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Comparison between Two-Photon Treatment Planning Techniques 3D-Conformal Radiotherapy and the Volumetric Modulated Arc Therapy for Head and Neck Carcinoma

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ABSTRACT

Introduction: Achieving precise dose delivery in head and neck cancer is challenging, requiring effective tumor control while minimizing toxicity. This study compares Volumetric-Modulated Arc Therapy (VMAT) and 3D Conformal Radiotherapy (3D-CRT), focusing on target coverage, Organs At Risk (OARs) sparing and treatment efficiency.

Material and Methods: For 7 randomly selected patients, Two plans (3D-CRT and VMAT) were created using Monaco TPS. The prescribed doses were 70/63/56Gy for Five patients and 69.96/59.4/54Gy for Two, in 35 and 33 fractions. The t-test was used for statistical analysis. VMAT plans underwent pretreatment quality control.

Results: The mean D_{mean}, D_{max}, and $V_{95\%}$ of PTV_{70Gy} were 70.86/70.23Gy, 78.95/75.28Gy, and 95.35% / 96.97% for 3D-CRT and VMAT. The D_{max} for the spinal cord, brainstem and chiasma were 49.98/40.76Gy, 64.05/50.00Gy, and 54.27/47.78Gy. The mean dose for the Left (L) and Right (R) parotids was 66.93/44.18Gy and 67.79/44.98Gy. The D_{max} for L/R optic nerves and eyes were 60.17/50.41Gy, 59.44/48.49Gy, 48.4/39.88, and 44.09/36.93Gy. The 0.03cc of the L/R temporal lobes received 73.37/69.59Gy and 73.17/68.33Gy. The mean dose in 2cc of the mandible was 72.88/66.99Gy. The mean volume of the larynx with 66Gy was 23.72% / 0.76%. The Homogeneity and Conformity Index were 0.12/0.08 and 0.95/0.97. The treatment time and MUs for 3D-CRT/VMAT were 3.35/6.36 min and 806.86/621.53 MUs. VMAT gamma index passing rate was 98.6%.

Conclusion: The VMAT limits irradiation, reduces OARs toxicity, assures higher target dose and avoids cold and hot spots. This study shows that VMAT provides superior normal tissue protection as compared to 3D-CRT.

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Introduction

The incidence of head and neck cancer is increasing in developing countries, and globally, it ranks as the sixth most common cancer. Approximately 70% of these cases require radiotherapy, either as a primary treatment, in combination with chemotherapy or targeted therapies, or as post-operative or palliative care [1]. Radiotherapy has advanced significantly, becoming a highly sophisticated process involving new imaging technologies, advanced delivery systems, and improved patient immobilization techniques [2]. Intensity-modulated radiation therapy (IMRT) is particularly effective for treating irregularly shaped target volumes while minimizing radiation exposure to organs at risk (OARs). This approach overcomes the limitations of conventional 3D conformal radiotherapy (3D-CRT), such as under-dosing of the target area and excessive radiation to nearby healthy tissues [1–6]. The head and neck region (H&N) is especially suitable for IMRT due to its complex anatomy and the potential for both acute and long-term radiation related toxicities (for example: xerostomia, cataract, blindness), usually distance between Clinical Target Volume (CTV) and critical structures such as parotids, mandible, chiasma, optic nerves, brainstem, spinal cord is within few millimeter's, therefore, in many cases, specially, with high risk, one part of the OARs and or normal tissues included in the Planning Target Volume (PTV) [2, 5, 7-9]. In an attempt to provide answer, we proposed to compare the dosimetric and technical aspects of 3DCRT and Volumetric-Modulated Arc Therapy (VMAT) for seven patients treated with VMAT for High-risk head and neck cancer.

Materials and Methods

Seven high-risk Head and Neck carcinoma (Six nasopharyngeal and One oropharynx) patients referred

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to our department for an external beam irradiation to the primary tumor and the nodes (neck and supraclavicular nodes) were considered for this dosimetric comparative analysis. Patient's characteristics are described in Table1.

Table1. Patient's characteristics

Patients number	7
Male/Female	4 / 3
Average age in Years (range)	53 (33 - 79) ± 15.5
Primary Radiotherapy (RT)	7/7
Chemotherapy	7/7

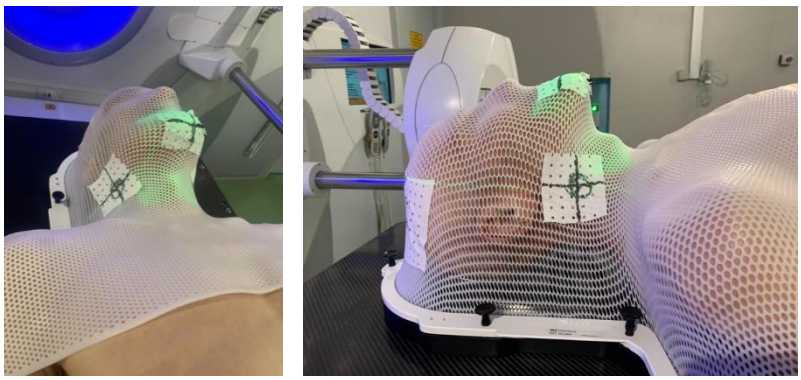
All patients were immobilized with the individual thermoplastic H&N mask (Figure1) and a Computed Tomography (CT) scan (using a Siemens Scanner 16 Barrettes and 82 cm FOV) with slice thickness 3 mm of the H&N region was made and reconstructed on 1 mm. The clinical target volumes CTV1,2 were delineated according to the initial diagnostic CT scan and an MRI which done on the same simulation position. CTV1 encompasses the area of the primary tumor or the postoperative tumor bed, including any lymph nodes confirmed as pathological. The intermediate target volume CTV2 covers the regions of the neck treated as an adjuvant measure, even in the absence of histological or clinical evidence of pathological lymph node changes. The planning target volumes PTV1,2 were defined based on CTV1,2 with an appropriate 3D safety margin. Specifically, PTV1 was created by adding a 5 mm margin to CTV1, while PTV2 included PTV1 along with the lymph nodes in CTV2, expanded by a 3 mm margin. The low risk planning target volume PTV3 was the elective nodes irradiation (nodes negative at risk level) CTV3 with a 3D margin of 3 mm. The delineated organs at risk were the spinal cord, brainstem, chiasma, parotids, optic nerves, eyes, lenses, temporal lobes, larynx, oral cavity and mandible. The Patients received VMAT Simultaneous Integrated Boost (SIB) treatment, Five days a week, 35 fractions, each time with a single dose of 2 Gy on PTV1, 1.8 Gy on PTV2 and 1.6 Gy on PTV3.

VMAT treatment plan

VMAT plans were created using the Monaco Treatment Planning System (TPS), version 5.11.02, employing the Monte Carlo Algorithm with a 2.5 mm dose grid resolution, 1% statistical uncertainty per calculation, a minimum segment width of 5 mm, and 360 control points per arc. The dose was prescribed to 50% of PTV1, ensuring that at least 95% of the prescribed dose covered the PTVs, while no more than 2% of the volume received over 107% of the dose. The isocenter was positioned at the center of PTV3 to meet pretreatment quality control requirements, ensuring all beamlet projections aligned with the IBA Dosimetry MatriXXEvolution phantom (24x24 cm²) to maximize data collection.

3D-CRT treatment plan

The all cases were replanned with the mono-isocentric technique 3D-CRT using the Monaco Treatment Planning System Collapsed Cone Algorithm. For the first phase (40 Gy), the primary tumor and the upper neck nodes were planified with 2 laterals shapes formed by Multileaf Collimators (MLCs) plus one or two segments to avoid the hot spots, and the lower neck nodes and the supraclavicular nodes with one anterior field, matched to inferior border of the 2 laterals plan at the isocenter (50 Gy). In the second phase, 10 Gy was giving to the upper part with 2 laterals by hiding the spinal cord (the shielding parts were completed with two Electrons lateral fields 3 Gy on 3 fractions to have 50 Gy in the PTV2. In the third phase, 2 lateral fields photons for the primary tumor and electrons for the nodes to have 70 Gy in the PTV1. The first goal for the two techniques was to treat homogeneously all the target volumes and sparing the spinal cord, chiasma, brainsteam and optic nerves. The second goal was to reduce the risk of xerostomia by decreasing the mean dose (Dmean) to the parotid glands which were usually partially included in PTV of the high risk head and neck carcinoma. On general, in the treatment of nasopharyngeal carcinoma precise dose delivery essential to achieve locoregional control and to minimize the complications.



(a) (b)

Figure1. Setup of patient

Data analysis and statistical study

Dose Volume Histograms (DVHs) statistics were analyzed comparing dose in PTVs and OARs. The Conformity and Homogeneity Index (CI and HI) were calculated using formulas 1 [10] and 2 [11-12]:

$$HI = (D2\% - D98\%) / D50\% \quad (1)$$

where, Dn% is the minimum dose in n % of the volume of the PTV (the ideal is close to zero) .

$$CI = TV / PTV \quad (2)$$

where, PTV is the planed target volume and TV is the treated volume covered by the reference dose (the ideal is one).

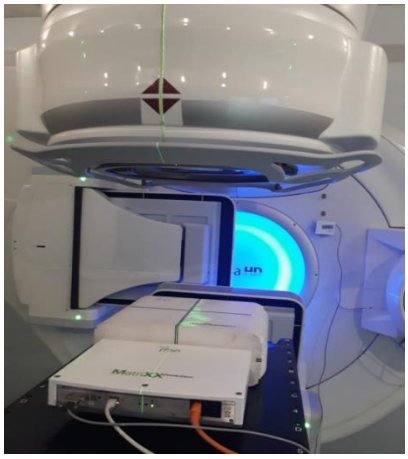


Figure 2. The MatriXX^{Evolution} phantom Setup

Regarding the efficiency of treatment delivery, we compared Monitor Units (MUs) and Treatment Time (TTT) for the 3D-CRT and VMAT techniques. The statistical analysis was performed using the Microsoft Excel Software 2010 't-test student program' where a p-value less or equal 0.05 was considered significant. The second part of this study was the validation of the accuracy of VMAT delivery, using the phantom MatriXXEvolution (Matrixx ionization detector arrays), IBA Dosimetry (1020 ionization chambers in an active area of 24.4 x 24.4 cm2, effective point of measurement: 3mm from surface) and My QA patient' Software (version 2.13, IBA Dosimetry) with an angle-dependent correction lookup-table for lateral beam directions. The setup of the MatriXXEvolution is shown in Figure 2. And the pre-treatment quality control plans was done on Four steps: the preheating of the Phantom, the Calibration of the Gantry Angle using the Correction Angle Sensor (CAS) tool, the application of the treatment plan to a dosimetric phantom then the comparison of the measured and the calculated phantom dose distribution using the Gamma Index (GI) criteria. The VMAT clinical cases passed with more than 95% for the set criteria of 3% Dose Difference (DD) and 3 mm Distance to Agreement (DTA).

Results

PTV1, 95%: The mean values were 95% (89.49% - 100%) for 3D-CRT and (96.97% - 99.67%) for VMAT, with a p value 0.25. This constraint was reached in all patients with VMAT, compared to only 5 cases with 3D-CRT. The two patients for whom the PTV1, 95% constraint was not reached by 3D-CRT, the values were 89.49%, 93.71%, as compared to 95%, 96.5% with VMAT. The average of the Dmean and Dmax were 70.86 / 70.23 Gy (p = 0.24) and 78.95 / 75.28 Gy (p = 0.07), respectively for the both techniques 3D-CRT/VMAT. The mean of Dmax was 112% of the prescribed dose with the 3D-CRT (Hot spots) versus 107% for the VMAT (Table.2). Conformity and Homogeneity Index (CI and HI): The average values were 0.95 (0.89 - 1) and 0.12 (0.073 - 0.253) for 3D-CRT and 0.97 (0.95 – 1) and 0.08 (0.059 – 0.111) for VMAT. The difference was statistically significant p = 0.023 for the CI and the VMAT technique allowed us more homogeneity distribution when compared to 3D-CRT approach.

Organs at risk

The spinal cord, brainstem, temporal lobes, eyes, optic verves, larynx, chiasma and mandible constraints were reached for the all patient using the VMAT technique and with significant differences compared to 3D-CRT, see Table.3. The average of the left and right parotids mean dose were 66.93/44.18 (p=0.00087) and 67.79/44.98 (p=0.00036) with 3D-CRT/VMAT, significantly different but the constraint was reached just for one patient with VMAT 25.04 Gy compared to 68.831 Gy with 3DCRT because of the advanced stage of the cancer.

Table 2. The mean of the $PTV_{1,95\%}$, D_{mean}, D_{max} , the conformity and the homogeneity index for 3D-Conformal Radiotherapy (3D-CRT) and Volumetric-Modulated Arc Therapy (VMAT) where the $PTV_{1,95\%}$, D_{mean} and D_{max} are the volume of Planning Target Volume1 (PTV_1) received 95% of the prescribed dose, the mean and max dose in the PTV_1 respectively

	3D-Conformal Radiotherapy	Volumetric-Modulated Arc Therapy	p-value
Mean $PTV_{1,95\%}$ (%)	95.35	96.97	0.25
Mean D_{mean} (Gy)	70.86	70.23	0.24
Mean D_{max} (Gy)	78.95	75.28	0.07
Mean Conformity Index	0.95	0.97	0.023
Mean Homogeneity Index	0.12	0.08	0.177

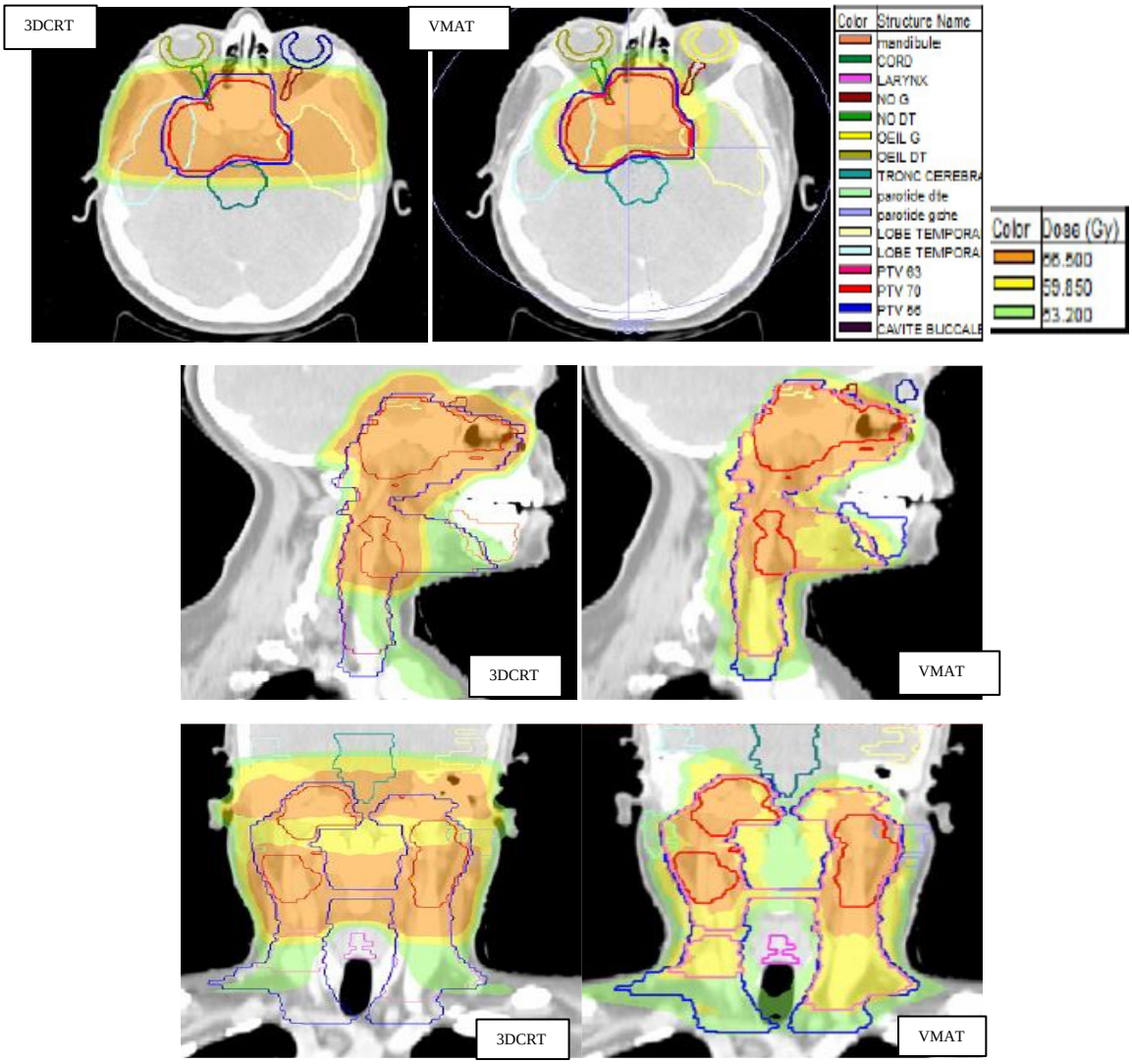


Figure 3. The transversal, Sagittal and coronal doses distribution for Volumetric-Modulated Arc Therapy (VMAT) and 3D Conformal Radiotherapy (3D-CRT); the Brown, Yellow and green isodoses correspond to 95% of the prescribed doses 70.0, 63.0 and 56.0 Gy respectively; and the Red, Pink and Blue contouring correspond to the Planning Target volumes PTV_1, PTV_2, PTV_3 respectively

Table 3. Organs At Risk (OARs) average doses with the 3D- Conformal Radiotherapy (3D-CRT) and Volumetric-Modulated Arc Therapy (VMAT) techniques where the $D_{50\%}$, D_{xcc} are the dose in 50% and in x cm^3 of the volume of the OARs, respectively and the $V_{66\%}$ is the volume of the larynx received 66 Gy.

Organs At Risk	Average		P value
	3D- Conformal Radiotherapy	Volumetric-Modulated Arc Therapy	
D_{max} Spinal cord	48.98	40.766	0.000
D_{max} Brainstem	64.059	50.00	0.000
D_{max} Chiasma	54.27	47.78	0.220
D_{mean} L Parotid	66.93	44.18	0.001
D_{mean} R Parotid	67.79	44.98	0.000
$D_{50\%}$ L Parotid	69.33	44.47	0.001
$D_{50\%}$ R Parotid	69.57	45.08	0.000
$D_{0.03cc}$ L Temporal lobe	73.37	69.59	0.007
$D_{0.03cc}$ R Temporal lobe	73.17	68.33	0.023
D_{max} L Optic nerve	60.17	50.41	0.045
D_{max} R Optic nerve	59.44	48.49	0.029
D_{max} L Eye	48.4	39.88	0.150
D_{max} R Eye	44.093	36.93	0.064
D_{2cc} Mandible	72.88	66.99	0.003
V_{66Gy} Larynx	23.72	0.76	0.014

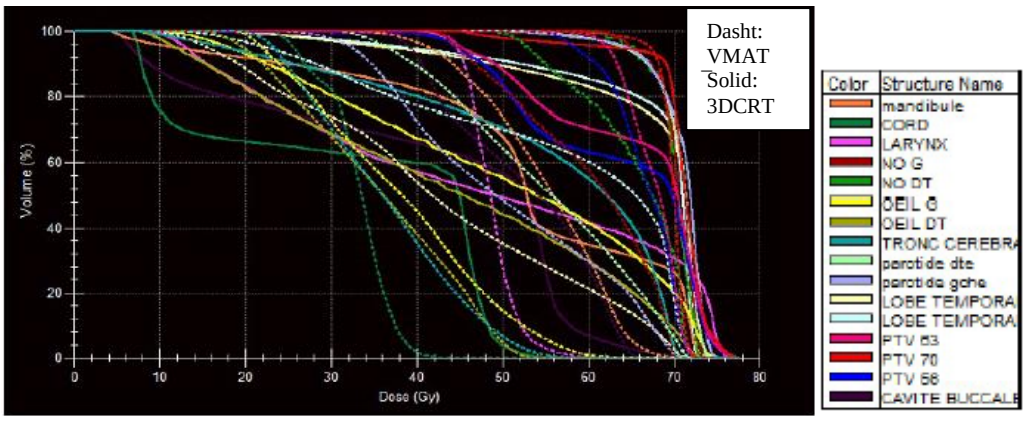


Figure 4. The Dose Volume Histograms (DVHs) of the Planning Target Volumes (PTVs) and the Organs At Risk (OARs) for the both approaches Volumetric-Modulated Arc Therapy VMAT (Dash) and 3D Conformal Radiotherapy 3D-CRT (Solid), show that the dose in OARs is the reduced and the coverage of the PTV_2 with VMAT

Table 4. The mean of Monitor Units (MUs) and Treatment Time **(**TTT) for the 3D Conformal Radiotherapy (3D-CRT) and Volumetric-Modulated Arc Therapy **(**VMAT) approaches (MUs Mean, TTT Mean (min) are the mean of the MUs number and treatment time, respectively)

	3D- Conformal Radiotherapy	Volumetric-Modulated Arc Therapy	P value
Monitor Units Mean	806.86	621.53	0.068
Treatment Time Mean (min)	3.35	6.36	0.001

Treatment efficiency of the both techniques and the pretreatment quality control of the VMAT plans

The mean of the MUs and the TTT were 806.86 / 621.53 and 3.35 / 6.36 min for 3D-CRT and VMAT, respectively, with p values 0.068 and 0.001, as shown in Table.4. A dosimetric evaluation of VMAT was conducted using a 2D-array with angle correction in a homogeneous phantom. Gamma index analysis revealed a mean passing pixel percentage of 98.6% for the 3% / 3 mm criterion, with values ranging from 96.7% to 99.9%.

Table 5. The plans' mean passing pixel percentage for the Volumetric-Modulated Arc Therapy technique

Patient	Passing pixel percentage (% pass)
1	97.8
2	98.6
3	96.7
4	99.1
5	98.4
6	99.9
7	99.7
Mean	98.6

Discussion

Radiotherapy plays a crucial role in managing head and neck cancer, with over Two-Thirds of patients requiring either definitive or post-operative radiation therapy [13]. Compared to Conventional Radiotherapy (3D-CRT), IMRT provides superior sparing of healthy tissues, thereby reducing toxicity [5]. This technique allows precise adjustment of the radiation beam to the irregularly shaped planning target volume while minimizing exposure to surrounding tissues and organs at risk [5, 8,9, 13-17].

S. Clavel et al reported Grade 2 or higher acute mucositis in 75% of patients (57.5% for Grade 3) treated with IMRT, compared to 77% (40% for Grade 3) with 3D-CRT [16]. Similarly, Nutting CM et al. and Gopa Ghosh et al. observed xerostomia rates of 38% and 45% with IMRT, respectively, compared to 74% and 72.5% with 3D-CRT [5, 17].

Although IMRT has significantly advanced in recent years, rotational treatment techniques, such as VMAT, offer additional benefits. These methods aim to reduce treatment time by incorporating greater flexibility, including variations in gantry speed, dose rate, collimator angles, and dynamically shaped fields [18-22]. For instance, the average beam-on time for RapidArc was 2.14 ± 0.43 minutes, significantly shorter than the 9.16 ± 2.5 minutes required for IMRT ($p < 0.00001$) [23]. Moreover, delivering a dose of 200 cGy per fraction required an average monitor unit (MU) of 523 ± 16 MU for Rapid-Arc and 2127 ± 570 for the 9 fields IMRT plan ($p < 0.0001$) [23]. Florian Stieler et al [24] show that the VMAT was the fastest treatment option (6.2 ± 1.0 min) comparing to tomotherapy (12.8 ± 1.7 min); IMRT 7 fields (7.6 ± 0.3 min) and IMRT 9 fields (8.5 ±0.4 min), furthermore, the number of the MUs was the lowest 512 ± 53 Versus 2551 ± 349, 945.2 ± 201 and 925 ± 234 respectively. Large reduction in dose to OARs have previously been reported when shifting from IMRT to VMAT [25]. The low dose volumes are increasing, the high dose volumes in the normal tissue are reduced and the planning objective values for OARs were improved when comparing the VMAT plans to the IMRT and with equal or better target coverage as well as conformity [26]. The study of Andrei Caraman [27] show that the IMRT and VMAT improved OARs sparing and provided superior planning

target volume coverage compared to the 3D-CRT, besides there were no significant differences in the dose to spinal cord and the DVH for Chiasma were very similar for the IMRT and VMAT plans. Also, the mean dose of chiasma was statistically similar for all three plan types. However, the mean dose brainstem was significantly lower for 3D-CRT (1730 cGy) compared to IMRT (2970 cGy) and VMAT (2830cGy), and the average of the max dose was 52.14 Gy (3D-CRT) Vs 52.68 Gy VMAT ($p = 0.87$) [27], in contrast our study show that the difference was statistically significant ($p = 0.000$) compared the max dose average of 3D-CRT (64.059 Gy) to VMAT (50.00 Gy). The tumor volume coverage was better with VMAT than 3D-CRT with: Conformity Index (CI) 1.204/1.062 and Homogeneity Index (HI) 0.276/0.12, which is the case of our investigation HI 0.12 /0.08 and CI 0.95/0.97. The concept of CI was first introduced by the Radiation Therapy Oncology Group (RTOG) in 1993 and detailed in Report 62 of the International Commission on Radiation Units and Measurements (ICRU) [11-12]. Similarly, Knoos T et al. proposed a Radiation Conformity Index (RCI) in 1998 [28]. According to the RTOG guidelines, an ideal CI equals 1, indicating perfect conformity. A CI of less than 1 means that the Target Volume (TV) is not fully irradiated, whereas a CI greater than 1 indicates that the irradiated volume extends beyond the TV, including normal tissues. In this study, CI values for both techniques were less than 1, demonstrating that the prescribed dose volume was smaller than the PTV. However, better dose conformity was achieved with the VMAT technique compared to 3D-CRT.

The findings of this study, along with those of Andrei Carman [27], confirm that the VMAT approach provides significant sparing of organs at risk and healthy tissues while maintaining adequate target volume coverage and with much lower MUs compared to 3D-CRT.

The limitation of the current work is the absence of the toxicity assessment and follow-up because of the limited number of patients, which will be the goal of our clinical study in head and neck cancer.

Conclusion

VMAT technique is an efficient and makes advanced fluency modulated treatment more accessible to the patients with head and neck cancer. The MUs with VMAT were lesser than 3D-CRT then the largely reduction of the secondary cancer's potential risk which can increase with the MUs (because the collimator transmission as scattered from the Linac is proportional to the number of MUs). The planning objective values for OARs were improved using the VMAT approach and thus the coverage of the target volume with best conformity and homogeneity dose distribution. In conclusion, our findings and many other studies show that the volumetric modulated arc therapy is the standard radiation therapy technique for head and neck cancer.

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