Pan Arab Journal of Oncology

Original Article

Comparison of Patient Setup Error Effect on Target Evaluation Parameters in 3D-CRT, IMRT and VMAT for Gioblastoma

Mahmoud Mohamed Al-Fishawy[1*], Amin El-Sayed Amin[2], Abdelsattar Mohamed Sallam[3], El-Sayed Mahmoud El-Sayed[3]

1. **Medical physicist, Radiation oncology department, International Medical Center**
2. **Professor of Radiation Physics, Radiation Oncology Department, Faculty of Medicine, Ain-Shams University**
3. **Professor of Biophysics, Physics Department, Faculty of science, Ain shams University**

ABSTRACT

Purpose: Radiotherapy is one of the bases for glioblastoma (GBM) standard treatment. Three-dimensional conformal radiotherapy (3DCRT) is most common technique to treat GBM, but Intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) are becoming widely used. This study compares patient setup error effect on target dose evaluation parameters [target mean dose, homogeneity index (HI), conformity index (CI) and conformity number (CN)] for different techniques.

Patients and methods: 9 GBM patients with target prescribed dose 60 Gy are selected. The accepted plans by different techniques were recalculated after applying a simulation setup error by shifting the isocenter 3mm, 5mm, 7mm. Recalculation and analysis of target evaluation parameters of all accepted plans (27 origin plans) and new simulation setup error plans (81 plans) to compare the effect of patient setup error.

Results: Measurements of the setup error effect for shifting isocenter till 7mm between 3DCRT, IMRT and VMAT show that the planning target volume (PTV) mean dose has a percentage error (0.5%, 2.1%, and 1.9%), for HI (1.9%, 22.2%, and 16.5%), for CI (2.6%, 11%, and 15.3%), while for CN (3.7%, 41.6%, and 39%) respectively.

Conclusions: For GBM patients the setup error effect on delivered dose appeared clearly in HI, CI and CN which more sensitive to patient setup error that appears in VMAT and IMRT technique while effect decreases with 3DCRT technique. So IMRT and VMAT are more complex techniques than 3DCRT which need more accurate verification for target position by using advanced imaging techniques to avoid any setup errors.

Keywords
Setup errors,
HI,
CI,
CN,
3DCRT,
IMRT,
VMAT,
GBM

INTRODUCTION

Glioblastoma multiforme (GBM) is the most common primary malignant brain tumor in adults that have been around 70% of high-grade gliomas. The GBM patients' prognosis has been poor with a median survival time about 1-2years [1].

The standard treatment for GBM patients involves maximal surgical resection then adjuvant chemo-radiotherapy [2]. The standard dose is 60 Gy in 30 fractions. The difficulty of GBM radiotherapy is to spare organs at risk (OARs) such as brainstem, optic chiasm, optic nerves, lens and cochlea.

The basic goal of external radiation therapy is to deliver a pre-

scribed dose to the target while minimums dose to OARs. There are a lot of Radiation therapy techniques (3DCRT, IMRT, VMAT, Proton therapy, Radiosurgery, Intra-operative radiotherapy)

3DCRT is the most common technique to treat GBM, but the new techniques such as IMRT and VMAT become available to compete the 3DCRT in GBM which can spare OARs more than 3DCRT and give better dose coverage and conformity.

The treatment plan quality is evaluated by the static dose volume histogram (DVH) parameters. Use a safety margin to insure that 95% of the prescribed isodose line covers the planning target volume (PTV) to make sure that the tumor has been covered. The coverage of PTV could be used as an indicator for clinical target volume (CTV) coverage with geometric uncertainties. So target coverage based on only PTV coverage would be accepted. Unfortunately, in special cases because of a complex patient geometry, physicians should make a compromise between PTV coverage and OARs doses. Patient setup errors at radiotherapy sessions can cause dose variations within the body, which may lead to underdose to a tumor and/or radiation overdose to OARs may be delivered. To reduce this setup errors some methods can be used such as portal image and cone-beam computed tomography (CBCT) [3].

The uses of a portal image by adjusting it with a digitally reconstructed radiograph (DRR) that delivered from treatment planning system (TPS). [The DRR has reconstructed from patient computed tomography (CT) images]. Another advanced method which more accurate that presents in new linears is CBCT can make CBCT at same time of session which can be adjusted with patient CT delivered from TPS [4].

New techniques have highly conformal nature for dose distributions that make it very sensitive to patient setup error.
The aim of this study is to compare the effect of patient setup error on the sensitivity of the delivered dose by different radiotherapy techniques (3DCRT, IMRT, and VMAT). So in this work, we study the effect of patient setup errors on the target evaluation parameters from the origin plans to simulated plans.

MATERIALS and METHODS

A set of 9 GBM cases have a target volume close to OARs are selected. Patients were immobilized in the supine position using an individualized head thermoplastic mask. Computed tomography CT and magnetic resonance imaging (MRI) scan with 3mm slide thickness starting from above head ending under shoulders were used to aid tumor delineation. The CT and MRI are imported into the treatment planning system (TPS) to fuse them for more accurate delineation by a radiation oncologist. The optic nerve, optic chiasm, brain stem, cochlea, eyes and lenses were the structures contoured as OARs.

Plans were designed for treatment by TrueBeam (S.no.1397) linear accelerator system with HD 120 MLC (High Definition Multi-Leaf Collimator, 64 inner leaves with 2.5 mm and 56 outer leaves with 5 mm), 6MV beams were used for all the plans. The plans were performed using the Anisotropic Analytical Algorithm (AAA) photon dose calculation algorithms implemented in the treatment planning system Eclipse version 11.0 designed by (Varian Medical Systems, Palo Alto, CA, USA).
Gross tumor volumes (GTVs) were delineated as the contrast-enhanced area in MRI that were fused with CT [5]. The clinical target volume (CTV) was contoured as the GTV plus a 2cm margin and restricted by the anatomical boundaries such as skull bones, ventricles, and OARs [6]. The planning target volume (PTV) was defined as a 0.5cm geometrical expansion of the CTV.
For each case in this study, three basic plans were generating using the three different techniques (3D-CRT plan, IMRT plan, and VMAT plan). To simulate a systematic setup error that may occur at treatment session an artificial setup error was applied in all plans. That error was considered as an isocenter shift of 3mm, 5mm or 7mm. So in the three techniques, each case had one basic plan plus three plans with setup errors, so the total number is 12 plans for each case. In VMAT dual full arc technique were used in all cases, while in IMRT and 3DCRT the number of beams and beams directions varies from case to another to obtain the optimum plan according to lesion position in each patient.
In all 12 treatment plans, dose distribution was calculated for all cases as well as target evaluation parameters. The difference in target evaluation parameters between the basic plan and setup error plans for each technique were calculated. Comparison of the effect of patient setup error (isocenter shift) in the three different techniques (3D-CRT, IMRT and VMAT) was performed. To compare the effect of patient setup error in different techniques, we used DVH analysis for OARs and PTV to evaluate the plans data like the homogeneity of dose distribution and target dose conformity for the PTV.

Homogeneity index HI: is defined as a ratio between the minimum dose and maximum dose **[7]:**

$$HI = D_2 / D_{98} \quad \textbf{(1)}$$

Where D_2 = minimum dose in 2% of the Planning Target Volume (PTV), indicating the "maximum dose", and D_{98} = minimum dose in 98% of the PTV, indicating the "minimum dose". The lower (closer to one) the index, the better is the dose homogeneity.
Conformity index CI: is defined as the ratio of the target volume and the total volume inside the prescription dose isodose surface, CI is generally used to indicate the volume of a prescription dose that is delivered inside the PTV. CI is expressed as **[8] :**

$$CI = \frac{PTV\,(PD)}{PIV} \quad \textbf{(2)}$$

Conformity number (CN): is defined as a relative measurement of dosimetric target coverage and sparing of normal tissues in a plan of treatment. The CN is expressed as:

$$CN = \frac{PTV\,(PD)}{PTV} x \frac{PTV\,(PD)}{PIV} \quad \textbf{(3)}$$

PTV (PD) refers to PTV coverage at the prescription dose and PIV represents prescription isodose surface volume. When the value is close to unity represents a better target conformity of radiation dose in the plan of treatment, Figure 1 compare between theses definitions

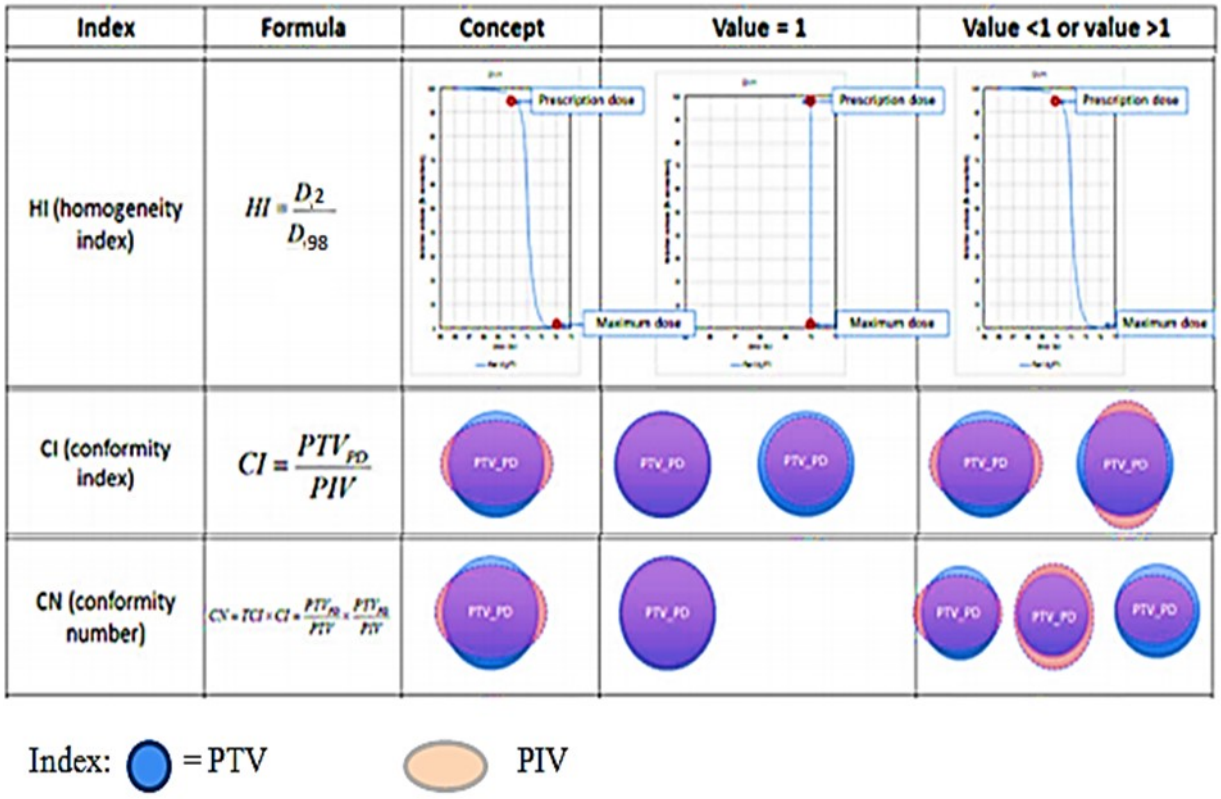

Figure 1. Illustrate the definitions of HI, CI and CN.

Table 1. Example of comparison of PTV dose coverage parameters and OAR dose

Plan parameter	3D	IMRT	VMAT
HI	1.022	1.018	1.004
CI	0.687	0.938	0.903
CN	0.606	0.868	0.883
PTV minimum dose (cGy)	5209	5135	5539
PTV maximum dose (cGy)	6282	6272	6398
PTV mean dose (cGy)	6071	6144	6107
Brainstem maximum dose (cGy)	4375	4018	3927
Brainstem V54Gy(cc)	0	0	0
Brainstem PRV maximum dose (cGy)	5390	5522	5683
Chiasm maximum dose (cGy)	4114	4000	3912
RT optic nerve maximum dose (cGy)	485	508	631
LT optic nerve maximum dose (cGy)	2972	2332	2124
RT lens maximum dose (cGy)	154	696	567
LT lens maximum dose (cGy)	138	564	513

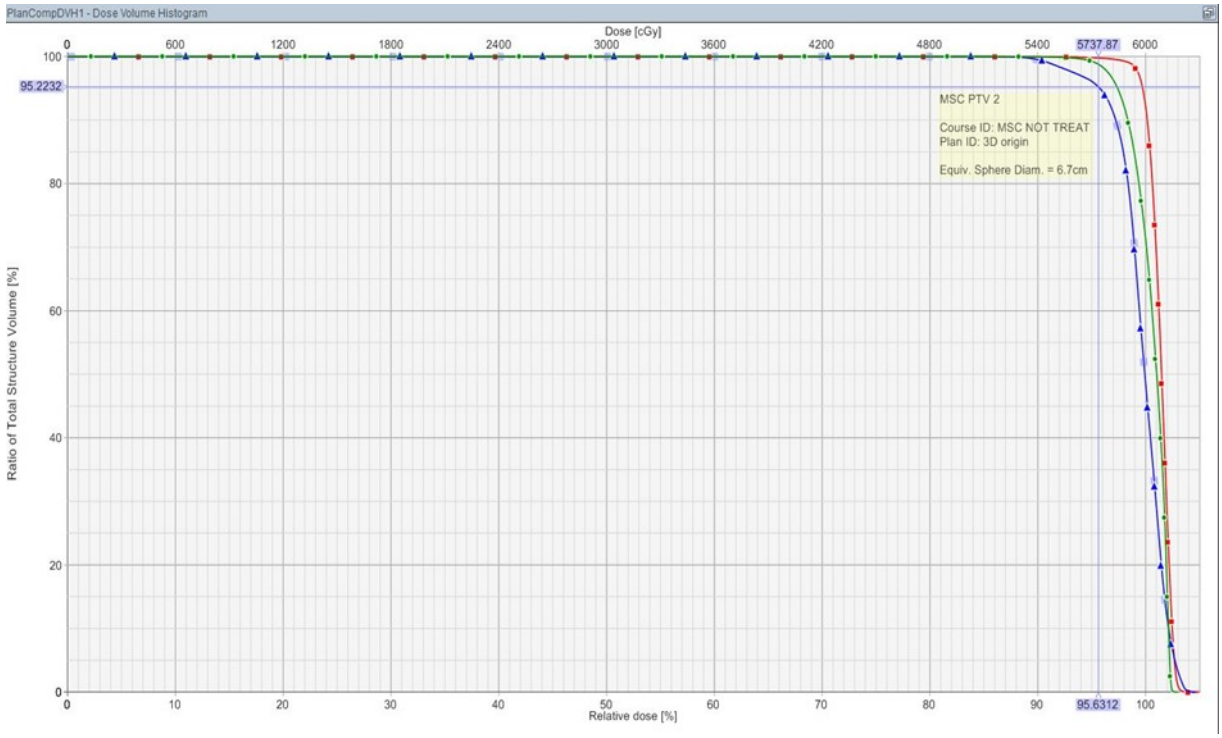

Figure 2. Comparison of PTV in DVH between origin plans of three different techniques (3DCRT blue, IMRT green and VMAT red).

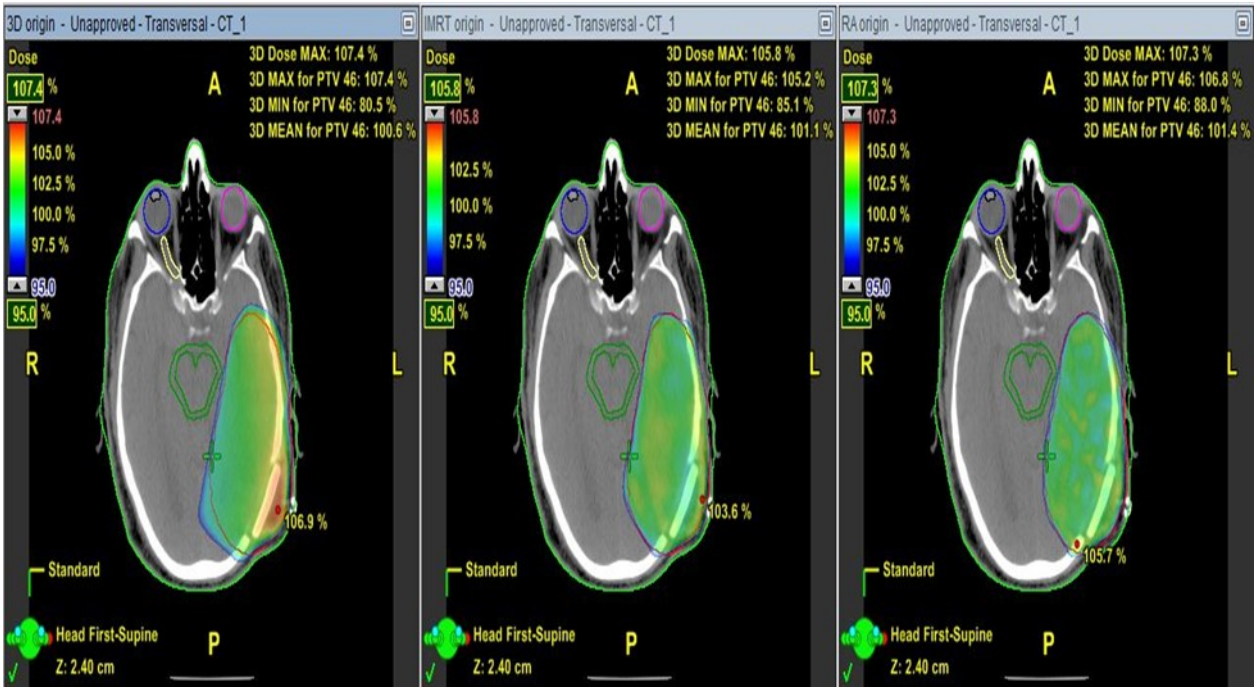

Figure 3. 95% colors wash dose distribution comparison between origin plans of three different techniques (3DCRT, IMRT, and VMAT) in an axial view,

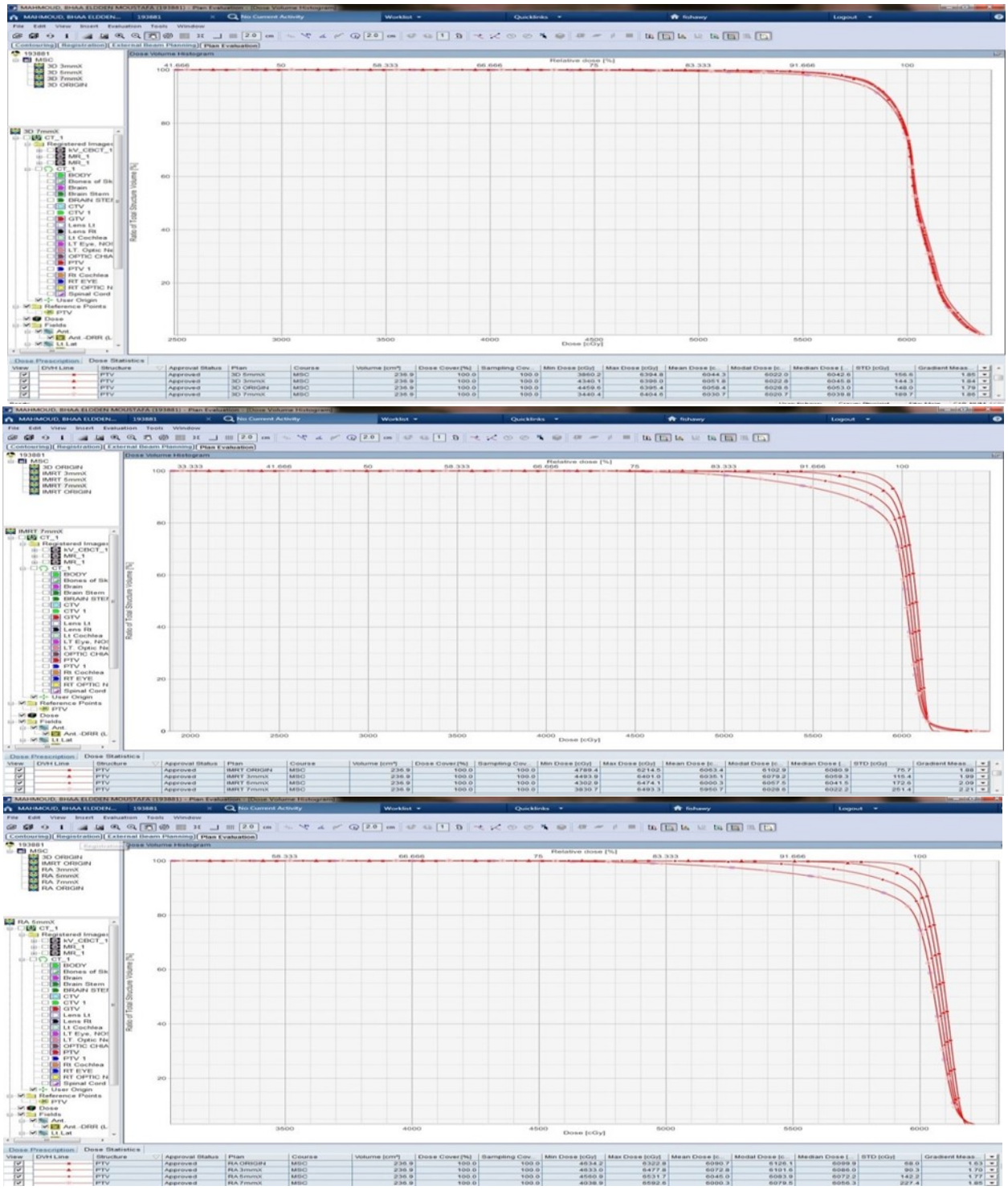

Figure 4. A,B,C. Comparison of PTV in DVH between Tolerated setup error plans in the same technique. (A) 3DCRT - (B) IMRT – (C) VMAT

Table 2. Average percentage of setup error effect on target dose coverage parameters

	HI			CI		
	3D	IMRT	RA	3D	IMRT	RA
3mm error	1.9034	4.7869	3.2642	2.6484	1.4125	3.2591
5mm error	1.0476	11.9040	9.0331	2.0872	5.1228	8.4925
7mm error	0.9929	22.2149	16.4562	0.4612	11.0626	15.3394
	CN			PTV MEAN		
	3D	IMRT	RA	3D	IMRT	RA
3mm error	3.7697	12.7482	12.4831	0.0600	0.5790	0.4444
5mm error	3.3890	25.5194	25.4435	0.1173	1.2403	1.0451
7mm error	1.0563	41.6023	39.0815	0.5638	2.1736	1.9502

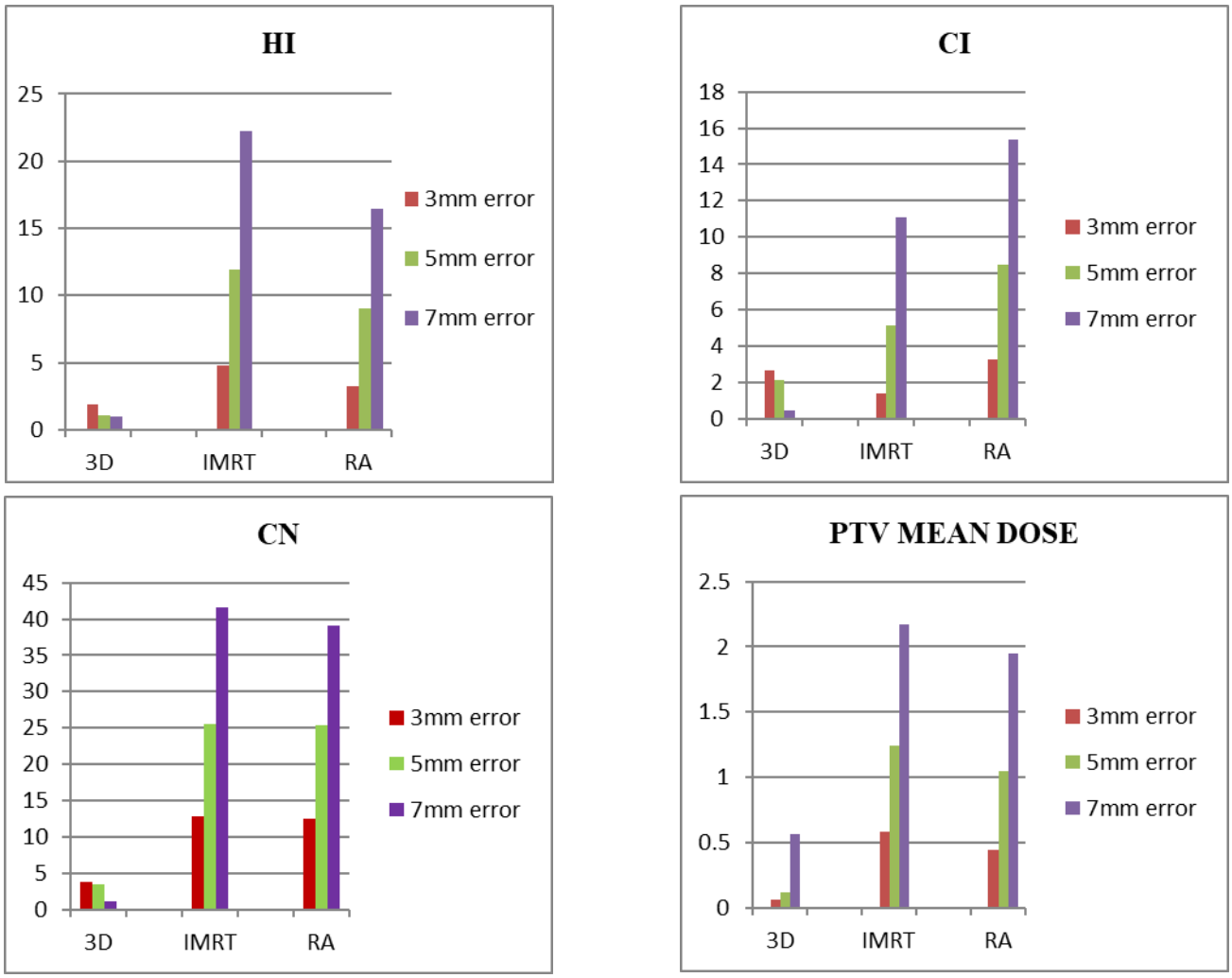

Figure 5. Chart comparison of average percentage of setup error effect on target dose coverage parameters (HI, CI, CN and PTV mean)

RESULTS AND DISCUSSION

In this study the comparison between original plans without error for different techniques gives that both VMAT and IMRT are comparable in OAR sparing and PTV coverage but VMAT is more achieved acceptance criteria, also VMAT is the best choice for easy delivery of treatment and timeless on the machine, while the 3DCRT techniques is last one of the three techniques in target coverage which under coverage for target volume to protect the critical structures.

techniques (3DCRT, IMRT, and VMAT) in an axial view,

When applied the artificial error the dose distribution and plan evaluation parameters were highly affected in VMAT then IMRT while the lowest effect was found in 3DCRT. The setup error effect on delivered dose has appeared clearly in target evaluation parameters (HI, CI, and CN) which the most difference appear in VMAT and IMRT while the effect of setup error is lower in 3DCRT.

The mean dose to the **PTV** from 3mm; 5mm and 7mm setup error was a percentage error range (0.06% to 0.5%) in 3DCRT technique, for IMRT (0.57% to 2.1%), however for VMAT (0.4% to 1.9%).

For the **homogeneity index HI** the effect of setup error due to isocenter shifts in 3DCRT has percentage error range (1% to 1.9%), while increased in IMRT (4.8% to 22.2%) and (3.3% to 16.5%) for VMAT.

For **conformity index CI** the study present that the percentage error range (0.4% to 2.6%) in 3DCRT in the error simulated plans, while in IMRT is (1.4% to 11%) and (3.2% to 15.3%) for the VMAT.

Furthermore for the **conformity number CN** established the large difference between the 3DCRT, IMRT and VMAT due to 3mm, 5mm and 7mm isocenter shifts which give a 3DCRT percentage error range (1% to 3.7%) but for IMRT the range (12.7% to 41.6%) and (12.5% to 39%) for the VMAT.

Then the study explains that the effect on PTV mean dose is less than 3% for all cases until 7mm in three different techniques, while the effect of setup error is very large for CN even it only 3mm shift, however for CI and HI its intermediate effect which is not high sensitive for 3mm setup error but very sensitive to error more than 3mm shift except in 3DCRT technique.

Figure 4 (A, B, C) shows the comparison between PTV curve in DVH for origin plan and isocenter shifted plans (3mm, 5mm & 7mm) in each technique. Which in figure (A) histogram we see a very slight difference between curves in 3DCRT technique while in (C) histogram for VMAT the difference between curves is more apparent and it intermediate in (B) histogram for IMRT.
Table 2 explains the average percentage of errors depending on origin plans of the different technique for all cases that result from isocenter shifted (3mm, 5mm & 7mm). This table contains HI, CI, CN and PTV mean dose percentage errors. This data also illustrates in figure 5 as a chart

CONCLUSIONS

The present study showed that VMAT and IMRT without setup error are comparable in PTV coverage and OAR sparing, however VMAT is more achieved acceptance criteria and more preferable due to easy delivery of treatment and timeless on the machine, on the other hand the 3DCRT techniques is last one of the three techniques in target coverage to protect the critical structures.

The study explains that the setup error effect is appeared clearly in planning target evaluation parameters which shows PTV mean dose percentage error is less than 3% for all cases until 7mm in the three different techniques, while the effect is very large for CN even it only 3mm shift, however for CI and HI its intermediate which is not high sensitive for 3mm shift but very sensitive to error more than 3mm shift except in 3DCRT technique which the effect of setup error was decreased.

Then the used techniques contain a risk because even a small error in treatment planning or delivery may lead to negative effects. For this reason, new verification systems allow to verify the patient position and minimize the patient setup error to treat and cure patients with minimal side effects. So the more advanced techniques are highly complicated which are the most sensitive to the effect of the setup errors.

Then decision of plan selection should not depend on DVH only especially when two competitor techniques that similar in PTV coverage and OAR sparing.

Finally, there is important to make sure that the patient is correctly positioned during advanced treatment techniques to avoid the setup error that's by using verification techniques like the portal image, KV image and cone beam computed tomography and other advanced option.

REFRENCES

1. Miranda, A., et al., Breaching barriers in glioblastoma. Part I: Molecular pathways and novel treatment approaches. International journal of pharmaceutics, 2017. 531(1): p. 372-388.
2. Stupp, R., et al., Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5 -year analysis of the EORTC-NCIC trial. The lancet oncology, 2009. **10**(5): p. 459-466.
3. Wu, Q.J., et al., Adaptive radiation therapy: technical components and clinical applications. The Cancer Journal, 2011. **17**(3): p. 182-189.
4. Steininger, P., et al., Auto-masked 2D/3D image registration and its validation with clinical cone-beam computed tomography. Vol. 57. 2012. 4277-92.
5. Kulkarni, B.S.N., et al., CT- and MRI-based gross target volume comparison in vestibular schwannomas. Reports of Practical Oncology and Radiotherapy, 2017. 22(3): p. 201-208.

6. Minniti, G., et al., Patterns of failure and comparison of different target volume delineations in patients with glioblastoma treated with conformal radiotherapy plus concomitant and adjuvant temozolomide. Radiotherapy and Oncology, 2010. 97(3): p. 377-381.
7. Kataria, T., et al., Homogeneity Index: An objective tool for assessment of conformal radiation treatments. Journal of medical physics/Association of Medical Physicists of India, 2012. 37(4): p. 207.
8. Lee, S., Y.J. Cao, and C.Y. Kim, Physical and Radiobiological Evaluation of Radiotherapy Treatment Plan, in Evolution of Ionizing Radiation Research. 2015, InTech.