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A Dosimetric Comparison of VMAT and IMRT Plan Quality for Nasopharyngeal Cancer Treatment using Varian Eclipse TPS

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Abstract
Aim: *The aim of this study is to compare the dosimetric difference for radiotherapy of nasopharyngeal carcinoma (NPC) between volumetric-modulated arc therapy (VMAT) and dynamic intensity-modulated radiation therapy (IMRT) using Varian Eclipse TPS following simultaneously integrated boost (SIB) protocol.*
Patients and Method: *Fifteen patients with NPC underwent SIB protocol were retrospectively selected for this study. The Gross tumour volume (GTV) of NPC contained nasopharynx gross target volume and the positive neck lymph nodes, PTV1 contained the clinical target volume (CTV) of high-risk sites and the whole nasopharynx and PTV2 contained the CTV of low-risk sites. The prescription dose of PTV1 was 69.96 Gy/33 fractions, and for PTV2 59.4 Gy/33 fractions. VMAT (two full arcs) and IMRT (9 equally spaced fields) plans were designed for each patient using SIB strategies. The dose constraints were set for a high conformal and homogenous dose distribution to the PTV with minimal dose to the organ at risks (OAR).The plan was first done for IMRT, using the same dose constraints VMAT plans were generated. The monitor unit (MU) and other dosimetric difference between IMRT and VMAT were compared.*
Results: *The fraction of prescribed dose received by 95%of PTV volume showed a better result for IMRT, resulting in a significant difference with $p < 0.05$, while no significant differences were found for Homogeneity Index and Conformity Index ($p > 0.05$). Similarly for OARs and remaining volume at risk no significant differences were found between IMRT and VMAT. The total MU for IMRT (1837.67 ± 141.54) is more than VMAT (625.33 ± 49.02) with $p < 0.05$.*
Conclusion: *This study shows that VMAT can achieve similar target coverage and homogeneity as IMRT except with fewer MUs and less delivery time compared to IMRT in cases of nasopharyngeal carcinomas.*
Keywords: *Nasopharynx, carcinoma, IMRT, VMAT, Monitor Unit, Dosimetry.*

Introduction

Nasopharyngeal carcinoma (NPC) is the predominant tumor type arising from the epithelial lining of the nasopharynx. NPC is endemic in Southern China, including Hong Kong, and India, in Nagaland[1]. NPC has always been a challenge to radiation oncologists because of the relative lack of surgical access to the deep anatomical location of the nasopharynx and its proximity to critical neurovascular structures[2,3]. Due radio-sensitive

and chemo-sensitive nature of NPC, radiotherapy (RT) is the treatment of choice. Despite encouraging clinical outcomes, several challenging aspects are inherent to the use of RT for NPC[1].

Various methods have been used to improve local control by increasing the target coverage, including three-dimensional conformal radiotherapy (3D CRT) and intensity-modulated radiotherapy (IMRT). Various reports have found that Simultaneous Integrated Boost (SIB) delivery of IMRT achieved improved normal tissue sparing compared with sequential delivery after either whole neck IMRT or conventional fields [5]. IMRT enables the simultaneous delivery of different doses to different target volumes, representing an ideal technique for localized dose escalation [2]. However, although IMRT has become a standard technique for NPC radiotherapy, the concern regarding its high number of monitor units (MUs) and prolonged treatment time is still under discussion [4]. With the advent of Volumetric-modulated arc therapy (VMAT), where the gantry moves continuously, with the MLC leaves and dose rate varying throughout the arc. It has more flexibility of dose delivery through a full range of angles (gantry rotation) with continuous modulation of beam aperture, variable dose rate [15] and a capability of delivering a highly conformal dose distribution within a short time interval.

In a VMAT treatment, the treatment planning system (TPS) computes the dose by sampling the delivery at several discrete gantry angles. In order to create a satisfactory dose plan with a single arc, it is necessary to optimize the field shapes and beam intensities from a large number of gantry angles. However, the field shapes are restricted in that the MLC leaves must be able to move to their new positions within the time required for the gantry to rotate between samples. Unfortunately, the larger the number of sampled gantry angles, the more difficult it is for the TPS to optimize within the MLC leaf motion constraints5. Various reports have compared VMAT and IMRT for NPC. They have found that VMAT provides significantly faster delivery time and fewer MU with a minimal advantage of better target coverage and OAR sparing compared to the IMRT. Therefore, we have undertaken this dosimetric study to compare the plan quality between VMAT and IMRT for Nasopharyngeal cancers using Varian Eclipse TPS.

Materials and Method

A. Study Population And Simulation

Fifteen patients with NPC who had undergone radiotherapy using the SIB technique were retrospectively selected for this study. Patients were immobilized in the supine position with the neck extended but keeping the neck straight using a base plate with a headrest and thermoplastic mould (Orfit). 3-dimensional (3D) volumetric Computed Tomography (CT) scan images were acquired (Phillips Brilliance Big Bore CT) with 3.0mm slice thickness using intravenous and oral contrast enhancement. The CT images were transferred to Eclipse TPS (15.6v) for structure delineation and planning.

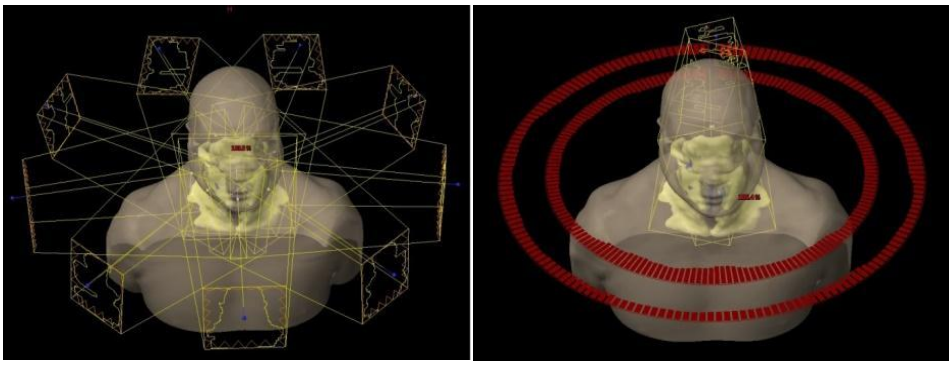

Figure 1: Beam arrangement for IMRT (left) and VMAT (right).

B. Target Volume Delineation

The target volumes and critical structures were delineated slice by slice in enhanced contrast images 3mm thickness in Eclipse 15.6v TPS. The target volumes are delineated according to International Commission of Radiation Units, and Measurements (ICRU) Reports 58 and 60 and Radiation Therapy Oncology Group (RTOG) guidelines. Gross tumor volume (GTV) was contoured from the CT scan images. GTV was defined as the nasopharynx primary gross target volume or/and the positive neck lymph nodes. CTV1 encompass the high-risk sites of microscopic extension and the whole nasopharynx; CTV2 was defined as the CTV1 plus a 5 to 10 mm margin (2 to 3 mm margin posteriorly in some cases) to encompass the low-risk sites of microscopic extension, Planning target volumes for CTVs were generated using 5 mm margins isotropically which were labelled as PTV1, PTV2 and PTV3. PTV3 is for the area of PTV2, subtracting PTV1 with a 5mm margin. Organs at risk (OARs), such as – Eyes, Optic Nerves, Parotids, Optic Chiasms, Brainstem, Spinal Cord, Mandible, Oral Cavity, etc., were contoured following DAHANCA, EORTC, GORTEC, HKNPCSG, NCIC, CTG, NCRI, RTOG, TROG consensus guidelines.

Table 1: Dose constraints for different organs at risk.

OARs	Constraints	OARs	Constraints
Mandible	Max = 70Gy	**Optic Nerve**	Max = 54Gy
Brainstem	Max = 54Gy	**Eye**	Max = 26Gy
Spinal Cord	Max = 45Gy	**Oral Cavity**	Max = 70Gy
Lens	Max = 6Gy	**Lips**	Mean = 20Gy
Cochlea	Max = 54Gy	**Parotid Total**	Mean = 33 Gy

C. Treatment Planning Specification

According to various literatures, it is recommended to prescribe different doses per fraction to two regions 10, 22, 23. The prescribed dose was 69.96Gy to PTV1 and 59.4Gy to PTV2 in 33 fractions with the SIB technique. The IMRT plans were designed using nine equally distributed co-planar 6MV beams with different collimator angles, and the dose rate was set at 400MU/min. The VMAT plans use two full arcs (179°-181°) and (181°-179°) with collimator rotation of 15° and 345°, respectively and a maximum dose rate of 600MU/min of 6MV beams. The collimator position and size were adjusted based on the size of the PTV2. The plans were calculated using the anisotropic analytical algorithm (AAA 15.6v). IMRT plans were planned such that 97% of the target volume received at least 95% of the prescribed dose, and less than 2cc of the target volume was received by 107% of the prescribed dose. The doses to all the OARs were reduced as much as possible without compromising the target dose coverage. The ability to spare these structures depends on the location and volume of the tumor and its extent. The maximum doses to the OAR structures were restricted so as not to exceed their tolerance doses, which were as follows: 54 Gy for the brainstem; 45 Gy for the spinal cord; 6 Gy for the lens; 54 Gy for optic nerves; 33 Gy for total parotids. After fully optimized and calculated, IMRT and VMAT plans were delivered to the Varian Trilogy accelerator with Varian millennium 80 MLC.

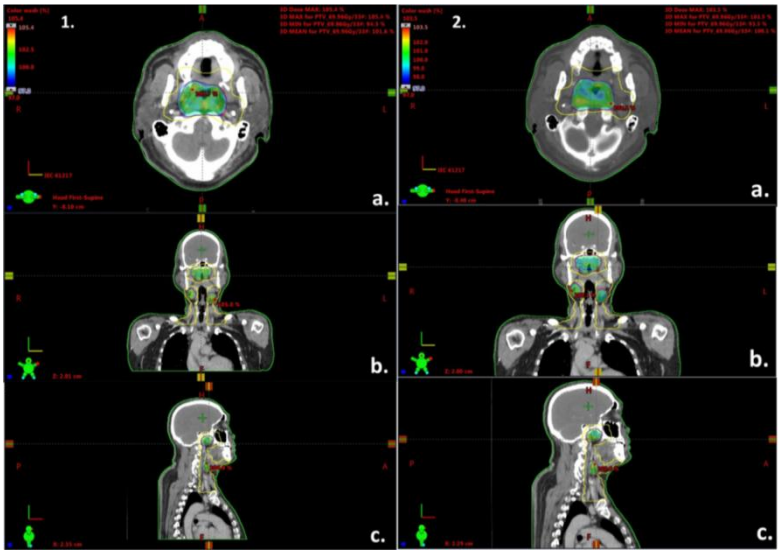

Figure 2: Isodose distribution of 97% for PTV1 using 1. IMRT 2. VMAT

D. Planning Evaluation

For PTV, according to ICRU Report No.83, dose homogeneity characterized the uniformity of dose distribution within the target volume. It was defined as homogeneity index

(HI) = [D2% - D98%]/(D50%)

where D2%, D98% and D50% were defined as the dose received by 2%, 98% and 50% of the volume of the PTV. According to Radiation Therapy and Oncology Group (RTOG) report, dose conformity specifies the degree to which the high-dose region conforms to the target volume. It is used for comparing the degree of conformity between plans and was calculated using two formulas conformity index (CI) = VRI/TV, Where VRI was the volume of reference isodose, and TV was the Total Volume of the PTV. Moreover, according to the Salt Lomax report, Dose conformity was calculated using the formula

CI = TVRI/TV,

where TVRI was PTV covered by reference isodose. Apart from CI and HI, the plans are also evaluated on D95% (defined as the dose received by 95% of the volume of the PTV) and V107% (cc) (Volume receiving 107% of the prescribed dose). OAR doses were assessed with: the maximal dose to the spinal cord, lens, eye, mandible, brain stem, and oral cavity and the mean dose to the total parotid glands and lips. The constraints are shown in table 1.

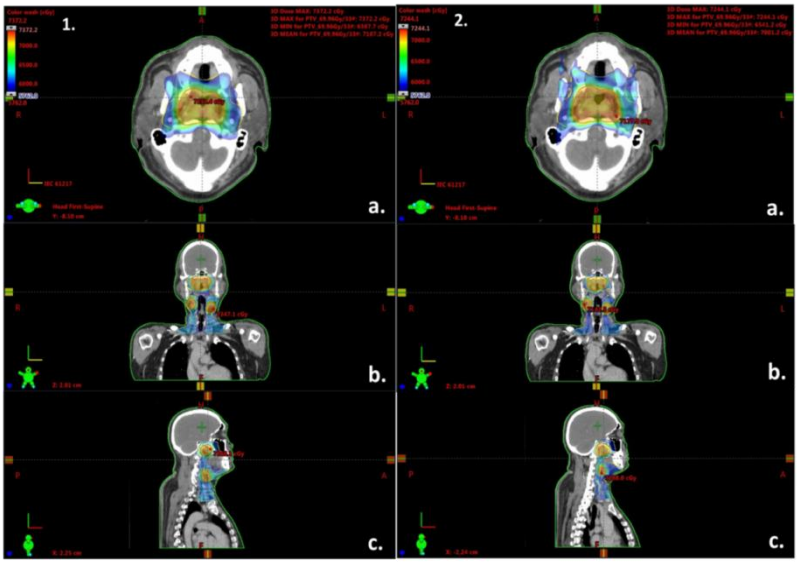

Figure 3: Isodose distribution of 5762cGy for PTV2 using 1. IMRT 2. VMAT

E. Statistical Method

For qualitative analysis between IMRT plans and VMAT plans, an Independent sample t-test run on an SPSS (Statistical Package for the Social Sciences) system provides a very suitable statistical method of investigation. Differences are considered to be statistically significant if p-values < 0.05.

Results

Tables 2 and 3 show detailed numerical findings from DVH analysis on PTVs and OARs, respectively. The axial, sagittal and coronal dose distributions produced by the two techniques for PTV1 are shown in figure 2, and for PTV2 are shown in figure 3. Figure 4 shows the DVH of the PTVs, and OARs using IMRT and VMAT. Figure 5 shows a graphic representation comparing IMRT and VMAT for PTV1, and figure 6 shows a graphic representation comparing IMRT and VMAT for PTV2 and PTV3.

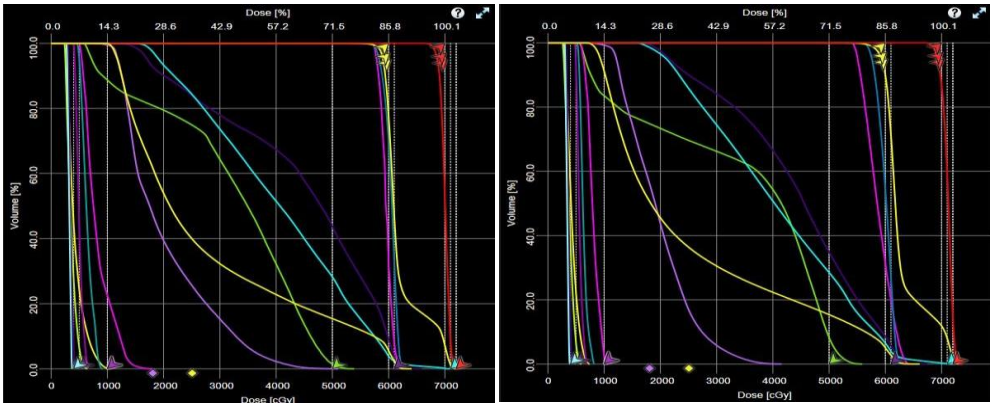

Figure 4: DVH of PTV and OAR for IMRT (left), VMAT (right)

I. Target Coverage and Dose Homogeneity

As shown in Table 2, the objective of D95% ≤ 97% (in PTV1) showed a better result for IMRT with a mean D95% of 97.35(%), resulting in a significant difference ($p < 0.05$) compared to VMAT. V107% (cc) was achieved by both the plans for PTV1, showing no significant differences between the two plans ($p > 0.05$). CI and HI for PTV1 and PTV2 showed no significant differences between the plans. However, V107% (cc) for PTV3 in IMRT was found to be superior to VMAT ($p < 0.05$).

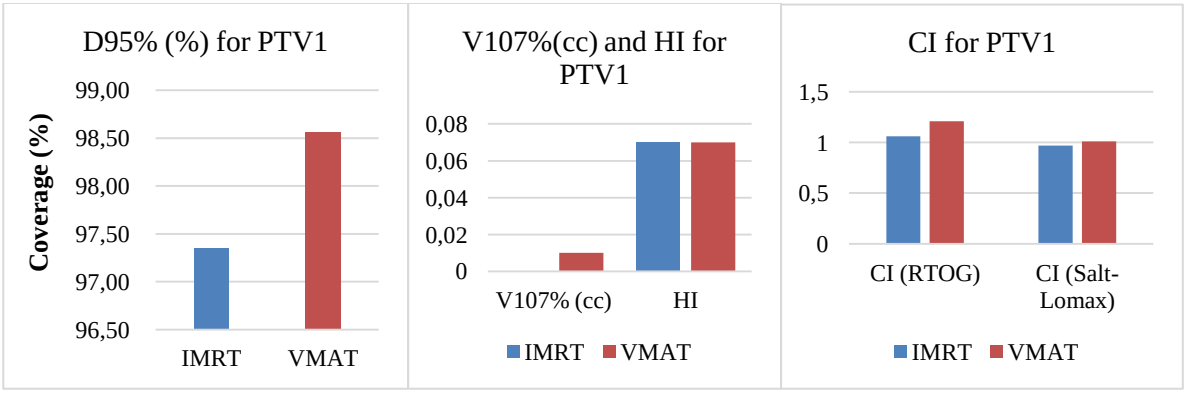

Figure 5: Plot of D95% (left), V107%(cc) and HI (middle), CI (right) for PTV1

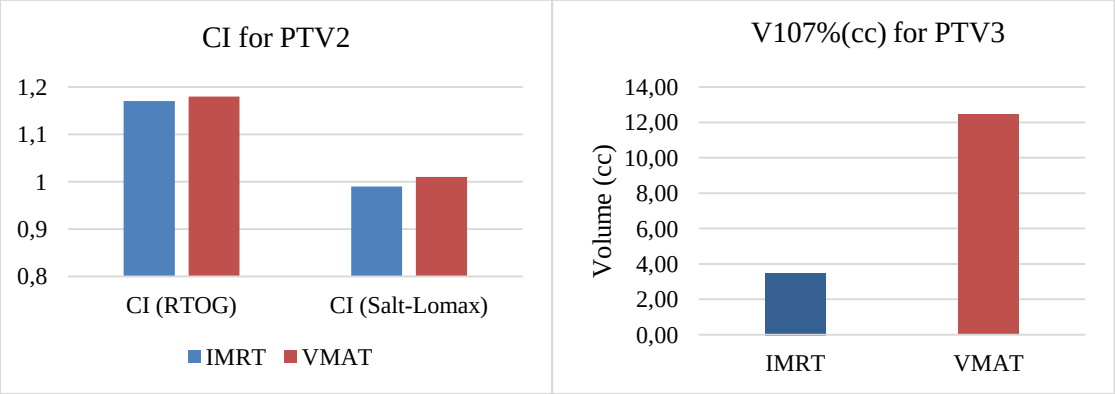

Figure 6: Plot of CI for PTV2 (left), V107%(cc) PTV3 (right).

II. Organs at Risk

Figure 7: shows a graphical representation of the difference between IMRT and VMAT for the OARs. Table 3 provides the statistical data for different OARs, showing no statistically significant differences.

Table 2: Statistical Data statistically comparing IMRT with VMAT for PTVs

Structure	Dosimetric Parameter	IMRT (mean±sd)	VMAT (mean±sd)	p-value
PTV1 (69.96 Gy)	D95% (%)	97.35±0.35	98.56±0.96	<0.001
	V107% (cc)	0±0.01	0.01±0.04	0.323
	HI	0.07±0.01	0.07±0.01	0.8
	CI (RTOG)	1.06±0.04	1.21±0.41	0.177
	CI (Salt-Lomax)	0.97±0.02	1.01±0.09	0.097
PTV2 (59.4Gy)	CI (RTOG)	1.17±0.1	1.18±0.11	0.789
	CI (Salt-Lomax)	0.99±0.05	1.01±0.08	0.539
PTV3 (59.4-69.96_5mm)	V107% (cc)	3.49±1.43	12.45±7.1	<0.001

a. Brainstem: The planning objective of Dmax ≤ 54Gy was met for both plans and showed no significant difference between the two plans.
b. Spinal Cord: The two techniques achieved their planning objective of Dmax ≤ 45Gy. Similar to the brain stem, the mean values of Dmax showed no significant difference.
c. Optic Nerves: Both the optic nerves were analyzed separately with the plan objective Dmax≤54Gy, and it was found that the mean Dmax for both right and left optic nerves showed no significant difference.
d. Oral cavity, Mandible and Lips: Both the plans achieved their objectives and showed no significant differences.

Table 3: Statistical Data statistically comparing IMRT with VMAT for different OARs

OAR	Parameter	IMRT (Mean ± SD)	VMAT (Mean ± SD)	p-value
Brainstem	Dmax (cGy)	5277.91 ± 304.09	5472.57 ± 209.69	0.052
Spinal Cord	Dmax (cGy)	4261.68 ± 200.66	4309.77 ± 286.99	0.599
Right Optic Nerve	Dmax (cGy)	3158.08 ± 1637.03	2624.61 ± 1688.67	0.387
Left Optic Nerve	Dmax (cGy)	2774.51 ± 1633.84	2427.63 ± 1707.55	0.574
Right Eye	Dmax (cGy)	2901.73 ± 671.34	2760.1 ± 810.53	0.606
Left Eye	Dmax (cGy)	2826.87 ± 769	2673.41 ± 746.96	0.584
Right Lens	Dmax (cGy)	798.47 ± 221.3	751.05 ± 167.91	0.514
Left Lens	Dmax (cGy)	768.31 ± 213.56	775.91 ± 168.58	0.915
Right Cochlea	Dmax (cGy)	5944.45 ± 773.16	6062.15 ± 886.86	0.701

Left Cochlea	Dmax (cGy)	5820.49 ± 899.74	5931.82 ± 977.88	0.748
Oral Cavity	Dmax (cGy)	7095.25 ± 269.28	7160.49 ± 292.16	0.53
Mandible	Dmax (cGy)	7052.07 ± 372.39	7112.07 ± 389.83	0.67
Lips	Dmean (cGy)	2067.59 ± 69.02	2054.41 ± 158.57	0.771
Parotid Total	Dmean (cGy)	3342.85 ± 460.28	3380.54 ± 541.78	0.839

e. Eyes, Lens and Cochlea: Both eyes (Dmax ≤ 26Gy), lens (Dmax ≤ 6Gy) and cochlea (Dmax ≤ 54Gy) were analyzed separately, with their respective plan objectives. The mean Dmax for both eyes, lens, and cochleae, showed no significant difference

f. Parotid Total: The planning objectives for total parotid Dmean ≤ 33Gy were met by both plans and showed no significant difference.

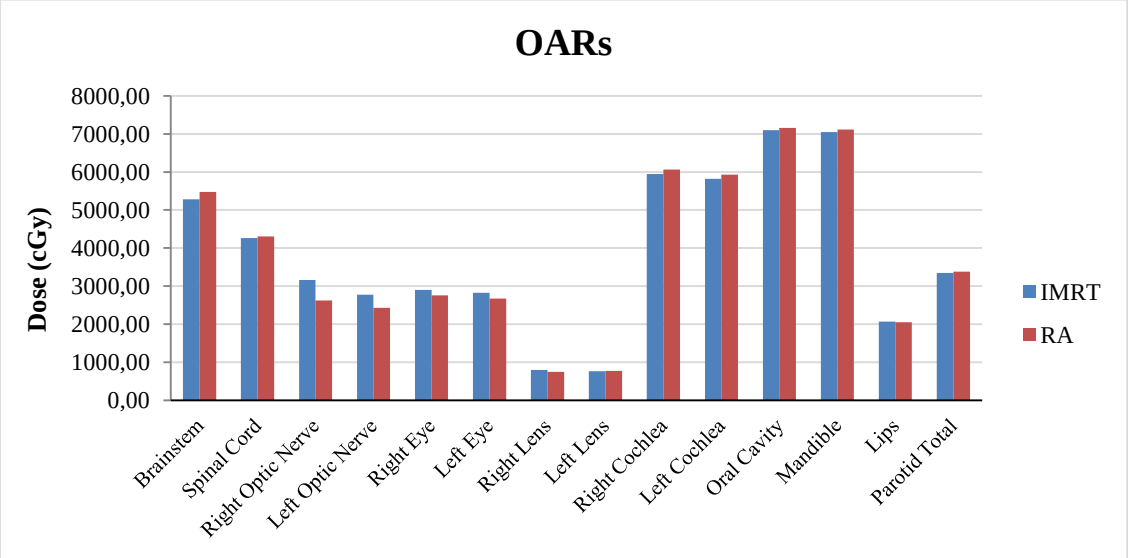

Figure 7: Plot of maximum dose and mean dose (lips and parotid total) for different PTV

III. Remaining Volume At Risk (RVR)

The application of RVR was to reduce the low dose received by the remaining healthy tissue. Table 4 gives the detailed numerical values on V5Gy(cc) (volume in cc receiving 5Gy), V10Gy(cc) (volume in cc receiving 10Gy), V20Gy(cc) (volume in cc receiving 20Gy), V30Gy(cc) (volume in cc receiving 30Gy), V50Gy(cc) (volume in cc receiving 50Gy), Dmax(Gy) and Dmean(Gy). There is no significant difference shown between the two plans. However, total MU showed a significant difference between the plans, where IMRT has a mean total MU three times that of VMAT plan with p value less than 0.001.

Table 4: Statistical Data statistically comparing IMRT with VMAT for RVR.

RVR = [Body - (PTV+OARs)]	IMRT (MEAN±SD)	VMAT (MEAN±SD)	p-value
Dmax (cGy)	7230.19 ± 228.8	7152.63 ± 259.6	0.393
Dmean (cGy)	947.82 ± 266.77	931.32 ± 272.21	0.868
V5Gy(cc)	3773.1 ± 1132.65	3724.83 ± 1133.44	0.908
V10Gy(cc)	3046.26 ± 885.9	2937.32 ± 836.02	0.732
V20Gy(cc)	2147.77 ± 519.8	2066.41 ± 523.41	0.673
V30Gy(cc)	1443.7 ± 349.14	1390.48 ± 319.14	0.666
V50Gy(cc)	457.17 ± 229.46	484.67 ± 210.55	0.735
MU Total	1837.67 ± 141.54	625.33 ± 49.02	<0.001

Discussion

Over the past few decades, there have been significant advances in the delivery of radiotherapy, and newer radiation techniques, e.g. Intensity Modulated Radiotherapy (IMRT), have been developed. Following its success, treating nasopharyngeal cancer using the IMRT delivery technique was considered a standard modality. Since NPC occurs near tissues and organs nearby, IMRT has become the principal radiation therapy technique for head and neck carcinoma using SIB protocol [4,8,18,19,21]. The main advantage of IMRT is to maximise target dose distribution while lowering the dose to the normal tissue, therefore reducing normal tissue complication probability by increasing local tumor control.

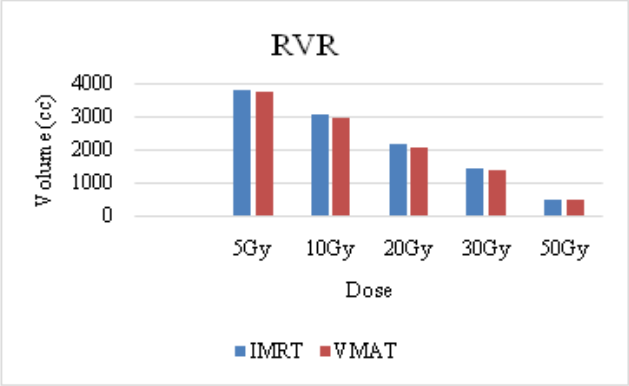

Figure 8: graphical representation for different does receive by the RVR

However, since IMRT usually requires 5-9 fields, treatment time is relatively long, which increases the probability of error due to patient discomfort and may compromise the treatment outcome, while the treatment time using the VMAT treatment technique is shortened.

Otto 7 introduced the concept of VMAT, which achieves intensity-modulation through continuous gantry motion, with MLC (multi leaf collimator) leaves and varying dose rates throughout the arc. E.J. Hall 6 reported that a high number of MU could increase scatter radiation and collimator transmission, therefore, increases the risk of secondary tumors. Studies by Lee 2 and Stieler 18 reported that the main difference between VMAT and IMRT was a significantly faster delivery time and lower number of MU for VMAT with a minimal advantage of better target coverage and OAR sparing as compared to the IMRT. Mellon 16, showed that VMAT had more homogeneous target coverage and a shorter treatment delivery compared with seven fields IMRT for prostate cancer treatment. Mahantshetty 17, compared IMRT vs VMAT in the treatment of Ovarian cancers using whole abdomen radiotherapy, and concluded that PTV conformity index, homogeneity, and OAR sparing were better in the cohort of patients treated by VMAT. Contradictory conclusions revealed that the mean dose of the parotid gland for 9-field IMRT was significantly reduced compared to those for VMAT plans 12. Based on this, an attempt was made in this study to design two plans - IMRT plans with 9-beams, and VMAT plans with two full arcs.

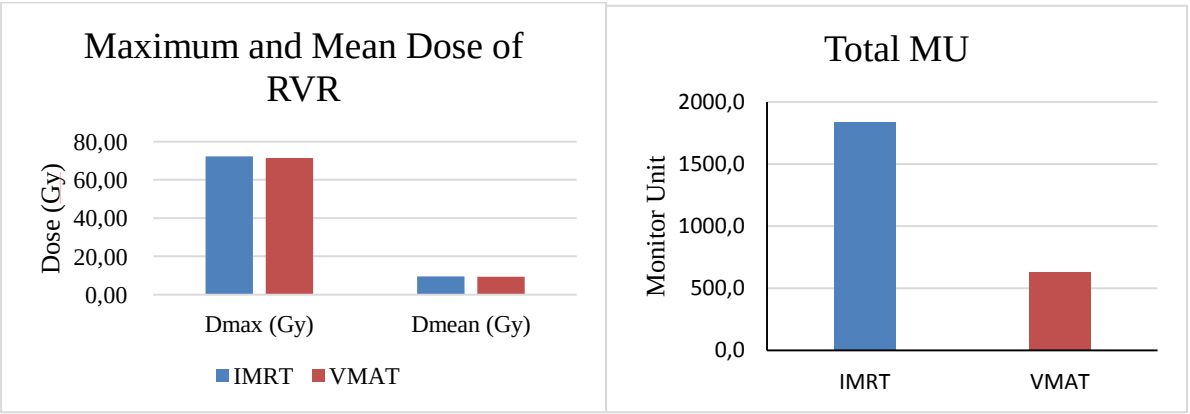

Figure 9: graphical representation of maximum and mean dose for RVR (left), and Total MU (right).

In radiotherapy, an optimal treatment technique can deliver high-dose conformity to the PTV with minimal dose to OARs. With respect to this dosimetric study, no technique was superior in all respects. Since in a SIB protocol, there are two different PTV with different prescribed dose, a PTV3 is contoured such that PTV1 is subtracted from PTV2 with 5mm margin such that a smooth dose gradient from PTV2 to PTV1 exist. The dose constraints to PTV3 were given in order to achieve the small volume of the PTV3 receiving V107% of the PTV2 prescribed dose, along with good dose homogeneity and conformity. However, by using the same optimization parameter in the VMAT plans as the IMRT plans as a reference, results have shown that comparing the two techniques for D95% (%) on PTV1 and V107% (cc) on PTV3, IMRT showed superiority compared to VMAT. On comparing the two techniques for total MU, VMAT shows superiority to IMRT.

In the case of OARs, both treatment techniques achieved desired dose constraints per QUANTEC guidelines. The study showed no statistically significant difference in OARs sparing between the two plans. It was observed that for a maximum number of patients, some portion of the parotid volume is included inside the PTV. To save the rest of the parotid, a structure termed (Right Parotid-PTV) and (Left Parotid-PTV) were contoured, and dose constraints are given accordingly. However, since it is nearer or overlaps with PTV, parotid's dose was high. For OAR and RVR, the treatment modality rendered no significant difference and nearly equivalent target dose conformity and homogeneity, reducing the dose spillage to the healthy tissues.

Conclusion

In summary, IMRT and VMAT provide satisfactory target dose coverage and improved efficiency with reduced normal tissue dose. VMAT provides less MU, machine wearing and treatment time compared to IMRT. VMAT, therefore, has a good perspective on radiation therapy application.

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