RESEARCH ARTICLE

Dose Planning Study of Target Volume Coverage with Intensity-Modulated Radiotherapy for Nasopharyngeal Carcinoma: Penang General Hospital Experience

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Abstract

Background: To compare the dosimetric coverage of target volumes and organs at risk in the radical treatment of nasopharyngeal carcinoma (NPC) between intensity-modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3DCRT). Materials and Methods: Data from 10 consecutive patients treated with IMRT from June-October 2011 in Penang General Hospital were collected retrospectively for analysis. For each patient, dose volume histograms were generated for both the IMRT and 3DCRT plans using a total dose of 70Gy. Comparison of the plans was accomplished by comparing the target volume coverage (5 measures) and sparing of organs at risk (17 organs) for each patient using both IMRT and 3DCRT. The means of each comparison target volume coverage measures and organs at risk measures were obtained and tested for statistical significance using the paired Student t-test. Results: All 5 measures for target volume coverage showed marked dosimetric superiority of IMRT over 3DCRT. V70 and V66.5 for PTV70 showed an absolute improvement of 39.3% and 24.1% respectively. V59.4 and V56.4 for PTV59.4 showed advantages of 18.4% and 16.4%. Moreover, the mean PTV70 dose revealed a 5.1 Gy higher dose with IMRT. Only 4 out of 17 organs at risk showed statistically significant difference in their means which were clinically meaningful between the IMRT and 3DCRT techniques. IMRT was superior in sparing the spinal cord (less 5.8Gy), V30 of right parotid (less 14.3%) and V30 of the left parotid (less 13.1%). The V55 of the left cochlea was lower with 3DCRT (less 44.3%). Conclusions: IMRT is superior to 3DCRT due to its dosimetric advantage in target volume coverage while delivering acceptable doses to organs at risk. A total dose of 70Gy with IMRT should be considered as a standard of care for radical treatment of NPC.

Keywords: Intensity-modulated radiotherapy - 3D conformal radiotherapy - nasopharyngeal carcinoma

Introduction

Nasopharyngeal carcinoma (NPC) is prevalent in China and the South-east Asian region with a peak incidence rate of 20 per 100,000 person-years in HongKong (Law et al., 2007). NPC is the fifth commonest malignancy in Peninsular Malaysia with an incidence rate of 8.5 and 2.6 per 100,000 populations for males and females respectively according to the latest available incidence report by the National Cancer Registry for Peninsular Malaysia in 2006 (Malaysian Cancer Statistics, 2006). The only curative treatment of NPC is with radiotherapy (RT) though the addition of chemotherapy to RT has been conclusively shown to be beneficial for locally advanced NPC. Two meta-analyses involving more than 2500

patients and ten randomized trials reported an absolute survival benefit of 4-6% at 5 years and this benefit was most pronounced with concurrent chemoirradiation (Langendijk et al., 2004; Baujat et al., 2006). As such the key to improving survival for NPC lies in advancement of RT technique and this area has seen remarkable progress over the last decade. Treatment have progressed from two-dimensional techniques in the early 1990s to three-dimensional conformal radiotherapy (3DCRT) and most recently intensity-modulated radiotherapy (IMRT) (Lee at al., 2002; Langendijk et al., 2004; Baujat et al., 2006; Kwong et al., 2006; Ng et al., 2006; Lin et al., 2009; Wang et al., 2012). RT for NPC is fraud with danger as the nasopharynx is surrounded by many radiosensitive structures such as the spinal cord, brainstem, temporal

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lobes, optic chiasm, optic nerves, retina, lenses, middle and inner ears and the parotid glands. NPC also has a propensity to spread along all directions often making the RT target volume large and irregular. This is especially so in stages III and IV disease where complicated target volumes which lie very close to critical organs like the spinal cord and brainstem making it impossible to be treated with adequate high dose with conventional 2D or 3DCRT. However, IMRT has been shown to be able to deliver high dose to the target areas despite these obstacles (Cheng et al., 2001; Waldron et al., 2003). The most important aim of RT is maximization of the therapeutic index which essentially means maximal radiation dose to the target volumes while delivering as little dose as possible to the organs at risk (OAR). Clinically, this should be expected to translate to maximal local control and survival with as little toxicity as possible. Comparison of dosimetry for NPC treatment between 3DCRT to IMRT has been done in several studies and these studies have collectively shown advantages of IMRT over 3DRT with regards to tumour coverage and OARs (Cheng et al., 2001; Hunt et al., 2001; Kam et al., 2003; Kristensen et al., 2007). However, these studies were done with different protocols from that of our institution and included different total doses to different target volumes. As such it is prudent for all institutions that are starting their IMRT service for NPC to perform an analysis of their own to compare the dosimetry of IMRT and 3DCRT. We consider this especially important in view of a recent study performed in our institution which revealed a worryingly low 5 years overall survival(OS) rate of only 33.3% for our NPC patients from a cohort of 285 patients treated in 2001-2005 (Phua et al., 2011). The treatment during that period of time was either with conventional 2DRT or 3DRT. As IMRT was only recently introduced in our institution, we hope with this advancement in RT technique the local control and survival rate will improve. With this study we set out to demonstrate the superiority of IMRT compared to 3DCRT regarding the target volume coverage while maintaining acceptable dosage to the OARs.

Materials and Methods

Patients

Data from 10 consecutive patients treated with IMRT from June-October 2011 in Penang General Hospital were collected retrospectively for analysis. The patients had a mean age of 50.4 years with a range of 36-72 years. There were 7 males and 3 females. All had good performance status with either ECOG PS 0-1. The patients' clinical T, N and overall AJCC stages are presented in table 1. Neo-adjuvant chemotherapy was given to 6 patients while 5 patients received concurrent chemoirradiation during IMRT with weekly cisplatin at 30mg/m2.

IMRT planning

Patients were immobilized with a tailored beam directional shell in a comfortable neck position. Intravenous contrast-enhanced CT using 3mm slice from the vertex to below the clavicles was performed using the CT simulator. CT data were then imported to the treatment planning system. Targets and organs at risk (OAR) were localized on the CT images. The gross tumour volume (GTV70) included all known gross disease in the primary area and the neck area determined from CT, MRI, clinical information and endoscopic examination. Enlarged neck nodes included any lymph nodes >1cm or nodes with a necrotic center. The clinical target volume (CTV70) to account for microscopic spread was obtained by giving a margin of 1cm circumferentially around the GTV. A second clinical target volume (CTV59.4) which is bigger than the CTV70 was delineated to account for all potential routes of spread for the primary and the nodal regions. These included the entire nasopharynx, parapharyngeal space, pterygopalatine fossa, posterior third of the nasal cavity and maxillary sinuses, inferior sphenoid sinus, posterior ethmoid sinus, base of skull (including the foramen ovale and rotundum bilaterally) and anterior half of the clivus. The cavernous sinus was also included for high risk patients.

As for the nodal region, the CTV59.4 included the nodes in the junctional, parapharyngeal, retropharyngeal, submandibular regions, level II, III, IV, V nodes and supraclavicular fossa bilaterally. Subsequently, separate planning target volumes (PTV) were obtained by providing a margin of 0.5 cm around the CTV to account for variabilities of treatment set up and internal organ movement resulting in PTV70 and PTV59.4. Margins were reduced to as low as 1 mm for target volumes in close proximity to critical OARs i.e. the brainstem and spinal cord. The treating radiation oncologist modified these final PTVs accordingly based on the surrounding critical OARs. The contoured OARs included the spinal cord, brainstem, optic chiasm, optic nerves, eyes, lenses, cochlea, parotid glands, oral cavity, larynx, mandible, temporomandibular joints and brachial plexus.

Inverse planning for IMRT was performed using the CMS XiO version 4.60. The prescribed doses were 70Gy to the PTV70 in 33 fractions at 2.12Gy per fraction and 59.4Gy in 33 fractions to the PTV59.4 at 1.8Gy per fraction. With regards to the OARs, the critical organs were the spinal cord and brainstem. Maximal allowable dose to any part of the spinal cord was 45Gy and for the brainstem it was 54Gy without any compromise. The optic nerves and eyes were kept below 50Gy while the optic chiasm was kept below 54Gy. If the doses of any of these optic apparatus were exceeded due to extensive disease informed consent for blindness was obtained from the patient prior to plan approval. The maximal allowable dose for the brachial plexus was 66Gy unless there was gross disease in its vicinity. Dose constraints for the OARs chosen by our institution were based on papers published by Emami in 1991 and the more recent publication in 2010 by the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) initiative (Emami et al., 1991; Marks et al., 2010).

Dose volume histogram (DVH) was generated for all the target volumes and OARs. For evaluation of the DVH, the treating oncologist used the following guideline for acceptability of a plan: 95% of any PTV70 was at or above 70Gy and 99% of PTV70 was at or above 65.1Gy. In addition, no more than 20% of the PTV70 was at or

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above 77Gy and no more than 5% of the PTV70 was at or above 80Gy. Plans fulfilling the criteria for PTV70 needed to be within the dose constraints for OARs as outlined above. Quality assurance for the finalized plan was done using the MapCHECK tool for point dose and fluence testing. Verification of isocentre was subsequently done by checking orthogonal fields using the SimViewNT Siemens Simulator. IMRT was delivered via seven fixed angles with an Elekta Precise Linear Accelerator. Portal imaging was done weekly using the Elekta iview electronic portal imaging version 3.4. Acceptable overall treatment time (OTT) was set at 7 weeks. Treatment was delivered once daily, 5 fractions per week, over 6 weeks and 3 days. All targets were treated simultaneously.

3DCRT planning

The above 10 patients were treated with IMRT. We then retrospectively performed 3DCRT planning for each of these patients to allow comparison between IMRT and 3DCRT for these 10 patients. The target volumes and OARs used were unchanged from that used in the IMRT for each patient. Total dose prescribed was the same at 70Gy. The best possible plan was obtained using at least 2 phases to ensure that the total brainstem and spinal cord doses were not exceeded as per the IMRT constraints i.e. 54Gy for the brainstem and 45Gy for the spinal cord. The doses to the eye apparatus were respected as well if possible unless they were very close to the target volumes. There was no limit to the number of fields used in each phase. Plans were modified accordingly to obtain the best possible therapeutic index i.e. maximizing tumour coverage while strictly not exceeding the tolerance doses of the brainstem and spinal cord, and minimizing doses to other OARs.

Comparison of IMRT and 3DCRT plans

For each patient, the DVHs were generated for both the IMRT and 3DCRT plans using a total dose of 70Gy. Comparison of the plans were done by comparing the volume of the target receiving the full dose (70Gy or more), V70 for PTV70 and 95% of the prescribed dose (66.5Gy or more), V66.5 for PTV70. The mean dose for the PTV70 was also compared, mean PTV70. As for the second target volume PTV59.4, comparison was done using the volume of the target receiving 59.4Gy or more, V59.4 for PTV59.4 and 95% of the prescribed dose (56.4Gy or more), V56.4 for PTV 59.4.

For the OARs, the maximum dose was obtained for the brainstem, spinal cord, right and left optic nerves, optic chiasm, right and left eyes, right and left lenses and right and left temporal mandibular joint (TMJ) for comparison between the IMRT and the 3DCRT plans. For the cochlea, the volume receiving 55Gy or more, V55 was used for comparison. For the oral cavity and larynx, the mean doses received were compared. The parotids were compared using the volume of the parotid receiving 30Gys or more, V30.

The means of the comparison items listed above for target volumes and OARs were obtained for both the IMRT and the 3DCRT. These means were tested for statistical significance using the paired Student t-test

utilizing SPSS version 18.0. A p-value of less than 0.05 was considered as statistically significant.

Results

The means of the targets volumes i.e. V70 and V66.5 for PTV70, V59.4 and V56.4 for PTV59.4 and the mean for mean PTV70 are found in Table 2. Also included in Table 2 are the means for the OARs including the means for the maximum doses of the brainstem, spinal cord, right and left optic nerves, optic chiasm, right and left eyes, right and left lenses, right and left TMJs, the means for the mean dose for the oral cavity and larynx and lastly the means for the V55 for the cochlea and V30 for the parotids.

The differences between these means for the IMRT and 3DCRT are found in Table 3. Included in this table are the 95% confidence interval for the differences of the means and the p-value for these differences. For the target volumes, all 5 comparative measures showed advantage of IMRT over 3DCRT which were statistically significant.

Table 1. Clinical Stage of 10 Patients

Tumour stage	T1	3
	T2	2
	T3	1
	T4	4
Nodal Stage	N0	2
	N1	0
	N2	6
	N3	2
AJCC stage	I	2
	II	0
	III	3
	IV	5

Table 2. Mean Target Volumes and Organ at Risk of 10 Patients

	Mean		Standard deviation	
	IMRT	3DCRT	IMRT	3DCRT
Target volumes (PTV70 and PTV59.4) and organs at risk				
V70 for PTV70	90.20%	50.90%	5.50%	10.70%
V66.5 for PTV70	96.70%	72.60%	2.30%	11.40%
Mean PTV70	73.3 Gy	68.2 Gy	1.1 Gy	2.1 Gy
V59.4 for PTV59.4	91.20%	72.80%	6.10%	10.00%
V56.4 for PTV59.4	97.00%	80.50%	2.20%	6.10%
Brainstem	50.4 Gy	50.7 Gy	3.0 Gy	3.6 Gy
Spinal cord	40.1 Gy	45.9 Gy	3.2 Gy	1.5 Gy
Right optic nerve	47.5 Gy	40.2 Gy	4.4 Gy	9.3 Gy
Left optic nerve	45.7 Gy	40.4 Gy	4.7 Gy	7.2 Gy
Optic chiasm	51.1 Gy	43.7 Gy	3.8 Gy	4.1 Gy
Right eye	39.2 Gy	31.4 Gy	8.0 Gy	11.7 Gy
Left eye	38.2 Gy	32.6 Gy	8.1 Gy	12.1 Gy
Right lense	8.0 Gy	5.3 Gy	5.1 Gy	5.3 Gy
Left lense	8.4 Gy	5.2 Gy	6.1 Gy	5.1 Gy
V55 right cochlear	27.20%	14.20%	43.40%	30.90%
V55 left cochlear	47.90%	3.60%	49.20%	7.20%
Oral cavity	49.6 Gy	51.7 Gy	5.4 Gy	10.2 Gy
Larynx	53.8 Gy	63.4 Gy	5.8 Gy	15.3 Gy
Right TMJ	71.9 Gy	65.0 Gy	2.7 Gy	20.3 Gy
Left TMH	73.9 Gy	70.7 Gy	3.3 Gy	1.9 Gy
V30 right parotid	52.70%	67.10%	7.20%	3.20%
V30 left parotid	53.10%	66.20%	6.60%	2.30%

The most glaring difference came from the V70 for PTV70 which is the percentage volume covering 70Gy or more, which showed an absolute difference of 39.3% (p value<0.000). The arguably most important measure which is the V66.5 for PTV70 which is the percentage volume covering 95% or more of the prescribed dose also showed a remarkable 24.1% absolute difference (p-value<0.000). The V66.5 for PTV70 using IMRT had a mean of 96.7% which is highly acceptable to ensure an adequate dose to the PTV as compared to only 72.6% using 3DCRT. The mean dose to the PTV70 was also higher for IMRT compared to 3DCRT at 73.3Gy versus 68.2Gy. Essentially, all 5 measures showed remarkable advantage in favour of IMRT.

Comparison of measures between IMRT and 3DCRT for the OARs which achieved statistical significance were the spinal cord, right and left optic nerve, optic chiasm, right eye, right lens, left cochlea, left TMJ and both parotids. The mean spinal cord dose was lower with IMRT at 40.1Gy versus 45.9Gy for 3DCRT (p-value=0.001). This advantage is important especially if patients have large posterior neck nodes which often times cannot be treated adequately with posterior electron field with 3DCRT technique in view of the tolerance of the spinal cord. The other mean measure that showed superiority for IMRT over 3DCRT was the V30 for the parotids. The mean V30 for the right parotid was 14.3% less while the left side was 13.1% less with IMRT. Unfortunately, the absolute percentage of the V30 for parotid glands with IMRT was still high at 52.7% for the right side and 53.1% for the left side. Ideally, V30 should be kept below 45% to reduce the risk of chronic xerostomia which is the commonest late effect of curative RT for NPC. Meanwhile, the OARs that showed advantage in favour of 3DCRT which achieved statistical significance were the right and left optic nerve, optic chiasm, right eye, right lens, left cochlea and left TMJ. With regards to the optic apparatus, none of this small absolute advantage in maximal dose in these structures can result in a clinical advantage as the mean doses for both IMRT and 3DCRT were below the threshold doses for serious late toxicity. The optic nerves have a threshold of 50Gy for a 5% complication rate in 5 years for neuropathy which can lead to blindness. The IMRT technique yielded a mean dose of 47.5Gy for the right nerve and 45.7Gy for the left nerve compared to 40.2Gy and 40.4Gy for the 3DCRT. Though there is an advantage in terms of lower doses with 3DCRT but both techniques yielded doses below the toxicity threshold of 50Gy. In fact, it is an in-built feature of inverse planning for IMRT treatment to push the limits of the tolerance doses of the OARs in order to achieve the best possible coverage for the target volumes. The same goes for the optic chiasm where the threshold is 54Gy and the means for IMRT and 3DCRT were 51.1Gy and 43.7Gy respectively. Both means were below the threshold level of 54Gy. The right eye mean doses were 39.2Gy and 31.4Gy for the IMRT and 3DCRT respectively. Both means were below the threshold of 50Gy for retinopathy. The right lens mean doses were 8.0Gy and 5.3Gy for the IMRT and 3DCRT respectively. These were below the tolerance dose of 10Gy for cataract formation. The

Table 3. Difference of Mean Values of Target Volumes and Organ at Risks between IMRT and 3DRT

	Difference of mean value between IMRT and 3DCRT	Std. Deviation of the difference	95%Confidence Interval of the Difference		P value (2-tailed)
			Lower	Upper	
Target Volumes (PTV70 & PTV59.4) & Organ at risks					
V70 for PTV70	39.30%	7.90%	33.60%	44.90%	0
V66.5 for PTV70	24.10%	10.70%	16.40%	31.70%	0
Mean PTV70	5.1 Gy	1.9 Gy	3.8 Gy	6.5 Gy	0
V59.4 for PTV59.4	18.40%	11.30%	10.30%	26.50%	0.001
V56.4 for PTV59.4	16.40%	6.60%	11.70%	21.10%	0
Brainstem	-0.2 Gy	5.5 Gy	-4.1 Gy	3.6 Gy	0.893
Spinal cord	-5.8 Gy	3.7 Gy	-8.4 Gy	-3.1 Gy	0.001
Right optic nerve	7.2 Gy	7.5 Gy	1.9 Gy	12.6 Gy	0.013
Left optic nerve	5.3 Gy	6.9 Gy	0.3 Gy	10.2 Gy	0.037
Optic chiasm	7.3 Gy	4.3 Gy	4.3 Gy	10.4 Gy	0
Right eye	7.8 Gy	8.5 Gy	1.7 Gy	13.9 Gy	0.017
Left eye	5.6 Gy	8.3 Gy	-0.3Gy	11.6 Gy	0.061
Right lense	2.6 Gy	3.8 Gy	0.0 Gy	5.3 Gy	0.05
Left lense	3.2 Gy	5.2 Gy	-0.4 Gy	6.9 Gy	0.079
V55 right cochlear	12.90%	56.70%	-27.60%	53.40%	0.489
V55 left cochlear	44.30%	46.90%	10.80%	77.80%	0.015
Oral cavity	-2.1 Gy	6.4 Gy	-6.6 Gy	2.5 Gy	0.339
Larynx	-9.6 Gy	13.5 Gy	-19.2 Gy	0.1 Gy	0.051
Right TMJ	6.9 Gy	21.5 Gy	-8.4 Gy	22.2 Gy	0.337
Left TMH	3.2 Gy	3.0 Gy	1.0 Gy	5.3 Gy	0.009
V30 right parotid	-14.30%	6.20%	-18.80%	-9.90%	0
V30 left parotid	-13.10%	6.30%	-17.60%	-8.50%	0

V55 of the left cochlea should ideally be kept below 5% to reduce the risk of neurosensory hearing deficit. The 3DCRT performed better with a mean of 3.6% compared to 47.9% (p-value=0.015) with IMRT. In addition, there were 5 out of the 10 patients who exceeded the 5% limit for doses at or above 55Gy with the IMRT treatment. With the 3DCRT, only 1 patient exceeded the 5% limit. Lastly, the mean doses for the left TMJ were 73.9Gy with IMRT and 70.7Gy with 3DCRT. Both the means exceeded the tolerance dose of 70Gy for a 5% complication rate at 5 years, thus there is no clinical advantage even though a lower mean dose was achieved with 3DCRT.

Discussion

NPC is one of the cancers where major advancement in the RT technique has been achieved in the last decade with the introduction of IMRT. This is especially relevant in the field of oncology as RT remains the only curative treatment modality for NPC. This is made all the more significant in view of our low survival rate as mentioned earlier and the fact that the majority of our patients present with advance disease (Phua et al., 2011). Presentation with AJCC stage 3 or 4 disease accounted for 79.3% of patients in the cohort treated from 2001-2005 in our institution. A similar situation was found in another study in University Hospital, Kuala Lumpur which revealed an even higher proportion at 94% (Prasad et al., 2000). The latest available data in Malaysia based on NPC patients treated in six major tertiary referral centers from July 2007 to February 2008 still showed 75% of patients presented with stage III or IV diseases (Pua et al., 2008). The recent usage of IMRT treatment for NPC patients in our institution presents an opportunity to achieve better

local control and survival rates. Although 3DCRT allows manual optimization of beam orientation, beam weighting and beam eye view shaping, there is still suboptimal conformity to the concave target volume required in NPC treatment. With the advent of IMRT, one more degree of freedom is gained where dose intensity modulation within each individual beam is possible (Kam et al., 2003). In addition, the dose constraints assigned to critical OARs in the optimization process allow better preservation of organ function than that achieved by 3DCRT.

The results of this study confirms the dosimetric advantage of IMRT over 3DCRT using the treatment protocol adopted by our institution. All 5 measures for tumour coverage showed huge absolute advantage with IMRT treatment. In fact the tumour coverage with 3DCRT was abysmal. The V70 and V66.5 for PTV70 was only 50.9% and 72.6% with 3DCRT compared to 90.2% and 96.7% with IMRT. This was due to the target volumes which lie close to the brainstem and the spinal cord where no compromise could be accepted. Doses kept below 54Gy for the brainstem and 45Gy for the spinal cord could not be compromised and with 3DCRT where the target volumes curved around these structures, the coverage of the target volumes would naturally be reduced to keep within the tolerance of these critical OARs. The other major obstacle with 3DCRT occurred when patients had advance nodal disease in the posterior cervical area. To keep within the tolerance of the cord, a second phase of treatment was needed where the photon beam avoided the spinal cord. This area was then compensated with a posterior neck field with electron treatment. Unfortunately, this often proved to be inadequate as the target volumes were still very close to the cord and though electron treatment allowed a rapid dose falloff beyond a certain distance there would still be dose deposited in the cord. As such higher energy electrons which could penetrate further to cover more of the target volume could not be used thus compromising the overall percentage of tumour coverage.

With regards to the dosimetric comparison of IMRT and 3DCRT for OARs, the OARs that had both clinical and statistical significant difference were the spinal cord, left cochlear and both parotids. IMRT produced lower dose to the spinal cord compared to 3DCRT. As the spinal cord serves as one of the critical OAR that limits the total dose that can be given, 3DRCT has been shown to be severely lacking in tackling this problem. Often times large posterior cervical neck nodes cannot be treated adequately with posterior electron therapy which is required once the tolerance dose of the cord has been reached when treating with lateral opposing photon fields in phase 1 treatment of 3DCRT. Morever, it is undesirable to split the field over any gross tumour volume but it is unavoidable with 3DCRT for off cod purpose. This problem is averted in IMRT where only 1 phase of treatment is required and the lower dose to the spinal cord can assure adequate coverage of nodal target volumes.

Xerostomia is the most significant side effect of 2DRT and 3DCRT. This affects the patients' speech, taste, deglutition and oral hygiene. Long time survivors' quality of life is often compromised due to this debilitating side effect. The parotids contribute 60-70% of the total salivary gland secretion (Kam et al., 2003). A study evaluating the impact of parotid sparing with IMRT and 3DCRT found that total salivary production reported a threshold parotid dose of 32Gy (Chao et al., 2001). It is best to aim for a V30 of parotids to below 45% if at all possible to allow as much recovery of salivary flow as possible. Our study shows an absolute reduction of 13-14% in the V30 with IMRT compared to 3DCRT. However, the mean V30 for both glands with IMRT were still above 45% at about 53%. It is important to note that the parotids lie very close to the retropharyngeal and jugulodigastric nodes which are part of the CTV59.4 and thus with expansion to account for set-up and internal organ movement to form the PTV59.4, the deep lobe of the parotids would inevitably be included in the PTV. We believe any compromise of the CTV or PTV to obtain a better V30 for the parotids cannot be justified as these are not critical OARs. Moreover, as alluded earlier the result of treatment for our patients from a cohort in 2001-2005 was poor and as such our primary aim should be to improve our local control and survival rates. The only advantage of 3DCRT over IMRT in our study which had both statistical and clinical significance was the lower V55 for the left cochlear. The cochlea lies in close proximity to the clivus and the upper parapharygngeal space, both of which are part of the CTV59.4 and PTV59.4. Ideally, the V55 of the cochlea should be less than 5% to reduce the chance and severity of hearing deficit. In our study, 5 patients exceeded this percentage with IMRT as compared to only 1 patient with 3DCRT. However, this is exactly the reason why 3DCRT is unable to achieve acceptable target volume coverage as it is unable to curve around the OAR which is the brainstem in this situation, and as such the lateral opposing fields have a sharp cut off to avoid the brainstem. In the same instance, this allows a lower dose to the cochlea but compromise the target volume coverage. As the cochlea is not a critical OAR, again there can be no justification to lower the dose to the cochlea by compromising coverage of the target volumes.

In conclusion, our study has shown clear dosimetric superiority of IMRT over 3DCRT for NPC treatment using our treatment policy with a total dose of 70Gy. Poor efficacy of NPC treatment can be due to inadequate dose to target volumes, intrinsic radioresistance or geographical miss. This study shows 3DCRT using our treatment protocol will result in severe inadequate dose to the target volumes and may be a contributing reason to the poor OS demonstrated for our cohort of patients treated in 2001-2005. It is imperative that IMRT be instituted as the standard of care for NPC treatment in our institution. Furthermore, we need to actively collect efficacy and late toxicity information of these patients treated with IMRT to guide future management.

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