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*RESEARCH ARTICLE*

# COMPARISON OF COPLANAR AND NON- COPLANARVMAT FOR BRAIN CANCER BY USING THE DOSIMETRICAL AND RADIOBIOLOGICAL INDICES

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## *Abstract*

**Background:** Recent techniques of radiotherapy such as volumetric modulated arc therapy (VMAT) that delivered in Coplanar technique or non-coplanar technique allows to deliver high doses to the brain tumors, at the same time reducing the risk of normal tissues as compared with intensity modulated radiotherapy (IMRT) and the three-dimensional conformal radiotherapy (3D-CRT).

**Aim:** The aim of the current work is to compare dosimetrical and radiobiological indices of treatment plans for brain tumor using CO-VMAT and NC-VMAT techniques to choose the optimum technique for the treated cases.

**Patients and methods:** Twenty-one cases with brain tumors were performed for the treatment planning study. The cases are planned by using the coplanar and non coplanar VMAT techniques and optimized to evaluate and compare dosimetrical and radiobiological parameters related to PTV dose coverage and sparing of organs at risk. The total dose of CO-VMAT and NC-VMAT plans is 60 Gray in 30 fractions during a single phase with a daily dose of 2 Gray.

**Results:** In dosimetrical calculations, CO-VMAT and NC-VMAT techniques gave similar (homogeneity index HI, modified homogeneity index MHI, conformity index CI and quality factor QF) values for the PTV, while CO-VMAT was the higher in (target coverage index TCI, prescription isodose to target volume ratio PITV and conformity number CN) values and the lower in (gradient index GI, gradient measure GM) values, and NC-VMAT was the lower in Monitor units MUs values. In radiobiological calculations, equivalent uniform dose EUD values, tumor control probability TCP and complication free tumor control probability P+ were large in CO-VMAT and normal tissue complication probability NTCP was less in NC-VMAT.

**Conclusion:** While the previous studies showed that CO-VMAT technique was used when the tumor is far from the organs at risk, the present work found CO-VMAT can be used when the tumor is near to or far from organs at risk (OARs) because it can achieve the target dose coverage and sparing of OARs together. We strongly recommend that NC-VMAT technique should be used when the OARs are located inside the tumor to be able to achieve more sparing of them.

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## Introduction:-

Brain is a soft mass that consists of cerebrum, the cerebellum, the brainstem, nerve cells and the supportive tissues. All these together along with the spinal cord constitute the Central Nervous System (CNS). The expression ‘‘glioma’’ is used to describe a rapidly spreading primary brain tumor. Brain tumor is a heterogeneous tumor and surrounding organs that have less tolerance to radiation (Shantta, & Basir, 2018). Many different types of brain tumors exist. Some brain tumors are noncancerous (benign), and some brain tumors are cancerous (malignant). The growth rate as well as the location of a brain tumor determines how it will affect the function of the nervous system. Brain tumor treatment options depend on the type of brain tumor, as well as its size and location. (Figure 1). The difficulty of treatment planning for brain tumor is the complex shape of target volumes with sparing critical tissues. Due to this complication, the brain planning makes a challenge in development radiotherapy techniques (warnick, & Gozal, 2018).

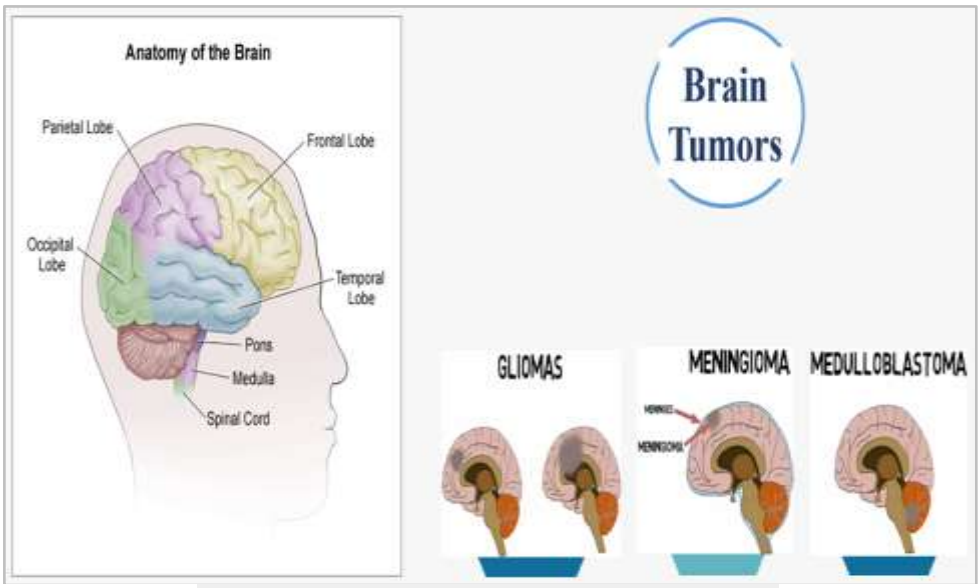



**Figure1:-** Anatomy of the brain and brain tumor types.

Currently, radiation treatment alone or combined with other modalities is the preferred therapy for over 50% of all cancer pathologies due to achieve a high level of killing clonogenic tumor cells within planned treatment volumes (PTVs) while producing minimalor acceptable damage to the normal tissues that will inevitably be exposed to some dose of radiation during the treatment. (Chapman, & Nahum, 2015). Due to the low conformity of PTV inconventional radiation therapy, adjacent organs often fall into the high dose region resulting in less effective treatment (Podgorsak2003). Optimization a plan of treatment in 3D-CRT needs not only the design of optimal field apertures but also number of fields, appropriate beam directions, beam weights and intensity modifiers (Khan 2010). On the other hand, IMRT allows for the radiation dose to conform more precisely to the three-dimensional (3-D) shape of the tumor by modulating or controlling the intensity of the radiation beam in multiple small volumes but due to its complexity, IMRT does require slightly longer daily treatment times and safety checks before the patient can start the treatment (Mayo Clinic, 2022). Thevolumetric modulated arc therapy (VMAT) is an advanced radiotherapy technique that uses arcs of radiation, rather than individual beams used in other types of radiotherapy. This makes the treatment much more targeted and accurate than single beam-based radiotherapy (Otto, 2008 & Shaffer et al, 2010). In addition, it has fewer monitor unit and a shorter delivery time compared to IMRT. Consequently, VMAT is the preferred technique in many clinics (Teoh et al, 2011). VMAT can be delivered through a single arc, or multiple arcs. Multiple arcs may be delivered in a coplanar technique or non- coplanar technique. The coplanar VMAT technique consists of multiple arcs planned in a single axial plane to facilitate the delivery of higher doses in regions of beam intersection. The non-coplanar VMAT technique utilizes multiple beam geometries strategically planned using non-standard couch angles (Cao, 2014).

The ICRU Reports provide clear definitions of target volumes that help in delineating tumors and normal tissues for use in the planning process so the treatment results can be compared, shown in (Figure 2). The organs at risk are usually located nearby tumors and sometime included inside treated volumes, with a risk that the radiation may affect their normal functioning, so the treatment planshould be prepared carefully to avoid damage this OARs function.

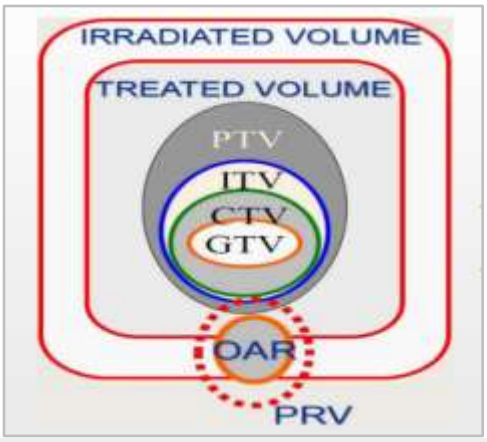



**Figure2:** International Commission on Radiation Units (ICRU) reports 50 and 62 target volumes used in the treatment planning.

For some tumors, PTV may be treated with a plan where normal tissues are not exceeded the accepted tolerance doses. But sometimes the oncologist needs to make a relative risk of normal tissue damage to control the tumor (Barrett et al. 2009). The organs at risk during radiotherapy are: brainstem, chiasm, optic nerves, eyes, lenses, right and left cochlea, and pituitary (Mlynarski et al. 2020).

The aim of the current work is to compare the dosimetrical and radiobiological parameters of CO-VMAT and NC-VMAT treatment plans with regard to the coverage of planning target volume (PTV) and the sparing of organs at risk (OARs) for brain tumor.

## Materials and Methods: -

Twenty-one cases with brain tumors that previously diagnosed at Oncology Department, Ain Shams University Hospitals were performed for the treatment planning study. The CT images was imported into the treatment planning system (TPS) to perform more accurate delineation. TPS was used in this study to achievethe aim of radiation therapy which provides the maximum dose to the target and the minimum dose to the OARs. The cases are planned using the Coplanar and Non coplanar VMAT techniques and optimized to compare the radiobiological and dosimetrical parameters. In treatment setup and imaging, patients were imaged and treated in the supine position and immobilized with a system consisting of a standard carbon support, a carbon headrest and a personalized mask (Figure 3).

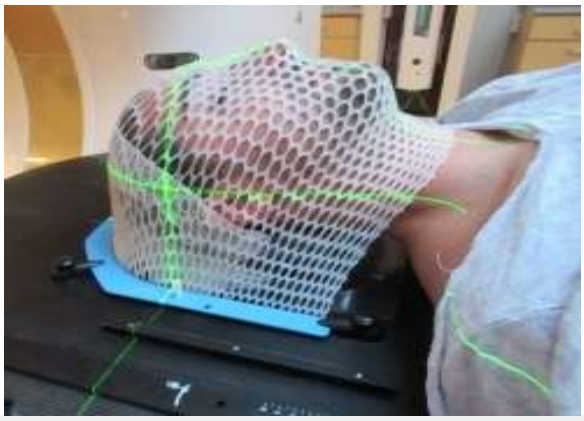


**Figure3: -**Immobilizing system, by thermoplastic mask, used in brain radiotherapy.

CT images of patients were taken in separate axial cuts with 3mm slice thickness from above head to under shoulders on multislice CT scanner. CT scan has DICOM 3.0 features to enhance the images and fixed laser light that used for helping in patient positioning (Figure 4).

**Figure4: -**CT scanner in radiotherapy.

The treatment planning system (TPS) used in radiotherapy is Eclipse version 13.5 designed by Varian Medical Systems planning software using a DICOM network connection with the Anisotropic Analytical Algorithm (AAA) photon dose calculation algorithms in order to simplify modern radiation therapy planning for all techniques of treatment. Treatment plans were generated by TrueBeam linear accelerator system designed by Varian Medical Systems, it was used in this study with millennium 120 Multi-Leaf Collimators (MLCs), 64 inner leaves with 2.5 mm and 56 outer leaves with 5 mm (Figure 5).

**Figure 5:** Varian Unique Linear Accelerator.

All cases were planned using a coplanar and non-coplanar volumetric modulated arc therapy techniques. All VMAT plans were created two half arcs with 6 MV photon beams energy at a maximum dose rate of 600 monitor unit per minute (Figure 6). The single isocenter for all VMAT plans was specified at the center of the tumor. Field sizes were formed by the arc geometry tool in treatment planning system. Both the Co-VMAT and NC-VMAT treatment plans were evaluated for each case and radiobiological and dosimetrical parameters were taken for calculations and analysis.

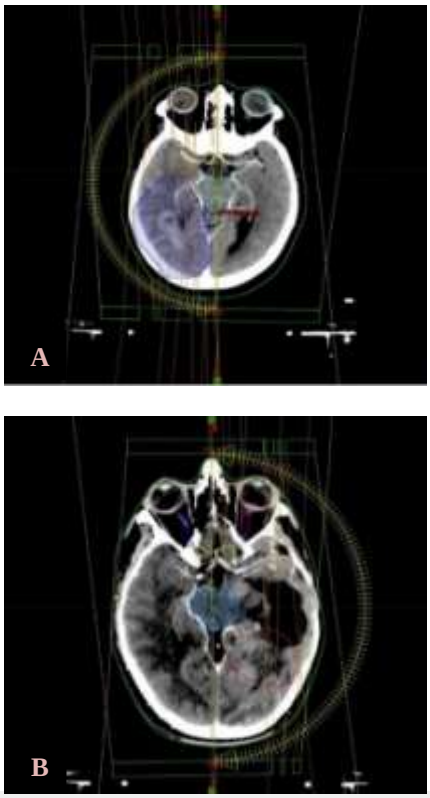
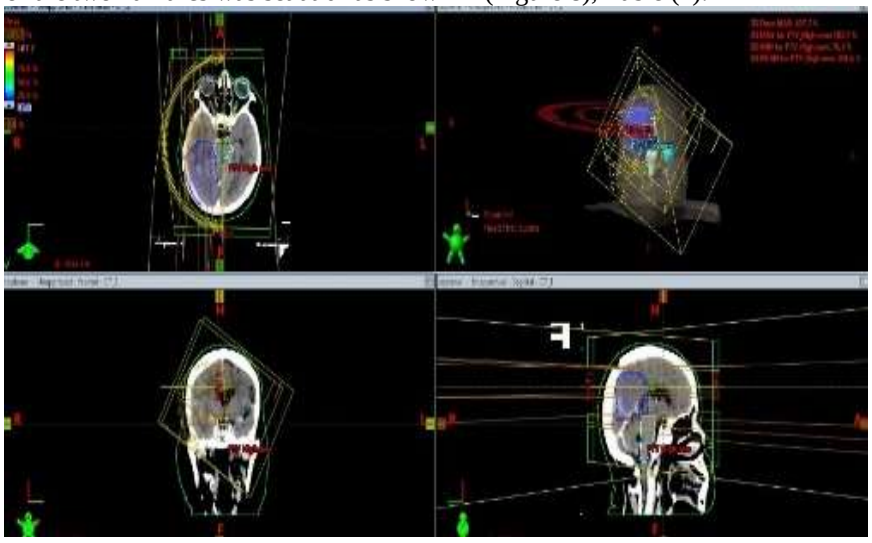



**Figure 6:-** VMAT plans created with two half arcs in the right (A) and leftside (B) of the brain.

In CO-VMAT plans, the first arc rotated with gantry angle clockwise from 181° to 0° and the second arc rotated with gantry angle counter-clockwise from 0° to 181° for cases with PTV on the right side of the brain. While for cases with PTV located at the left side of the brain, the gantry angle of the two half arcs was set counter-clockwise from 179° to 0° and clockwise 0° to 179° of both arcs, the collimator rotation was set at 30° for clockwise arc and 330° for counter-clockwise arc and the couch angle were set at 0° as shown in (Figure 7), Table (1).

In NC-VMAT plans, the couch angle was set at 25° for clockwise arc and 15° for counter-clockwise arc and the gantry angle for both arcs were set from 0° to 181°and 181° to 0° for cases with PTV on the right side of the brain. While for cases with PTV located at the left side of the brain, the couch angle was set at 350° for clockwise arc and 10° for counter-clockwise arc and the gantry angle for the two arcs was set from 0° to 179° and 179° to 0°. The collimator rotation for the two half arcs was set at 0° as shown in (Figure 8), Table (2).



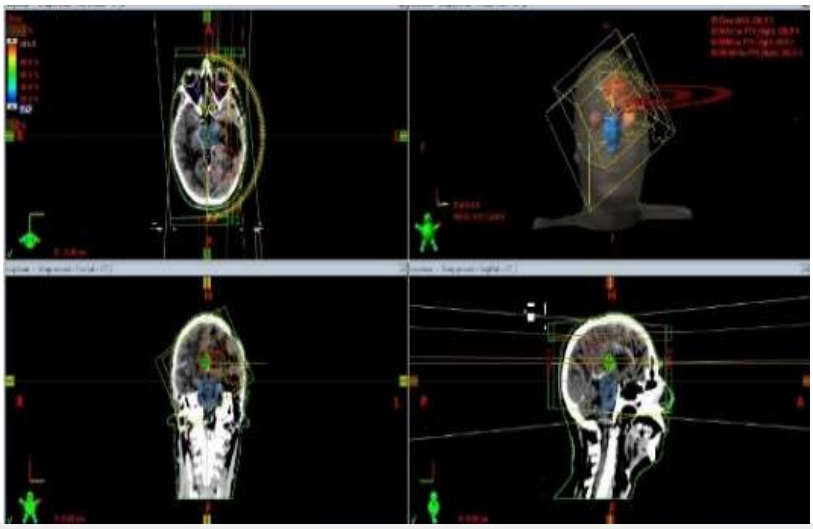


**Figure7:-** CO-VMAT plans fields arrangement in the right and left side of the brain.

**Table 1:-** CO-VMAT plans geometry:

| | | | | |
|---|---|---|---|---|
| PTV right | **Field** | **Gantry angle** | **Collimator angle** | **Couch angle** |
| | Field 1 | 181° to 0° - cw | 30 | 0 |
| | Field 2 | 0° to 181° - ccw | 330 | 0 |
| PTV left | **Field** | **Gantry angle** | **Collimator angle** | **Couch angle** |
| | Field 1 | 0° to 179° - cw | 30 | 0 |
| | Field 2 | 179° to 0° - ccw | 330 | 0 |

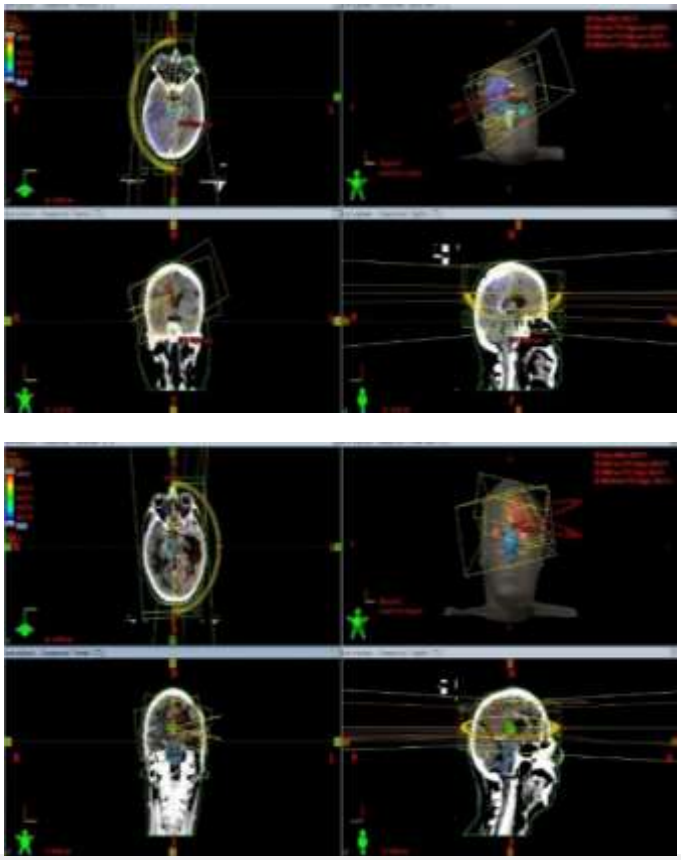


**Figure8: -**NC-VMAT plans fields arrangement in the right and left side of the brain.

**Table 2: -** NC-VMAT plans geometry:

| | | | | |
|---|---|---|---|---|
| PTV right | **Field** | **Gantry angle** | **Collimator angle** | **Couch angle** |
| | Field 1 | 181° to 0° - cw | 30 | 25 |
| | Field 2 | 0° to 181° - ccw | 330 | 15 |
| PTV left | **Field** | **Gantry angle** | **Collimator angle** | **Couch angle** |
| | Field 1 | 0° to 179° - cw | 30 | 350 |
| | Field 2 | 179° to 0° - ccw | 330 | 10 |

The CO-VMAT and NC-VMAT plans were prepared to deliver a daily dose of 2 Gy for a total dose of 60 Gy in 30 fractions in a single phase. Dose distribution was normalized and defined on PTV dose. VMAT plans were generated to deliver a high dose to PTV while sparing the surrounding critical organs that may be affected if exposed to radiotherapy more than the required tolerance dose. For this reason, tolerance limits of organs at risk are applied as shown in Table (3) (Maguire et al, 2010).

**Table 3:-** PTV and OARs tolerance limits for all VMAT plans:

| **Target coverage** | **Dose constraints (Gy)** |
|---|---|
| PTV | ◆ $D_{max}$ < 108% of prescription dose (60 Gy)<br>◆ $D_{min}$ > 90% of prescription dose<br>◆ $D_{95\%} \geq 95\%$ |
| **Critical normal organs** | **Dose constraints (Gy)** |
| Brainstem | $D_{max} < 54$ Gy |
| Optic chiasm | $D_{max} < 54$ Gy |
| Optic nerves | $D_{max} < 54$ Gy |
| **Other normal organs** | **Dose constraints (Gy)** |
| Eyes | $D_{mean} < 35$ Gy, $D_{max} < 50$ Gy |
| Lens | $D_{max} < 7$ Gy |
| Cochlea | $D_{mean} \leq 45$ Gy |
| Pituitary | $D_{mean} < 45$ Gy, $D_{max} < 50$ Gy |

Physical dosimetric and radiobiological indices are very useful parameters that can help in evaluating the target dose coverage and OARs doses from treatment plan to other for comparison. An isodose distribution and DVH for the evaluation of advanced treatment planning techniques were insufficient. As a result, there are several quantitative evaluation indexes that may represent target conformity and dose homogeneity such as:

**Prescription isodose to target volume (PITV) ratio:** is obtained by dividing prescription isodose surface volume (PIV) by target volume (TV), and is defines as:

$$PITV = PIV/TV \quad (1)$$

The PITV ratio is a measure of conformity and a value of 1.0 does not necessary means that both PIV and TV are the same. (Lee, & Cao, et al. 2015)

**Homogeneity index (HI):** is defined as the ratio of minimum dose delivered to the PTV (Dmin) divided by the maximum dose delivered to the PTV (Dmax), and is expressed as:

$$HI = Dmin/Dmax \quad (2)$$

HI of close to 1 (Lower values) indicates the ideal uniform dose homogeneity within the PTV. (Kataria, &Sharma, et al. 2012)

**Modified homogeneity index (MHI):** is similar to HI equation; in this study we described the term of Dmax = $D_{95}$ and the term of Dmin = $D_5$.

$$MHI = D_5/D_{95} \quad (3)$$

**Target coverage index (TCI):** is defined as the ratio of the target volume at least the prescription dose ($PTV_{PD}$) and the total target volume (TV), is classified as:

$$TCI= PTV_{PD}/TV \quad (4)$$

**Conformity index (CI):** is defined as the ratio of target volume that coverage at the prescription dose ($PTV_{PD}$) and the total volume inside the isodose surface that corresponds to the prescription dose (PIV), is explained as:

$$CI= PTV_{PD}/PIV \quad (5)$$

CI represents that 100% of a prescribed dose is delivered to a target, and no dose is delivered to adjacent tissues. Higher CI values refer to poorer dose conformity to the PTV.

**Conformity number (CN):** is a relative measurement of dosimetric target coverage and normal tissues sparing in a plan of treatment, and is described as:

$$CN= PTV_{PD}/PTV \times PTV_{PD}/PIV \quad (6)$$

The CN value (that is close to unity) indicatesa better target conformity of radiation dose in a treatment plan. (Feuvret, & Noel, et al. 2006).

**Gradient index (GI):** is defined as the ratio of the volume covered by at least 50% of the prescription dose ($V_G$) to the volume covered by the full prescription dose ($V_P$) is explained as:

$$GI= V_G/V_P = V_{50}/V_{100} \quad (7)$$

GI value (that is closer to unity) indicates a lower dose to critical structures in the treatment plan (Paddick et al. 2006).

**Gradient measure (GM):** is a quantity determined to express the dose gradient value in centimeters by Eclipse treatment planning software.

**Monitor units (MUs):** is used as a measure of a patient's radiation time on the machine in each treatment plan. More radiation time on the machine can lead to setup error.

**Quality factor (QF):** is evaluating the quality of an entire plan and mainly used to compare the conformity of various treatment plans, and is expressed as:

$$QF= [2.718 \exp (-\sum_{i=1}^{N} Wi\ Xi)] \quad (8)$$

$X_i$ represents all PTV indices and $W_i$ represents the weighting factor (Kim et al, 2018).

To investigate the radiobiological effect for the target volume and different OARs, the **tumor control probability(TCP)**, **normal tissue complication probability(NTCP)**and **tumor control without normal tissue complications or complication free tumor control probability ($P^+$)** were determined from cumulative DVH utilizing various optimization algorithms for radiation therapy techniques.

**Equivalent uniform dose (EUD)** is known as the dose with uniform distribution over a structure, which would produce a similar outcome as the dose calculated by the DVH. The EUD determined by Niemierko's phenomenological model is expressed as:

$$EUD=(\sum_{i=1} V_i D_i^a)^{\frac{1}{a}} \quad (9)$$

Where a is unitless model parameter that is derived from normal tissues or tumor of interest, $V_i$ indicates to the $i^{th}$ partial volume that received a dose of $D_i$ in Gy and $D_i^a$is the biologically equivalent physical dose of 2 Gy.

**TCP**is a common term used to predict the target control at a specific time. The TCP model is expressed as:

$$TCP= 1/(1+(TCD_{50}/EUD) \hat{}\gamma_{50} \quad (10)$$

**NTCP** is similar to TCP, it used to express the complication rate of a normal tissue at a defined end point. The NTCP model is described as:

$$NTCP= 1/1+(TD_{50}/EUD) \hat{}\gamma_{50} \quad (11)$$

$TCD_{50}$ is the target dose to control 50% of the target when irradiated homogeneously, $TD_{50}$ is the tolerance dose for a 50% complication probability at a specific time interval and $\gamma_{50}$ is a unitless parameter derived from the slope of the dose-response curve that is particular to normal organ or tumor of interest.

During this study, the different radiobiological parameters such as: the value of parameter a, $\gamma_{50}$, $TCD_{50}$, $TD_{50}$, DEF, and $\alpha/\beta$ that were used to calculate TCP and NTCP were taken, as tabulated in Table (4).

**$P^+$** is a term gives a single value that takes into regard TCP and NTCP values from a plan of treatment to predict outcomes of treatment. $P^+$ is determined as:

$P^+ = TCP\ (1-NTCP)$

$P^+ = TCP-NTCP+\delta \cdot 1-TCP \cdot NTCP \quad (12)$

where $\delta=0.2$, defines the patients fraction TCP and NTCP (Zhao, 2010).

**Table 4:-** Radiobiological parameters for calculating TCP and NTCP.

| Parameters | Tumor and OARs | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Brain Tumor** | **Brainstem** | **Chiasm** | **Optic nerve_Rt.** | **Optic nerve_Lt.** | **Lens_Rt.** | **Lens_Lt.** |
| **A** | -13 | 7 | 25 | 25 | 25 | 3 | 3 |
| $\boldsymbol{\gamma_{50}}$ | 2.28 | 3 | 3 | 3 | 3 | 1 | 1 |
| $\boldsymbol{TCD_{50}/TD_{50}}$ | 51.77 | 54 | 54 | 54 | 54 | 18 | 18 |
| **DEF** | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| $\boldsymbol{\alpha/\beta}$ | 10 | 3 | 3 | 3 | 3 | 3 | 3 |
| **References** | Gay, &Niemierko, 2007 | Emami et al, 1991 | | | | | |

## Results:-

The process of evaluation radiotherapy plan is depending on target dose coverage and sparing organs at risk by dose statistics from the DVH, which used to compare CO-VMAT and NC-VMAT techniques of the treatment plans. The results of this study include comparing dosimetrical and radiobiological indices in CO-VMAT and NC-VMAT techniques to choose the optimum technique for the treated cases.

In DVH curves the lines with triangle indicate to CO-VMAT while the lines with squares symbolize to NC-VMAT (Figure 9). This figure shows that CO-VMAT curve gives the better PTV coverage in comparison NC-VMAT curve.

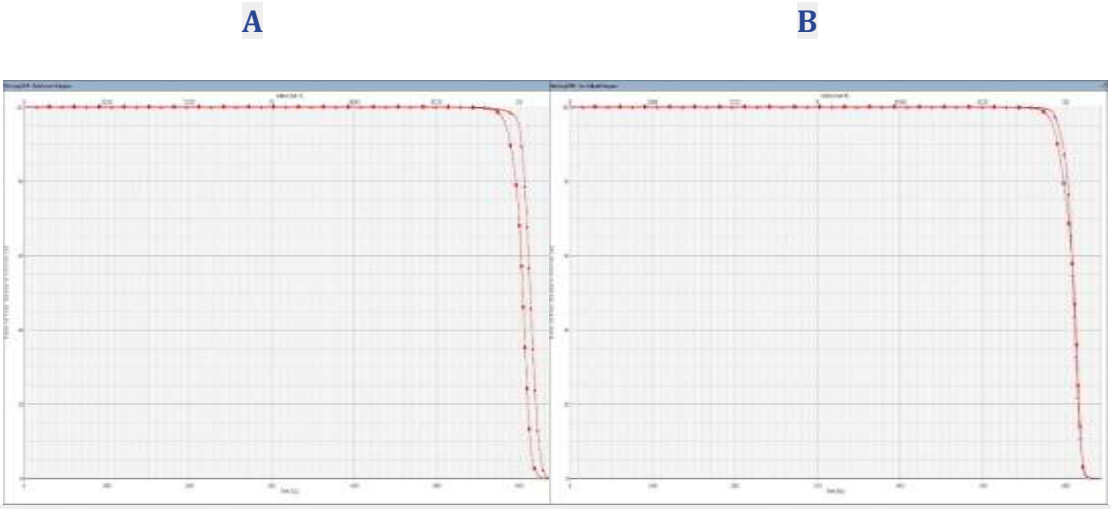



**Figure 9:**- DVH comparison of PTV left (A) and PTV right (B) between CO-VMAT (Δ) and NC-VMAT (■)

Dose distribution is one of important radiation therapy method in process of plan analysis and evaluation. (Figure 10 and 11) illustrate comparison of the target dose distribution (95% of the target dose – 57Gy) between coplanar and non-coplanar VMAT techniques in the same CT slices respectively. The dose distributionfor both techniques were approximately the same. The CO-VMAT dose volumetric values were slightly higher compared to the NC-VMAT values. Furthermore, the overall dose volumetric parameters of CO-VMAT and NC-VMAT keep somewhat similar and still within the limits of tolerance dose were shown in Table (5), Chart (1).

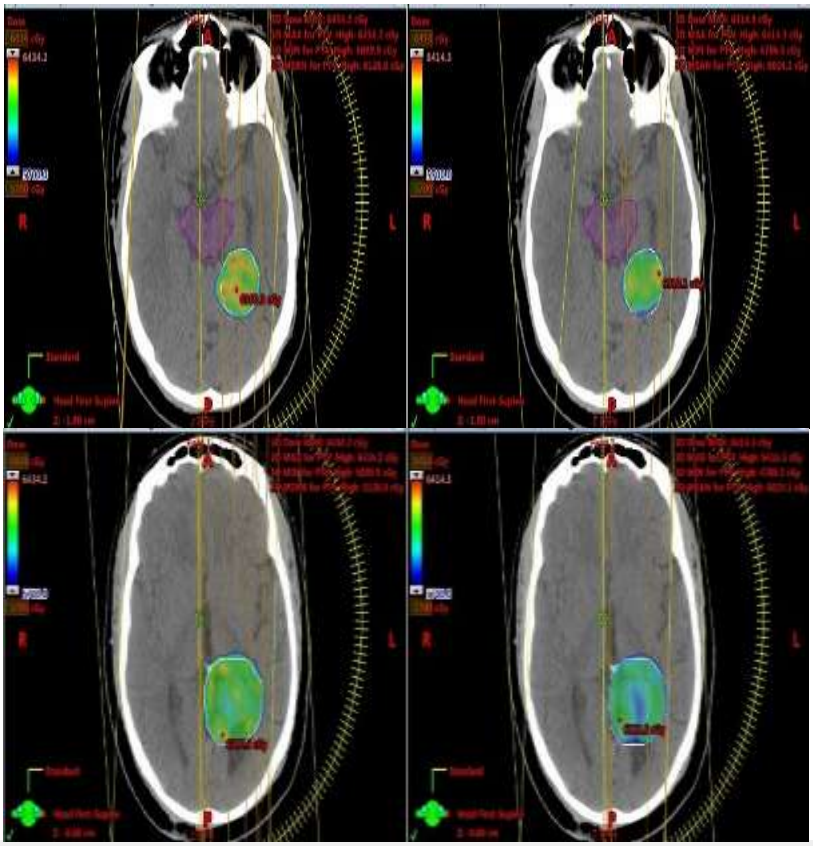


**Figure 10:**- Dose distribution comparison of PTV left for CO-VMAT and NC-VMAT.

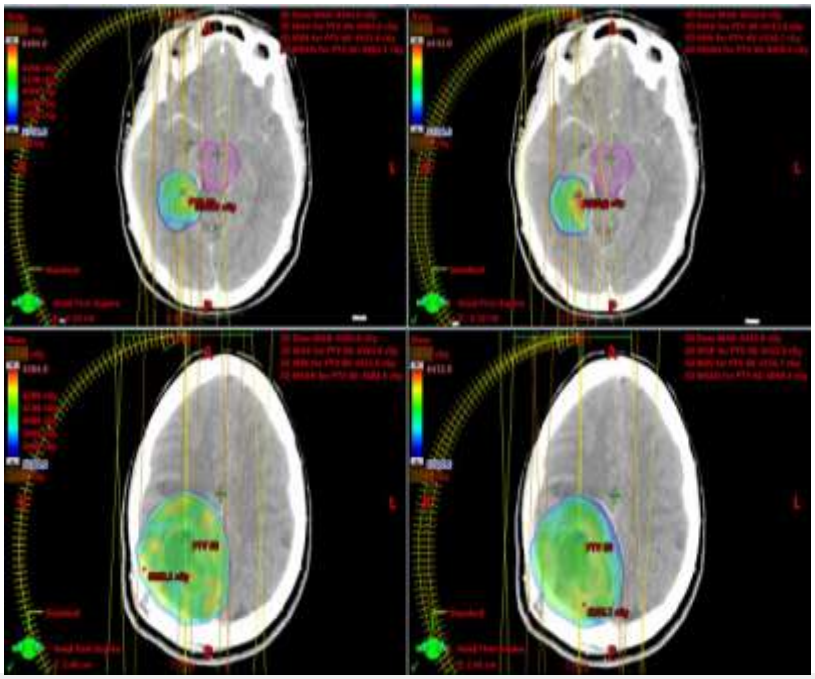
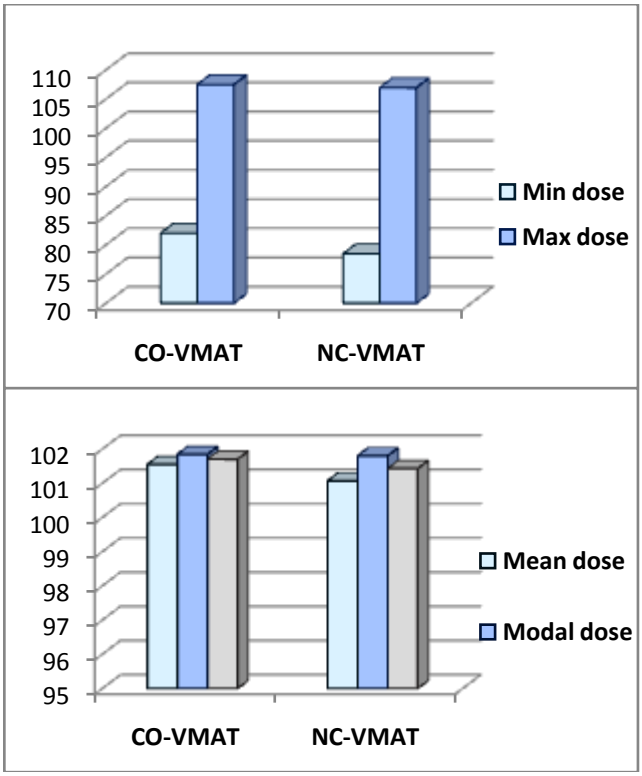


**Figure 11:-** Dose distribution comparison of PTV right for CO-VMAT and NC-VMAT.

**Table 5: -**The dose volumetric statistics of PTV for both CO-VMAT and NC-VMAT with STD statistics.

| Index | Dmin | | Dmax | | Dmean | | Modal Dose | | Median Dose | | STD | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Technique | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC--VMAT |
| AVG | 81.99 | 78.46 | 107.45 | 106.93 | 101.55 | 101.07 | 101.84 | 101.80 | 101.70 | 101.43 | 0.99 | 1.12 |
| p-value | 0.002310 | | 0.012543 | | 0.001396 | | 0.714702 | | 0.032790 | | 0.000262 | |



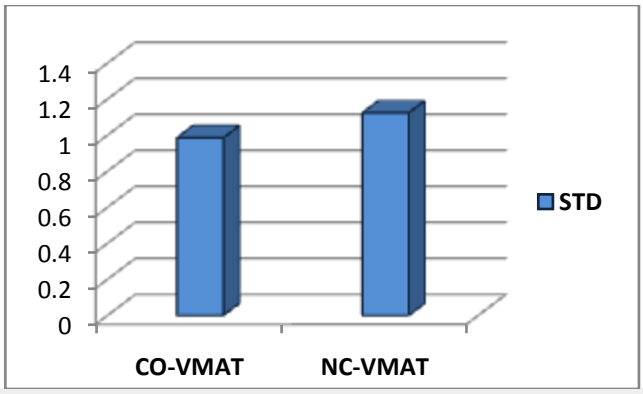



**Chart 1:-** The dose volumetric parameters for CO-VMAT and NC-VMAT.

The comparison of (HI, MHI, TCI and PITV values) between the CO-VMAT and NC-VMAT plans for all cases were tabulated in Table (6), Charts (2). The HI and MHI average results of PTV60 were in this study (1.09, 1.10) and (1.05, 1.06) for CO-VMAT and NC-VMAT. In addition, the average variance percentage and P-value were (1.05%, 0.004282) and (0.71%, 0.000494). For the TCI and PITV average, the results represented in the study were (0.86, 0.79) and (0.93, 0.83) for the both techniques of VMAT (CO-VMAT and NC-VMAT). And also, the average variance percentage and P-value were (-9.96%, 0.000542) and (-12.38%, 0.000253).

CI, CN, GI, GM, MU and QF values comparison for all cases between the CO-VMAT and NC-VMAT plans were represented in Table (7), Charts (3). The CI and CN average results for the two VMAT techniques (CO-VMAT and NC-VMAT) were in the study (0.93, 0.95) and (0.81, 0.75). And also, the average variance percentage and P-value were (2.00%, 0.003526) and (-7.69%, 0.001097).

For the average of GI and GM, the results in this study were (3.13, 3.42) and (1.53, 1.62) for CO-VMAT and NC-VMAT. In addition, the average variance percentage and P-value were (7.10%, 0.007075) and (5.49%, 0.000645). The study shown that the MUs and QF average results for the two techniques of VMAT were (330.29, 321.43) and (2.50, 2.49) in CO-VMAT and NC-VMAT. And, the average variance percentage and P-value were (-2.94, 0.046024) and (-0.28, 0.030024).

Table (8), Chart (4) illustrates the average variance percentage data of HI, MHI, TCI, PITV, CI, CN, GI, GM, MU, QF for the both VMAT techniques. The upper column indicates that CO-VMAT has a feature while the lower column is the inverse

**Table 6:-** HI, MHI, TCI and PITV values comparison for all cases.

| Index | HI | | MHI | | TCI | | PITV | |
|---|---|---|---|---|---|---|---|---|
| Case | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT |
| 1 | 1.08 | 1.09 | 1.05 | 1.05 | 0.90 | 0.89 | 0.94 | 0.94 |
| 2 | 1.09 | 1.10 | 1.05 | 1.05 | 0.85 | 0.79 | 0.89 | 0.81 |
| 3 | 1.08 | 1.09 | 1.05 | 1.05 | 0.94 | 0.68 | 1.01 | 0.70 |
| 4 | 1.06 | 1.06 | 1.03 | 1.03 | 0.98 | 0.95 | 1.08 | 1.04 |
| 5 | 1.06 | 1.08 | 1.04 | 1.05 | 0.91 | 0.81 | 0.97 | 0.83 |
| 6 | 1.14 | 1.14 | 1.08 | 1.09 | 0.82 | 0.71 | 0.84 | 0.72 |
| 7 | 1.09 | 1.07 | 1.03 | 1.04 | 0.82 | 0.91 | 0.85 | 0.97 |
| 8 | 1.13 | 1.14 | 1.07 | 1.08 | 0.72 | 0.63 | 0.75 | 0.66 |
| 9 | 1.07 | 1.07 | 1.04 | 1.05 | 0.94 | 0.84 | 0.96 | 0.85 |
| 10 | 1.07 | 1.09 | 1.05 | 1.06 | 0.85 | 0.76 | 0.86 | 0.76 |
| 11 | 1.08 | 1.11 | 1.04 | 1.06 | 0.95 | 0.84 | 1.03 | 0.86 |
| 12 | 1.06 | 1.09 | 1.04 | 1.06 | 0.88 | 0.69 | 0.95 | 0.70 |
| 13 | 1.11 | 1.15 | 1.05 | 1.06 | 0.64 | 0.71 | 1.09 | 1.10 |
| 14 | 1.07 | 1.07 | 1.04 | 1.04 | 0.93 | 0.85 | 0.98 | 0.87 |
| 15 | 1.09 | 1.13 | 1.05 | 1.07 | 0.82 | 0.67 | 0.86 | 0.68 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 16 | 1.13 | 1.12 | 1.08 | 1.08 | 0.75 | 0.64 | 0.80 | 0.70 |
| 17 | 1.10 | 1.10 | 1.06 | 1.06 | 0.86 | 0.84 | 0.87 | 0.86 |
| 18 | 1.08 | 1.08 | 1.04 | 1.04 | 0.95 | 0.96 | 1.00 | 1.00 |
| 19 | 1.06 | 1.08 | 1.04 | 1.05 | 0.90 | 0.79 | 0.97 | 0.81 |
| 20 | 1.12 | 1.12 | 1.07 | 1.07 | 0.75 | 0.74 | 0.77 | 0.76 |
| 21 | 1.08 | 1.12 | 1.05 | 1.06 | 0.94 | 0.86 | 1.01 | 0.89 |
| **Average** | 1.09 | 1.10 | 1.05 | 1.06 | 0.86 | 0.79 | 0.93 | 0.83 |
| **p-value** | 0.004282 | | 0.000494 | | 0.000542 | | 0.000253 | |

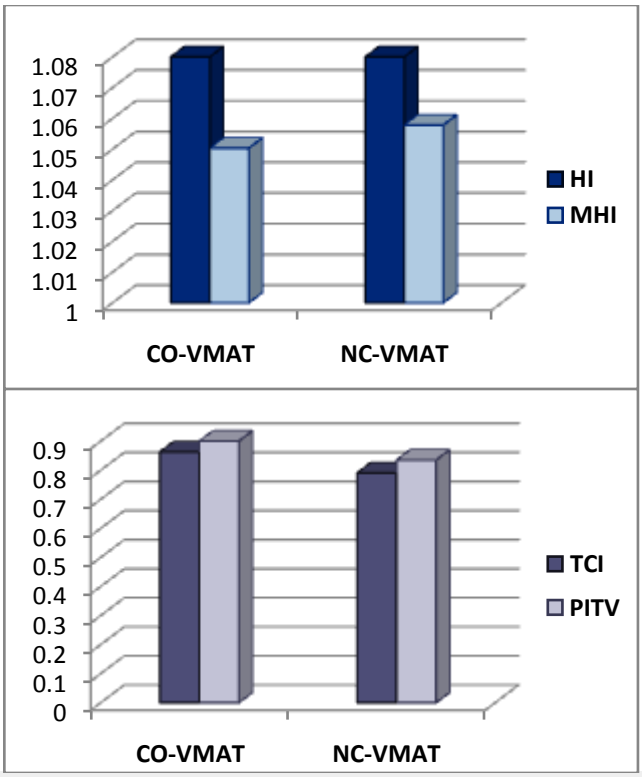
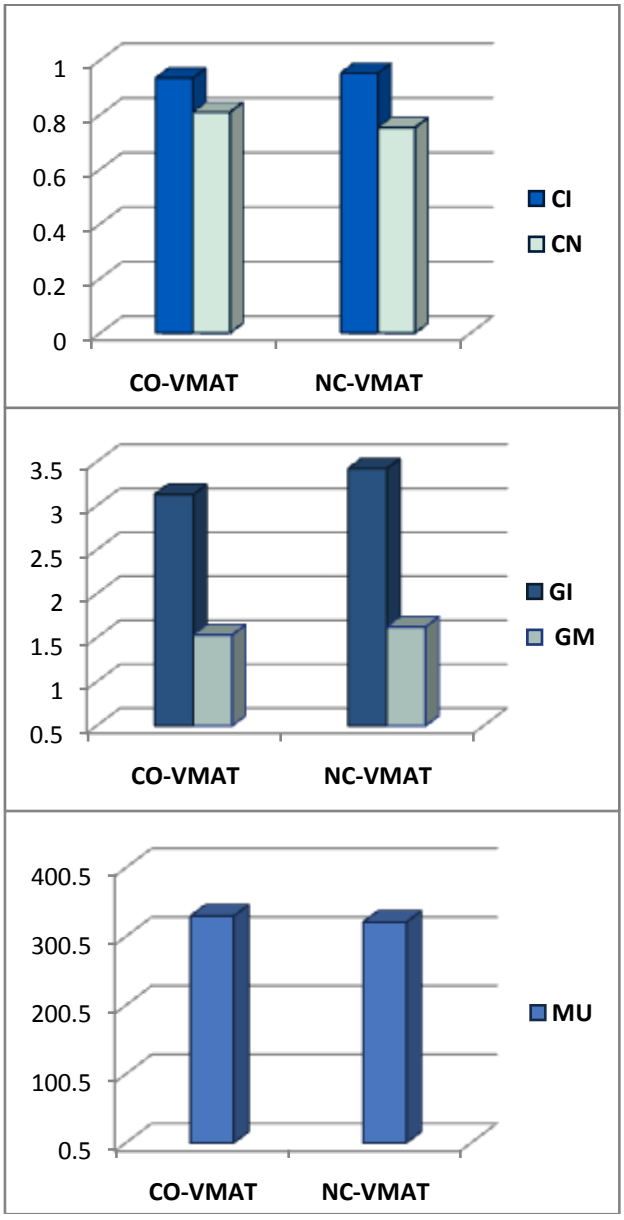



**Chart 2:-** HI, MHI, TCI and PITV comparison between CO-VMAT and NC-VMAT.

**Table 7:-** CI, CN, GI, GM, MU and QF comparison between CO-VMAT and NC-VMAT.

| **Index** | **CI** | | **CN** | | **GI** | | **GM** | | **MU** | | **QF** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Case** | **CO-VMAT** | **NC-VMAT** | **CO-VMAT** | **NC-VMAT** | **CO-VMAT** | **NC-VMAT** | **CO-VMAT** | **NC-VMAT** | **CO-VMAT** | **NC-VMAT** | **CO VMAT** | **NC-VMAT** |
| 1 | 0.95 | 0.95 | 0.85 | 0.85 | 2.81 | 2.79 | 1.55 | 1.53 | 324 | 311 | 2.50 | 2.50 |
| 2 | 0.96 | 0.98 | 0.82 | 0.77 | 2.78 | 3.03 | 1.44 | 1.54 | 313 | 305 | 2.51 | 2.50 |
| 3 | 0.93 | 0.97 | 0.88 | 0.66 | 4.28 | 5.30 | 1.34 | 1.4 | 419 | 399 | 2.46 | 2.45 |
| 4 | 0.90 | 0.92 | 0.88 | 0.88 | 3.22 | 3.38 | 1.53 | 1.58 | 361 | 341 | 2.48 | 2.48 |
| 5 | 0.94 | 0.97 | 0.85 | 0.79 | 3.15 | 3.81 | 1.4 | 1.6 | 351 | 352 | 2.50 | 2.47 |
| 6 | 0.98 | 0.98 | 0.80 | 0.69 | 2.63 | 3.00 | 1.47 | 1.63 | 259 | 251 | 2.52 | 2.51 |
| 7 | 0.97 | 0.94 | 0.79 | 0.86 | 3.26 | 3.28 | 1.24 | 1.28 | 352 | 335 | 2.51 | 2.49 |
| 8 | 0.96 | 0.96 | 0.69 | 0.61 | 3.57 | 3.87 | 1.56 | 1.62 | 264 | 301 | 2.49 | 2.49 |
| 9 | 0.98 | 0.99 | 0.92 | 0.83 | 3.09 | 3.75 | 1.57 | 1.81 | 325 | 332 | 2.49 | 2.47 |
| 10 | 0.99 | 0.99 | 0.84 | 0.76 | 3.19 | 3.67 | 1.7 | 1.87 | 344 | 306 | 2.49 | 2.47 |
| 11 | 0.93 | 0.98 | 0.88 | 0.83 | 2.50 | 2.99 | 1.39 | 1.61 | 343 | 346 | 2.51 | 2.50 |
| 12 | 0.93 | 0.99 | 0.82 | 0.68 | 3.09 | 4.06 | 1.35 | 1.58 | 302 | 281 | 2.50 | 2.48 |
| 13 | 0.59 | 0.65 | 0.38 | 0.46 | 2.90 | 2.92 | 1.9 | 1.82 | 410 | 406 | 2.52 | 2.51 |
| 14 | 0.95 | 0.98 | 0.89 | 0.84 | 3.60 | 3.80 | 1.59 | 1.6 | 326 | 324 | 2.47 | 2.47 |
| 15 | 0.95 | 0.99 | 0.78 | 0.67 | 2.66 | 3.23 | 1.78 | 2.02 | 307 | 274 | 2.51 | 2.49 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 0.94 | 0.92 | 0.70 | 0.59 | 3.69 | 4.13 | 1.81 | 1.92 | 292 | 257 | 2.48 | 2.47 |
| 17 | 0.98 | 0.98 | 0.84 | 0.83 | 2.86 | 2.78 | 1.67 | 1.61 | 289 | 313 | 2.50 | 2.50 |
| 18 | 0.95 | 0.96 | 0.91 | 0.92 | 3.54 | 2.44 | 1.37 | 1.37 | 336 | 327 | 2.48 | 2.52 |
| 19 | 0.93 | 0.97 | 0.84 | 0.77 | 2.87 | 3.50 | 1.39 | 1.59 | 342 | 309 | 2.51 | 2.49 |
| 20 | 0.98 | 0.98 | 0.74 | 0.73 | 3.28 | 3.27 | 1.82 | 1.81 | 286 | 296 | 2.49 | 2.49 |
| 21 | 0.93 | 0.96 | 0.88 | 0.82 | 2.75 | 2.88 | 1.29 | 1.3 | 391 | 384 | 2.51 | 2.51 |
| **AVG** | 0.93 | 0.95 | 0.81 | 0.75 | 3.13 | 3.42 | 1.53 | 1.62 | 330.29 | 321.43 | 2.50 | 2.49 |
| **p-value** | 0.003526 | | 0.001097 | | 0.007075 | | 0.000645 | | 0.046024 | | 0.030024 | |



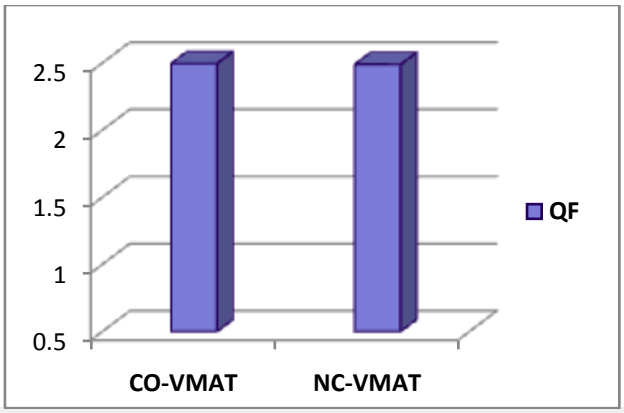



**Chart 3:-** CI, CN, GI, GM, MU and QF values comparison for all cases.

**Table 8:-** Average variance percentage comparison for indices:

| *Variance percentage between coplanar VMAT and non-coplanar VMAT in HI, MHI, TCI, PITV, CI, CN, GI, GM, MU, QF* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| ***Index*** | **HI** | **MHI** | **TCI** | **PITV** | **CI** | **CN** | **GI** | **GM** | **MU** | **QF** |
| ***AVG*** | 1.05 | 0.71 | -9.96 | -12.38 | 2.00 | -7.69 | 7.10 | 5.49 | -2.94 | -0.28 |

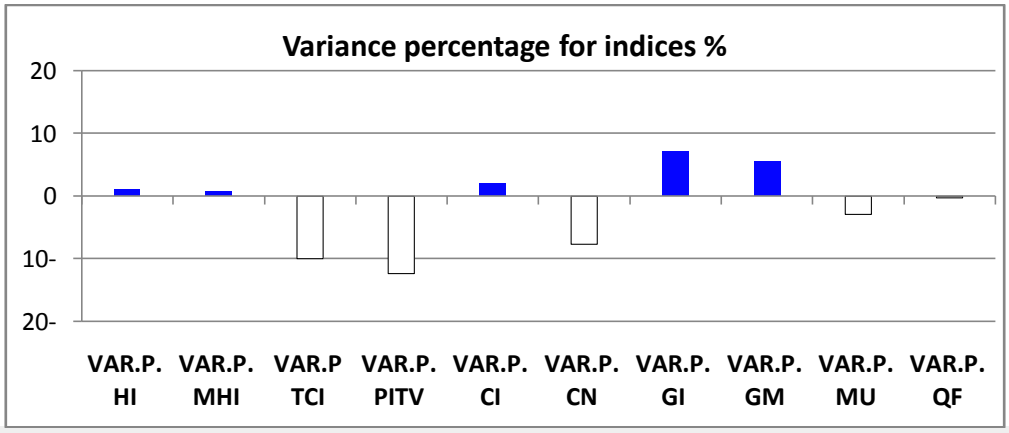



**Chart 4:-** Average variance percentage comparison between CO-VMAT and NC-VMAT for dosimetrical indices.

The maximum and mean doses statistics of the OARs that resulted from the two VMAT techniques were listed in Tables (9 and 10), Chart (5) for brainstem, chiasm, right optic nerve, left optic nerve, right eye, left eye, right lens, left lens, right cochlea, left cochlea, pituitary.

The NC-VMAT technique was the best in sparing of OARs compared to the CO-VMAT technique. Furthermore, the overall maximum and mean doses statistics of CO-VMAT and NC-VMAT still within the dose tolerance limits.

Table (11), Chart (6) represents the average variance percentage in OARs doses for the both VMAT techniques, the upper column in the chart means that CO-VMAT has an advantage over NC-VMAT while the lower column indicates to the opposite.

The study results that related to the average of the maximum dose for organs at high risk such as brainstem, chiasm, right optic nerve and left optic nerve in the CO-VMAT technique were (3632.14, 2076.26, 1208.39 and 1686.72 cGy), while in the NC-VMAT technique were (3463.89, 1913.80, 1208.39 and 1456.47 cGy). And, the average variance percentage and P-value were (-7.83%, 5.0219E-07), (-22.17%, 0.004991), (-27.52%, 0.003352) and (-27.09%, 0.004336).

For organs at intermediate risk such as right eye, left eye, right lens and left lens, the average results of the maximum dose in CO-VMAT technique were (1274.92, 1383.95, 446.91 and 418.40 cGy), while in NC-VMAT technique were (1109.53, 1248.62, 382.76 and 334.42 cGy). And also, the average variance percentage and P-value were (-17.26%, 0.005151), (-39.84%, 0.169030), (-19.74%, 0.002953) and (-38.49%, 0.000292).

The average data of mean dose for organs at low risk such as right cochlea, left cochlea and pituitary were (782.75, 730.68 and 515.53 cGy) in CO-VMAT technique, while in NC-VMAT technique were (760.59, 490.52 and 505.04 cGy). Furthermore, the average variance percentage and P-value were (-12.97, 0.639509), (-137.74%, 0.010836), (-7.37%, 0.742975).

**Table 9:-** Brainstem, chiasm, optic nerves and eyes dose statistics comparison for CO-VMAT and NC-VMAT.

| Organ | Brainstem Dmax | | Chiasm Dmax | | Optic nerve_Rt. Dmax | | Optic nerve_Lt. Dmax | | Eye_Lt. Dmax | | Eye_Lt. Dmax | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO VMAT | NC-VMAT |
| AVG | 3632 | 3463 | 2076 | 1913 | 1458 | 1208 | 1686 | 1456 | 1274 | 1109 | 1383 | 1248 |
| p-value | 5.0219E-07 | | 0.004991 | | 0.003352 | | 0.004336 | | 0.005151 | | 0.169030 | |

**Table 10:-** Lenses, right/left cochlea and pituitary dose statistics comparison for CO-VMAT and NC-VMAT.

| Organ | Lens_rt. Dmax | | Lens_Lt. Dmax | | Cochlea_Rt. Dmean | | Cochlea_Lt. Dmean | | Pituitary Dmean | |
|---|---|---|---|---|---|---|---|---|---|---|
| Case | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT | CO-VMAT | NC-VMAT |
| AVG | 446.91 | 382.76 | 418.40 | 334.42 | 782.75 | 760.59 | 730.68 | 490.52 | 515.53 | 505.04 |
| p-value | 0.002953 | | 0.000292 | | 0.639509 | | 0.010836 | | 0.742975 | |

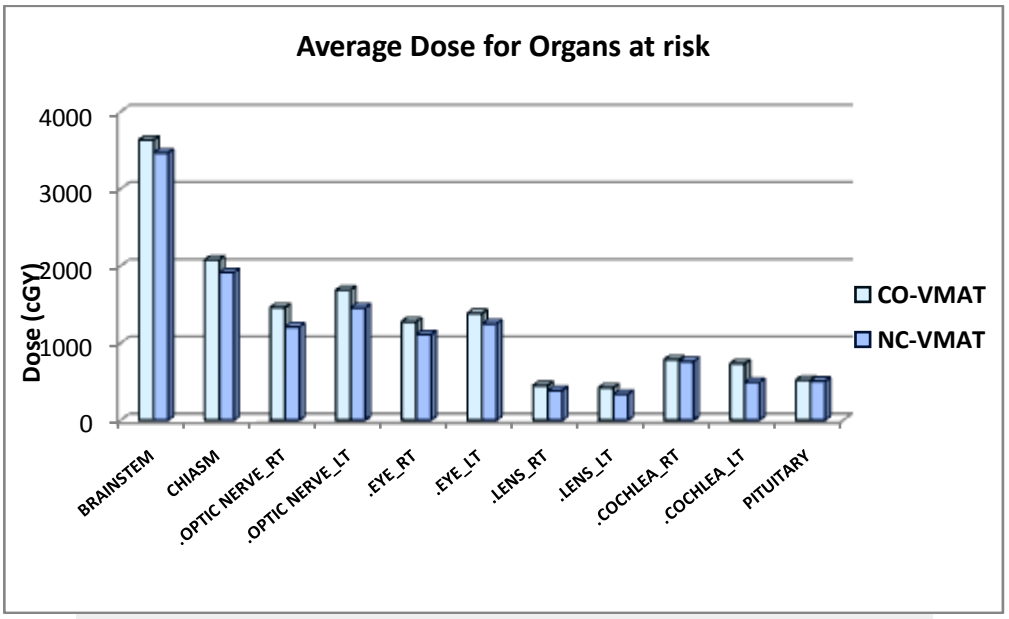



**Chart 5:-** Average dose statistics of OARs for both CO-VMAT and NC-VMAT.

**Table 11:-** Average variance percentage comparison for OARs.

| *Variance percentage for organs at risk data* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Brainstem | Chiasm | Optic nerve_Rt | Optic nerve_Lt | Eye_ Rt | Eye-Lt | Lens _Rt | Lens _Lt | Cochlea _Rt | Cochlea _Lt | Pituitary |
| AVG | -7.8 | -22.1 | -27.5 | -27.1 | -17.2 | -39.8 | -19.7 | -38.4 | -12.9 | -137.7 | -7.3 |

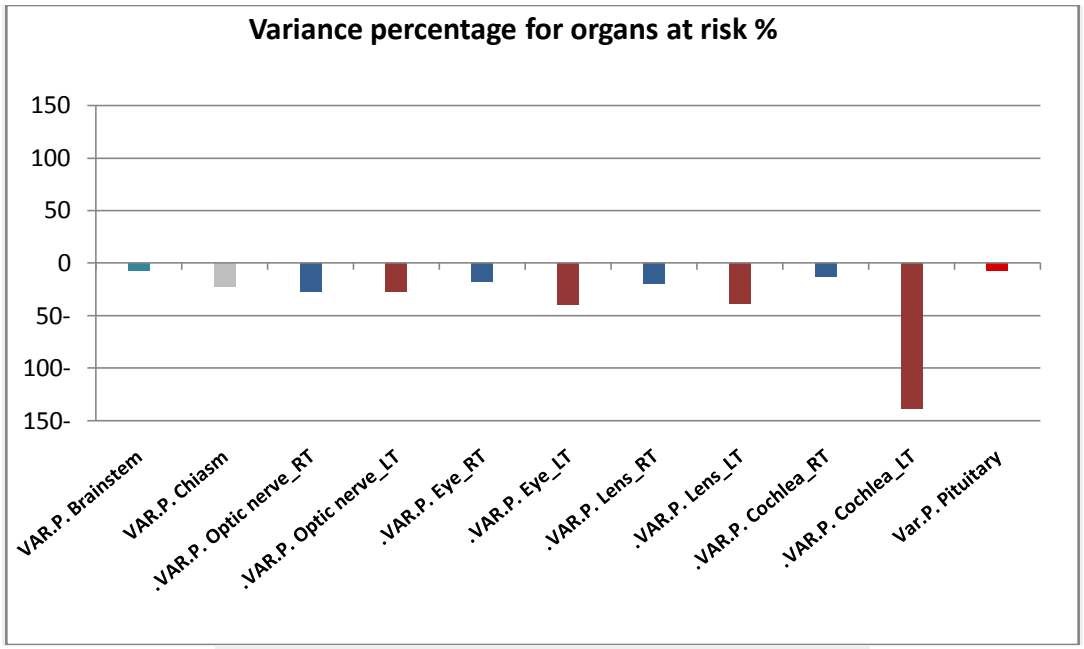



**Chart 6:** Average variance percentage comparison for OARs.

The radiobiological parameters impact of CO-VMAT and NC-VMAT plans was compared by using MATLAB program for brain tumors. The TCP values of brain tumor and NTCP values of brainstem, chiasm, right optic nerve, left optic nerve, right lens and left lens with its averages and all results of EUD model average for the two VMAT techniques were listed in the Tables (12, 13 and 14), Charts (7 and 8).

**EUD model comparison:**
The EUD model average result of TCP between the CO-VMAT and NC-VMAT plans were (60.82, 60.44 Gy). And for NTCP, the CO-VMAT plans got the higher result of EUD model average in comparison to the NC-VMAT plans. The EUD model averages (Gy) for NTCP were (17.53, 15.18 for brainstem), (14.08, 12,63 for chiasm), (9.14, 7.35 for right optic nerve), (10.82, 9.01 for left optic nerve), (2.22, 1.92 for right lens) and (2.13, 1.63 for left lens) in the CO-VMAT and NC-VMAT respectively.

**TCP and NTCP modelscomparison:**
In this study, all the results showed that the TCP average of the CO-VMAT plans were 81.25% while in NC-VMAT plans were 80.35%. This meaning that the TCP by CO-VMAT was larger than NC-VMAT, where P-value = 0.000622.

The NTCP average were compare in CO-VMAT and NC-VMAT plans for OARs such as: brainstem (0.00014%, 0.000021%), chiasm (0.00084%, 0.00015%), right optic nerve (0.00015%, 0.000059%), left optic nerve (0.000045%, 0.000018%), right lens (0.00046%, 0.00026%) and left lens (0.00038%, 0.00016%). This meaning that the NTCP of the NC-VMAT technique was less, and this a lowering in complication means a slight damage to normal organs, where P-value = 0.029820, 0.144558, 0.328077, 0.052115, 0.021914, 0.001981. variance percentage comparison between CO-VMAT and NC-VMAT techniques for OARs.

**P+ value comparison:**
In Chart (9), P+ average comparison was shown between CO-VMAT and NC-VMAT techniques for cases. The CO-VMAT technique obtained the highest value of P+ in this chart, while the NC-VMAT technique achieved the lowest P+ value. The P+ value of CO-VMAT was 81.09% and the P+ value of NC-VMAT was 80.30%.

**Table 12:-** TCP comparison between two techniques of VMAT.

| TCP | | |
|---|---|---|
| **Case** | **CO- VMAT** | **NC- VMAT** |
| **Average** | 81.25% | 80.35% |

| | | |
|---|---|---|
| **EUD average (Gy)** | 60.82 | 60.44 |
| **p-value** | 0.000622 | |

**Table 13:-** NTCP comparison for brainstem and chiasm.

| **Normal tissue complication probability (NTCP)** | | | | |
|---|---|---|---|---|
| **Organ** | **Brainstem** | | **Chiasm** | |
| **Technique** | **CO-VMAT** | **NC-VMAT** | **CO-VMAT** | **NC-VMAT** |
| **Patient data** | < 0.08 | < 0.01 | < 0.07 | < 0.05 |
| **Average** | 0.00014 | 0.000021 | 0.00084 | 0.00015 |
| **EUD average (Gy)** | 17.53 | 15.18 | 14.08 | 12.63 |
| **p-value** | 0.029820 | | 0.144558 | |

**Table 14:-** NTCP comparison for optic nerves and lenses.

| **Normal tissue complication probability (NTCP)** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Organ** | **Optic nerve_Rt.** | | **Optic nerve_Lt.** | | **Lens_Rt.** | | **Lens_Lt.** | |
| **Technique** | **CO-VMAT** | **NC-VMAT** | **CO-VMAT** | **NC-VMAT** | **CO-VMAT** | **NC-VMAT** | **CO-VMAT** | **NC-VMAT** |
| **Patient data** | < 0.0003 | < 0.00001 | < 0.04 | < 0.02 | < 0.09 | < 0.07 | < 0.09 | < 0.06 |
| **Average** | 0.00015 | 0.000059 | 0.000045 | 0.000018 | 0.00046 | 0.00026 | 0.00038 | 0.00016 |
| **EUD average (Gy)** | 9.14 | 7.35 | 10.82 | 9.01 | 2.22 | 1.92 | 2.13 | 1.63 |
| **p-value** | 0.328077 | | 0.052115 | | 0.021914 | | 0.001981 | |

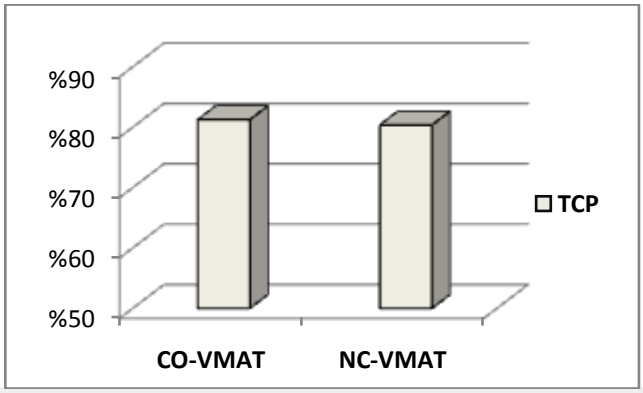



**Chart 7:-** TCP comparison between CO-VMAT and NC-VMAT.

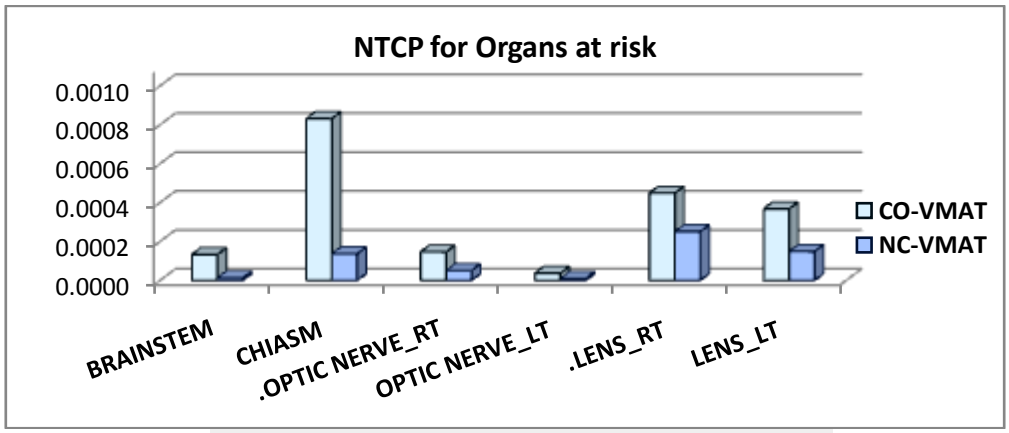



**Chart 8:-** NTCP values comparison of OARs for all cases.

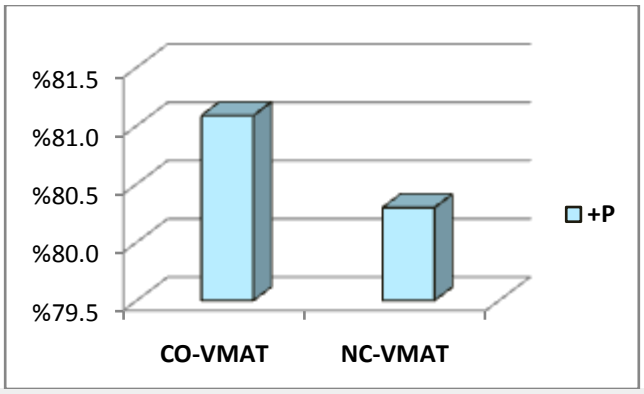



**Chart 9:** -Comparison between CO-VMAT and NC-VMAT for P+ average values of OARs for all cases.

## Conclusion:-

In the current study of the brain tumors treatment, the comparison of the dosimetrical and radiobiological parameters related to PTV dose coverage and sparing of OARs for two treatment techniques of VMAT showed thatDVH and Dose distribution of NC-VMAT plan for cases appeared in small part of PTV because of the sparing of OARs but it can be covered by 93%. In the plan of CO-VMAT, this underdose didn't occur in PTV despite the sparing of OARs.

1. CO-VMAT and NC-VMAT techniques gave a similar (HI, MHI, CI and QF) values for the PTV.CO-VMAT were the higher in (TCI, PITV and CN) values and the lower in (GI, GM) values, while NC-VMAT was the lower in MUs values.
2. According to the integral dose and the probability of occurrence secondary malignant cancer, the comparison study showed that NC-VMAT technique was much lower than that of CO-VMAT technique due to it has less MUs and short treatment time on the machine.
3. Concerning of the normal tissue doses, NC-VMAT technique has the preference over CO-VMAT technique in the high, intermediate and low risk organs.
4. TCP and P+ were large in CO-VMAT while NTCP was less in NC-VMAT.
5. The results of study showed that NC-VMAT technique is the lowest in tumor dose coverage which be within the tolerance dose limits, where it can maybe accept by the oncologist.
6. According to sparing of OARs, we found a slight difference in doses of all organs at risk surrounding brain tumor in NC-VMAT technique compared to CO-VMAT technique.
7. While the previous studies showed that CO-VMAT technique was used when the tumor is far from the organs at risk, the present work found that CO-VMAT can be used when the tumor is near to or far from OARs because it can achieve the target dose coverage and sparing of OARs together.
8. Based on what previous studies have shown, the current work found that NC-VMAT technique should be used onlyin cases of brain tumors that require to spare OARs which located within the tumor because the delivery efficiency of NC-VMAT plans takes a long time and it can lead to collisions between the machine and patient and also affects intrafraction patient motion through the treatment fraction.

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