Volume 23, No 3 | International Journal of Radiation Research, July 2025

Quantitative assessment of treatment planning dosimetric parameters in 3D-CRT with the mixed photon-electron beams versus IMRT for the nasopharyngeal carcinoma

H. Ahmadpour[1], A. Mohammadkarim[2*], A. Kazemian[3], G. Geraily[4], P. Hejazi[1], M. Yadollahi[5], M. Najafi[6], N. Gorjizadeh[6]

[1]*Department of Medical Physics, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran*
[2]*Radiation Sciences Research Center (RSRC), Aja University of Medical Sciences, Tehran, Iran*
[3]*Radiation Oncology Research Center (RORC), Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*
[4]*Department of Medical Physics and Biomedical Engineering, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*
[5]*Department of Radiology Technology, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[6]*Department of Radiation Oncology, Cancer Institute of Iran, Tehran University of Medical Sciences, Tehran, Iran*

► ***Short Report***

Corresponding author:
Alireza Mohammadkarim, Ph.D.,
E-mail:
mohammadkarim.medphys@gmail.com

Received: April 2024
Final revised: November 2024
Accepted: November 2024

Int. J. Radiat. Res., July 2024; 23(3): 809-812

DOI: 10.61186/ijrr.23.3.38

Keywords: *Nasopharyngeal carcinoma, conformal radiotherapy, intensity-modulated radiotherapy, tumor control probability.*

ABSTRACT

Background: External radiotherapy procedures as an important tool for curing nasopharyngeal carcinoma (NPC) are commonly performed with one of the well-known techniques, three-dimensional conformal radiotherapy (3D-CRT) or intensity-modulated radiotherapy (IMRT). ***Materials and Methods:*** In this study, the therapeutically dosimetric parameters including conformity index (CI), homogeneity index (HI), and tumor control probability (TCP) were extracted from the dose volume histogram (DVH) curves of fifteen patients in two designed treatment plans including, 3D-CRT and IMRT. 3D-CRT plans were performed in three phases by considering the mixed photon-electron beams in the second phase with a total dose of 70 Gy in 35 fractions. The prescribed dose of IMRT plans was 70 Gy in 33 fractions by employing 9 fields of photon beams. ***Results:*** A significant statistical difference was observed in TCP and CI between 3D-CRT and IMRT plans. The average value of TCP in IMRT is 5.65 times that of 3D-CRT. Also, IMRT showed a 123% increase in the average value of CI compared with 3D-CRT.There were no significant statistical changes in HI between the two treatments. ***Conclusion:*** Although the IMRT procedure is more effective than 3D-CRT in the dose delivery process, 3D-CRT with mixed photon-electron beams can create dose homogeneity.

INTRODUCTION

Radiotherapy (RT) is a crucial treatment modality for head and neck cancers, particularly nasopharyngeal carcinoma (NPC), where it serves as the primary approach for early-stage tumors and is often combined with surgery and chemotherapy for advanced cases. Effective NPC treatment requires delivering high doses of radiation to localized regions adjacent to vital structures such as the spinal cord, brainstem, and salivary glands [1].

Recent reports indicate that, the mixed photon-electron beams in three-dimensional conformal radiotherapy (3D-CRT) technique are more effective for treating head and neck tumors compared to procedures utilizing solely photon irradiation [2-5]. The mixed electron-photon beams can leverage the advantages of electron beams to enhance the dose delivery while minimizing the overshadowing of deep organs at risk such as the spinal cord [2]. On the other hand, due to the advancement of RT equipment, intensity-modulated radiotherapy (IMRT) is now selected as a therapeutic modality for a considerable number of NPC patients [1, 3].

To assess the effectiveness of a specific treatment plan, the therapeutically dosimetric parameters such as the conformity index (CI), homogeneity index (HI) and tumor control probability (TCP) are the essential characteristics for predicting the reliability of the dose delivery process to the planning target volume (PTV). Among these, TCP plays a vital role in estimating the probability of eradicating or controlling tumor growth through RT. This estimation is based on mathematical models that account for the tumor's response to the administered dose. CI evaluates the accuracy of delivering the prescribed dose to the target volume, reflecting the precision and accuracy of the RT process. Furthermore, assessing the HI is known as a reliable tool for determining the uniformity of dose distribution within the target volume [6, 7].

To our knowledge, no report provides a

[DOI: 10.61882/ijrr.23.3.38]

comparison between the dosimetric parameters of IMRT and mixed photon-electron beams in 3D-CRT for NPC treatments. Therefore, the main aim of the present study was to compare the dosimetric parameters of IMRT and 3D-CRT utilizing mixed photon-electron beams, thus evaluating the potential of this technique as an alternative to conventional methods.

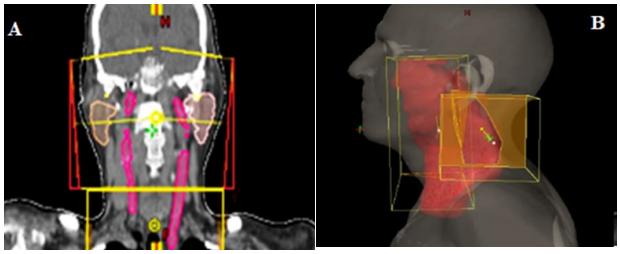
MATERIALS AND METHODS

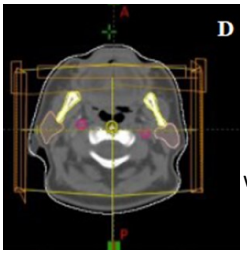
Treatment planning

The sequential computed tomography (CT) images of fifteen Iranian male patients without a history of tumor surgery (age=66.8±7.4 years) with various stages of NPC disease were used for treatment planning with two techniques 3D-CRT and IMRT. All of the subjects were referred to the Cancer Institute of Imam Khomeini Hospital in Tehran after the ethical committee approving the study (May 23, 2022, Approval ID: IR.SEMUMS.REC.1401.047). Clinical target volume (CTV) and gross tumor volume (GTV) are defined based on ICRU 50. Moreover, the organ at risk volume was countered as the safety margins around each vital area such as the brainstem, spinal cord, chiasm, optic nerves, parotid and mandible (8). The Monte Carlo algorithm in the treatment planning system (TPS) software package was utilized to calculate the dose profiles and optimize the plan design. All calculations were performed using the Monaco Synergy 5.11.02 TPS (Elekta, Sweden).

In the treatment planning of 3D-CRT, the prescribed dose of the tumor was approximately 70 Gy with the regime of 2 Gy per fraction, administered 5 times per week. In 3D-CRT treatment planning, three phases were defined. In the first step, two lateral fields for covering the expanded tumor area in the head along with the supraclavicular and posterior fields for covering the target in the upper neck region were applied to surround the PTV (figure 1a). Following the administration of a total dose of 46 Gy in 23 sessions, the spinal cord was excluded from the lateral fields, and two opposite electron fields were applied to cover the lymph nodes without affecting the spinal cord in 7 fractions (figure 1b). In the third phase, two parallel lateral fields were modified to cover the gross tumor volume in the last five treatment sessions (figure 1c). After performing each plan, the dose volume histogram (DVH) curve was yielded for the PTV receiving 60 Gy (PTV60) and the PTV for the primary NPC tumor (PTV70) (figure 1d).

Treatment planning with the IMRT technique was carried out, administering a total prescribed dose of 70 Gy for 33 fractions. Therefore, a 2.12 Gy dose per fraction should be considered over 5 sessions per week. Nine coplanar fields with the same consecutive angle difference (0°, 40°, 80°, 120°, 160°, 200°, 240°, 280° and 320°) were used for each treatment planning (figure 2a). Dose constraints of well-known organs at risk were defined according to the QUANTEC tables and optimized dose distribution was approved based on the routine clinical protocol [9]. Figure 2b displays a sample of DVH curves for PTV60 and PTV70, derived from the IMRT technique.





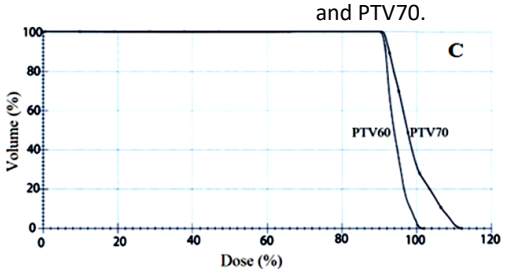
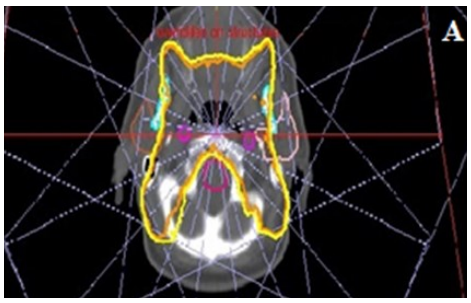


Figure 1. The process of NPC treatment planning with the 3D-CRT technique in three phases: **(a)** two lateral fields in the head along with anterior-posterior fields in the neck [phase 1], **(b)** two opposite lateral fields of photon beams combined with two lateral electron fields [phase 2], **(c)** lateral fields to cover the gross of tumor [phase 3], **(d)** a sample of DVH curves for a patient for PTV60 and PTV70.



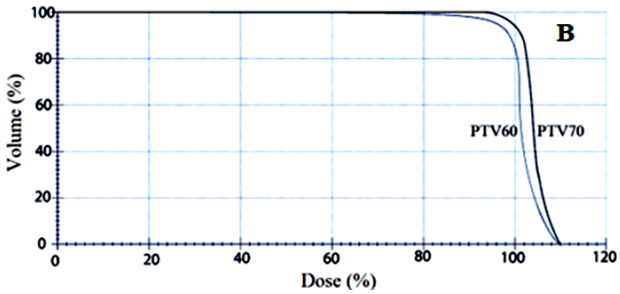


Figure 2. (a) A view of applying IMRT fields in the inverse planning of a selected NPC patient, **(b)** a sample of extracted DVH curves for a patient for PTV60 and PTV70.

Calculation of therapeutically dosimetric parameters

In this step, we analyzed therapeutic dosimetric parameters, including CI, HI and TCP for NPC patients

[DOI: 10.61882/ijrr.23.3.38]

while two treatment planning techniques were performed separately performed on the CT images for each patient and DVH curves were extracted. The CI is defined as the ratio between the volume covered by the 95% isodose (V_{RI}) and the target volume (TV) delineated as the PTV [10].

$$CI = \frac{V_{RI}}{TV} \quad (1)$$

The HI parameter is defined by equation (2). In this formula, D_5 and D_{95} are the dose values for 5% and 95% of the target volume, respectively. Additionally, D_p represents the prescribed dose [11].

$$HI = \frac{D_5 - D_{95}}{D_P} \times 100 \quad (2)$$

Evaluation of TCP was performed by applying the equivalent uniform dose (EUD) model and implementing of equation (3). The EUD for the tumor target is defined as the biologically equivalent dose which, if given uniformly, will lead to the same cancer cell kill in the TV as the actual non-uniform dose distribution. A free open-source program (eudmodel.m), modified in MATLAB software, was used to calculate Niemierko's EUD-based TCP for all subjects [12].

$$TCP = \frac{1}{1+(\frac{TCD_{50}}{EUD})^{4\gamma_{50}}} \quad (3)$$

In above formula, TCD_{50} is the tumor dose to control 50% of the malignancies while the target is homogeneously irradiated [12].

Statistical analysis

Statistical Package for the Social Sciences (SPSS) software (version 24, SPSS Inc.) was used to perform statistical analysis. To compare the IMRT plan of each patient with the corresponding 3D-CRT plan, paired t -test analysis was employed. P-values less than 0.05 were considered statistically significant in our analyses.

RESULTS

The outcome of the HI parameter shows no significant difference between the mentioned data for cancer treatment (P>0.05). Therefore, the uniformity of dose distribution in the NPC volume is not affected by altering these two treatment techniques. However, the results indicated that CI and TCP parameters in IMRT plans are significantly higher than those in 3D-CRT. It should be noted that to verify the dose delivery in each IMRT plan, a process of dose measurement including the reference point dose and the dose distribution in two directions with the 2D-array detectors was performed by employing a specific uniform phantom, and all of the studied plans were confirmed.

To evaluate the relative effects of the IMRT procedure in comparison with the 3D-CRT technique, three dosimetric parameters of the PTV during the external RT with the IMRT methodology were normalized against the results obtained from the 3D-CRT technique across three phases. Figure 3 shows that treatment of NPC with mixed photon-electron beams can create dose homogeneity similar to IMRT treatment.

Table 1. Mean value ± standard deviation of the therapeutically dosimetric parameters including TCP, CI and HI for IMRT and 3D-CRT plans.

Parameter	IMRT	3D-CRT	P-Value
TCP	0.745 ± 0.025	0.112 ± 0.191	0.022
CI	0.98±0.01	0.44±0.24	0.049
HI	0.22±0.03	0.26±0.11	0.512

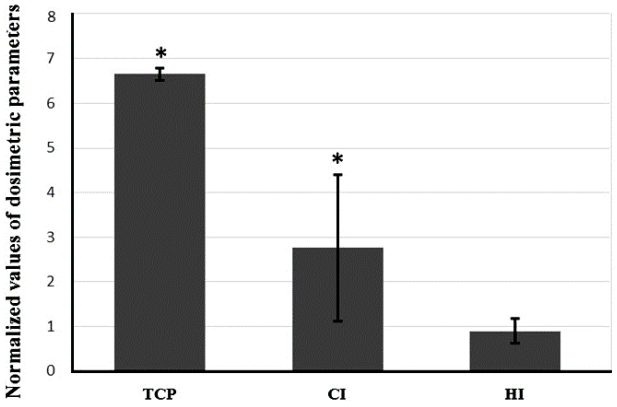


Figure 3. Alteration of TCP, CI and HI while normalizing the IMRT parameters against the results of 3D-CRT. "#" represents statistically significant difference.

DISCUSSION

Before the commercialization of inverse planning algorithms, the 3D-CRT technique was effectively used as a prominent method for the treatment of NPCs. Currently, the IMRT procedure is employed for the treatment of nasopharyngeal tumors, while the 3D-CRT technique remains an acceptable option for these malignancies. The outcomes of previous publications [13-15] make it necessary to compare the feasibility of NPC treatment with different modalities such as IMRT and mixed photon-electron beams in 3D-CRT.

The present study focused on some indicators of mixed photon-electron beams in the 3D-CTR technique quantitatively for the treatment of NPC tumors when only access to this technology is possible. Conversely, 3D-CRT is performed as an authentic alternative technique for the treatment of stage-I NPC diseases in advanced clinical centers according to the previous report [16]. Based on the results presented in table 1, the IMRT technique ensures a higher level of precision in containing high dose levels near the target areas. Furthermore, the 3D-CRT procedure in three phases with photon and electron beams combined can create uniform dose distribution as well as the IMRT technique. A similar

[DOI: 10.61882/ijrr.23.3.38]

previous report, illustrated that both IMRT and 3D-CRT techniques, by employing two parallel photon beams lead to similar uniform dose distribution [6, 17]. In addition, another study about the treatment of lymphoma carcinoma concluded that the IMRT technique with 5-7 fields leads to better dose coverage compared with the 3D-CRT protocol which employs the combination of three fields of photon-electron beams [17]. Moreover, Vitolo et. al. indicated that employing the IMRT plans leads to higher dose delivery to the GTV and CTV compared with the 3D-CRT plans in three phases when accounting for the mixed photon-electron beams [18].

This study employed a DVH-based model, recognized for its accuracy, to compute the TCP parameter as a dependable metric for evaluating cancer treatment efficacy [6]. As expected, the statistical analysis illustrates a higher value of TCP in IMRT plans compared with 3D-CRT once (figure 3). This conclusion confirmed Tai *et. al.*'s published study [6]. In a similar study, Mesbahi et. al. reported that seven coplanar fields of IMRT improved the dose coverage of PTV compared with the 3D-CRT which had been planned by photon beams in three phases. Moreover, a higher precision of dose delivery was reported for IMRT plans [19]. In addition, it has been proven that the TCP values in RT of NPC can be improved by developing the treatment phases for the IMRT procedure [20]. Consequently, it seems that this report can be considered together with our outcome. In other words, employing the electron beams along with the photons can be effective in improving the quality of treatment in all modalities of RT.

CONCLUSION

This study assessed the therapeutic effectiveness of the mixed photon-electron beams with three phases in 3D-CRT planning in comparison to the IMRT for NPC patients. Taken together, our results suggest that the utilized protocol of 3D-CRT can be considered a reliable RT procedure for NPC cases. It is noteworthy that the 3D-CRT with the mixed photon-electron beams can create dose homogeneity in the target volume as well as IMRT dose for treating NPC. All in all, the 3D-CRT with the mixed photon-electron beams improves the dose delivery to the PTV compared with that when only photon beams were used. Therefore, it is advisable to consider using this technique in cases where IMRT is not feasible.

ACKNOWLEDGEMENT

The authors would like to thank the members of Cancer Institute of Iran.

***Funding*:** None.

***Conflicts of interest*:** None.

***Ethical consideration*:** This study has been approved by ethic committee of SEMUMS (May 23, 2022, Approval ID: IR.SEMUMS.REC.1401.047)

***Author contribution*:** A.M., was responsible for drafting the manuscript as the main faculty member supervisor. Data analysis was performed by H.A. as a Master's student. Other authors had substantial role in the project and in manuscript preparation and revision.

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[DOI: 10.61882/ijrr.23.3.38]