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The Dosimetric and Radiobiological Assessment of Three Intensity-Modulated Radiotherapy Techniques for The Treatment of Oropharyngeal Cancer

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Abstract

Objectives: A comparison of the treatment-plans quality and the radiobiological impact of dynamic field (Sliding Window (SW/IMRT), Volumetric Modulated Arc-Therapy (VMAT) and Helical Tomotherapy (HT) plans for oropharyngeal carcinoma.

Methods: Three cohorts of patients were selected, planned and treated with one of three IMRT techniques and the plans compared dosimetricaly and radiobiologically. In-house software computed Equivalent Uniform Dose (EUD); a second piece of software was developed to compute NTCP using the Lyman Kutcher Burman models. The risk of cancer induction was estimated from the integral dose (ID).

Results: The three types of IMRT plan yielded similar dose distributions. The hot spot in HT yielded Dmax < 105% of Dpres. The EUDs were maximized over the PTVs and reduced for all structures treated by HT compared to SW and VMAT. All NTCPs were less than 5% except for the parotid glands. The second cancer risk varied with the type of IMRT.

Conclusion: EUD, NTCP and ID assessment in addition to dosimetric parameters evaluation confirm that the three techniques are equivalent dosimetrically, but HT offers better radiobiologically sparing of structures in case of oropharyngeal cancer.

Advances in Knowledge: This paper is a complete study compared to all studies given above in a lot of journals. It concerns three novel IMRT techniques of treatment, where we find the dosimetric evaluation and the biologic impact of each modality of treatment at the first time and we give an estimation of induced second cancer for each one in the second part.

Abbrevations: IMRT: Intensity modulated radiotherapy, HT: Helical Tomotherapy, VMAT: Volumetric modulated arc therapy, EUD: Equivalent uniform dose, NTCP: normal tissue complication probability, ID: Integral dose

Introduction

Intensity modulated radiotherapy (IMRT) has been routinely employed in Europe over the past decade, comprising several different modalities of intensity modulation [1-4]. The use of dynamic-field Sliding Window "SW/IMRT", Volumetric Modulated Arc Therapy "VMAT" or Helical Tomotherapy (HT) requires increased attention. In the case of dynamic IMRT, the gantry is positioned at a specific angle and the leaves of the MLC continuously change their position; VMAT involves gantry rotation with dynamic leaf motion and varying dose rate. Tomotherapy combines the variable beamlet intensity with image guidance (IGRT). All three 'flavours' of IMRT enable the delivery of a highly conformal and homogeneous dose to the target volume in comparison with so-called 3D conformal therapy [5]. Consequently, there is a need to assess the advantages and disadvantages of each technique.

Numerous dosimetric and treatment planning have compared treatment plans for several tumors sites particularly head and neck. Among the authors who have compared dosimetrically these three IMRT techniques we can cite: Cao et al. [6] whose made a treatment planning comparison between IMAT and helical tomotherapy (HT), Verbal et al. [7] whose compared the planning and dosimetry of Rapid Arc to conventionnal IMRT for head and neck patients, finding similar dose distributions; and Fogliata et al. [8] who compared the plans for RA, HT and IMRT for 12 patients with benign brain tumours. These studies demonstrated that these three techniques yield comparable plan quality. Although, most of the investigations carried out

concerned dosimetric comparisons, certain authors have emphasized the risk of second cancer induction [9-12]. Taking the above-cited studies as our starting point, we decided to include in our study a radiobiological assessment of IMRT modality. This was made using the concept of Equivalent Uniform Dose [13,14]. Predictive models like normal tissue complication probability [15-17] and the calculation of integral dose (ID) [18].

Methods

Patients and Prescription

Three cohorts of patients with oropharyngeal cancer treated with IMRT, VMAT and HT were selected for this study. The treatments took place in different periods. Thirty-four patients were treated with SW/IMRT (median age 60 years), thirty others treated with VMAT (median age 64.5 years) and thirty-three patients (median age 61 years) treated with HT. None of these patients presented with distant metastasis (M0) (Table 1). In order to compare these IMRT techniques, the same prescription was used: Prescribed dose of 70 Gy to the PTV70, 66 Gy to the PTV66 and 56 Gy to the PTV56, delivered in 35 fractions using simultaneous integrated boost (SIB). The goal of the treatments was to deliver the prescribed dose to at least 95% of the PTV [19]. The maximum "cut-off" dose to the spinal cord was not allowed to exceed 40 Gy in all cases. The planning constraints and the objectives for the target volumes and the critical structures were defined according to RTOG0522 [20]. The different target volumes (GTVs) were generated according to ICRU50 and 62 [21,22]. A margin of 5 mm was added to each targets volume (PTV70, PTV66 and PTV56).

Table 1: Patient demographics.

		SW			VMAT			HT	
		Gender	Age		Gender	Age		Gender	Age
	P1	F	62	P8	M	72	P6	M	77
	P5	M	64	P14	M	70	P8	F	65
	P9	F	62	P24	F	72	P12	M	55
	P11	M	78	-	-	-	P24	M	49
	P13	H	55	-	-	-	P26	M	67
	P21	H	63	-	-	-	P27	M	53
Stage I	P22	M	68	-	-	-	P34	M	54
	P25	M	53	-	-	-	-	-	-
	P26	M	56	-	-	-	-	-	-
	P28	F	65	-	-	-	-	-	-
	P32	F	49	-	-	-	-	-	-
	P12	M	57	P2	M	42	P1	M	69
	P14	F	67	P4	M	46	P4	M	68
Stage II	P18	F	65	P7	F	69	P5	M	73
	P27	M	70	P10	F	59	P10	F	63
	P29	M	56	P18	F	69	P11	F	56
	P30	M	66	P21	F	68	P19	M	53
	P31	M	53	P22	F	67	P21	M	77
	P33	M	61	P23	M	75	P23	M	58
	P34	M	58	P27	M	67	P25	M	60
	-	-	-	P29	M	64	P30	M	65
	-	-	-	P30	M	66	-	-	-
Stage III	P2	M	57	P1	M	57	P2	M	53
	P10	M	49	P25	M	66	P3	M	52
	P15	F	59	-	-	-	P7	F	79
	P20	M	54	-	-	-	P9	M	52
	-	-	-	-	-	-	P15	M	62
	-	-	-	-	-	-	P22	M	53
	-	-	-	-	-	-	P33	M	64
Stage IV	P7	M	50	P3	M	57	P13	M	55

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	P8	M	68	P6	M	55	P16	M	65
	P16	F	66	P17	F	70	P17	M	51
	P17	M	80	P19	M	60	P29	M	60
	P19	M	63	P20	M	58	P31	M	51
	P23	M	53	P26	M	58	-	-	-
	P24	M	54	P28	M	67	-	-	-
	P3	M	67	P5	M	70	P14	M	69
Unknown	P4	M	68	P9	M	65	P20	F	71
	P6	M	49	P11	M	83	P28	M	57
	-	-	-	P12	M	70	P32	M	56
	-	-	-	P13	M	67	-	-	-
	-	-	-	P15	F	56	-	-	-
	-	-	-	P16	M	65	-	-	-

F: Female; M: Male

Treatment Planning

IMRT and VMAT plans were generated for 6 MV beam energy on an HD Linac 21EX (Varian Medical Systems, Palo Alto, CA, and Brainlab, Inc., Germany). For each treatment modality the machine was equipped with a Multi-leaf Collimator (MLC) with 80 leaves with a dose rate of 400 MU/at the isocentre (SW/IMRT) and 120 leaves with 600 MU/at the isocentre (VMAT) respectively. Dose and MU calculations for IMRT were performed for sliding window delivery. For each sliding window IMRT, seven co-planar beams were planned for delivery at different gantry angles 0; 20; 75; 130; 230; 285; and 340 degrees using an isocentric technique. Plans were created using inverse planning software (EclipseTM, Helios, version 8.6.10, Varian Medical Systems, Palo Alto, CA, USA).

The VMAT technique consisted of 2 arcs moving in opposing directions with complementary collimator rotations. A double-arc plan was created for each patient using the Rapid Arc (Varian Medical Systems) software. The two complete coplanar-arc beams each comprising 360 degrees of rotation were delivered in clockwise and counter-clock-wise directions respectively. All IMRT and VMAT plans were calculated with software options (AAA "Anisotropic Analytical Algorithm V8 and later version" [23,24]). In the case of HT, plans were derived by the Tomotherapy Hi-art system, version2.0 (Accurray). This involves a convolution and superposition algorithm [25].

Assessment of the planning

Dosimetric Tools

Dose Volume Histograms (DVH) were generated to aid in the assessment of the treatment plans of the three different cohorts. In this way, Dmax, Dmin and Dmean were collected and compared for tumors and critical structures. Initially, a quantitative comparison was established between the above three dose metrics for tumors. Conformity index (CI95%) was defined as the ratio between the maximum dose and the minimum dose received by 95% of the volume of PTV.

Dosimetric comparison was then performed for all critical structures for the three techniques (SW/IMRT, VMAT and HT). The results for the tumors and for the various normal-tissue-volumes were compared and analyzed using the T-test for paired samples and the nonparametric Wilcoxon test, with the threshold for significance set at $P < 0.05$.

Radiobiological Tools

In the second step of this study, software was developed to compute Equivalent Uniform Dose (EUD) (Eqt.1) for tumor and organ at risk [26].

$$\mathrm{EUD} = \left(\sum_{i=1}^{k} v_i D_i^a\right)^{(1/a)} \equiv \mathrm{gEUD} = \left(\frac{1}{N}\sum_{i=1}^{k} D_i^a\right)^{(1/a)} \quad (1)$$

A second piece of software was developed related to normal tissue complication probability using the Lyman- Kutcher-Burman models [27]. The expression employed for the NTCP is given by equation 2:

$$NTCP = (2\pi)^{-1/2} \int_{-\infty}^{t} \exp\left(\frac{-x^2}{2}\right) dx \equiv NTCP = \frac{1}{2}\left[1 + erf\left(\frac{t}{\sqrt{2}}\right)\right] \quad (2)$$

with :

$$t = (d_{réf} - TD_{50}(v_{eff})) / (m.TD_{50}(v_{eff})) \quad (3)$$

where :

$$v_{eff}^{(j)} = v_j \left(\frac{d_j}{d_{réf}}\right)^{1/n} \quad and \quad v = \sum_{j=1}^{k} v_{eff}^{(j)} \quad (4)$$

and:

TD_{50}: is the dose at NTCP =50%, this parameter for each critical structure was obtained from Emami et al (1991) (Table 2).

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Table 2: Specific parameters given for tumors and critical structures obtained from Emami et al.

Structures	a (W et al. [18]	δ_{50} (Gamma50)	TD_{50}(Gy)	TCD_{50}(Gy)	n	m	Endpoint
Head and Neck tumors	-8	2	-	72	-	-	-
Critical Structures (OARs)							
Brainstem	4.6	3	65		0.16	0.14	Necrosis
Spinal Cord	7.4	4	66.5		0.05	0.175	Myelitis
Parotid (Lt-Rt)	5	6	46		0.70	0.18	Xerostomia
Larynx	4.6	4	80		0.11	0.75	Necrosis

(1991) used as input parameters to calculate EUD(Gy) and NTCP.

v_j is the irradiated volume which receiving dose d_j (Kutcher et al. [27].

TCD_{50}, the dose that yields a tumour control probability of 50% for tumors that receive a uniform dose; TD50, tolerance dose for a 50% complication rate at a specific time interval.

Integral Dose

Another important clinical metric is the integral dose (ID) for each structure. The integral dose function is defined as the sum of the product of a given dose (Di), the volume of tissue receiving that dose (Vi) and the density of the tissue volume (ρ_i), as represented by the following equation [28]:

$$IntegralDose = \sum_i D_i \times V_i \times \rho_i \quad (5)$$

where the normal tissue concerns the spinal cord, the brainstem, the left and the right parotid glands and the larynx. The target volume was excluded. The value for the density (ρ_i) is taken as equal to one. Therefore, the unit of integral dose is Gykg. The integral doses were calculated directly from the dose volume histogram data.

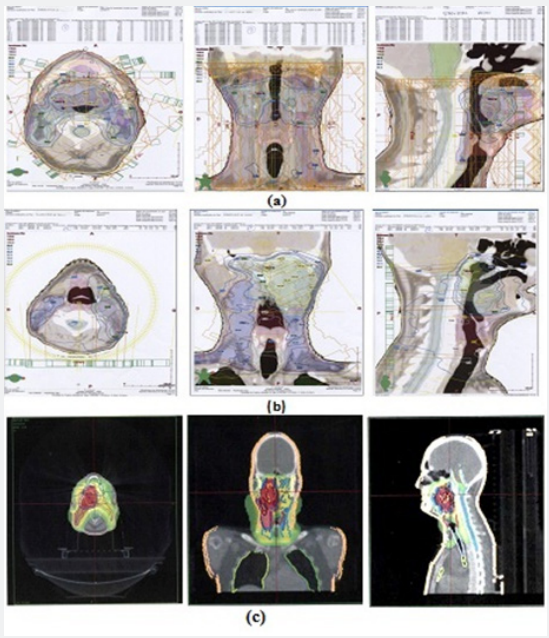

Figure 1: Dose distributions obtained for targets volumes plotted in three different planes: sagittal, coronal and cranio-caudal directions for the three different cohorts treated at different times by the three IMRT modalities: SW (a), VMAT (b) and HT (c).

Results

Quantitative Assessment

Targets

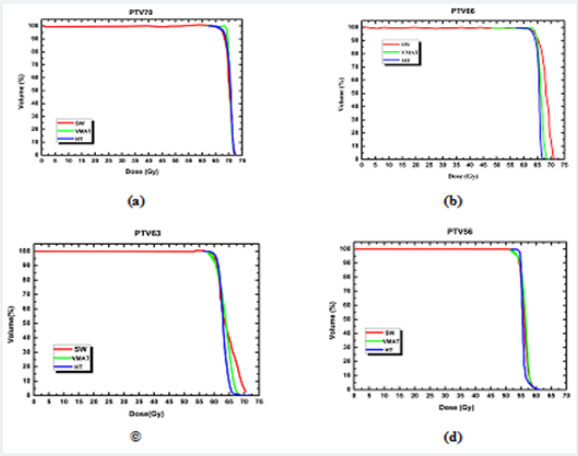

Figure 2: Dosimetric comparison between target volumes (PTV70, PTV66) in case of three different cohorts of patients treated with the three IMRT techniques at different periods of time.

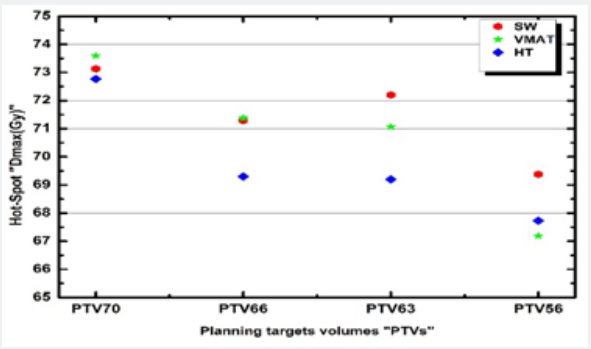

Figure 3: Comparison of the "Hot-Spot" in the PTVs for the three IMRT treatments techniques of oropharyngeal cancer.

Dose distributions for the target volumes and critical structures were obtained in three different planes: sagittal, coronal and cranio-caudal directions for the three IMRT modalities SW/IMRT (Figure-1a), VMAT (Figure-1b) and HT (Figure-1c). All these plans correspond to different patients treated in different time periods. All these plans were analyzed and compared dosimetrically (Figure 2). Table 2 summarizes also all the dosimetric results obtained for targets and structures

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for the three IMRT treatments types. Both HT and VMAT achieve superior coverage of the target volumes compared to SW. The evaluation of the- 'hot-spot' shows that HT delivered the lowest maximum doses (Dmax < 105% Dpres) to the different target volumes compared to SW and VMAT (Figure 3).

The differences in Dmean for the VMAT and HT treatments compared to SW were: lower relative mean dose (ΔDmean) of PTV70 [2.19 vs 1.54%], PTV66 [1.01 vs (-) 0.43%], PTV63 [0.78 vs 0.15%] and PTV56 [1.48 vs (-)0.26%]. These results show that these three techniques exhibit differences less than ± 2.5%. The comparison of Dmean with the prescribed dose, demonstrates that HT achieves a better conformity index than SW and VMAT (Table 3).

Dmin, minimum dose; Dmax, maximum dose; Dmean, mean dose; Vmean, mean volume ; CI, conformity index

$$\Delta D_{mean} = \frac{D_{mean}(\text{VMAT,HT}) - D_{mean}(\text{IMRT})}{D_{mean}(\text{IMRT})} \times 100\% \qquad \text{Conformity index} = \frac{D_{max}}{D_{pres}}$$

Critical Structures

For all patients, DVHs for critical structures (brainstem, spinal cord, left and right parotid and larynx) were calculated and analyzed. Representative DVHs for the IMRT, VMAT and HT treatments are plotted in Figure 4. Table 3 depicts the dosimetric comparison for these structures calculated for each modality of treatment. These results revealed that HT delivered the lowest mean doses to the spinal cord (15.40 Gy); the Lt-parotid (25.18 Gy) and the larynx (37.31 Gy). However, the comparison of the corresponding Vmean revealed that the HT treatments irradiates more volume compared to SW and VMAT that is the case of the spinal cord (23.88 cc), brainstem (27.68 cc) and the larynx (32.85 cc).

Table 3: Statistics on Doses (±SD) of SW vs VMAT and HT.

Tumours	Dose volume index	SW	VMAT	HT
		mean±SD	mean±SD	mean±SD
PTV70	D_{min}	58.26±5.87	63.32±3.53	60.82±2.80
	D_{max}	73.13±1.71	73.59±0.95	72.77±0.82
	D_{mean}	68.65±3.68	70.16±0.32	69.71±0.15
	V_{mean}	147.46±103.13	112.27±104.92	181.58±105.42
	CI	1.04	1.05	1.03
PTV66	D_{min}	53.68±4.67	56.80±2.92	53.56±4.94
	D_{max}	71.29±1.50	71.38±1.34	69.30±0.79
	D_{mean}	66.10±0.81	66.77±0.37	65.81±0.25
	V_{mean}	158.99±108.00	146.06±75.02	197.20±110.09
	CI	1.08	1.08	1.05
PTV63	D_{min}	53.95±0.21	55.02±1.68	54.46±4.93
	D_{max}	72.20±1.97	71.07±1.08	69.20±1.97
	D_{mean}	63.80±1.13	64.30±0.18	63.90±1.48
	$V_{meanù}$	101.5±1.41	168.25±40.17	89.10±63.61
	CI	1.14	1.13	1.09
PTV56	D_{min}	41.96±4.30	45.23±3.47	38.54±7.04
	D_{max}	69.38±2.5	67.19±2.35	67.73±2.43
	D_{mean}	56.41±0.52	57.25±0.59	56.26±1.26
	Vmean	332.88±84.65	348.59±120.67	339.39±113.89
	CI	1.23	1.19	1.21
Structures				
Spinal Cord	D_{min}	1.02±2.25	0.40±0.53	0.60±1.38
	D_{max}	39.09±1.83	38.73±2.61	38.83±2.77
	D_{mean}	21.04±4.41	20.10±5.75	15.40±3.52
	V_{mean}	21.20±2.79	23.17±2.81	23.88±4.33
Brainstem	D_{min}	2.10±2.02	2.00±1.21	3.45±4.38
	D_{max}	33.02±14.21	33.51±13.06	33.35±7.16
	D_{mean}	9.11±7.58	9.85±7.72	12.99±7.66
	V_{mean}	25.11±6.36	26.81±7.35	27.68±11.05

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Rt-Parotid	D_{min}	6.50±3.64	5.05±2.37	7.42±6.31
	D_{max}	65.52±5.35	62.44±5.34	63.51±7.52
	D_{mean}	27.55±9.53	24.00±5.64	26.79±10.26
	V_{mean}	25.87±10.02	23.42±7.99	23.79±6.53
Lt-Parotid	D_{min}	5.68±2.84	7.65±8.13	5.63±2.16
	D_{max}	64.84±5.26	65.90±8.93	62.25±6.47
	D_{mean}	25.04±5.11	32.25±14.54	25.19±6.47
	V_{mean}	25.83±9.15	23.82±8.07	23.12±5.98
Larynx	D_{min}	22.40±5.80	24.02±7.86	20.5±12.35
	D_{max}	62.87±6.60	62.08±5.84	66.70±5.77
	D_{mean}	37.48±7.48	41.15±9.45	37.31±11.70
	V_{mean}	22.52±11.90	27.81±13.68	32.85±10.01

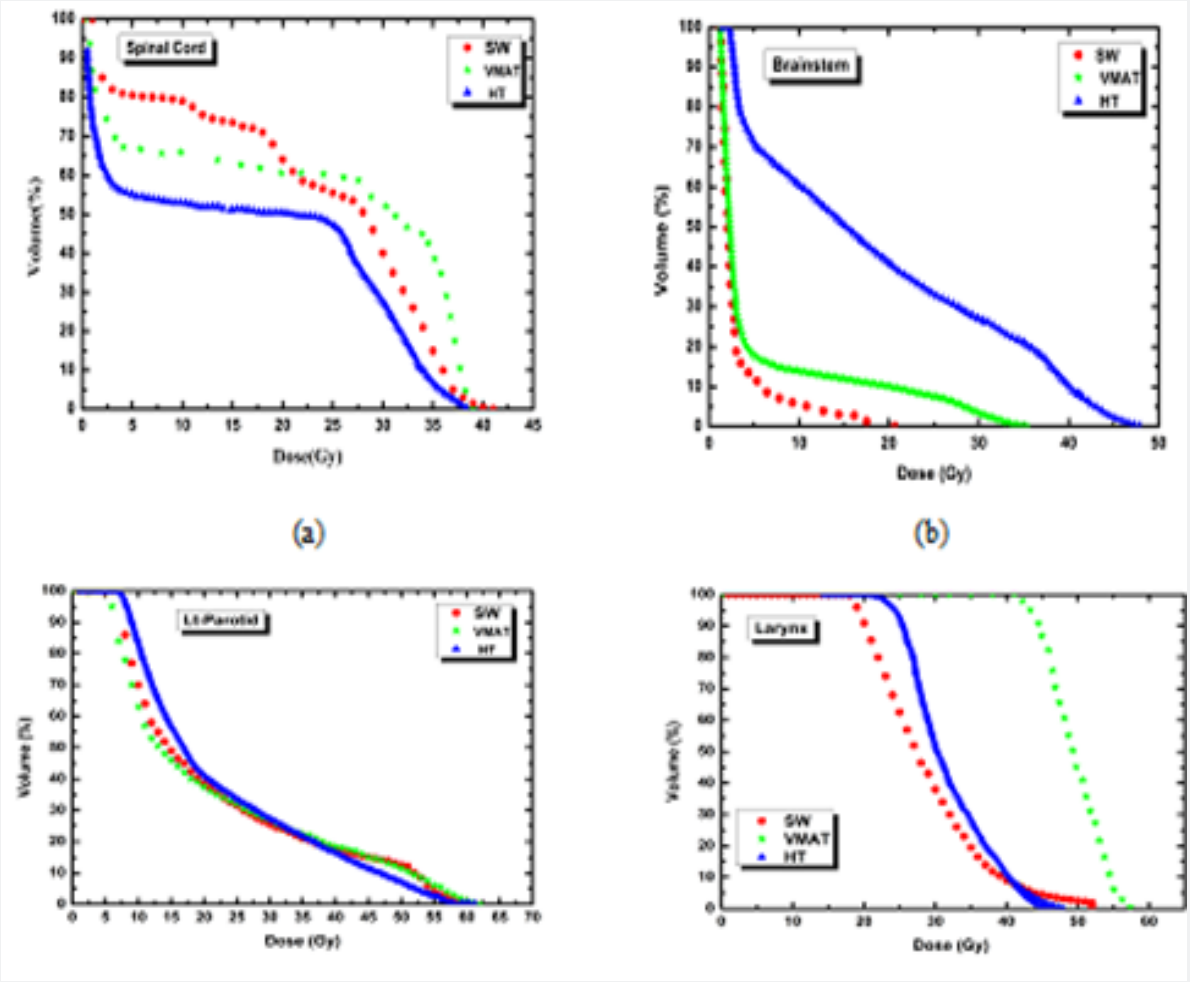

Figure 4: Dosimetric comparison between critical structures (Spinal Cord, Lt-Parotid gland) in case of three different cohorts of patients treated with three different IMRT techniques at different periods of time.

The relative differences in the mean dose were calculated for VMAT and HT compared to SW. In the case of the spinal cord, it was found (-) 4.46% vs (-) 26.80% ; 8.12% vs 42.59% in the case of the brainstem; (-) 12.88% vs (-) 4.93 % for the right parotid and 28.79 vs % 0.55% for the left-parotid and 9.79 % vs (-) 0.45% for the larynx. From these results; one can infer that the sparing of the spinal cord and larynx is greater with HT –e.g- the left- parotid gland received a mean dose less than 26 Gy (Dmean < 26 Gy). This result confirms that this organ was well protected in the case of IMRT and HT, so there is a very low risk of Xerostomia Hey et al. (2011). In the case of the right-Parotid gland, VMAT provided better protection than SW or HT.

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Qualitative Assessment

PTVs volumes and structures

Table 4: Comparison of EUDs to PTVs and the relative increase ΔEUD (%) between SW, VMAT and HT plans in the case of oropharyngeal cancer.

Radiobiological index EUD(Gy) of PTVs					
Tumours	**SW**	**VMAT**	**HT**	**Relative increase** ΔEUD (%)	
	mean±SD	mean±SD	mean±SD	VMAT vs SW	HT vs SW
PTV70	78.61±7.30	82.62±4.50	86.77±4.73	5.10	10.38
PTV66	75.27±6.17	78.35±5.89	82.73±3.89	4.09	10.0
PTV63	75.90±8.46	78.13±7.37	78.08±5.66	2.93	2.87
PTV56	67.45±17.46	70.81±7.94	79.49±6.04	4.98	17.85

The concept of EUD has been applied to three cohorts of patients treated with SW, VMAT and HT. To enable comparison between these treatment techniques, all plans were established, and dose volumes were generated and compared. The EUD over all the different planning targets' volumes were calculated for each modality of treatment (Table 4). Indeed, a paired comparison analysis showed significantly improved equivalent uniform dose for VMAT compared to SW on the PTV70 (p<0.0074 vs p<0.010); PTV66 (p<0.434 vs p<0.27); PTV63 (p<0.071 vs p< E-5) and PTV56 (p<0.121 vs p<6.55E-6). In the case of HT, the EUD is maximized on the different PTVs volumes where PTV70 (p<8.41E-7); PTV66 (p<0.336); PTV63 (p < 0.863); PTV56 (p < 0.779).

Table 5: Comparison of EUDs to structures with corresponding Normal Tissue Complication Probability (NTCP) and Integral dose between IMRT, VMAT and HT plans in the case of oropharyngeal cancer.

Radiobiological indices (EUD(Gy), NTCP(%) and ID (Gykg) for critical structures				
Structures		**SW**	**VMAT**	**HT**
Spinal cord	EUD	15.72±3.14	17.04±2.97	12.82±3.46
	NTCP	0.014±0.009	0.018±0.007	0.012±0.13
	ID	439.89±77.50	458.31±116.29	369±106.5
Brainstem	EUD	8.93±6.79	8.74±6.07	8.00±2.94
	NTCP	0.0372±0.18	< 0.05	0.0029±0.0119
	ID	231.32±210.01	265.60±237.45	323.3±162.18
Rt-Parotid	EUD	22.66±6.14	20.32±4.83	19.66±7.41
	NTCP	0.101±0.23	0.12 ±0.25	0.20±0.33
	ID	716.80±344.43	552.31±188.64	651.93±368.42
Lt-Parotid	EUD	22.29±6.29	25.82±7.64	20.48±5.83
	NTCP	0.08±0.25	0.22±0.30	0.15±0.27
	ID	644.97±270.20	792.58±491.70	573.9±164.27
Larynx	EUD	30.98±8.43	29.26±6.37	30.67±7.24
	NTCP	0.029±0.15	< 0.05	0.0035±0.019
	ID	833.67±442.77	1165.04±802.01	1086±465.87

EUD, equivalent uniform dose

Relative increase, $\Delta EUD\ (\%) = [(EUD_{SW} - EUD_{VMAT,HT})/EUD_{SW}]x100$

Table 5 depicts also the biological assessment results obtained for the different structures. EUDs (Gy) and NTCPs calculation were performed in the case of SW vs VMAT and SW vs HT respectively. The critical structures being analyzed were the spinal cord, the brainstem, the left and the right parotid as well as the larynx. For these structures we found significantly improved paired comparison in case of HT. Spinal cord (p=0.89 vs p=0.06) and (p=0.89vs p=0.009); Brainstem (p<0.05 vs p=0.0066); and (p<0.05 vs p=0.44); Rt-Parotid (p=0.76 vs p=0.65) and (p=0.76 vs p=0.09); Lt-Parotid (p= 0.94 vs p=0.66) and (p= 0.94 vs p=0.93); larynx (p=0.012 vs p=0.09) and (p=0.05 vs p=0.65). The EUD evaluation of critical structures sparing showed that all organs were protected. In fact, all EUDs values are lower than Dmean which means that HT treatment assures a better protection of all organs. On the other hand, excluding the case of larynx, VMAT assures a better protection and gave an EUDs values lower than SW and HT ones.

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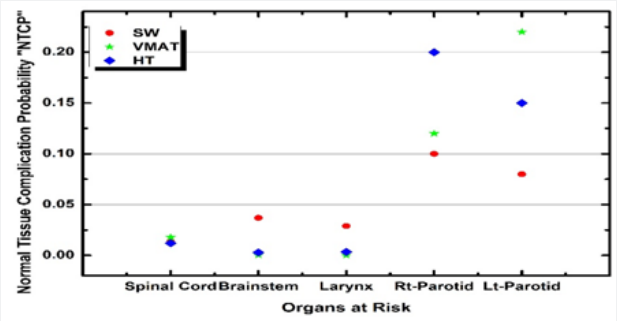

Figure 5: Normal tissue complication probability calculated for each structure for the three IMRT techniques.

The normal tissue complication probabilities (NTCP) were calculated in the case of the spinal cord, the Brainstem, the Lt and the Rt-parotid glands and the larynx for the three cohorts. The results are illustrated in Figure 5. The results of NTCPs for critical structures are consistent with doses received by these organs. As HT delivered lower mean doses to the spinal cord, to Lt-and Rt-parotid glands and to the larynx, the NTCP were thus lower for all critical structures and the values were < 0.05 for the three cohorts especially for the case of Lt and Rt-parotid gland.

Toxicity of Critical Structures

Table 5 lists all the integral doses (ID) calculated in GyKg, for each structure. Through the analysis of the biological comparison of SW, VMAT and HT we found that the spinal cord is better protected with the HT treatment than VMAT and SW. It was found also, that VMAT is not appropriate for the Lt-parotid and that HT is better than both SW and VMAT. In this study, it was noticed that when treatment is given by VMAT, 8 patients presented a mean dose > 50 Gy in the Lt-parotid gland. Consequently, the integral dose was more important with VMAT compared to IMRT and HT. For the right parotid, 5 patients received a mean dose Dmean > 26 Gy whereas 2 patients received Dmean > 50 Gy, which leads us to conclude that VMAT is a more protective technique for this OAR compared to HT and SW. In the case of larynx and brainstem, the results obtained with HT are higher than those of VMAT and SW. Hence, the former represents a superior technique because it ensures better protection. A higher integral dose is delivered by HT compared to SW and VMAT.

Discussion

Quantitative and qualitative assessments have been performed on SW, VMAT and HT treatments. They have been compared in terms of plan quality by comparing firstly different dosimetric parameters like Dmin, Dmax, Dmean, conformity CI and hot-spot-in case of tumors (Table 2). Through this comparison, it was noticed that HT scored over VMAT by achieving a lower PTV maximum, calculated in terms of Dmax in the PTV63 and PTV56 compared to SW, otherwise a higher maximum dose was obtained in PTV70 and PTV66 with VMAT compared to both SW and HT (Table 2). These results were similar to those obtained by Brogg, et al. [29].

Through the dosimetric comparison of the different structures to the constraints dose defined in the QUANTEC reports [30] we found that: The spinal cord is well protected by all three IMRT techniques where Dmax < 50 Gy so the myelopathy risk is lower than 0.2%; The brainstem is well protected also because Dmax < 54 Gy for all the three techniques of IMRT so the risk of neuropathy or necrosis is eliminated; In case of larynx we found Dmax < 66 Gy in case of SW and VMAT, the risk of vocal dysfunction is < 20% contrarily the Dmax for HT exceed 66 Gy so the risk of edema is < 20%. Finally, both the parotid glands received a Dmean < 39 Gy so the risk of xerostomia is < 50%, which can be eliminated for the patients treated with IMRT and HT (Dmean (Lt-Parotid) < 26 Gy) [31]. Secondly, in the radiobiological assessment (Table 4), we have demonstrated that the HT treatment is more effective than VMAT and SW as all EUDs values for the different PTVs were maximized in case of the HT treatments. HT treatments achieve better normal-tissue sparing which was noticed for serial (the spinal cord and brainstem) and parallel organs (larynx and Lt-and Rt-parotids glands) after comparison of Dmax and Dmean with the dose constraints defined in the QUANTEC reports.

In fact, a better sparing of structures was noticed with lower values of EUD and NTCP for spinal cord, brainstem, Lt-and-Rt-parotid glands. The results obtained for the different structures (Table 5) were recorded respectively in case of SW vs VMAT and SW vs HT and gave us (-8.39%) and (18.44%) in the case of the spinal cord; (2.12 %) and (10.41%) in the case of the brainstem. We found also (10.32%) and (13.23%) in the case of Rt-parotid gland; (-15.83%) and (8.12%) in the case of the Lt-parotid gland and finally (5.55 %) and (1%) in the case of the larynx. Similarly, the values of NTCP were lower than 0.05 in the case of all the studied structures expectedly the Rt-and-Lt-parotids glands (Table 5). Increased sensitivity to dose constraints was noticed with HT compared to IMRT and VMAT which was revealed by an increase in spinal cord sparing. This was similar to the finding of White et al. [32].

At the end of this project, the integral dose was calculated for each type of IMRT treatment in order to assess the risk of radiotherapy-induced carcinogenesis. The spinal cord, Lt-parotid gland and larynx received a lower integral dose in the case of HT compared to SW [33,34]. A decrease of 11% for the Lt-parotid gland, with HT compared to SW. These results confirm the benefit of NT sparing by HT. An increase of 39.7% in soft- tissue dose was observed for brainstem in case of HT, and 14.8% for VMAT compared to SW. On the other hand, the Rt-parotid gland showed a decrease in integral dose compared to HT and SW with values of (9%) and (22.9%) in the case of HT and VMAT respectively compared to SW. Finally, lower doses irradiation tissue to the larynx confirms better sparing of this structure with the SW technique.

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Conclusion

Dosimetric comparison and radiobiologic evaluation where studied in this project to assess the benefit of three IMRT techniques. The in-house software was developed using EUD-based objective function for tumors and structures and predictive models "NTCP" for NT structures. All obtained results demonstrate that HT remains the most beneficial treatment for oropharyngeal cancer with better sparing of structures and NT. The estimation of the risk of second cancer revealed that it's depending on the treatment with lower or the maximum irradiated of normal tissue.

Competing Interests

The authors declare that they have no competing interests.

References

1. S Vieillot, P Fenoglietto, CL Moscardo, N Aillères, C Lemanski, et al. (2010) Quelle radiothérapie conformationnelle avec modulation d'intensité ? De la technique « step and shoot » à l'arcthérapie, point de vue de l'oncologue Radiothérapeute. Cancer/Radiothérapie 14(2010): 550-553.
2. Verbakel WF, Cuijpers JP, Hoffmans D, Bieker M, Slotman BJ, et al. (2009) volumetric intensity-modulated arctherapy vs. conventional in head-and-neck cancer: a comparative planning and dosimetric study. Int J Radiat Oncol Biol Phys 74(1): 252-259.
3. A Clivio, A Fogliata, A Franzetti-Pellanda, G Nicolini, E Vanetti, et al. (2009) Volumetric-modulated arc radiotherapy for carcinomas of the anal canal: A treatment planning comparison with fixed field Radiother Oncol 92(1): 118-124.
4. L Cozzi, KA Dinshaw, SK Shrivastava, U Mahantshetty, R Engineer, et al. (2008) A treatment planning study comparing volumetric arc modulation with RapidArc and fixed field for cervix uteri radiotherapy. Radiother Oncol 89(2): 180-191.
5. Clark CH, Bidmead AM, Mubata CD, Harrington KJ, Nutting CM, et al. (2004) Intensity-modulated radiotherapy improves target coverage, spinal cord sparing and allows dose escalation in patients with locally advanced cancer of the larynx. Radiother Oncol 70(2): 189-198.
6. D Cao, TW Holmes, MKN Afghan, DM Shepard (2007) Comparison of plan quality provided by intensity-modulated arc therapy and helical tomotherapy. Int J radiat Oncol Biol Phys 69(1): 240-250.
7. W Verbakel, JP Cuipers, D Hoffmans, BM Bieker, BJ Slotman, et al. (2009) Volumetric intensity-modulated arc therapy vs conventionnel IMRT in head and neck cancer. A comparative planning and dosimetric study. Int J Radiat Oncol Biol Phys 74(1): 252-259.
8. A Fogliata, A Clivio, G Nicolini, E Vanetti, L Cozzi (2008) Intensity modulation with photons for benign intracranial tumours: A planning comparison of volumetric single arc, helical arc and fixed gantry techniques. Radioth Oncology 89(3): 254-262.
9. Randall ME, Ibbott GS (2006) Intensity-modulated radiation therapy for gynecologic cancers: pitfalls, hazards, and cautions to be considered. Semin Radiat Oncol 16(3): 138-143.
10. Hall EJ (2006) Intensity-modulated radiation therapy, protons, and the risk of second cancers. Int J Radiat Oncol Biol Phys 65(1): 1-7.
11. Hall EJ, Wuu CS (2003) Radiation-induced second cancer: the impact of 3D-CRT and IMRT. Int J Radiat Oncol Biol Phys 56(1): 83-88.
12. Dorr W, Herrmann T (2002) Second primary tumours after radiotherapy for malignancies, Treatment-related parameters. Strahlenther Onkol 178(7): 357-362.
13. kavanagh BD, Timmerman RD, Benedict SH, Wu Q, Schefter TE, et al. (2003) How should we describe the radiobiological effect of extracranial stereotaxic radiosurgery: equivalent uniform dose or tumour control probability? Med Phys 30(3): 321-324.
14. Niemierko A (1997) Reporting and analyzing dose distributions: a concept of equivalent uniform dose. Med Phys 24(1): 103-110.
15. Lyman JT (1992) Normal tissue complications probabilities: variable dose per fraction. Int J Radiat Oncol Biol Phys 22(2): 247-250.
16. Terahara A, Niemierko A, Goitein M, Finkelstein D, Hug E, et al. (1999) Analysis of the relationship between tumour dose inhomogeneity and local control in patients with skull base chordoma. Int J Radiat Oncol Biol Phys 45(2): 351-358.
17. Thieke C, Bortfeld T, Niemierko A, Nill S (2003) From physical dose constraints to equivalent uniform dose constraints in inverse radiotherapy planning. Med Phys 30(9): 2332-2339.
18. Detlef Bartkowiak, Nicole Humble, Peter Suhr, Juliane Hagg, Katharina Mair, et al. (2012) Radiotherapy and Oncology 105(2012)122-126.
19. ICRU (1993) ICRU Report50. Prescribing, recording and reporting photon beam therapy. Bethesda: Intenational Commission on Radiation Units and Measurements.
20. RTOG0522 (2016) Protocol Information. A randomized phase III trial of concurrent accelerated radiation and cisplatin versus concurrent accelerated radiation. Cisplatin, and Cetuximab (C225) for stage III and IV head and neck carcinomas.
21. ICRU (1999) ICRU Report 62. Prescribing, recording and reporting photon beam therapy, Supplement to ICRU50. Bethesda: International Commission on Radiation Units and Measurements.
22. Gregoire V, Levendag P, Ang KK, Bernier J, Braaksma M, et al. (2003) CT-based delineation of lymph node level and related CTVs in the node-negative neck. DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines-Radiation Oncol 69(3): 227-236.
23. Bragg C, Windate K, Conway J (2008) Clinical implications of the anisotropic analytical algorithm for treatment planning and verification. Radiother Oncol 86(2): 276-284.
24. Ulmer W, Pyyry J, Kaissl W (2005) A3D photon superposition/convolution algorithm and its foundation on results of Monte Carlo calculations. Phys Med Biol 50(8): 1767-1790.
25. Claude J Bailat, sébastien Baechler, Raphael Moeckli, Marc Pachoud, Olivier Pisaturo, et al. (2011) The concept and challenges of Tomotherapy accelerators. Rep Prog Phys 74.
26. A Niemierko (1990) A generalized concept of equivalent uniform dose (EUD). Med Phys 26: 1100.
27. Kutcher GJ, Burman C, Brewster L, Goitein M, Mohan R (1991) Histogram reduction method for calculating complication probabilities for 3-dimensional treatment planning evaluations. Int J Rad Onc Biol Phy 21(1): 137- 146.
28. VJ Estall, D Eaton, KE Burton, SJ Jefferies, R Jena, et al. (2010) NG Burnet Intensity-Modulated Radiotherapy plan optimization for skull base lesions: Practical class solutions for dose calculation. Clinical Oncology 22(2010): 313-320.
29. Jeremias Hey, Juergen Setz, Reinhard Gerlach, Martin Janich, Guido Hildebrandt, et al. (2011) Parotid gland-recovery after radiotherapy in the head and neck region: 36 months follow-up of a prospective clinical study. Radiation Oncology 6: 125.
30. Quantec (2010) (Quantitative Analysis of Normal Tissue Effects in the Clinic), Joint AAPM-ASTRO working group, Special Issue of IJROBP 76(3).
31. Sara Broggi, Lucia Perna, Francesco Bonsignore, Giuseppe Rinaldin, Claudio Fiorino, et al. (2014) Static and rotational intensity modulated

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DOI: 10.19080/CTOIJ.2019.12.555850.

techniques for head-neck cancer radiotherapy: A planning comparison. Physica Medica 1-7.

32. Peter White, Kit Chi Chan, Ka Wai Chen G, Ka Yiu Chan, Ming Chun Chau, et al. (2013) Volumetric intensity-modulated arc therapy vs conventiona intensity-modulated radiation therapy in nasopharyngeal carcinoma: a dosimetric study. Journal of Radiation Research 54: 532-545.

33. Followill D, Geis P, Boyer A (1997) Estimates of whole-body dose equivalent produced by beam intensity modulated conformal therapy. Int J Radiat Oncol Biol Phys 38(3): 667-672.

34. Schneider U, Lomax A, Pemler P, Besserer J, Ross D, et al. (2006) The impact of IMRT and proton radiotherapy on secondary cancer incidence. Strahlenther Onkol 182(11): 647-652.

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