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Research Article

Correlation between Target Volume and Organs at Risk Doses in Stage Ii-Iva Nasopharyngeal Carcinoma Patients Treated With Helical Tomotherapy: A Prospective Single Institution Study from Northeast India

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ABSTRACT
Background: Nasopharyngeal carcinoma (NPC) is a relatively rare head and neck cancer globally, accounting for only about 0.7% of all cancers The peak incidence arises between 15 and 25 years of age, with the second peak of 50 and 59 years of age. The majority of patients present with locally advanced disease (stage II–IVA) requiring combined modality therapy .The aim of the study is to examine the relationship between target volume and organ-at-risk (OAR) doses in nasopharyngeal carcinoma (NPC) patients treated with image-guided helical tomotherapy.
Material and Methods: In this prospective single-institutional study, 30 patients with histologically confirmed stage II–IVA NPC were treated with helical tomotherapy to a dose of 70 Gy in 35 fractions with concurrent Cisplatin chemotherapy. The target volumes and key Organs at Risk (spinal cord, brainstem, bilateral cochlea, parotids, larynx, oral cavity) were delineated. Dose–volume histogram parameters (maximum dose Dmax, mean dose Dmean, and V50Gy for selected structures) were recorded. Pearson correlation coefficients (r) between GTVp and OAR dose metrics were computed and a p value <0.05 was considered significant.
Results: The GTVp volume ranged between 10–210 cm^3 (mean ~78 cm^3). Larger GTVp was significantly associated with higher doses to the right cochlea and oral cavity. Specifically, GTVp had a positive correlation with right cochlea Dmax ($r \approx 0.77$, $p=0.005$) and Dmean ($r \approx 0.84$, $p=0.004$), and with oral cavity mean dose ($r \approx 0.68$, $p=0.030$) .No other OAR parameters showed significant correlations (all $p>0.05$).
Conclusions: Thus in Nasopharyngeal Cancer treated with helical tomotherapy, increasing tumor volume was linked to higher doses to the right cochlea and oral cavity. These findings underscore the impact of tumor extent on OAR exposure and highlight the need for careful dose optimization, especially to auditory and mucosal structures, in patients with large GTVs.

Keywords: GTV: Gross tumour volume, CTV: Clinical target volume, PTV: Planning target volume, IMRT: Intensity modulated Radiotherapy, IGRT: Image guided Radiotherapy, NPC: Nasopharyngeal Carcinoma, OAR: Organs at risk, MVCT: Megavoltage Computed tomography, TPS: Treatment planning system, DICOM: Digital imaging and communications in medicine, SPSS: Statistical Package for the Social Sciences.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a relatively rare head and neck cancer globally, accounting for only about 0.7% of all cancers (~120,000 new cases/year)[1] However, its incidence shows marked geographic variation and is endemic in East and Southeast Asia (with age-standardized rates up to ≈ 6–20 per 100,000 in high-risk areas)[2]. In India, NPC incidence is

generally low except in the northeastern states where rates can exceed 15 per 100,000.[3] The peak incidence arises between 15 and 25 years of age , with the second peak of 50 and 59 years of age. The majority of patients present with locally advanced disease (stage II–IVA) requiring combined modality therapy. Current standard management of locoregionally advanced NPC is definitive radiotherapy with concurrent platinum-based chemotherapy.[4]

Intensity-modulated radiotherapy (IMRT), often with image guidance, has become the technique of choice for NPC due to its ability to achieve excellent tumor control while better sparing adjacent organs at risk (OARs) compared to conventional 2D radiotherapy.[5] Various meta-analyses have shown that IMRT yields superior locoregional control and overall survival, also with substantially lower rate of late toxicities such as xerostomia and cranial neuropathies relative to older techniques .Helical tomotherapy (HT) represents an advanced IG-IMRT platform that delivers highly conformal dose distributions with in-built imaging for precise patient positioning. By modulating beam intensity around the patient, HT can deliver high dose to targets while minimizing dose to nearby critical structures.

Despite these technical advances, NPC treatment can still impart significant toxicity, including xerostomia, dysphagia, and sensorineural hearing loss, often related to the dose received by salivary glands, oral mucosa, and the cochlea.[6] In practice, larger tumor volumes may require larger treatment fields or higher target margins, potentially increasing incidental OAR dose. However, there is limited data quantifying how target volume affects OAR dosimetry in NPC. Yao et al. performed a large prospective study (148 patients) and found that greater gross tumor volume (GTV) was strongly predictive of higher doses to multiple OARs (including brainstem, cochlea, temporal lobes)

This study is an attempt to investigate the correlation between target volume (GTVp) and OAR dose parameters in NPC patients treated with helical tomotherapy focussing on key normal structures (spinal cord, brainstem, cochleae, parotids, larynx, oral cavity) that can impact critical functions. Thus identifying statistically significant dose-volume relationships could improve planning strategies, especially in large tumors where OAR sparing is challenging.

MATERIALS AND METHODS

This Prospective study was carried out in the Department of Radiation Oncology, State Cancer Institute, GMC. Prior approval for conducting this study was obtained from the Institutional Ethics Committee.

Participants

Thirty histologically confirmed Nasopharyngeal Carcinoma patients of Stage II–IVA, aged 27-58 years with M:F ratio of 2:1 were enrolled in this study.

Treatment Planning

All patients were immobilised using 5 clamp thermoplastic head and neck mould. Intravenous Iodine contrast was used for optimum differential tissue enhancement and proper delineation of target structures. The CT simulation was done for all the patients in the Siemens® SOMATOM® DEFINITION AS-20 CT scanner with the proper traction. After acquisition, the images were transferred to the Accuray® Precision TPS in DICOM format, registered and fused.

Targets and OARs were contoured on planning CT (and MRI fusion) according to the international guidelines put forward by Lee et al. [7] The primary gross tumor volume (GTVp) was delineated, and a 5 mm margin (adjusted for anatomical boundaries) defined the CTVp1. CTVp2 was contoured as GTVp + 10 mm alongwith the nasopharynx , at least 5 mm of choana,5 mm from posterior wall of maxillary sinus, skull base foramina i.e; the foramen ovale, rotundum, lacerum, petrous tip, anterior 1/3rds of clivus, inferior half of sphenoid sinus, (whole if T3-T4), parapharyngeal space, the pterygoid fossa. GTVn was contoured and a margin of 5mm was given to define the CTVn1. Bilateral level II,III,IV,Va, retro-pharyngeal lymph nodal stations were contoured and alongwith the CTVn1 plus a margin of 5 mm designated as CTVn2. CTVp1 and CTVn1 were combined using Boolean operator to designate the CTV 70, likewise CTVp2 and CTVn2 were combined to formed the CTV 60. Respective PTVs were created giving adequate margins according to the institutional protocol. The prescribed dose to the primary PTV70 was 70 Gy in 35 fractions, the PTV 60 was treated to a dose of 60 Gy in 30 fractions.[8]

OARs contoured included the spinal cord, brainstem, bilateral cochleae, bilateral parotid glands, larynx, oral cavity, and other relevant structures. Treatment planning was done using 6 MV photons in a sequential plan. Dose–volume histograms (DVHs) were generated for each plan. For each OAR we recorded relevant dose metrics: maximum dose (Dmax) and

mean dose (Dmean) in Gy, and select volume metrics (e.g. V50Gy for larynx and cochlea, V30Gy for parotids) as per standard reporting. All patients received radiotherapy with daily image guidance using MVCT in the Accuray® Radixact X9 tomotherapy machine.

Statitical Analysis

After treatment planning and dose calculation, data analysis was performed using statistical software IBM SPSS Statistics (Version 26.0); IBM Corp., Armonk, NY, USA**.**

Pearson correlation coefficients (r) were computed between the primary target volume (GTVp) and OAR dose volume parameter. Values closer to 1 or -1 indicate linear relationships. Correlation coefficients were reported with corresponding 95% confidence intervals (CI). Correlation coefficients yielding *p-values* <0.05 were considered statistically significant.

RESULTS

Table 1 Summarises The Baseline Demographic And Clinical Characteristics Of All 30 Patients.

Categories	Frequency
Age	
Less than 50 years	16 (53.3 %)
More than 50 years	14 (47.7 %)
Gender	
Male	20 (66.7%)
Female	10 (33.3%)
T stage	
T1	5 (16.6%)
T2	7 (23.3%)
T3	14 (46.6%)
T4	4 (13.3%)
N stage	
N0	0
N1	9 (30%)
N2	12 (40%)
N3	9 (30%)
M stage	
M0	30 (100%)
M1	0
Stage group	
I	0
II	7 (23.3%)
III	14 (46.6%)
IVA	9 (30%)
IVB	0
Clinical symptoms	
Neck swelling	20 (66.6%)
Nasal obstruction, epistaxis	15 (50%)
Headache	10 (33.3%)
Hearing problem, tinnitus	12(40%)
Histology	
Keratinising SCC	11 (36.6%)
Non Keratinising SCC	15 (50%)
Undifferentiated	4 (13.3%)
EBV association	
Positive	14 (46.6%)
Negative	16 (53.3%)

All 30 patients completed planned therapy. Tumors exhibited significant volumetric heterogeneity (GTVp range ≈10–210 cm^3, mean ≈78 cm^3). By design, all plans met target coverage goals while respecting standard OAR constraints. Table 2 summarizes the Pearson

correlation analysis between target volume (GTVp) and key OAR dose parameters.

Table 2. Correlation between Gross Tumor Volume (Gtvp) and OAR Dose Metrics (N=30).

OAR	Dose parameter	Pearson Coefficient [r]	p-value
Right cochlea	Dmax	0.77	0.005
	Dmean	0.84	0.004
Oral cavity	Dmax	0.206	0.052
	Dmean	0.68	0.03
Left cochlea	Dmax	0.048	0.8
	Dmean	0.095	0.793
Spinal cord	Dmax	0.62	0.055
Brainstem	Dmax	0.473	0.4
Right parotid	Dmean	0.390	0.265
	V30	0.379	0.28
Left parotid	Dmean	0.532	0.113
	V30	0.379	0.27
Larynx	Dmax	0.504	0.134
	Dmean	0.019	0.957
	V50	0.137	0.705

The table highlights that larger GTVp was significantly associated with higher doses to the right cochlea and to the oral cavity. The strongest correlations were observed for the right cochlea ($r \approx 0.77$ for Dmax, $r \approx 0.84$ for Dmean; both $p<0.05$) and for the oral cavity mean dose ($r \approx 0.68$, $p \approx 0.03$). No other OAR parameter showed a statistically significant correlation with tumor volume (all other $p>0.05$). For example, left cochlea Dmean showed a trend ($r \approx 0.68$) but did not reach the $p<0.05$ threshold ($p=0.051$). Similarly, mean doses to the parotids, brainstem, spinal cord, and larynx had low correlation coefficients ($|r|<0.6$) with p-values >0.05.This indicates that patients with larger NPC primaries tended to receive higher doses in the vicinity of the right inner ear and oral cavity structures when treated with standard tomotherapy plans. In contrast, other OARs – including the contralateral cochlea and bilateral parotids – did not show significant volume-related dose increases in this cohort.

DISCUSSION

This prospective analysis of 30 NPC patients treated with IGRT in helical tomotherapy demonstrates that increasing primary tumor volume correlates significantly with higher doses to the right cochlea and oral cavity. These findings are consistent with prior observations that tumor bulk influences normal tissue exposure in NPC. In a large series, Yao et al. reported that greater GTV was a better predictor than T-stage for dose elevation to multiple OARs (including brainstem, temporal lobes and cochlea). Our results extend this to an IGRT-based setting, highlighting the sensitivity of cochlear and oral doses received to the tumor size.

Anatomically, the nasopharynx lies just above the level of the skull base and pharynx. Larger tumors often extend laterally into the parapharyngeal space or inferiorly toward the oropharynx. Thus, larger PTVs may abut or envelop the petrous temporal bone containing the cochlea, leading to higher cochlear doses. The particularly strong correlation on the right side may reflect asymmetry in our cohort's tumors or beam arrangements, but it emphasizes that even with advanced planning, cochlear sparing becomes more difficult as tumor volume increases. The oral cavity mean dose also rose with GTV, likely reflecting more inferior tumor extent . In practice, higher oral cavity dose predicts worse mucositis and swallowing toxicity, just as higher cochlear dose is associated with sensorineural hearing loss.[9-10] Indeed, radiation-induced hearing loss is a known late effect in NPC: grade ≥2 hearing impairment occurs in up to ~42% of patients receiving IMRT[11].

Interestingly, none of the other OARs showed statistically significant volume–dose correlations. Bilateral parotid Dmean values remained largely un-correlated with GTV ($r \approx 0$–0.4), reflecting consistent parotid-sparing across cases. Likewise, spinal cord and brainstem doses were well controlled and did not rise with volume, likely due to strict

planning constraints for these serial structures. This suggests that our planning approach effectively mitigates OAR dose escalation for most structures, except in the case of cochlea and oral cavity where proximity to large targets is unavoidable.

Our results have practical implications. First, they suggest that in NPC patients with very large GTVs, planners should pay special attention to auditory and oral cavity structures. Whenever feasible, tighter margins or advanced techniques (e.g. non-coplanar beams, adaptive replanning) might be considered to limit cochlear and oral doses. Second, these correlations highlight the value of IGRT: daily image guidance helps ensure dose is delivered as planned, but it cannot fully compensate for the geometric necessity of treating a large volume. In high-volume tumors, closer follow-up of audiometric function may be warranted.

This study is limited by its small sample size and single-institution design. The 30-patient cohort, while prospective, may not capture the full variability seen in larger populations. Correlation analysis also cannot prove causation, and it is possible that underlying anatomical factors or patient positioning differences contributed to the results. Nonetheless, our findings provide an important quantitative insight in an Indian NPC cohort treated with modern IGRT.

CONCLUSION

In a 30-patient prospective series of locoregionally advanced NPC treated with Image Guided-helical tomotherapy, we found that larger primary tumor volumes were significantly associated with higher radiation doses to the right cochlea and to the oral cavity. These volume–dose relationships were not observed for other OARs. The results depicts the impact of tumor size on normal tissue exposure even with conformal IMRT/IGRT techniques, and highlight the need for diligent planning to spare cochlea and oral structures in patients with large nasopharyngeal tumors.

Conflict of Interest: None

Ethical Clearance: obtained from IEC, State Cancer Institute , GMC, Guwahati

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