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Evaluation of Radiation Doses Received by Organs at Risk in 3D Conformal and Intensity Modulated Radiotherapy for Head and Neck Cancer

Hunar A. Hassan[1], Kharman A. Faraj[2], Zarean Y. Saeed[1]

[1]*Zhianawa Cancer Center, Sualimani City, Kurdistan Region, Iraq*
[2]*Department of Physics, College of Science, University of Sulamani, Sulaimani City, Kurdistan Region, Iraq.*
Email:kharman.faraj@univsul.edu.iq

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Abstract

The purpose of this study was to evaluate the doses delivered to the critical structures located close to the target volume during head and neck radiotherapy by 3D-CRT and IMRT technics in order to select possible treatment technic proper to head and neck regions. We have used all data collected from the Treatment Planning Systems (TPS) to conduct a pilot comparison between the two modalities. The comparison included the parameters of the target coverage, dose conformity and homogeneity for the planning target volume (PTV), the maximum and mean doses for organs at risk (OARs), the time required to deliver the prescribed dose, and number of Monitor Units (MU). The results showed that the dose conformity with IMRT plans for both PTV high and low risk was significantly better than those obtained with 3D-CRT plan. The dose uniformity in the PTV low risk was better with IMRT plan; mean homogeneity Index (HI) was 37.476 but for 3D-CRT were 43.465. IMRT technic achieved better PTV coverage. IMRT tended to provide a significant better OAR avoidance than 3D-CRT. We concluded that the 3D-CRT plan could not provide adequate OAR avoidance where many OARs are close to the PTVs. The IMRT plan, even though it takes longer time and more MUs, is the optimal plan for head and neck cancer treatment that derives to a better outcome while avoiding complication in the surrounded normal tissue.

Introduction

Radiation therapy can be given in different treatment modalities, such as internal or external radiotherapy. The radiation is given to the patient in one or more modalities at the same time. Different types of radiation (such as X-rays or electrons) may be used for the patient one after the other, depending on the type, size and location of the tumor [1]. External radiotherapy includes several treatment technics such as two-dimensional radiotherapy (2D-RT), three-dimensional Conformal Radiotherapy (3D-CRT), and more advanced technics such as Intensity Modulated Radiation Therapy (IMRT), Rapid ARC or Volumetric Modulated Arc Therapy (VMAT), and Image Guided Radiotherapy (IGRT).

External beam radiotherapy can be delivered more precisely by using 3D-CRT technique, which is based on 3D images from a special computed tomography (CT scan). Due to CT scans, more powerful computers, improved dose calculation algorithms and Multi-leaf Collimators (MLCs), the 3D-CRT is able to shape the Radiotherapy Beam (RTB) closely to match the target shape and volume. In 3D-CRT the tumor and all organs are viewed in three dimensions and the radiation is delivered by using irregular beams with uniform intensity according to the tumor shape from different direction, and conform the irradiated volume to the tumor shape. In this technic every details can be obtain about the tumor and other organs such as organ volume and shape, maximum, minimum, mean doses, and doses delivered to each point included in the contoured area [2, 3].

Intensity Modulated Radiotherapy (IMRT) is an advanced form of 3D-CRT that can be used to treat any part of the body, and provides improved dose distribution producing a better coverage of the tumor and sparing healthy tissues [4, 5]. In IMRT treatment technic, the collimation leaves (MLCs) are carefully adjusted according to the shape, size, and location of the tumor just like 3D-CRT , but the intensity of each beam is modulated (not uniform) during the treatment time[6]. IMRT can deliver the same radiation dose to the tumor with fewer side effects as compared to the 3D-CRT or much higher dose to the tumor with the same dose to nearby organs. This is particularly effective when dealing with tumors that locate close to vital organs or structures within the body [7].

Head and neck cancer is the terminology used to describe a number of different malignant tumors that develop in or around the, larynx, pharynx, nasal cavity, sinuses, salivary glands and oral cavity, excluding the brain, the eye, the esophagus, thyroid glands, scalp, skin, bone [8]. Most head and neck cancers are squamous cell carcinomas. This type of cancer begins in the flat squamous cells that make up the thin layer of tissue on the surface of the structures in the head and neck [9]. Many head and neck cancers can be cured, especially if they are diagnosed in early stage. Although eliminating the cancer is the primary goal of treatment [10]. The treatment of head and neck cancers varies by primary site and stage. The most common treatment modalities for head and neck cancer are surgery, radiation therapy, chemotherapy, and targeted therapy. The treatment modality is depending on several factors such as type and stage of cancer, possible side effects, patient's preferences and overall health [11]. Surgery and RT with or without chemotherapy are the most frequently used modalities in head and neck cancer. Most patients with advanced tumors have their radiotherapy in two phases. Phase one is typically a large volume including the primary tumor with any lymph nodes, and any areas of microscopic spread. The volume of phase two is smaller and includes the primary tumor, and any involved lymph nodes. Other elective lymph nodes region may be included in first Phase but not in second phase. Elective lymph nodes irradiation is indicated when risk of microscopic disease exceeds (15-20%) [12, 13].

Organs at risk (OARs) are normal tissues whose radiation sensitivity may significantly influence the treatment planning and prescribed doses. Each organ has its tolerance dose level and this must be taken into account in the planning proses [14]. With regard to histopathological properties of tissue, organs at risk can be classified as serial, parallel and serial-parallel [15, 16].

The aim of the study was to evaluate the doses delivered to the critical structures (organs at risk) located close to the target volume during head and neck radiotherapy by both technics 3D-CRT and IMRT. In Zhianawa Cancer Center (ZCC) where a limited numbers of RT machines and requirements of both treatment technics 3D-CRT and IMRT are available for hundreds of patients in the waiting list. The improved dose distribution during the dose delivery is possible for both mentioned techniques with a better protection of the OAR for IMRT versus 3D-CRT. Therefore, it is necessary to consider the required time and the amount of doses delivered to OAR in the selection of any of the two technics to be decided.

Research Methods

Eight patients have received radiotherapy for head and neck cancers at Zhianawa Cancer Center were selected for this study. The dose prescriptions for the patients were different according to the cancer stage of each patient. Five patients had two Planning Target Volumes (PTVs) (54, 66) Gy, and three patients had three PTVs (54, 60, and 70) Gy.

We have used all data collected from the Treatment Planning Systems (TPS) to conduct a pilot comparison between IMRT and 3D-CRT technics. This comparison includes the parameters of the target coverage, dose conformity and homogeneity for the planning target volume (PTV), the maximum and mean doses for (OARs), the time required to deliver the prescribed dose, and number of Monitor Units (MU). The radiation beam dose amounts and intensities were verified as well through quality assurance procedures.

The target volumes were delineated (contoured) according to the recommendation of (ICRU) report No.50. GTV was contoured according to the information from CT-Scanner, MRI, pathology and oncology reports, then CTV, PTV were delineated. Normal tissues and nearby organs were contoured, (spinal cord, brain stem,

brain, parotids, optic nerves, optic chiasm, eyes, mandible, and both cochlea) delineated as OAR. The dose prescribed for all PTVs according to the type, size, and location of the tumor for each patient.

Three dimensional plans were created on XIO planning system for all eight patients. The plans were in two phases for patients with two PTVs and three phases for patients with three PTVs. The daily dose was 2Gy for all phases and the super possession algorithm was used in dose calculation.

Dose Volume histogram (DVH) created for the plans and several quantitative evaluation tools such as target volume coverage, Homogeneity Index (HI), Conformity index (CI), ORA, maximum dose and mean dose were used for evaluation the plans.

The maximum, minimum, mean dose values and DVH curves have been determined for all organs at risk (OARs) including (spinal cord, brainstem, eye lenses, optic nerves, optic chiasm, parotids, cochlea, and mandible). The obtained data were compared with the organs tolerance dose levels. Both IMRT and 3D-CRT plans for all patients were delivered with the Elekta Synergy Linac available at ZCC and the time needed for each plan was measured. The data of each patient is not present because the paper will be very long.

The Statistical analysis was performed by using t-test to compare the means of tumor coverage, CI, HI, OAR doses, delivery times and MUs.. The P-values less than 0.05 were considered as a significant.

Results

The radiation doses for all beams used for the treatment of all patients were measured with I'mRT phantom and compared with the calculated doses by the TPSs in the QA plans. The intensities of every beam were measured with the MatriXX and Omnipro software and compared with the calculated intensities with Omnipro software to obtain gamma index. The results showed in tables 1 and 2.

Table (1); Measured and calculated dose for all patients with both IMRT and 3D-CRT plans

Patients	3D-CRT dose (Gy)		IMRT dose (Gy)	
	Measured	Calculated	Measured	Calculated
Patient I	1.94	1.961	2.154	2.11
Patient II	2.11	2.118	2.060	2.04
Patient III	1.82	1.833	2.014	1.98
Patient IV	2.01	2.024	1.891	1.87
Patient V	1.78	1.796	1.715	1.7
Patient VI	1.98	1.986	2.143	2.13
Patient VII	1.88	1.903	1.96	1.987
Patient VIII	2.09	2.105	2.08	2.103

Table (2); Calculated gamma Indexes (%) for all patients with both IMRT and 3D-CRT plans

Patients	3D-CRT gamma Indexes %	IMRT gamma Indexes %
Patient I	1.2	2.1
Patient II	0.8	1.5
Patient III	0.9	1.7
Patient IV	1.2	0.9
Patient V	0.6	1.2
Patient VI	0.5	1.2
Patient VII	0.9	1.1
Patient VIII	0.8	1.0

Mean values of CI, HI and $V_{95\%}$ for both technics IMRT and 3D-CRT shown in table 3. The mean values of CI for PTV high risk were 1.640 and 2.705 and for PTV low risk were 1.315 and 1.641 for IMRT and 3D-CRT respectively. The CI with IMRT plan was significantly better than 3D-CRT for the PTV high risk and low risk and the p-values were 0.0005 and 0.005 respectively.

There is no significant deference (p=0.1351) between HI for PTV high risk in IMRT and 3D-CRT and the mean values of HI for PTV high risk in IMRT and 3D-CRT were 14.036 and 15.938 respectively. Regarding the mean values of HI for PTV low risk; IMRT was significantly (p= 0.034) better than 3D-CRT and the mean values of HI were 37.476 and 43.465 for IMRT and 3D-CRT respectively.

Mean values of V95% for PTV high risks were 96.77% and 96.29% in IMRT and 3D-CRT plans respectively and 97.48% and 95.10% for PTV low risks respectively. There was no significant deference between IMRT and 3D-CRT regarding to coverage of both PTVs.

Table (3); CI, HI, V95%, and P value for both high and low risk PTVs

	PTV high risk			PTV low risk		
	IMRT	3D-CTR	P value	IMRT	3D-CTR	P value
Mean CI	1.640	2.705	0.0005	1.315	1.641	0.005
Mean HI	14.036	15.938	0.1351	37.476	43.465	0.034
MeanV95%	96.77%	96.29%	0.3376	97.48%	95.10%	0.174

Mean doses received by organs (Cord, Brainstem, Rt parotid, Lt Parotid, Rt cochlea, Lt cochlea, Rt Optic nerve, Lt Optic nerve, Optic Chiasm, Rt eye, Lt eye, Rt lens, Lt lens, and Mandible) with IMRT and 3D-CRT shown in table 4. The mean doses received by organs (cord, Brainstem, both parotids, and mandible) high significantly lower with IMRT compared with3D-CRT plan and significantly lower observed for right and left cochlea. No significant difference was observed for the other organs.

Table (4); mean dose values received by OARs in IMRT and 3D-CRT plans

OAR	mean dose / Gy		P value
	IMRT	3D-CRT	
Cord	39.067	50.922	0.0002
Brainstem	44.456	50.339	0.0080
RT parotid	28.776	52.979	0.0002
Lt Parotid	29.572	55.500	0.0003
Rt cochlea	17.469	26.856	0.0171
Lt cochlea	20.174	30.315	0.0163
Rt Optic nerve	12.806	14.030	0.1970
Lt Optic nerve	12.774	14.094	0.2671
Optic Chiasm	11.036	10.517	0.4322
Rt eye	3.756	9.106	0.0777
Lt eye	4.040	6.888	0.1318
Rt lens	2.560	7.534	0.1470
Lt lens	2.408	5.807	0.1750
Mandible	47.727	53.517	0.0082

The time required to deliver a single IMRT fraction was higher than the delivery time required for a single 3D-CRT fraction for all patients. Regarding to MU in each fraction, the IMRT plans need more MUs than 3D-CRT to deliver the prescribed dose to the PTVs. The delivery time for a single fraction and fractional MU for each patient were shown in table 5.

The times required to deliver IMRT plans were significantly higher ($p= 5.32x10^{-7}$) than those for 3D-CRT plans. Mean delivery time was 12:14 min and 4:57min for IMRT and 3D-CRT plans respectively.

The mean Monitor Unit (MU) to deliver the prescribed doses of a single fraction for IMRT and 3D-CRT were 735.255 and 524.775 respectively. It was significantly (p=0.003) higher in IMRT compared to 3D-CRT.

Table (5); delivery time and monitor units for IMRT and 3D-CRT for all patients and the average

Patients	Delivery time / Mm:ss		MU / Fraction MU	
	IMRT	3D-CRT	IMRT	3D-CRT
Patient I	13:26	4:50	933.8	435.6
Patient II	12:18	5:46	704.5	585.6
Patient III	12:27	4:42	709.2	529.1
Patient IV	13:11	5:24	699.6	686.4
Patient V	12:27	4:50	648.2	455.9
Patient VI	9:33	4:46	647.6	566.4
Patient VII	12:59	4:11	769.2	456.4
Patient VIII	11:32	5:07	770	482.8
Average	12:14	4:57	735.25	524.775

Discussion

This study focused on tumor coverage deliberately to determine the difference between both IMRT and 3D-CRT plans regarding to CI, HI, doses of OAR, and delivery time when they have almost the same tumor coverage. The conformity of IMRT plans was significantly better than 3D-CRT for all PTVs due to the modulation of the radiation intensity in IMRT plan, according to the plan need. There was no significant difference between IMRT and 3D-CRT plans regarding HI values for high risk PTV, but for PTV low risk the difference was significant. These results are consistent with those published by William M. Mendenhall et.al (2006) which showed that IMRT may result in a dose distribution that is more conformal than that achieved with 3D-CRT, allowing dose reduction to normal structures and thus decreasing toxicity [17].
Parotid glands were over dosed in all 3D-CRT plans because parts of the parotids intersecting with the PTVs so sparing such organs with 3D-CRT plan almost impossible while in IMRT plan the doses to the parotids were within the acceptable limits. Petra M. Braam et.al (2006) showed that IMRT significantly reduces the number of parotid flow complications for patients with oropharyngeal cancer [18]. Leire Arbea et.al (2010) used IMRT vs.3D-CRT in locally advanced rectal cancer (LARC) and concluded that IMRT planning improves target conformity and decreases irradiation of the OAR at the expense of increased target heterogeneity. IMRT planning increases irradiated body volume (IBV) at 5 Gy or less but decreases the IBV at 20 Gy or more [19].

In this study the doses received by (spinal cord, brainstem, cochlea, and mandible) with IMRT technic were significantly better than 3D-CRT. In 3D-CRT plans spinal cord was over dosed for six patients and brainstem for four patients (the data were not shown). To solve this issue the doses must be reduced in overall plans and this lead to under coverage of PTVs. In such plans one has to choose between PTV coverage and doses received by OARs. Nancy Lee et.al (2002) used IMRT to treat nasopharyngeal carcinoma (NPC), their study showed that excellent local-regional control for NPC was achieved with IMRT and this technic provided excellent tumor target coverage which allowed the delivery of a high dose to the target with significant sparing of the salivary glands and other nearby critical normal tissues [20]. Christian Fiandra C. et,al(2012) concluded that IMRT techniques showed superior target coverage and OAR sparing and larger volumes of healthy tissues (lungs, breasts) receiving low doses [21].

In our study both IMRT and 3D-CRT delivered low doses to (eye lenses, optic nerves, optic chiasm), because these organs were far away from the tumor and outside the treatment fields, receiving just scattered doses. In IMRT plan the dose to these organs were slightly higher due to the high number of MU and longer irradiation time in IMRT plan which produce more scattering. Edvard Abel et.al (2017) concluded that IMRT has improved the long-term quality of life of head and neck cancer patients who have been treated with radiation therapy, but might cause more acute side effects [22].

Treatment time was significantly higher with IMRT plan because the MLCs needs time to move and make numbers of small sub-fields for each beam to modulate the intensity of the beams. Also these modulated beams are requiring more MUs to deliver the prescribed dose, as it's clear in the results of this study. Our results agree with the study done by Andrea Pirzkall et.al (2000) which showed IMRT increases number of MU significantly [23].

In our study the QA procedures showed that the delivered doses and beam intensities were almost the same (for both IMRT and 3D-CRT) with those calculated by the two TPSs. This confirms that the calculation results obtained with the TPS software used in this study are correct and we can rely on them.

Conclusions

Using different dosimetry techniques in radiotherapy planning leads to significant change in tumor control and sparing normal organs, as well as dose delivery time and MUs. Dose conformity and uniformity of dose distribution is much better in IMRT plan compared to 3D-CRT plan. 3D-CRT plan has a limitation of sparing organs near the tumor, IMRT plan is a good choice when dealing with treating PTVs near critical organs. IMRT plans require more MUs and time to deliver the prescribed doses as compared to 3D-CRT plans. The organs outside the treatment area receive slightly higher dose in IMRT due to higher number of MUs and irradiation time.

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