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ORIGINAL ARTICLE

The Role of Adaptive Radiotherapy in Definitive Radiation of Nasopharyngeal Cancer: A Review of Dosimetry

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OBJECTIVE

This study aimed to evaluate the dosimetry changes and provide an overview of the time for radiation planning adjustments.

METHODS

This prospective cohort study recruited nasopharyngeal cancer patients aged 18 or older. Radiation planning adjustment was performed if at least one normal organ at-risk or target volume deviated from the criteria.

RESULTS

A total of 11 patients were included as study subjects. After completing up to the 30th fraction of radiation, 8 of 11 patients lost more than 10% of their weight and required adjustments in their radiation plan. The analysis of the relationship between the fractionation time and planning adjustment showed the greatest increase in fractions 11 to 16, RR: 2.83 (1.74–4.61) and 4.76 (2.35–9.65), with a statistically significant result (p=0.000). The widest neck separation demonstrated the highest sensitivity of plan adjustment need (93.3%) and specificity (87.5%) at 1.21 cm with an area under the curve (AUC) of 0.951 and a 95% CI of 0.905–0.996 (p<0.001). The mastoid tip separation showed the highest plan adjustment need sensitivity of 93.3% and specificity of 40.6% at 0.435 cm with an AUC of 0.741, 95% CI 0.631–0.852 (p<0.001). The Δ body weight percentage showed the plan adjustment needs a sensitivity of 91.1% and specificity of 81.2% at 4.49 with an AUC of 0.911, 95% CI 0.844–0978 (p<0.001).

CONCLUSION

The radiation planning adjustment in patients with locally advanced nasopharyngeal cancer is suggested at the 16th fraction, the 3rd week. It is recommended at the widest lymph node area separation of 1.21 cm or a weight loss percentage of 4.49%.

Keywords: Nasopharyngeal cancer; radiation dosimetry; radiotherapy.
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INTRODUCTION

Radiotherapy has a critical role in the management of head-and-neck cancer, both definitively and adjuvant postoperatively, of which one of the most common cases is nasopharyngeal cancer.[1] Over the past decades, nasopharyngeal cancer has become an endemic disease in East Asia, Southeast Asia, North Africa, and

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the Middle East.[2] Based on 2020 global cancer observatory data, nasopharyngeal cancer is ranked 5th in the number of new cases in Indonesia.[3]

Several studies reported that patients with head-and-neck cancer experienced significant body contour changes in the radiation area in the 6–7th week of radiation, one of which was due to a reduction in tumor size.[4] Barker et al.[5] reported that there were changes in the geometry and volume of 14 head-and-neck cancers with tumor size and lymph nodes ≥4 cm at irradiation observed from frequent evaluation computed tomography (CT) scans. Gross tumor volume (GTV) decreased by a median of 0.2 cm^2 per irradiation session/day. These anatomical changes are concerning due to the possibility of overdosage of organs at risk (OAR). Apart from shrinking the size of the tumor, weight loss is another factor that can cause changes in the patient's anatomy. Li et al.[6] reported that 56% of 159 patients with nasopharyngeal cancer lost more than 5% of their weight during radiation, with a median weight loss of 6.9 kg. This contributed to the change in dosimetry during radiation. The study conducted by Khaldoon with a phantom representing patients before and after radiation demonstrated that there were differences in the average dose of OAR in the treatment planning system (TPS) ranging from 3.5 gy to 29.8 gy.[7]

The dosimetry changes may cause a decreased therapeutic ratio due to body contour changes that occur during radiation, manifested as the loosening of the head-and-neck thermoplastic mask. Stauch et al.[8] reported that in head-and-neck cancer, an average change in neck separation of 1.06 cm led to an increase in the average dose of OAR, such as in the parotid, which experienced an average dose increase of 3.9 Gy, the spinal cord of 1.5 Gy, and the brainstem of 0.2 Gy. An adaptive radiation was then emerged as the imaging feedback control strategy, with replanning as the response to variations or changes that occur in patients.[9,10]

Hansen et al.[1] stated that replanning is mostly a clinical decision, taking into account how significant the size of the tumor, weight loss, or looseness of the mask make the position unsuitable with the initial radiation plan. There is no guideline yet on when replanning should be carried out. Wang et al. recommended performing a CT simulation again before the 25th fraction, with a significant difference at week 2. Stauch et al.[8] reported that in head-and-neck cancer, the average neck separation of 1.06 cm led to an increase in the average dose in OARs such as the parotid, which experienced an average increase in dose of 3.9 Gy, the spinal cord of 1.5 Gy, and the brainstem of 0.2 Gy. In Indonesia, verification methods are generally made according to the circumstances of each radiotherapy center to achieve results with minimal workload. In Ciptomangunkusumo Hospital, Jakarta, radiation planning adjustments are carried out if the immobilization device is inadequate or loose, but there is no data evaluating the dosimetry changes. Therefore, this study aimed to evaluate the dosimetry changes and provide an overview of the time for radiation planning adjustment. Furthermore, significant mask loosening was reviewed for changes in dosimetry planning to maintain dosimetry accuracy on the target and OAR.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Radiation Oncology Integrated Service Unit of Cipto Mangunkusumo Hospital, Jakarta, from March to June 2022.

The subjects were patients aged 18 years or more who were diagnosed with nasopharyngeal cancer. The inclusion criteria were patients subjected to kilovoltage cone beam CT (kV-CBCT) with a thickness of 2 mm by scanning the area from the vertex to below the clavicle, radiation planning carried out at TPS Monaco, and radiation at Versa using kV-CBCT every 5 fractions. Patients who did not complete the planned radiation, who had previously undergone external radiation, and patients with a radiation gap of >5 consecutive days or a total of 10 days were excluded.

The patients underwent a CT simulator with a thickness of 2 mm per slice, which includes the head vertex up to 2 cm below the sternoclavicular joint, to calculate the radiation dose exposed to the brain that may receive further toxic effects due to radiation. In the delineation, the images produced by the CT simulator were fused with previous images, either in the form of magnetic resonance imaging (MRI) or positron emission CT (PET-CT) scans. In nasopharyngeal cancer, MRI was used to determine the target delineation of the primary tumor (GTVp) more accurately and was done within 2–3 weeks before the simulation, while PET-CT is more used as a guide in identifying tumors, especially in small lymph nodes that can be missed on CT and MRI scans. It is recommended to make clinical target volume (CTV) adjustments based on the nature of tumor invasion and its anatomical relationship with surrounding soft tissue. The cranial base is not considered a strong barrier like other cortical bones, so delineation adjustments were not necessary after 5 mm of expansion into the cranial base.[11] The recommended dose for CTV was three dose levels, or administering three doses simultaneously in one radiation session, where CTV1 is an expansion of GTV, CTV2 cover areas or regions that are at high risk of microscopic spread, and CTV3 cover areas or regions that are at low risk of microscopic spread. All of the patients underwent a 33-fraction scheme (2.12 Gy per fraction) with 3 dose levels of 69.96 Gy, 63 to 59.4 Gy, and 54 Gy.[12]

The following are delineation recommendations for nasopharyngeal cancer CTV:[11]

a. High Dose CTVp1
   - Margin of GTVp: GTVp + 5 mm (± Whole Nasopharynx)
   - Minimum margin if near a critical organ: GTVp + 1 mm.
b. High Dose CTVn1
   - Margin of nodal GTV (GTVn): GTVn+5 mm (consider 1 cm if there is extracapsular extension).
c. Intermediate Dose CTVp2
   - Margin of GTV: GTVp + 10 mm + Whole Nasopharynx
   - Nasal cavity, the posterior part: At least covers the anterior 5 mm of the choana
   - Maxillary sinus, posteriorly: Extends at least 5 mm anteriorly from the posterior wall of the maxilla
   - Posterior ethmoid sinuses: Covers the vomer area
   - Base cranial: Includes the foramen ovale, rotundum, lacerum, and the petrous edge
   - Sinus cavernous: Included area of T3-T4 tumor on the involved side
   - Pterygoid fossa: Insert the entire fossa into the CTV area
   - Parapharyngeal space: Inserted into the CTV area
   - Sphenoid sinus: Inserted ½ inferior parts if the tumor is T1-T2, and the entire sphenoid is inserted if it is T3-T4
   - Clivus: Insert 1/3 of the area if there is no clivus invasion and insert the whole if there is clivus invasion
   - Minimum margin if the tumor is close to critical organs: GTVp + 2 mm.
d. Intermediate dose CTVn2
   - Margin of GTVn: CTVn1+5 mm
   - Bilateral negative lymph nodes: Include levels II, III, Va, VIIa, VIIb, and at least 1 level below the level of the involved lymph nodes
   - Level Ib: Included if lymph nodes are positive at level Ib, submandibular nodes are involved, there is the extracapsular extension at level II, and there is the involvement of structures with major drainage at level Ib
   - If there is no involvement, the level Ib ipsilateral area can be excluded.
e. Low dose CTVn3
   - IV and Vb levels up to the clavicle are included if cervical lymph nodes are involved.

The dose prescription was conducted based on a study conducted by Lee et al., specifically that ≥95% of the prescription dose covers 100% of the volume of the planning target volume (PTV), or ≥93% of the prescription dose covers ≥99% of the volume of the PTV. Meanwhile, for OAR in nasopharyngeal cancer, the dose limits were given according to the recommendations by Lee et al.[12]

The CT data sets were sent to the Eclipse TPS for contouring. The contouring was carried out by medical residents and reviewed separately by two radiation oncologists based on international guidelines for the delineation of the CTV for nasopharyngeal carcinoma. Afterward, the patients were given a dose prescription. Simultaneous Integrated boost with a dose of 70/60/54 Gy in 33 fractions, and constraints were determined according to the Deviation Protocol on target organs and OAR.

Radiation planning was made by two medical physicists after receiving the dosage prescription and dose limits to normal organs that had been previously determined. The radiation planning was then reviewed separately by two radiation oncologists. The positioning was verified using kV-CBCT in the first fraction and each of the next 5 fractions in each patient. The kV-CBCT images and the images used for radiation planning or CT planning were verified through automatic and manual co-registration based on the bone and soft tissue anatomy with a displacement tolerance of 3 mm from the isocenter. This was conducted by a radiation oncology resident under the supervision of a radiation oncologist. The radiation was then given to the Versa HDlinear Accelerator (LINAC).

To compare the dosimetry, contouring was performed on the kV-CBCT image in each fraction against the target volume, and OAR was selected based on clinical preference. Fusion was performed between the kV-CBCT image on the Versa HD LINAC and the CT simulator planning image carried out previously by 2 radiation oncologists and 1 medical physicist to reduce bias due to the selection of differ-

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Table 1 Characteristics of study subjects who required radiation planning adjustment

Patient	Age (years)	Stage	Δ weight decrease (%)	Δ widest lymph node separation (cm)	Δ mastoid tip separation (cm)	Fraction required radiation planning adjustment	Causes of radiation planning adjustment
1	66	III	9.62	2.56	2.16	21	Left optic nerve, GTVp, GTVn, PTV54
2	23	IVA	12.58	2.57	1.05	26	GTVn
3	47	IVA	6.82	1.54	0.55	16	Left optic nerve, PTV54
4	45	IVA	22.77	2.39	2.49	16	PTV54
5	38	IVA	31.25	3.06	2.65	6	GTVn
6	68	IVA	1.52	0.67	1.71	No radiation planning adjustment	None
7	60	IVB	16.05	3.26	0.81	16	PTV60
8	68	IVA	10.66	1.71	0.93	16	PTV70, PTV60, spinal cord, brain stem, left optic nerve
9	38	IVB	14.52	3.53	1.36	1	PTV54
10	47	III	15.28	3.07	1.19	16	GTVn, left and right optic nerve
11	55	IVA	13.64	4.35	2.29	1	CTV70, PTV70, GTVn

GTVp: Primary gross tumor volume; GTVn: Nodal gross tumor volume; PTV: Planning target volume; CTV: Clinical target volume

ent bone landmarks. For each patient, all planning parameters were recalculated using kV-CBCT images. Using the kV-CBCT calibration curve, the simulated dose distribution based on the kV-CBCT weekly fraction image was evaluated. Dosimetry evaluation results were recorded on the OAR and target volume for each kV-CBCT. Radiation planning adjustment was carried out in the presence of a deviation in at least one normal OAR or target volume according to the specified criteria. If the dosimetry deviation criteria were met but occurred in fraction 31, the radiation planning adjustment was unnecessary.

The dosimetry data were analyzed with the Statistical Program for the Social Science version 23.0. The analysis of the numerical data distribution was carried out using Shapiro-Wilk. The relationship between numerical variables and the radiation planning adjustment criteria conducted with logistic regression and sensitivity analysis as presented in the receiver operating curve. Chi-square and Fischer exact tests were carried out to determine the relationship between categorical variables.

RESULTS

There were 13 patients with nasopharyngeal cancer who met the study criteria and had been confirmed to undergo definitive locoregional radiation therapy. Of them, there were 2 patients who did not undergo kV-CBCT: 1 did not undergo kV-CBCT verification in fraction 6, and 1 patient did not undergo kV-CBCT in fraction 31, leaving a total of 11 patients as our study participants.

The mean age of the subjects was 50±15.14 years, and the mean body weight was 62.2±11.16 years.

After completing up to the 30th fraction of radiation, 8 of 11 patients lost more than 10% of their weight and required adjustments in their radiation plan. For the widest neck separation, 10 out of 11 patients were found to have decreased neck separation of more than 1.5 cm and required adjustment to radiation planning, while the results for changes in mastoid tip separation were varied. There were only 1 out of 11 patients who did not require adjustment to radiation planning with a body weight decrease of 1.52%, a widest lymph node separation of 0.67 cm, and a mastoid tip separation of 1.71 cm in the 30th fraction. Changes in dosimetry of GTVn were the most common cause of radiation planning adjustments. The characteristics of study subjects who required radiation planning adjustments are presented in Table 1.

Periodic measurements of all study participants during radiation included body weight, widest neck separation, and mastoid tip separation. When compared to before undergoing radiation, all three parameters showed increased values after radiation, as can be seen in Figure 1.

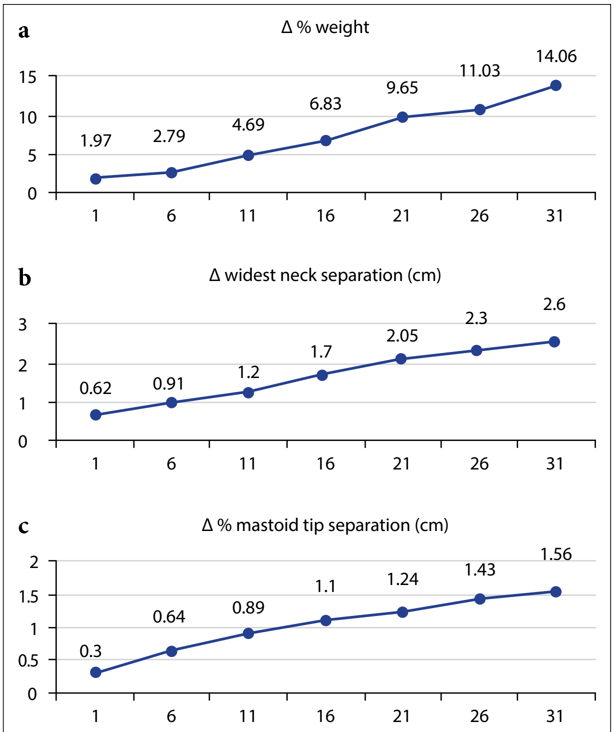

Fig. 1. The percentage of changes in (a) body weight, (b) widest neck separation, and (c) mastoid tip separation during radiation.

The target volume of GTVn had a dosimetry change at D_{100} that widens as the number of fractions received increases, with a significant change at the 16th fraction, while for the mean dosimetry of GTVp, target volume changes tend to be unstable. For Target CTV, the dosimetry changes were also wider, with changes of up to 2–3 times in the 31st fraction when compared to the first fraction. The largest increase in CTV dosimetry changes occurred in the 16th fraction compared to the 11th fraction in V95 CTV70 and V95 CTV54. There was an increase in PTV in dosimetry changes as the number of fractions increased in V95 PTV70 and V95 PTV60, but it tended to be unstable in V95 PTV54. Normal organs at risk of the optic chiasma, spinal cord, and brainstem showed an increase in dosimetry changes, but the right optic nerve showed a decreasing trend of dosimetry changes in the 20th fraction, and the left optic nerve decreased after the 26th fraction as can be seen in Table 2.

The bivariate analysis was conducted with Chi-square and Fischer tests to investigate the relationship between time of fractionation and radiation planning adjustment, as can be seen in Table 3. The relative risk ratio showed the greatest increase in fractions 11–16, from 2.83 (1.74–4.61) to 4.76 (2.35–9.65).

Table 2 Dosimetry changes in target volume and normal organs at risk during radiation

Target volume and OAR	Parameters	Fractions						
		1	6	11	16	21	26	31
Δ %GTVp	$D_{95\%}$	2.97±0.62	3.79±3.58	3.53±2.97	2.52±1.46	3.75±3.81	4.08±5.25	2.5±1.67
Δ %GTVn	$D_{95\%}$	5.07±8.0	3.14±3.5	3.12±4.25	5.54±5.17	9.5±11.07	12.43±8.67	14.89±13.78
Δ % CTV V95 70 gy	$V_{95\%}$	1.94±1.91	1.85±1.76	2.22±1.97	2.79±1.83	3.6±1.81	3.6±1.84	4.57±2.63
Δ % CTV V95 60 gy	$V_{95\%}$	0.48±0.38	0.65±0.68	0.78±0.85	1.08±1.14	1.35±1.25	1.24±1.43	1.44±1.48
Δ % CTV V95 54 gy	$V_{95\%}$	0.32±0.59	0.57±0.9	0.43±0.89	1.67±3.38	2.41±5.52	1.72±2.29	1.3±2.19
Δ % PTV V95 70 gy	$V_{95\%}$	3.9±2.87	3.76±2.78	3.29±2.19	4.21±3.64	4.12±2.83	3.982.55	4.42±4.09
Δ % PTV V95 60 gy	$V_{95\%}$	1.87±0.76	2.08±1.4	2.11±1.09	2.86±3.04	3.02±2.9	2.76±2.71	3.12±3.39
Δ % PTV V95 54 gy	$V_{95\%}$	8.35±19.39	5.15±11.46	5.38±8.99	8.24±15.73	7.78±11.7	7.0±11.03	5.36±7.48
Δ Brain stem (cGy)	$D_{0.03cc}$	176.45±108.76	152.72±159.17	254.63±156.54	178.72±212.53	282.45±166.36	283.63±172.78	273.0±2.57
Δ Chiasm (cGy)	$D_{0.03cc}$	185.45±126.76	218.09±104.31	277.18±169.71	253.09±237.67	295±193.14	379.54±189.29	361.63±224
Δ Left optic nerve (cGy)	$D_{0.03cc}$	157±122.26	254±129	305.45±163	387.36±204	398.81±174.31	430.27±176.97	286.54±176.71
Δ Right optic nerve (cGy)	$D_{0.03cc}$	131.90±131.65	194.81±138.26	296.27±99.31	347.36±153.83	328.81±194.74	283.72±236.40	221.81±174.02
Δ Spinal cord (cGy)	$D_{0.03cc}$	131±101.33	135.54±78.7	179.63±153.09	290.90±285.26	301.45±191.39	223.63±235.13	364.81±251.64

OAR: Organ at risk; GTVp: Primary gross tumor volume; GTVn: Nodal gross tumor volume; CTV: Clinical target volume; PTV: Planning target volume

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Table 3 Relationship between fractionation time and indications of radiation planning adjustment

Variables	RR (95% CI)	p (Chi-square)
Fraction 1	Reference	Reference
Fraction ≥6	2.34 (1.52–3.61)	0.006*
Fraction ≥11	2.83 (1.74–4.61)	0.000
Fraction ≥16	4.76 (2.35–9.65)	0.000
Fraction ≥21	5.25(2.04–13.51)	0.000
Fraction ≥26	6 (1.56–22.98)	0.000
Fraction 31	5.167 (0.78–34.07)	0.021*

*: Fischer test. RR: Risk ratios; CI: Confidence interval

The cutoffs of the three clinical parameters were evaluated using the receiver operating characteristic. The widest neck separation demonstrated the highest sensitivity (93.3%) and specificity (87.5%) at 1.21 cm with an area under the curve (AUC) of 0.951 and a 95% CI of 0.905–0.996. The results were statistically significant ($p<0.001$). As can be seen in Figure 2.

DISCUSSION

Patients with nasopharyngeal cancer in this study had a mean age of 50 years, with a higher proportion of males (72.7%). The male-to-female ratio was 2.6:1. All patients were at a locally advanced stage, namely stage III, IVA, or IVB. The highest proportion of stages was stage IVA (63.6%). All patients in this study received chemoradiation. This is in accordance with a study conducted by Gondhowiardjo et al.[13] in 2013, which was also conducted at Ciptomangunkusumo Hospital. Their study demonstrated a median age of 47 years, a predominance of stage IVA (33.9%), and a male-to-female ratio of 2.4:1.

The majority of the patients in this study used a thermoplastic Orfit mask (72.7%), while the remaining (27.3%) used a clear thermoplastic mask. The difference between these two masks is that there are more fixation points on clarity, namely 9 points, while Orfit has only 4 points. The current Orfit mask is a recycled mask, while the Klarity mask is disposable or a maximum of one-time recycled.

The results of the dose-volume histogram CT planning evaluation showed that the patients received a mean of 66.5 Gy, indicating the minimum dose needed to reduce the risk of local recurrence.[14] Meanwhile, V95% CTV and V95% PTV have met the optimal criteria based on international guidelines and The Danish Head and Neck Cancer Group protocol. For critical normal organs at risk, specifically the optic chiasma, optic nerve, brainstem, and spinal cord, all were within the replanning threshold of tolerance.

As with other head-and-neck cancers, clinically significant changes in the form of the reduced size of the primary tumor and lymph nodes and weight loss occurred in nasopharyngeal cancer when external radiation was performed. Cheng et al. demonstrated a mean reduction in tumor size in the lymph nodes and primary tumor of 16.2% and 9.1% at 30 Gy and 28.7% and 13.1% at 50 Gy, respectively. It was difficult to determine the GTV in the kV-CBCT data set so that the existing contours were the result of the registration of the contours in CT planning, which was then adjusted based on the area that exits the body contour. Nonetheless, Cheng et al. showed a response to reduced tumor size in accordance with the measurement of the widest neck separation, which underwent a 3-fold change in separation compared to the first fraction, where the Δ of the widest lymph node separation in the first fraction changed from 0.62±0.51 cm to 1.7±0.87 cm in the 16th fraction, which corresponds to week 3 or having received a dose of 30 Gy. At the mastoid tip, the Δ separation increased from 0.3±0.3 to 1.1±0.5 at week 3.[15]

Weight loss often occurs in cases of nasopharyngeal cancer. Cheng et al.[15] showed a mean weight loss at 30 Gy and 50 Gy of 5.4% and 9.3%, respectively, compared to before radiation. Our study showed a higher mean weight loss, in which before receiving the 16th fraction, the weight decreased by 6.83%, and before receiving the 26th fraction, the mean body weight decreased by 11.03%.

The distribution of doses to the target volume and normal organs at risk may experience a shift or change of doses along with the anatomical changes that occur during radiation. Fung et al.[16] made two adaptations of radiation planning in 10 cases of nasopharyngeal cancer that were treated with radiation at Hi-Art Tomotherapy using the latest CT set data and delineation contours for use in radiation compared to the original contour or the first contour through the fusion system, then used to adjust radiation planning. There was an increase in the dose at the target volume, while normal organs at risk also received higher doses compared to dosimetry on the contour, which is indeed used for adaptive radiation. In this study, the results were in accordance with Fung et al., in which the radiation doses increased but at the target volume, dosimetry changes tended to decrease, which could be due to changes in anatomy, the type of mask used, and decreased body weight.

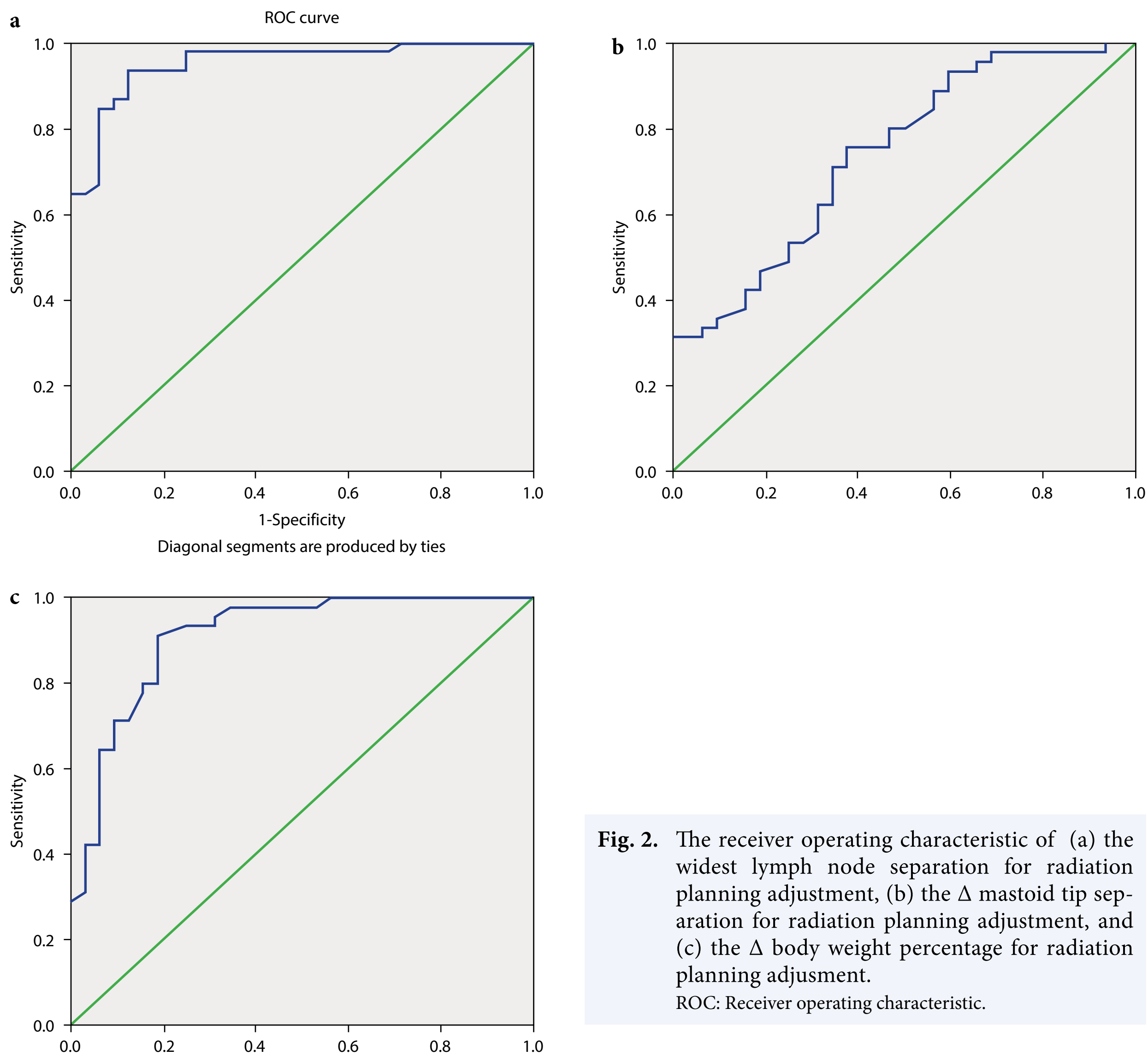

Fig. 2. The receiver operating characteristic of (a) the widest lymph node separation for radiation planning adjustment, (b) the Δ mastoid tip separation for radiation planning adjustment, and (c) the Δ body weight percentage for radiation planning adjusment.
ROC: Receiver operating characteristic.

There are no guidelines yet on the best time to perform radiation planning adjustments. Gregoire et al.[17] proposed that adaptive radiation therapy should be based on clinical needs, taking into account the changes in the patient's anatomy during the radiation session. On the other hand, Wang et al.[18] recommended that a CT simulation be performed again before the 25th fraction with a significant difference in the 2nd week. Cheng et al.[15] also suggested adaptive radiotherapy due to significant weight loss because it can increase the dose on PTV and also on critical organ structures. The Evolution of Radiation Therapy Oncology Group 1016 Protocol recommends replanning in conditions of >10% weight loss or significant shrinkage of lymph nodes in cases of head-and-neck cancer.

In this study, the replanning was carried out based on the determined criteria and when tolerance was interfered with. Starting from the 6th fraction, there was a statistically significant relative risk of 2.34 (1.52–3.61) for replanning, with the most significant increase in the 16th fraction (RR 4.76, 2.35–9.65). Among the three studied clinical parameters, the widest separation had the highest sensitivity and specificity at 1.21 cm with an AUC of 0.951, 95% CI 0.905–0.996. The widest separation parameter was better than the separation on the mastoid tip, which has the best sensitivity at 0.435 cm, namely 93.3%, but with a specificity of 40.6% and an AUC of 0.741 (95% CI 0.631–0.852). The weight loss body had the highest sensitivity (91.1%) and specificity (81.2%) at 4.49% with an AUC of 0.911, 95% CI 0.844–0.978.

Advanced toxicity in nasopharyngeal cancer can reduce the patient's quality of life. Radiation techniques with IMRT are currently associated with reduced toxicity compared to 2DRT. Several studies reported that with the IMRT technique, toxicity to the neural system has a low rate, such as the incidence of temporal lobe radionecrosis, which is 0.2%. In the area of the chiasma and optic nerve, the incidence of radiation-induced optic neuropathy is quite low, with a D_{max} of <55 Gy in radiation and a fraction of 2 Gy. Lee et al. recommended giving a dose of $D_{0.03}$ cc at PRV <54 Gy and maximum acceptance criteria (MAC) <60 Gy. In this brainstem case, Lee et al.[12] recommended $D_{0.03}$ cc at PRV <54 Gy and MAC 60 Gy. In the cochlea, the most common toxicity is hearing loss. The maximum recommended cochlear threshold is ≤55 Gy with consideration of the size of the tumor and the location of the tumor, which causes the average dose below 45 Gy not to be achieved. In the larynx, toxicity may manifest as a decrease in voice quality, which gets worse with increasing doses, and laryngeal edema that can occur after radiation. The recommended dose was reduced to a mean dose of ≤35 Gy, where previously the recommendation was for a mean dose of ≤45.30 Gy with a standard deviation of 2.4 Gy compared to the initial radiation plan. In the lens, doses below 5 Gy do not cause visual disturbances. Visual disturbances caused by lens opacity occur at doses above 15 Gy. In the oral region, the toxicity that interferes with therapy is mucositis. Chemoradiation is known to increase the risk 4 times higher than radiation alone for the risk of developing grade 3 mucositis. The recommended average dose is ≤40 Gy, with a maximum threshold below 50 Gy. In the mandibular region, osteoradionecrosis is a further toxic effect, one of which is influenced by the radiation dose in addition to the patient's own dental status. The recommended dose is $D_{2\%}$ ≤70 Gy with a maximum threshold of <75 Gy.

Limitations of the Study

This study has several limitations, including poor image quality produced by kV-CBCT compared to CT simulators, the use of partially recycled masks, and different fixation points.

CONCLUSION

The radiation planning adjustment in patients with locally advanced nasopharyngeal cancer is suggested at the 16th fraction, or in the 3rd week. Weight loss and changes in neck separation significantly affect the dosimetry changes in locally advanced nasopharyngeal cancer patients. Adjustment of radiation planning in locally advanced nasopharyngeal cancer is recommended at the widest lymph node area separation of 1.21 cm or a weight loss percentage of 4.49%.

Peer-review: Externally peer-reviewed.

Conflict of Interest: All authors declared no conflict of interest.

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