Introduction

Cancer is leading cause of morbidity and mortality worldwide, with approximately 19.2 million new cases and 9.95 million cancers related deaths in 2020 [1]. Among Noncommunicable diseases (NCDs), cancers are now predominant cause for the majority of global deaths, and is expected to rank as the leading cause of death and the single most important barrier to increasing life expectancy in every country of the world in the 21st century. In the Indian scenario, 1.3 million new cancer cases were estimated, indicating India as a single country (of the 185 countries) contributing to 10.43% of the global cancer burden; mortality figures were 851678, contributing to 7.05% of global cancer deaths in 2020 [2].

Head and neck cancers (HNC) are included among the commonest carcinomas worldwide and in India, in both males and females but more prevalent in males. HNC account for 17.7% of all new cancers in India, with approx. 230,000, new cases per year [3].

Head and neck cancers (HNC) are the malignancies arising from the base of skull to the thoracic inlet. Quality of life in these patients is poor as they suffer from socially awkward condition. They are persistently symptomatic which comprises pain, bleeding, mucositis, dysphasia, difficulty in swallowing, excessive salivating and most disturbing is proliferative growth that disfigures the face.

The management of HCN is a multimodality approach which includes chemotherapy, surgery, radiation therapy and targeted therapy. Role of chemotherapy is as either neoadjuvant, along with radiation therapy as CTRT and in palliative setting [4].

Radiotherapy is main non-surgical treatment for squamous cell carcinoma of head and neck (HNSCC) [5] and main is to deliver a tumoricidal dose to the target and simultaneously spare the healthy structures in vicinity. For achieving this goal, technology prompt radiotherapy in future and that is how it advances from three-dimensional conformal radiotherapy (3D-CRT) to intensity modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT). In the past few years
IMRT has established as gold standard for organs at risk (OAR) sparing, target coverage and dose conformity. With the evolvement of rapid arc VMAT, an inter comparison is need of time to state the pros and cons of each technique. So, present study is formulated to evaluate the comparative efficacy of IMRT with VMRT for head and neck cancer with dosimetric parameters in terms of PTV coverage, homogeneity index, conformity index and Dose received by organs at risk (OAR).

Materials and Methods

Prospective randomised study was conducted at Acharya Tulsi regional cancer treatment and research institute, SPMC Bikaner, Rajasthan after acceptance from institutional ethical committee. Written consent was taken from all patients before recruitment in study.

Patient Selection and preparation

Total 50 patients of non-metastatic, non-palliative head and neck cancer patients were randomly selected in the study and divided in two groups. One group treated with IMRT technique plans and other with VMAT.

A pre-treatment evaluation was done which includes complete history and physical examination, CECT / MRI of head and neck, chest x ray or thoracic CT.

Patients were aligned in supine position and immobilised on a head support pad using thermoplastic mask. All patients were scanned from skull vertex to mid-chest in the CT simulator “G HIGH SPEED”. Intravenous contrast was used in order to help in the delineation of cervical nodes. CT images will then be transferred to the TPS “ECLIPSE”.

Target volume definition

Gross tumour volume (GTV) is defined as the macroscopic disease including all positive lymph nodes detected by clinical examination and radiological imaging. The clinical target volume (CTV GROSS) disease is composed of GTV with a 10-mm margin. Near the neural structures, the margin is reduced to as little as 1 mm. The CTV subclinical disease is composed of CTG gross disease in addition to other areas at high risk of harbouring microscopic spread. The planning target volumes (PTV) are generally a 5mm expansion of each of CTVs to account for potential setup errors and patient motion. Similarly, the margin around the CTV was limited to 1 mm near the neural structures [6]. Three PTVs were generated with different dose levels; PTV70Gy, PTV60Gy and PTV54Gy in both VMAT and IMRT plans.

Dose and Fractionation

The dose to the PTV 70 is prescribed as 70 Gy in 2.33 Gy per fraction, the dose to the PTV 60 is prescribed as 2 Gy per fraction, the dose to the PTV54 Gy was 54 Gy in 30 fractions. The prescribed doses were delivered in 30 fractions, once daily, five fractions per week using simultaneous integrated boost (SIB) technique. The BED calculated is 80.52 Gy.

Radiotherapy Treatment planning

IMRT and VMAT plans were created using 6 and 10 MV photons commissioned on a TRUE-BEAM equipped with a multi-leaf collimator 0.5 cm width, max. speed of 2.5cm/s per leaf. The upper and lower collimators comprise a complete field of 40*40 cm square. Variable dose rate up to 2400 Mu/min in TRUE-BEAM.

Plan evaluation parameters

A total dose of 70 Gy was delivered to the PTV boost and 54 Gy to the elective PTV. In all cases the target was to achieve 95% of the prescription dose to at least 95% of each PTV. No point dose outside PTVs was >107% of the prescribed dose, and no point dose within PTVs was >110% of the prescribed dose. For the OAR, maximum doses to the brainstem and spinal cord were tried to be kept below 54Gy and 45 Gy, respectively. Regarding the parotid glands, the aim was to restrict the mean dose to below 26Gy. For vestibulocochlear nerve, aim was to restrict dose below 54 Gy.

The DVH for PTV coverage, parotid, spinal cord and brain stem were generated. The PTV coverage was calculated using the ratio of target volume covered by 95% of prescribed isodose line divided by the volume of PTV. Minimum and maximum doses within the PTV, the D98% and D2% values were also recorded (dose received by 98% and 2% of the PTV volume). As per the ICRU 83, the homogeneity index (HI) was calculated using the following equation (D2% −D98%)/D50% (ratio of difference between the dose covering 2% and 98% to the dose received by 50% of the PTV volume). The conformity index (CI95%) was defined as the ratio between the patient volume receiving at least 95% of the prescribed dose and the volume of the PTV.

Results

The Statistical Package for Social Sciences (SPSS) version 16.0 was used. Paired t test was applied to compare the different dosimetric parameters.

Median age of the patients was 50 years (14-72 years) which is lower than stated by GLOBOCON 2020 which may be due to small sample size and maximum patients belonged (41-50 years) age group. Among 50 patients, 38 (12%) patients were in stage IVA, followed by stage III (36%) and II (26%). In total 50 cases, 40% were of oral cavity cancers followed by nasopharyngeal cancer (18%), hypopharyngeal cancer (14%), oropharyngeal cancer (12%) and laryngeal cancer (10%). The PTV volume was ranging from 80.3 cm³ to 941.6 cm³. The median PTV volume was 302.9 cm³. Patients with low PTV volume were mostly post-operative cases (early cases) while with the high PTV volume were with the high nodal burden

<table>
<thead>
<tr>
<th>Stage</th>
<th>VMAT</th>
<th>IMRT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>1.02</td>
<td>1.033</td>
<td>0.03</td>
</tr>
<tr>
<td>Stage III</td>
<td>1.029</td>
<td>1.076</td>
<td>0.018</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>1.056</td>
<td>0.969</td>
<td>0.063</td>
</tr>
</tbody>
</table>
Table 2. Homogeneity Index and Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>VMAT</th>
<th>IMRT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>0.0961</td>
<td>0.0969</td>
<td>0.063</td>
</tr>
<tr>
<td>Stage III</td>
<td>0.0988</td>
<td>0.104</td>
<td>0.023</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>0.0994</td>
<td>0.108</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 3 Average Dose to Different OARS for VMAT and IMRT

<table>
<thead>
<tr>
<th>Organs</th>
<th>VMAT (in cGy)</th>
<th>IMRT (in cGy)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotid Left</td>
<td>2702</td>
<td>3154</td>
<td>0.003</td>
</tr>
<tr>
<td>Parotid Right</td>
<td>2747</td>
<td>3205</td>
<td>0.031</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>4303</td>
<td>4514</td>
<td>0.32</td>
</tr>
<tr>
<td>Brainstem</td>
<td>4547</td>
<td>4993</td>
<td>0.0012</td>
</tr>
<tr>
<td>Vestibulocochlear nerve Left</td>
<td>3288</td>
<td>3606</td>
<td>0.0026</td>
</tr>
<tr>
<td>Vestibulocochlear nerve Right</td>
<td>3275</td>
<td>3696</td>
<td>0.001</td>
</tr>
</tbody>
</table>

resulting in high elective CTV volume and thus the PTV.

**Target volume coverage**

Dose D98% for PTV70 were 6533 cGy and 6514 cGy for VMAT and IMRT respectively. Dose D2% for PTV70 were 7244 and 7203 cGy respectively. Dose D50% PTV70 for VMAT was 7040 cGy and for IMRT D50% was 6984 cGy. No statistically significant difference (p>0.05) was found between PTV coverage values of VMAT and IMRT. PTV coverage values for VMAT and IMRT were also assessed in plans with different stage group of head and neck cancer patients. For VMAT plans, the average values of D98% for stage II, III and IVA were 6636, 6494 and 6498 cGy respectively. The D50% were 7041, 7021 and 7052, D2% were 7211, 7269 and 7243 cGy respectively for stage II, III and IVA. The difference in values of D98%, D50% and D2% for VMAT and IMRT were statistically insignificant (p>0.05).

For IMRT, the average D98% value for stage II, III, IVA were 6573, 6462 and 6526 cGy respectively. The D50% were 7022, 6958 and 6983 cGy for II, III and IVA. D2% values for stage II, III and IVA were 7210, 7207 and 7194 cGy respectively for stage II, III and IVA. The difference between values of D98%, D50% and D2% for II, III, IVA were statistically insignificant (p>0.05).

The conformity index for IMRT and VMAT plans were 1.067 and 1.037 respectively. The difference was also noted between homogeneity index which were 0.0984 for VMAT and 0.1041 for IMRT plans. The difference is statistically significant. The average conformity index in stage II, III, IVA were 1.020, 1.029 and 1.056 respectively for VMAT plans (Table 1). Similarly, for IMRT plans, conformity index was 1.033, 1.076 and 1.080 respectively. The difference was statistically significant in all the stage groups.

The average homogeneity index in stage II, III, IVA were 0.0961, 0.0988 and 0.0994 respectively for VMAT plans. Similarly, for the IMRT plans, homogeneity index was 0.0969, 0.01040 and 0.0108 respectively. The difference was statistically significant (p< 0.05) in stage III and IVA but insignificant in stage II (p> 0.05) (Table 2).

The conformity index was better for VMAT in all the PTV category compared to IMRT. The homogeneity index was also better in VMAT plans as compared to IMRT except for higher PTV volume where IMRT had better plans.

The mean dose to parotid were significantly lesser in parotid glands in VMAT plans. Also, the point max dose to spinal cord, brainstem, vestibulocochlear nerve was lesser. There was no significant difference in dose received by spinal cord in both arms. Dose to OARs were lesser in VMAT in higher stage irrespective of the type of OAR. Regarding mean dose to parotid, it was always lesser irrespective of the stage of disease and the difference was significant in higher stages. Dose to spinal cord was approximately similar, the difference was not significant. Dose to brainstem was lesser in VMAT Plans as compared to IMRT irrespective of the stage. Similarly, in vestibulocochlear nerve the dose was lesser in VMAT plans. The difference was statistically significant in brainstem and vestibulocochlear nerve (Table 3).

**Discussion**

VMAT is an advanced radiation treatment modality for cancers which has potential to prompt treatment plans for different anatomical sites which are comparable with corresponding IMRT plans. In present study IMRT plans were compared with VMAT in terms of various dose volume parameters to assess PTV coverage, homogeneity index, conformity index and OAR sparing.

On analysis there was no significant difference in PTV Coverage for PTV66 between IMRT and VMAT. Dose D98% for PTV70 was 65.33 Gy and 65.14 for VMAT and IMRT respectively. The difference was also not seen with D50% and D2% between IMRT and VMAT.

On subset analysis of stage and coverage, there was no significant difference between stage II, III and IVA for D98% in VMAT plans, and same holds true for stage II, III and IVA in IMRT plans. Similar results were observed in D50% and D2%. On analysis of PTV coverage for stage II plans in IMRT and VMAT, no significant difference for D98% and the difference was also not significant for D50% and D2%. This result was similar in stage III and IVA between both the plans. These findings were in accordance with the results of study done by Caraman et al [7] which stated that the minimum dose to the Planning Target Volume (D98%) was not significantly different for Intensity Modulated Radiotherapy and Volumetric Modulated Arc Therapy plans, while there was small difference in the maximum or mean dose to Planning Target Volume though statistically insignificant.

In present study it was observed that the conformity index was 1.037 and 1.067 for VMAT and IMRT plans respectively. The difference was statistically significant (p-value 0.038). On subset analysis also VMAT was more conformal to IMRT irrespective of the stage of primary disease. On another subset analysis of PTV volume versus conformity, the VMAT was more conformal.
Regarding homogeneity, HI was 0.0984 for VMAT and 0.1041 for IMRT. The VMAT technique gave more homogeneous plans over IMRT. This difference was statistically significant in stage III (p value 0.023) and IVA (p value 0.001) but insignificant (p value 0.063) in stage II. Similar Results were found on comparison of primary tumour wise homogeneity index in both the plans. However, on comparing with PTV volume, it was observed that VMAT was more homogeneous except for higher PTV volumes. These findings were similar with the study conducted by Lu et al which showed that VMAT and IMRT had similar PTV coverage with an average of 96%. Homogeneity was better in VMAT (1.06) than IMRT plans (1.07). Nagarajan et al. stated that VMAT achieved a better conformity index 95% (C95%) with value of 1.016 ± 0.014 compared to 1.033 ± 0.0012 in IMRT. Dosimetric parameters like D2%, D5%, D50% were higher in VMAT compared to IMRT. HI was higher for the IMRT with value of 0.035 ± 0.003 compared to 0.0058 ± 0.008 with VMAT.

On analysis, the mean dose to parotid were significantly lesser in parotid glands in VMAT plans. Also, the point max dose to spinal cord, brainstem, vestibulocochlear nerve was lesser. There was no significant difference in dose received by spinal cord in both arms. Mirestean et al found similar result with VMAT significantly decreased Dmean dose to right and left parotid glands.

On analysis of Dmax to spinal cord, the average Dmax dose was 43.03 Gy and 45.14 Gy for VMAT and IMRT respectively but it was statistically insignificant. Difference was more evident in early staged cancers as compared to late stage cancer. The max point dose to brainstem was 45.47 Gy for VMAT AND 49.93 Gy for IMRT (statistically significant). The difference was present irrespective of the stage of tumour. Similarly point max dose to right and left VCN was 32.75 Gy, 32.88 Gy for VMAT while it was 36.96 Gy and 36.06 for IMRT. The difference was statistically significant. Findings similar with study conducted by Lu et al [8] and Nagarajan et al [9] that VMAT had a better sparing effect on brainstem, spinal cord and parotid gland.

In conclusion, dosimetric plan quality parameters of VMAT are comparable with IMRT plans, more conformal and homogeneous dose is delivered via VMAT along with better OAR sparing like parotid gland, brainstem, vestibulocochlear nerve. This may result in better locoregional control and may prevent Radiotherapy related side effects like mucositis, xerostomia etc. However, present study has its own drawbacks like small number of sample size and is dosimetric study. For more conclusive results further clinical study should be conducted with large sample size.

References

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