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Data Availability Statement

The data supporting the findings of this study are publicly available and are included within this published article.

RESEARCH ARTICLE

Dosimetric Analysis with Intensity-modulated Radiation Therapy for Central Nervous System Irradiation in Patients with Brain Cancer Compared with Three-dimensional Conformal Radiation Therapy Treatment

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ABSTRACT

Intensity-modulated radiation therapy (IMRT) was put as the development of three-dimensional conformal radiation therapy (3D-CRT). The purpose of the present study is to compare the dosimetric analysis of two techniques of radiotherapy (IMRT) and 3D-CRT, which include target volume and organ at risk for both plans. The present study enrolled that nine patients with different types of brain cancer which previously irradiated from November 2018 to May 2019 were selected in Zhianawa Cancer Center in Sulaymaniyah; all cases were planned again by both techniques 3D-CRT and IMRT. IMRT planning provides reducing the dose of both right and left optic nerve mean dose for right optic nerve 13.70 Gy and left 14.93 Gy compared with the 3D-CRT plan (right optic nerve 23.54 Gy and left 19.13 Gy). $P = 0.2$ for the right optic nerve and $P = 0.56$ for the left optic nerve were statistically significant. IMRT plan reduces dose to the optic chiasm compared to 3D-CRT plan, the mean dose of optic chiasm for IMRT was 33.37 Gy relative to 3D-CRT which was 34.28 Gy and $P = 0.92$. IMRT plan was better than 3D-CRT for many organs at risk, especially for optic chiasm and both optic nerve deliver less dose than 3D-CRT.

Keywords: Brain cancer; Intensity-modulated radiation therapy; Radiotherapy; Reduce dose; Three-dimensional conformal radiation therapy

INTRODUCTION

Intensity-modulated radiation therapy (IMRT) was put as the development of three-dimensional conformal radiation therapy (3D-CRT) (Bentzen, 2005; Bortfeld, 2006) to improve tumor control and patient survival (Navarria et al., 2014). The target of radiotherapy is to deliver the prescribed dose to the tumor and organs at risk (OAR), receiving a minimum dose as much as possible. Nowadays, a different type of tumors is treated by radiotherapy with surgery and chemotherapy (Chui et al., 2001).

The tumors can affect the nervous system (Giglio and Gilbert, 2010). Nearly half of the patients who have cancer will receive radiotherapy as a section of their oncologic treatment (Kumar et al., 2013). 3D-CRT uses computed tomography to produce three-dimensional volumes of a patient's anatomy (Goyal, 2008) and also to visualize OAR and the tumor (Ghosh-Laskar et al., 2016; Nutting et al., 2011).

3D-CRT is a very available radiotherapy technique which considered as standard (Kortmann et al., 2003; Krasin et al., 2010; Chan, 2015).

Non-uniform radiation beam intensities use in IMRT by computer-based optimization to achieve better dose distribution (Tejpal et al., 2010). Furthermore, multileaf collimators that use in IMRT are dynamic or static, which delivers high doses while minimizing dose to the surrounding healthy tissues (Bhatnagar et al., 2006; Zelefsky et al., 2002; Heron et al., 2003). Distribution of dose is inversely determined in IMRT, which means that the treatment planner must decide the dose distribution for each organ at risk and after that, the computer will start calculating a group of the beam that will be generated (Spirou and Chui, 1998) and also is expected to improve radiotherapy by late morbidity of treatment and better covers the volume of the target (Lin et al., 2003; Scott-Brown et al., 2010).

IMRT contains the radiation field, in which the shape is in accordance with the projective shape of planning target volume (PTV) in the radiation beam. And then, multiple fixed angle beams are usually needed for better qualities (Xie et al., 2014), which patient's quality of life can be more improved (Sun et al., 2014; Zhou et al., 2017; Kuang et al., 2012).

The purpose of the present study is to compare the dosimetric analysis of two techniques of radiotherapy IMRT and 3D-CRT, which include target volume and organ at risk for both techniques.

MATERIALS AND METHODS

Patient's Selection

All of the patient's ages were ranged between 9 and 52 years, three males and six females. The prescribed dose for all the cases was 54 Gy with 30 fractions.

Forward Planning (3D-CRT)

The present study uses Xio (release 5.00.02) three-dimensional radiotherapy treatment planning system, the energy used to produce a plan in 3D-CRT for all types of brain cancer was 6MV photon. Three to four beams were designed for treatment planning. There are three main volumes to be into account in radiotherapy planning, the first volume is the position of the tumor and this is known as the gross tumor volume (GTV). The second volume surrounds the GTV and describes the extent of microscopic unexpected tumor spread; this is known as the clinical target volume (CTV). The original concepts of the GTV and CTV were detailed in report 50 from the International Commission on Radiation Units and Protection (ICRU), in 1993 (ICRU Report 50). In the third volume, the PTV is a geometric concept designed to confirm that the radiotherapy prescription dose is actually delivered to the CTV (Burnet et al., 2004). To cover, the PTV multileaf collimator (MLC) was used. A wedge also used to perform dose homogeneity in PTV.

Inverse Planning (IMRT)

Seven-field and nine-field were used for inverse planning with the energy of 6MV photon. For seven fields were used to cover PTV using (MLC) at gantry angle (80°, 120°, 160°, 200°, 240°, 280°, and 300°). For nine fields were used to cover PTV using (MLC) at gantry angle (0°, 40°, 80°, 120°, 160°, 200°, 240°, 280°, and 320°).

The Tolerance Doses for OAR for Both Parallel and Serial Organs

The maximum dose for OAR for the lens was 7 Gy, the optical nerve was 55 Gy, mean dose for cochlea was ≤45 Gy, mean dose for the eye was <35 Gy, brain stem was <54 Gy, and optic chiasm 55 Gy.

Prescription Dose and Dosimetric Analysis

The prescription dose for all patients was 54 Gy in 30 fractions, for each day, the patient received 1.8 Gy. Dose-volume histograms (DVHs) of both techniques used to evaluate maximum dose, mean dose for each organ at risk, and cover of PTV. All plans in both techniques depend

on DVHs to ensure that the 95% of the volume of PTV received 95% of the prescribed dose.

The DVHs are a tool to show the dose that is delivered to OAR and volume of the target (Guckenberger et al., 2006). Conformity index (CI) defines as an attempt to measure exactly how well the distribution of dose follows the shape of the target volume, and it is a ratio of the tissue volume which receives at least 95% of the prescription dose divided by the volume of the PTV, as shown in equation (1). CI is more conformal when its value closer to 1 (Foroudi et al., 2012).

$$CI = V_{95\%} / V_{PTV} \quad (1)$$

Homogeneity index (HI) is a common tool that is used to analyze dose homogeneity in the tumor volume, as shown in equation (2). It is used to compare the dose distributions of many treatment plans (Feuvret et al., 2006; Gong et al., 2008; Wu et al., 2003).

$$HI = D_{2\%} - D_{98\%} / D_{50\%} \quad (2)$$

Where $D_{2\%}$ and $D_{98\%}$ represent the doses of the PTV, respectively, $D_{98\%}$ means that at least 98% of the PTV receives this dose, and hence, $D_{2\%}$ means that at least 2% of the PTV receives this dose. $D_{2\%}$ is considered to be the maximum dose and $D_{98\%}$ is considered to be the minimum dose, lower HI values mean a more homogenous target dose (Yoon et al., 2007).

Statistical Methods

Statistical analysis was done using SPSS version 19 (IBM) statistical software package. Data described by the mean ± SD. *t*-test was used to compare the prescribed dose of both technique, and $P < 0.05$ was considered to be statistically significant.

Ethical Considerations

The present study was approved by the Research Ethics Committee of the College of Medicine at Hawler Medical University.

RESULTS

Table 1 represents the clinical characteristics of the patients.

IMRT planning provides reducing the dose of both right and left optic nerve mean dose for (right was 13.7 ± 12.15 Gy and left 14.93 ± 14.19 Gy) compared with 3D-CRT (right was 23.54 ± 18.77 Gy and left 19.13 ± 16.15 Gy), as shown in Figures 1 and 2.

3D-CRT shows reduce dose received to left cochlea, it was 15.8 Gy relative to IMRT that was 18.1 Gy. However, the

mean dose for the right cochlea was 20.01 Gy in IMRT and 21.14 Gy in 3D-CRT, as shown in Figures 3 and 4.

IMRT plan reduces dose to the optic chiasm compared to 3D-CRT plan, the mean dose of optic chiasm was 33.37 Gy relative to 3D-CRT which was 34.28 Gy. However, the 3D-CRT plan shows reduce dose received to the brain stem (mean dose was 37.18 Gy relative to IMRT), which was 41.4 Gy, as shown in Figures 5 and 6.

Table 1: Clinical characteristics of the patients

Cases	location of tumor volume of PTV (cm ³)	tumor type
1.	The middle part of the brain 290.128	brain stem glioma
2.	The lower middle part of the brain 128.708	diffuse intrinsic pontine glioma
3.	The right part of the brain 405.964	anaplastic ependymoma GIII
4.	The right part of the brain 331.533	supine brain tumor
5.	The right back part of the brain 78.695	meningioma
6.	The upper middle part of the brain 181.568	meningioma
7.	The right part of the brain 345.713	oligodendroglioma GII
8.	The middle back part of the brain 77.495	ependymoma GII (Cerebellar)
9.	The middle part of the brain 22.690	pituitary adenoma

PTV: Planning target volume

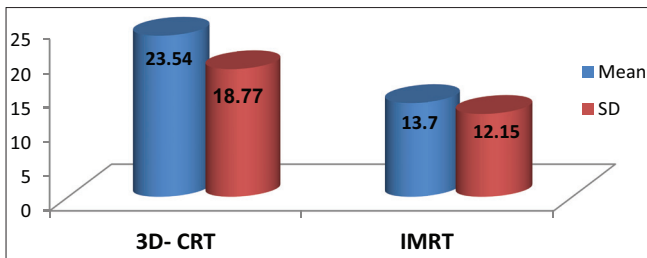


Figure 1: Mean±SD of the maximum dose for right optic nerve in IMRT versus 3D-CRT

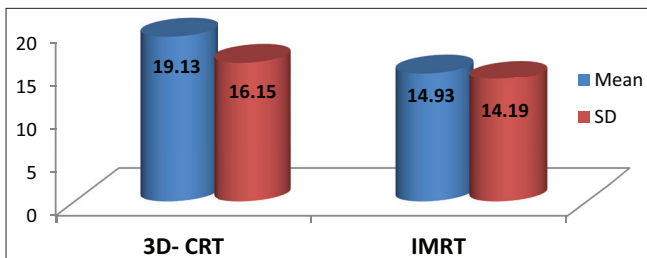


Figure 2: Mean and standard deviation (SD±) maximum dose for left optic nerve in IMRT versus 3D-CRT

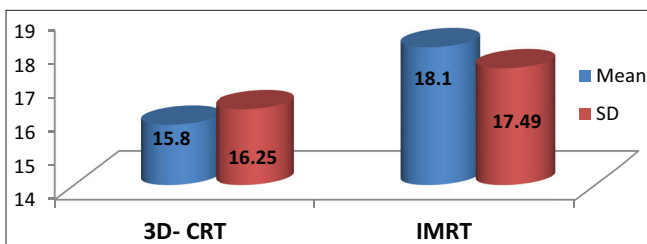


Figure 3: Mean and standard deviation (SD±) maximum dose for left cochlea in IMRT versus 3D-CRT

The mean dose of the right eye for both plans was slightly different for 3D-CRT was 13.15 Gy and for IMRT was 13.27 Gy. However, for the left eye, the mean dose was 8.41 Gy and for IMRT was 12.73 Gy. For the left lens, 3D-CRT shows reduce mean dose than IMRT for both was 2.46 Gy and 3.44 Gy.

IMRT plan was better for reducing the mean dose for the right lens, it was 2.88 Gy compared with 3D-CRT that mean dose was 6.75 Gy, as shown in Figure 7.

The organ at risk for both techniques was not statistically significant, right and left eye, $P = 0.98$ and 0.65 while for right and left cochlea, $P = 0.89$ and 0.75 . However, for both lenses, $P = 0.48$ and 0.56 was statistically significant. However, for both optic nerves $P = 0.2$ and 0.56 , for brain stem $P = 0.7$, and optic chiasm $P = 0.92$ are shown in Table 2.

Mean and standard deviation of CI for both plan 3D-CRT and IMRT was 0.97 ± 0.01 , 0.87 ± 0.31 , and $P = 0.33$, which is not statistically significant, while HI for 3D-CRT was 0.10 ± 0.04 and for IMRT was 0.12 ± 0.03 , ($P = 0.195$). $D_{5\%}$ and $D_{2\%}$ refer that volume (PTV) received 5%–2% of the

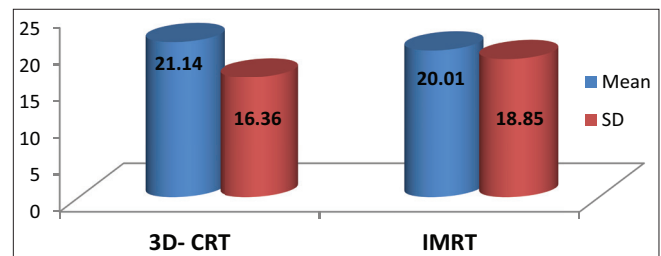


Figure 4: Mean and standard deviation (SD±) maximum dose for right cochlea in IMRT versus 3D-CRT

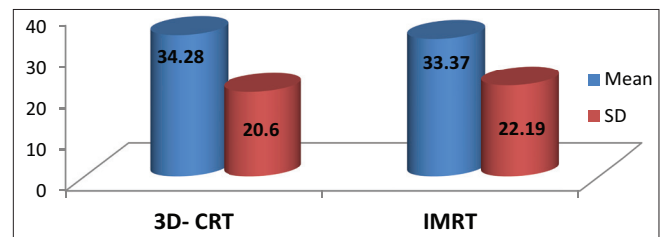


Figure 5: Mean and standard deviation (SD±) maximum dose for optic chiasm in IMRT versus 3D-CRT

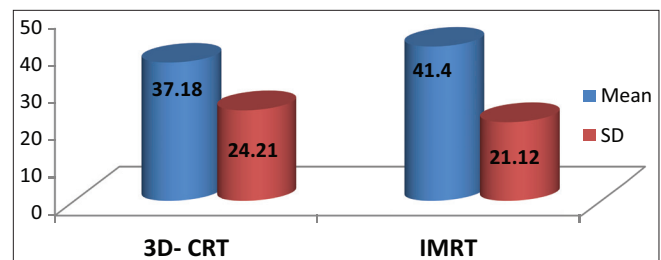


Figure 6: Mean and standard deviation (SD±) maximum dose for brain stem in IMRT versus 3D-CRT

Table 2: The mean dose of radiotherapy to organs at risk using different radiation modality

Organ at risk	3D-CRT Mean±SD	IMRT Mean±SD	P-value
Right eye	13.15±19.31	13.27±16.64	0.98
Right cochlea	21.14±16.36	20.01±18.85	0.89
Right lens	6.75±16.08	2.88±1.70	0.48
Right optic nerve	23.54±18.77	13.70±12.15	0.2
Brain stem	37.18±24.21	41.40±21.12	0.7
Optic chiasm	34.28±20.60	33.37±22.19	0.92
Left eye	8.41±13.08	12.73±15.52	0.65
Left cochlea	15.80 ±16.25	18.10±17.49	0.75
Left lens	2.46±4.37	3.44±2.31	0.56
Left optic nerve	19.13±16.15	14.93±14.19	0.56

3D-CRT: Three-dimensional conformal radiation therapy, IMRT: Intensity-modulated radiation therapy

Table 3: Dosimetric parameters of 3D-RT and IMRT plan

Dosimetric parameters	3D-CRT Mean±SD	IMRT Mean±SD	P-value
Conformity index	0.97±0.01	0.87±0.31	0.33
Homogeneity index	0.10±0.04	0.12±0.03	0.195
D _{98%}	50.95±1.04	51.21±0.67	0.3
D _{95%}	52.07±0.49	52.17±0.63	0.45
D _{5%}	56.97±1.09	57.58±0.99	0.013
D _{2%}	57.34±1.21	58.06±1.12	0.007

3D-CRT: Three-dimensional conformal radiation therapy, IMRT: Intensity-modulated radiation therapy

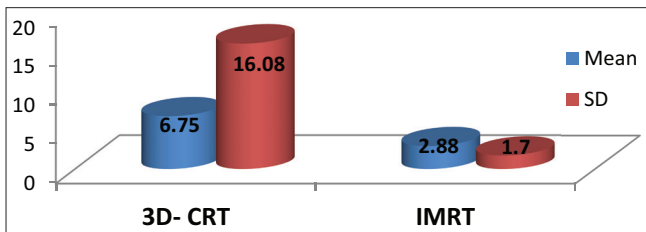


Figure 7: Mean and standard deviation (SD±) maximum dose for the right lens in IMRT versus 3D-CRT

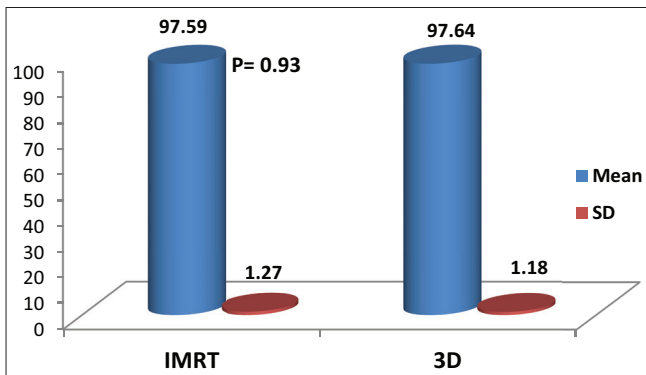


Figure 8: Mean and SD of PTV in 3D versus IMRT among brain tumors

prescribed dose, D_{5%} and D_{2%} were significant difference in IMRT compared with 3D-CRT and P = 0.013 for D_{5%} and 0.007 for D_{2%} which is statistically significant, as shown in Table 3.

PTV for both plans was not statistically significant, which for IMRT was 97.59% and for 3D-CRT was 97.64% and P = 0.93, as shown in Figure 8.

DISCUSSION

This study shows the dosimetric comparison between 3D-CRT plan and IMRT plan, resulting in the present study shows that both right and left optic nerves receive a less prescribed dose in the IMRT plan as relative to 3D-CRT, but for brain stem, 3D-CRT shows reduce dose received than IMRT. However, this result compares with a study done in Egypt by Al Zayat et al. and shows that in IMRT optic nerve receives a higher dose (38.86 Gy) than 3D-CRT (27.57 Gy). However, for brain stem, IMRT shows better plan (72.17 Gy) relative with 3D-CRT (73.05 Gy) (Al Zayat et al., 2014).

In 3DCRT plan which usually use two or three fields with wedges in relative with the IMRT plans which using more than three fields, using a small number of the fields given advantages to the 3D-CRT plan which is less monitor units, short time of treatment and make small low-dose areas. This is crucial because low-dose areas may induce secondary cancer (Moret et al., 2009; Fontenot et al., 2009; Zwahlen et al., 2009).

CONCLUSION

IMRT plan was better than 3D-CRT for many OAR,, especially for optic chiasm and both optic nerves deliver less dose than 3D-CRT, while PTV for both plans was slightly different. Both techniques can use to treat brain cancer, but if OARs were so close to PTV that it is better to use IMRT than 3D-CRT.

CONFLICTS OF INTEREST

The authors reported no conflicts of interest.

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