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The Role of Intensity Modulated Radiation Therapy (IMRT) Techniques in External Radiation Therapy on the Value of Organ at Risk (OAR) Nasopharyngeal Carcinoma: Literature Review

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ABSTRACT

Nasopharyngeal carcinoma (NPC) is a malignant disease that exists in Asia, the development of imaging techniques and radiation therapy in the last 5 years has utilized 75% of diagnoses as nasopharyngeal carcinoma without metastases. The development of radiotherapy techniques has changed from conventional 2-dimensional (2D) to 3-dimensional conformal radiotherapy (3DCRT) and intensity modulated radiotherapy (IMRT). IMRT technique is one of the newest treatments at this time, so this technique requires a high level of precision and specific requirements either in immobilization or dose distribution, so that the accuracy rate for random or random systems is better than conventional 2D and 3D-CRT techniques. This study uses a descriptive qualitative method with a literature review study approach by collecting and analyzing data that aims to determine the role of the IMRT technique in external radiotherapy on the dose value of OAR for nasopharyngeal carcinoma. Based on the literature that forms the basis for the assessment, several advantages of the intensity modulated technique are shown. IMRT radiotherapy is capable of producing highly conformal doses with complex dose gradients, as well as being able to increase dose distribution within the target volume and reduce OAR doses.

Keywords: The role of IMRT technique in OAR nasopharyngeal carcinoma, nasopharyngeal carcinoma, linac

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a malignant disease that exists in Asia, the development of imaging techniques and radiation therapy in the last 5 years has reached 75% of diagnoses as nasopharyngeal carcinoma without metastases, NPC appears in the nasopharynx area located in the superior throat and inferior nose area. With the development of improved treatment methods, patient survival and targeting against cancer is expected to become a significant major goal for radiation oncologists (1). NPC is an endemic disease in certain regions of the world, the standard incidence of NPC is 1.2 per 100,000 in men and 1.7 per 100,000 in women or about 0.7 per 100,000 annually (2). In China, especially in Guangdong province, it has the highest annual incidence of 20 to 60/100,000, with advances in treatment techniques especially in radiotherapy we have obtained an average of 60% to 70% overall survival (OS) each year in NPC (3). Southeast Asia has the prevalence is poor, especially in Indonesia, the average recorded is 6.2/100.000, with 13,000 new cases of NPC every year (4). The nasopharyngeal carcinoma irradiation technique can be performed using the Linear Accelerator (LINAC) modality. LINAC is a high-energy radiotherapy machine that has multiple electron and photon beam energies, namely the electron energy for radiotherapy is in the range of 4-22 MeV and for photon energy it is 6-8 MV. The existence of LINAC is very efficient in radiation therapy because LINAC has more than one energy, namely photons and electrons. The working principle of LINAC is that the emitted electrons will experience acceleration in an electromagnetic field to increase their kinetic energy (5). In the LINAC modality, there are several techniques, one of which is (2D) 2 Dimensional, (3DCRT) 3 Dimentional Conformal Radiotherapy and (IMRT) Intensity Modulated Radiation Therapy. The 2D technique consists of planning using conventional techniques on a simulator with energy suitable for target formation (6). 3D-

CRT is the treatment of choice for cancer for better target coverage and significantly lower toxicity to normal organs compared to 2D technique (7). IMRT is The latest innovation in the treatment of NPC, this technique is capable of producing highly conformal doses with complex dose gradients (8). Linear Accelerator Many normal tissues close to NPC are defined as organs at risk (OAR), including the temporal lobe, brainstem, spinal cord, optic nerve, parotid gland, submandibular gland, pituitary. Therefore, treatment planning is difficult in NPC, especially in critical normal tissues such as the brain stem, and temporal lobes, which are very close to the target volume, so that inaccurate depiction will pose a danger to treatment planning resulting in inadequate target volume for OAR (9). Target volume (TV) can change significantly during radiation therapy resulting in uncertainty of the resulting dose either to the target or to the OAR, due to the effects of weight loss or even changes in tumor position such as gross target volume (GTV) or clincal target volume (CTV) displacement.) and geometric changes greatly affect during the use of IMRT, GTV is all macroscopic diseases detected on CT diagnostics and tumor volume that can be detected on physical examination, CTV is tumor volume limited by tumor macroscopic spread (tumor infiltrative spread) (10). The NPC radiotherapy treatment plan has a dose tolerance limit, namely for brain stem 64 Gy, bone marrow 55 Gy, optic nerve 60 Gy, tumor 80 Gy, temporal lobe 70 Gy, brachial plexus 70 Gy, pituitary gland 54 Gy, thyroid 50 Gy, cochlea 55 Gy, parotid gland 35 Gy, mandibular and temporomandibular joint (TMJ) 75 Gy, oral cavity 50 Gy, pharyngeal muscles 55 Gy, larynx 35 Gy, submandibular gland <35 Gy (11). The development of radiotherapy techniques has undergone a change from conventional 2- dimensional (2D) to 3-Dimensional Conformal Radiotherapy (3DCRT) and Intensity Modulated Radiotherapy (IMRT). In this study, it was found that several cases of non-metastatic NPC experienced signs of disease return with a high category, but after the use of the IMRT technique, non-metastatic NPC decreased by about 7.4% (12). IMRT technique is one of the newest treatments at this time, so the technique This requires a high level of precision and specific requirements for either immobilization or dose distribution, so that the accuracy of the random or random system is better than conventional 2D and 3D-CRT techniques.

METHOD

Type and Design of Reserch

This study used a descriptive qualitative method with a literature review study approach by collecting and analyzing data that aims to determine the role of IMRT technique in external radiotherapy on the dose value of OAR for nasopharyngeal carcinoma.

RESULTS

The Role of IMRT Technique in External Radiation Therapy The effectiveness in irradiation can be viewed from

IMRT Advantage

Nasopharyngeal carcinoma is a differentiated disease in which the disease is caused by the frequently metastatic Epstein-Barr virus, and also optimizes target volume cover and allows much less radiation of healthy organs than conventional 2D or 3D radiotherapy leading to lower final toxicity rates. Nasopharyngeal carcinoma is very sensitive to radiation, therefore, radiotherapy has become one of the main therapeutic approaches. Radiotherapy, IMRT is a major breakthrough in the treatment of nasopharyngeal carcinoma (NPC). Clinically for NPC patients dosimetric overload of this technique has contributed to increased overall survival and reduced radiotherapy-related side effects such as xerostomia, IMRT is currently the mainstay of radiation oncology. Accurate delineation and precise dosing of target and risk organ volumes (OARs) is the key to the success of radiotherapy, IMRT can improve local control for tumor volume, repeated radiation administration, fractional dose and age are major factors for overall survival rate.

The Role of Radiation Techniques for IMRT KNF Radiation Therapy

For the overall survival rate after radiation or reradiation for local tumor control from the data of 239 patients there were a total of 120 patients who died and 119 patients experienced recovery/lived, where the cause of death included local recurrences ranging from 13 (10.8%),Regional recurrence (0%), metastases 22 (18.3%), radiation injury 83 (69.2%), and other causes about 2 (1.7%) and for cure/life status was disease free 98 (82.3%), local recurrence 8 (6.7%), metastases 9 (7.6%), local recurrence for metastases 4 (3.4%) (15).

Table 1: The Role of Radiation Techniques for IMRT KNF Radiation Therapy

Status at last Follow-up			No. patiens (percentage)
Death 120 Patients	Causeof death	Local recurrence	13(10,8%)
		Regional	0(0%)
		recurrence	22(18,3%)
		Distant metastasis	83(69,2%)
Alive 119 Patients		Radiation injuries	2(1,7%)
	Status	Others	98(82,3%)
		Disease free	8(6,7%)
		Local recurrence	9(7,6%)
		Distant metastasis	4(3,4%)
		Local recurrence +	
		distant metastasis	

Quality of Life for NPC Patients

Table 2: Results of Modified EORTC QLQ-H&N35 for KNF survivors

	2D-RT Mean±SD	3D-CRT Mean±SD	IMRT Mean±SD	p-value
Difficulty in speech	4.80±3.61	3.30±2.78	2.30±2.70	0.003
Difficulty in chewing	5.13±3.81	3.43±2.99	2.75±3.03	0.012
Swallowing ability	6.36±3.39	5.50±3.82	3.86±3.66	0.004
Sensation during meal	5.03±3.6	4.36±3.16	2.89±2.74	0.006
Drinking water to keep moist mouth	6.03±3.32	4.90±3.25	3.64±3.42	<0.001
Insomnia	3.70±3.50	3.26±3.14	2.93±3.17	0.58
Drinking water assessment by swallow	6.13±3.43	3.53±3.52	3.64±3.42	< 0.001
Drythroat withoutmeal	4.08±3.48	3.66±2.94	3.43±2.92	0.165

For the quality of life of patients after undergoing radiation therapy using either 2D, 3D, or IMRT techniques, there is a different percentage of comparison, in this case for the use of IMRT, the survival rate is better, as has been seen in previous studies or existing journals. that for the use of the 2D technique the difficulty in speaking was around 4.80±3.61, for the use of the 3D technique, 3.30 ± 2.78, and for the use of the IMRT technique, 2.30 ± 2.70. difficulty in chewing for IMRT was 2.75±3.03, the ability to swallow using the 2D technique was 6.36±3.39, the 3D technique was 5.50 ± 3.82, while using the IMRT technique was 3.86±3.66, dry throat sensation when eating and drinking, using the 2D technique was 5.03±3.66, the 3D technique was 4.36±3.16, while the IMRT technique was 2.89±2.74, insomnia, for the use of the 2D technique was 3.70 ± 3.50, the 3D technique was, 3.26 ± 3.14, while the IMRT technique was, 2.93 ± 3.17, patients treated using this technique showed a difference where the use of IMRT was more profitable because the quality of life was very good or in a smaller percentage than the use of 2D and 3D techniques (17).

How is IMRT Dosage Value Against Nasopharyngeal Carcinoma OAR

a. IMRT OAR Standard Dosage

The NPC radiotherapy treatment plan has a dose tolerance limit, namely for brain stem 64 Gy, bone marrow 55 Gy, optic nerve 60 Gy, tumor 80 Gy, temporal lobe 70 Gy, brachial plexus 70 Gy, pituitary gland 54 Gy, thyroid 50 Gy, cochlea 55 Gy, parotid gland 35 Gy, mandibular and temporomandibular joint (TMJ) 75 Gy, oral cavity 50 Gy, pharyngeal muscles 55 Gy, larynx 35 Gy,submandibular gland <35 Gy (11).

IMRT Dosage Against OAR

Table 3: IMRT dose analysis on OAR

Critical Structure	Mean Dose (Gy)	Range (Gy)
Brain Stem	22.62	5.94-48,51
Spinal Cord	12.77	0.62-37.21
Optic Chiasma	17.92	1.72-47.03
Optic Nerve	-	-
Left	17.12	1.27-55.51
Right	17.42	1.04-51.14
Lens	-	-
Left	3.67	0.41-12.05
Right	3.78	0.72-10.84
Temporal Lobe		
Left	14.31	0.48-46.46
Right	15.18	1.19-41.39
Parotid	-	-
Left	18.77	2.37-57.12
Right	18.20	3.28-38.42
Temporomandibular Joint	-	-
Left	26.52	8.66-47.27
Right	26.22	7.28-57.40
Pituitary	27.10	2.22-60.27

In the examination of nasopharyngeal carcinoma, of course, there are many organs at risk that must be protected, in order to achieve as much dose reduction as possible and maintain these organs, the indicated dose limits must be lower than the specified tolerance, for example for the brain stem the average dose is 22.6 Gy, with range approx. 5.94-48.51, spinal cord 12.77, range 0.62-37.21, optic chiasm 17.92, range, 1.72-47.03, left and right optic nerves approx. 17.15, range 1.04-55.51, left and right lens, 3.67, range 0.41-12.05, left and right temporal lobe, 14.31, range, 0.48-41, 46, left and right parotid 18.20, range 3.28-57.12, left and right temporomandibular joint 26.22, range 7.28-57.40, pituitary 27.10, range 2.22-60, 27. In this case, IMRT certainly achieves the radiation therapy plan, especially in organ maintenance at risk in nasopharyngeal carcinoma, IMRT results in a fairly good increase in dose distribution, the coverage can be seen in the dose data table presented in table 4.3 (15).

Dose of 3D-CRT OAR Compared to IMRT in NPC

Table 4: Radiation values of OAR for 3D-CRT and IMRT techniques

OAR	Average TNTCP ± SD (%) of OAR for Different Ranges of General Volume Between TPTV and OAR			
	Protocol.	**0 – 6 cm3**	**6-12 cm3**	**12 cm3**
Brain Stem	IMRT	0,01±0,01	0±0	0,01±0,1
	3DCRT	0,03±0,01	0,03±0,01	0,05±0,00
	p-value	0,339	0,081	0,035
Spinal Cord	IMRT	0±0	0±0	0±0
	3DCRT	0,03±0,01	0,03±0,01	0±0
	p-value	0.104	0,081	-
Optic Chiasma	IMRT	0±0	0±0	0,06± 0,06
	3DCRT	0,01±0,01	0±0	0±0
	p-value	0,339	-	0,351
Optic Nerve	IMRT	0±0	0,02±0,02	0,01±0,01
	3DCRT	0±0	0±0	0,03 ± 0,03
	p-value	-	0,347	0.351
Parotid Gland	IMRT	19.25±3	40.09±00.0	50.63±4.52
	3CRT	37.97± 0050	70.54± 0005	6.36±4,005
	p-value	P < 0,001	P< 0,001	0,005

Along with the rapid development of radiation therapy techniques, the development of 2D, 3DCRT, and IMRT techniques will certainly provide more benefits for both the way work in the field and the dose for organs at risk that is increasingly minimized, as in this journal, which is comparing the use of 3DCRT and IMRT, for example for the brain stem, at a depth of 0 – 6 cm3 3DCRT can give a dose of 0.03±0.01 Gy and IMRT 0.01±0.01 Gy, for a depth of 6-12 cm3 3DCRT can give a dose of 0.03±0 0,01 Gy and IMRT 0±0 Gy, and at a depth of 12 cm3 3DCRT gave a dose of 0.05±000 Gy, IMRT 0.01±0.01 Gy, spinal cord, depth 0-6 cm3 3DCRT 0.03 ±0.01 Gy, and IMRT 0±0 Gy, depth 6-12 cm3 3DCRT 0.03±0.01 Gy, IMRT 0±0 Gy and depth 12 cm3 3DCRT 0±0 Gy, IMRT 0±0 Gy, gland parotid, at a depth of 0-6 cm3 3DCRT 37.97±005 Gy, IMRT 19.25±3 Gy, a depth of 6-12 cm3 3DCRT 70.54±0005 Gy, IMRT 40.09±00.0 Gy, and a depth of 12 cm3 3DCRT 76.36±4005 Gy, IMRT 5 0.63±4.52 Gy (16).

CONCLUSION

Based on the results of the literature review that has been explained by the author, the role of IMRT technique in the success of radiation therapy is very effective compared to 2D and 3D techniques. This is evidenced from various research results that IMRT is able to provide optimal results after irradiation, in this case IMRT is also able to improve a better quality of life and the dose to OAR NPC received is smaller when compared to 2D and 3D techniques. For further research, a literature review will be conducted on IMRT with different objects.

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