dose equal to 107 %.

3. Results and Discussion

For 3D-Conformal radiotherapy recommendations according to ICRU 50. 62, is that the 95% isodose surface of prescription dose should encompass at least 95% of the PTV volume while sparing OARs.

The Figure 2. represents the dose distribution in a CT-scan axial plane of a 52-year-old patient, receiving 60 Gy on a PTV volume of 250 cc. In the right there is visible the 3D-view of the beam configuration (three wedged fields).

The DVH shows that the PTV volume (red line) has 100 % coverage by 95 % of dose prescription (57Gy). The maximum doses received by brainstem (yellow line) is 52.7 Gy, chiasm (light brown) 13.5 Gy, and the mean dose for the right cochlea (brown line) and left cochlea (pink line) where 19.9 Gy and 12.8 Gy respectively. (Dosimetric parameters calculated were HI = 0.1; CI= 0.7).

Patents selected were adults and their age range from 24 to 69 years old with an average of 59 years old.

They were 6 female and 27 men.

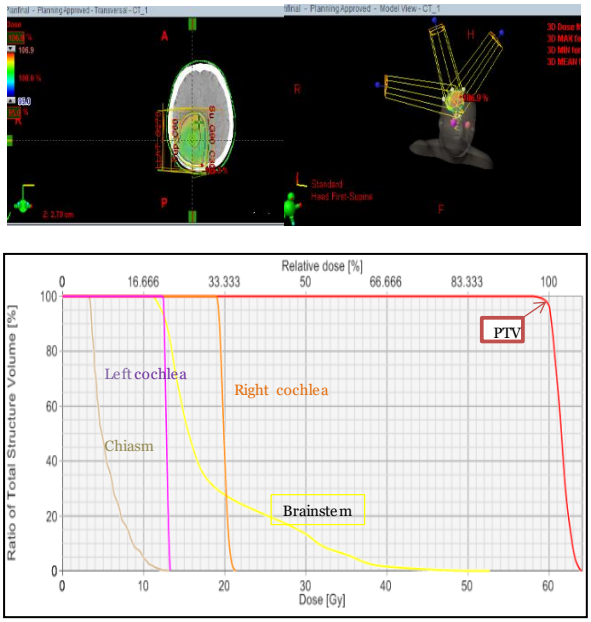

Figure 2. Dose distribution on PTV, Beam configuration in 3Dview and Dose volume Histogram for PTV and OARs Eclipse TPS.

Dosimetric parameters are extracted by histograms for each plan and the mean values and their ranges are tabulated in the Table2.

The mean GTV volume of tumours measured on planning CT imaging was 28.1 ± 16.5 cc (range 9.1 cc to 60.7 cc). The mean PTV volume was 270.8 ± 79.5 cc and a range from 97.2 cc to 458 cc.

The mean dose received by GTV volume was 60.8 ± 0.4 Gy with a range from 59.8Gy to 62.2 Gy.

The mean PTV volumes in percentage that received at least 95 % of 60 Gy (57 Gy), was 98.3 ± 1.9 % with a range from 94.4 to 100 %, in accordance to ICRU50 for tumour coverage.

Volume of PTV that takes the 107 % of Dose prescription of 60 Gy, is not present in plans, that means there is a good homogeneity within 95 to 107 %. D_{mean} and D50 % are in similar values and near equal to the point dose prescription that is 60 Gy.

Table 2. Target volumes GTV, PTV and planning indexes.

	Mean ± std	Range
PTV_volume (cc)	270.8 ± 79.5	(97.2 – 458.0)
GTV_volume (cc)	28.1 ± 16.5	(9.1 – 60.7)
GTV_Dmean (Gy)	60.8 ± 0.4	(59.8 - 62.2)
V95 % (%)	98.3 ± 1.9	(94.4 -100.0)
V107 % (%)	0.0 ± 0.0	(0.002 – 0.0)
Dmean (Gy)	60.9 ± 0.4	(60.03 - 61.5)
D 50 % (Gy)	61.13 ± 0.3	(60.5 – 61.9)
D 2% (Gy)	63 ± 0.4	(62.0 - 63.7)
D 98% (Gy)	57.4 ± 2.2	(51.0 - 60)
CI	0.8 ± 0.0	(0.7- 0.9)
HI	0.1 ± 0.0	(0.1 - 0.2)

std: Standard deviation; Vx% presents the PTV volume in percentage that receiving at least x % of prescribed dose; Dx % the dose received by x% of the volume of PTV; Dmean: mean dose received by PTV.

The mean values for CI and HI calculated according to formula (1) and (2) respectively, were CI = 0.8 (range: 0.7 – 0.9) and HI = 0.1 (range: 0.1 to 0.2). The values shows that treatment plans realized with 3D-CRT, for the 33 patients were optimal regarding the dose homogeneity and dose conformity to the PTV.

Glioblastoma is an infiltrative tumour in brain and treated with high doses (60 Gy). When its localization is nearby critical organs like optical pathways, brainstem or cochlea, it makes treatment plan difficult to achieve optimal tumour coverage while sparing OARs. Mean dosimetric data received by OARs in the 33 patients are tabulated in Table 3.

Table 3. Mean values of maximum and mean doses received by Organs at risk in 33 patients.

OAR	Mean (Gy) ± std
Brainstem (D_{max})	51.4 ± 11.7
Chiasm (D_{max})	31.3 ± 18.3
Right optic nerve (D_{max})	18.6 ± 16.2
Left optic nerve (D_{max})	16.9 ± 16.5
Right eye (D_{max})	9.8 ± 13.9
Left eye (D_{max})	11.3 ± 13.8
Right eye (D_{mean})	3.4 ± 3.3
Left eye (D_{mean})	3.9 ± 3.3
Right lens (D_{max})	2.6 ± 1.4
Left lens (D_{max})	2.8 ± 1.6
Right cochlea (D_{max})	16.8 ± 12.6
Left cochlea (D_{max})	17.4 ± 13.3

The mean value of the maximum doses received by brainstem was 51.4 ± 11.7 Gy and the mean value of maximum doses received by chiasm was 31.3 ± 18.3 Gy. From data in Table3, it seems that the mean doses received by eyes, lenses and cochlea, were in low dose values comparing to dose restrictions [10,13].

4. Conclusion

Treatment plans of 33 patients were analyzed retrospectively. Treatment plans were realized using 3D-CRT with the 6 MV FF photon beam. There were used 3 to 6 static fields, wedged and open one for treatment plans. The mean PTV volumes in percentage that received at least 95 % of 60 Gy (57 Gy), was 98.3 ± 1.9 % with a range from 94.4 to 100 %, within ICRU50 recommendations. Dose coverage of PTV volume is dependent from tumour volume and tumour localization nearby to organs at risk. Median dose to the PTV is close to the prescription dose, and the maximum doses were less than 107%. Conformity index and dose homogeneity were within recommendations.

Finally, 3D - CRT remains an effective modality of treatment for GBM regarding local disease control and cost – effectiveness compared with other modalities.

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