# ORIGINAL ARTICLE \_

# Dosimetric evaluation of nasopharyngeal carcinomas irradiated with different IMRT techniques

Sevim Ozdemir<sup>1</sup>, Yasin Coban<sup>1</sup>, Mustafa Akin<sup>1</sup>, Pinar Ambarcioglu<sup>2</sup>, Ozgehan Onay<sup>1</sup>, Cumhur Yildirim<sup>1</sup>, Esengul Uzel<sup>3</sup>, Omer Uzel<sup>1</sup>

<sup>1</sup>Cerrahpasa Medical Faculty, Department of Radiation Oncology, Istanbul; <sup>2</sup>Cerrahpasa Medical Faculty Department of Biostatistics, Istanbul; <sup>3</sup>Sisli Etfal Teaching and Research Hospital, Istanbul, Turkey

# Summary

**Purpose:** To evaluate the performance of volumetric arc therapy (VMAT), dynamic intensity modulated radiotherapy (IMRT) and step-and-shoot IMRT techniques in nasopharyngeal cancer (NPC) patients.

**Methods:** IMRT plans of 48 NPC patients treated between May 2010 and December 2012, were evaluated. Twenty two patients were planned with VMAT, 18 with dynamic IMRT and 8 with step-and-shoot IMRT. Conformity index (CI) and homogeneity index (HI), the dosimetry of the planning target volumes (PTVs) and organs at risk (OARs) and the monitor units (MU) were evaluated for each IMRT modality.

**Results:** The conformity indices of VMAT and dynamic IMRT were better than step-and-shoot IMRT plans (p<0.05). Step-and-shoot IMRT plans provided better homogeneity than VMAT (p=0.01). MUs for dynamic IMRT were much higher compared to VMAT (p<0.01) and stepand-shoot IMRT (p<0.01). There was no significant difference between the 3 techniques in terms of PTV70 mean doses. When compared with step-and-shoot IMRT, VMAT and dynamic IMRT had a better sparing effect on optic nerves, eyes and optic chiasm (p<0.05). VMAT plans performed better sparing for brain stem than dynamic IMRT (p=0.01). There was a remarkable decrease in the maximum doses of VMAT to the eye.

**Conclusions:** VMAT outperforms dynamic IMRT by effectively reducing the MU and the dose to some OARs, with adequate PTV coverage. Also, VMAT provides better sparing of normal tissue and conformity than step-and-shoot IMRT. Differences between step-and-shoot IMRT and dynamic IMRT are thought to be due to technical differences of linear accelerator devices like fiber size, variable fiber, dose rate and gantry.

*Key words: intensity modulated arc therapy, intensity modulated radiotherapy, nasopharyngeal carcinoma, radiotherapy* 

# Introduction

NPC is endemic in the southeast Asia and southern China. Radiotherapy (RT) has been the mainstay treatment for patients with non-metastatic NPC due to radiation sensitivity and complex geometry of the tumor. NPC needs complex treatment plan management, due to the contour of the target volume and the OARs.

Recently, great progress has been reported in the field of RT as a result of rapid technological advances [1]. IMRT improves the therapeutic ratio by maximizing tumor coverage and sparing normal tissues [2,3]. IMRT provides better dose distribution to the target volume with lower dose for OARs in NPC [4,5]. A novel technique, VMAT, an arced-based approach to IMRT, can be delivered with a linear accelerator with conventional multileaf collimator (MLC). During VMAT, the leaves of MLC move continuously as the gantry rotates [6]. It's shown that VMAT was able to apply high-quality NPC treatment plans with adequate PTV coverage, and normal tissue sparing in the literature [7].

This study was performed to evaluate the performance of VMAT, dynamic IMRT and step-and-shoot IMRT tecniques in NPC.

*Correspondence to*: Sevim Ozdemir, MD. Kenan Evler Kislasi Yolu Caddesi, Istanbul, Turkey, Tel: +90 5054950595, Fax: +90 2124143101, E-mail: drsozdemir@yahoo.com

Received: 19/05/2014; Accepted: 24/06/2014

# Methods

IMRT plans of 48 NPC patients treated between May 2010 and December 2012 were evaluated. Patient median age was 43 years (range 14-79) and 73% of the patients were male. Patients were classified according to American Joint Committee on Cancer (AJCC) staging system 2009 [8]. The majority of the patients had advanced clinical stages (stage III/IV:72.9%) with undifferentiated histology (70.8%). All of the patients were free of distant metastases.

## Planning CT

Immobilization of patients was provided with thermoplastic head and shoulder mask. Imaging was performed from the top of the head to the lower part of the sternoclavicular joint with 2.5 mm sliced images.

## Contouring

PET-CT or MRI images were fused with planning CT for all patients. The gross tumor volume (GTV70) was defined as the primary tumor and involved lymph nodes considering physical examination, endoscopic findings, CT, PET-CT, and magnetic resonance imaging. The clinical target volumes (CTVs) were created as CTV70: GTV+ 5mm margin, CTV60: entire nasopharynx, and CTV54 was defined as the low risk region (entire nasopharynx, posterior ethmoids, posterior third of the nasal cavity and maxillary sinuses, inferior sphenoid sinus, clivus, cavernous sinuses and elective nodal areas). While neck lymph node levels II-V were included in CTV54 in all cases, level Ib was included when an adjacent level was involved. Planning treatment volume (PTV) was created by adding 3 mm margin to CTV. Eyes, lenses, optic nerves, chiasm, pituitary gland, mandible, temporal lobes, brain stem, spinal cord, parotid glands, submandibular glands, oral cavity, temporomandibular joints, larynx, thyroid gland, cochleas, pharyngeal muscles and brachial plexus were delineated as OARs. Target volumes and critical organs were delineated according to RTOG Atlas [9].

# Planning

Doses to primary tumor and involved lymph nodes, high risk region, and uninvolved regional nodal areas were 70, 60, and 54 Gy, respectively and planned simultaneously over 33 fractions to 39 patients. Nine patients received 70 Gy to primary tumor and involved lymph nodes and 50 Gy for electively irradiated neck nodes with sequential boost tecnique.

Treatment goals were: at least 95% of the PTV should receive 100% of the prescribed dose, and maximum dose (Dmax) should not exceed 107%. 98% of PTV70 volume should receive 95% of the prescribed dose and no more than 2% of PTV70 volume should receive more than 107% of the prescribed dose. For OARs, dose constraints were taken from the Radiation Therapy Oncology Group (RTOG). According to this, maxi-

mum doses to spinal cord and brain stem were limited to 45 Gy and 54 Gy, respectively. At least one parotid gland mean dose was aimed to be less than 26 Gy or the volume receiving 30 Gy radiation should be less than 50% of the parotid volume.

## **Planning techniques**

#### VMAT plan

Twenty two patients were planned with VMAT plan, using Eclipse (v 8.6) treatment planning system. Varian Rapid-Arc linear accelerator, equipped with a millennium MLC with 120 leaves, was used for treatment. Six-MV photon beams were applied to treatment plans with a maximum dose rate of 600 MU/min.

#### Dynamic IMRT plan

Eighteen patients were planned with dynamic IMRT plan, using Eclipse (v 8.6) treatment planning system, which used 7–9 angles to evenly separate coplanar fields. Six-MV photon beams were applied and a fixed dose rate of 300 MU/min was selected.

#### Step-and- shoot IMRT plan

Eight cases were planned using Prowess Panther V5.01 planning system. The plan was delivered on an Electa Synergy Linac, equipped with an 80-leaf, 1cm MLC with step-and-shoot IMRT. Six MV photon beams were applied, 7-9 angles were used and a fixed dose rate of 600 MU/min was selected.

#### Dose evaluations

Conformity index (CI), homogeneity index (HI), monitor units (MU), dosimetry of PTV, and OARs were evaluated for each IMRT modality.

#### Statistics

Kruskal-Wallis test was used for statistical evaluation of each of the 3 tecnique. Mann Whitney U test was used for Npar analysis to compare dual groups. Statistical significance was set at p<0.05.

# Results

#### CI

There was no significant difference between VMAT and dynamic IMRT in conformity, while the conformity indices of VMAT (1.19) and dynamic IMRT (1.10) were better than step-and-shoot IMRT plans (1.35, p<0.05; Table 1).

# HI

Step-and-shoot IMRT plans provided better homogeneity (1.07) than VMAT (1.08, p=0.01).

			Dynamic IMRT Mean±SD	Step and shoot IMRT Mean±SD	p value			
		VMAT Mean±SD			VMAT vs dy- namic IMRT	VMAT vs step and shoot IMRT	Dynamic IMRT vs step and shoot IMRT	
PTV70	2 *	$106.02 \pm 1.36$	105.9 ± 1.36	106.74 ± 1.20	>0.05	>0.05	>0.05	
	98*	98.6 ± 1.13	97.9 ± 2.14	95.6 ± 3.35	0.15	0.00	0.16	
	Mean	$103.2 \pm 0.67$	$103.4 \pm 0.71$	$103.0 \pm 2.06$	>0.05	>0.05	>0.05	
	CI	$1.19 \pm 0.25$	$1.10 \pm 0.12$	$1.35 \pm 0.26$	0.31	0.04	0.00	
	HI	$1.08 \pm 0.01$	$1.08 \pm 0.03$	$1.07 \pm 0.01$	0.63	0.01	0.05	
MU		$548.1\pm249.8$	$1657.2\pm674.8$	$451.3\pm41.2$	0.00	0.59	0.00	

#### Table 1. Comparison of MU, CI and HI

\*: % prescribed dose, VMAT: volumetric modulated therapy, PTV: planning target volume, SD: standard deviation, MU: monitor units, CI: conformity index, HI: homogeneity index, IMRT: intensity modulated radiotherapy

#### MU

MUs for dynamic IMRT (1657.2) were much higher compared to VMAT (548.1, p<0.01) and step-and-shoot IMRT (451.3, p<0.01; Table 1). MU values were similar with VMAT and stepand-shoot IMRT.

## IMRT techniques

PTV coverage: There was no significant difference among the 3 techniques in terms of PTV70 mean doses. Two percent of PTV70 for VMAT, dynamic IMRT and step-and-shoot IMRT tecnique were  $106.02\pm1.36$ ,  $105.9\pm1.36$  and  $106.74\pm1.20$ , respectively. Ninety eight percent were  $98.6\pm1.13$ ,  $97.9\pm2.14$ , and  $95.6\pm3.35$  for the 3 modalities, respectively. Also PTV-70 Dmean were  $103.2\pm0.67$ ,  $103.4\pm0.71$  and  $103.0\pm2.06$ , respectively (Table 2).

## OAR

When compared with step-and-shoot IMRT, VMAT and dynamic IMRT had a better sparing effect on optic nerves, eyes and optic chiasm (p<0.05). VMAT plans performed better sparing for brain stem (max:53.2) than dynamic IMRT (max:56.5, p=0.01). There was a remarkable decrease to maximum doses to eyes with VMAT. There was no significant difference in the effect of parotid glands, cochlea, submandibular glands and spinal cord sparing among the 3 techniques. The mean or average doses to the OARs in the 48 NPC patients are listed in Table 2.

# Discussion

RT is fundamental for local NPC treatment. When compared to the other head and neck cancers, NPC has better treatment outcomes and life expectancy. Five-year survival can reach 85% at early-stage disease [10-12]. As mentioned above, because of complex geometry of the tumor and surrounding critical structures, treatment planning for NPC is difficult. Therefore, sparing normal tissues has become an important issue.

As a result of advances in planning and implementation of RT, various approaches have emerged. Improvement in tumor target coverage and significant sparing of adjacent critical structures allow the feasibility of IMRT for NPC. IMRT is characterized by multi-angular beams while gives the dose cross-sectional. Also, VMAT is a novel IMRT technology that uses a linear accelerator to implement modulated radiation dose to 360 degrees in a single gantry. Dose is given to all volume rather than sectional delivery. Treatment is performed using rotational or arc geometry instead many static beams, which is thought to deliver a more homogeneous dose in the target area. Dose rate, gantry rotation speed and MLC fiber velocity vary during treatment [13].

There are several studies that emphasized the comparison between VMAT and IMRT in head and neck cancer, including NPC [14-16]. According to a study by Vanetti et al. [17] VMAT provided a better sparing effect to OARs compared to conventional fixed field IMRT with similar target coverage in head and neck cancers. VMAT reduced the mean dose to the contralateral parotid gland by 13.5% while the decrement of maximal doses to the spinal cord and brain stem were 8.9% and 35.1%, respectively. According to the present study, VMAT provided better doses to some OARs such as brain stem, eves, optic chiasm and optic nerves, although we couldn't clearly mention a superiority in terms of PTV coverage. Besides, VMAT and dy-

			Dunamic	Step and shoot	p-value			
		VMAT Mean±SD	IMRT Mean±SD	IMRT Mean±SD	VMAT vs dy- namic IMRT	VMAT vs step and shoot IMRT	Dynamic IMRT vs step and shoot IMRT	
Spinal cord	Max	$44.7 \pm 1.49$	44.8 ± 2.5	$44.5 \pm 1.7$	>0.05	>0.05	>0.05	
Brain stem	Max	53.2 ± 3	$56.5 \pm 4.4$	54.6 ± 3	0.01	0.15	0.42	
Parotid	R mean	$33.7 \pm 9.4$	34.1 ± 16	$41.8 \pm 13.1$	>0.05	>0.05	>0.05	
	L mean	31.4 ± 9	36.5 ± 11	$42.1 \pm 14.4$	>0.05	>0.05	>0.05	
Eye	R max	$20.6 \pm 12.5$	26.6 ± 5.7	31.6 ± 12.3	0.00	0.02	0.12	
	L max	$19.2 \pm 10.4$	$27.1 \pm 6.8$	35.5 ± 15.9	0.00	0.02	0.09	
Lens	R max	5.9 ± 2.2	4.3 ± 0.9	7.8 ± 3.9	0.00	0.04	0.00	
	L max	5.9 ± 2.3	$4.4 \pm 0.9$	$11.7 \pm 11.4$	0.00	0.12	0.01	
Optic chiasm	Max	$18.8 \pm 16.8$	$50.9 \pm 16.07$	$54.6 \pm 14.4$	0.00	0.00	0.66	
Optic nerves	R max	$28.4 \pm 16.1$	47.9 ± 11	$47.5 \pm 10.9$	0.00	0.00	0.80	
	L max	$27 \pm 16$	47.5 ± 9.6	48.6 ± 10.5	0.00	0.00	0.66	
Cohlea	R mean	$43.9 \pm 8.6$	46.7 ± 15.2	55.1 ± 9.7	>0.05	>0.05	>0.05	
	L mean	$46.5 \pm 10.7$	44.7 ± 16.2	52.2 ± 9.4	>0.05	>0.05	>0.05	
Submandibu-	R max	55.5 ± 9.9	52.6 ± 11.9	56.4 ± 6.6	>0.05	>0.05	>0.05	
lar gland	L max	57.06 ± 8	51.1 ± 12	55.8 ± 5.4	>0.05	>0.05	>0.05	

 Table 2. Comparison of normal tissue doses

R: right, L: left, Max: maximum dose, Mean: mean dose. For other abbreviations see footnote of Table 1

namic IMRT demonstrated similar conformity, better than step-and-shoot IMRT did.

Our study has several limitations. First, it is a retrospective study. Second, the patient tumor volumes were different. Third, the number of patients were different in the groups, with relatively small sample size in the step-and-shoot IMRT group. Therefore, the varieties of plans should be considered. Verbakel et al. showed improved homogeneity with VMAT [14]. In the current study, step-and-shoot IMRT plans provided a better homogeneity than VMAT and similar to the dynamic IMRT.

IMRT for NPC requires complex plan management, more fields and MUs. This planning may require prolonged treatment time. In the case of prolonged fraction time, despite a very good immobilization, position shifts and increase in movement during swallowing may occur. Eventually, clinical efficacy may be reduced. Shibamoto et al. showed that the reduction of the treatment time may increase the biologic effect of RT [18]. Bradley et al. investigated swallowing function during treatment of head and neck cancers [19]. They reported that while swallowing frequency was 3–19 times in one treatment fraction, the time interval was 4.8 sec for swallowing and the shift of the target volume was 3.13–12.32 mm during treatment. The authors estimated that the swallowing movement and the position shift would decrease the accuracy of the target volume due to longer treatment delivery time. Compared with conventional IMRT, recent data indicates that VMAT reduces treatment time by using less monitor units [14,16] In the present study, MU values were similar with VMAT and step-andshoot IMRT techniques, while two-thirds less monitor units than dynamic IMRT were necessary. As a result, we may prefer VMAT due to increasing the accuracy of therapy, and improving the effectiveness of treatment by reducing the delivery time.

There is another important issue that needs to be addressed and interests physicists; for a sufficient VMAT plan, plan optimization will take more than 17 hrs for VMAT for one locally advanced NPC, while only 0.5–1 h for IMRT [20]. New strategies should be developed to reduce planning time for VMAT. This should be discussed in another study.

In conclusion, VMAT outperforms dynamic IMRT by effectively reducing MU and dose to some OARs, with adequate PTV coverage. Also, VMAT provides better sparing of normal tissue and conformity than step-and-shoot IMRT. Differences between step-and-shoot IMRT and dynamic IMRT are thought to be due to technical differences of linear accelerator devices like fiber size, variable fiber, dose rate and gantry. Future well-designed studies are required to evaluate clinical outcomes.

# References

- 1. Hong TS, Ritter MA, Tome WA, Harari PM. Intensity-modulated radiation therapy:emerging cancer treatment technology.Br J Cancer 2005;92:1819-1824.
- Kam MK, Chau RM, Suen J, Choi PH, Teo PM. Intensity-modulated radiotherapy in nasopharyngeal carcinoma: dosimetric advantage over conventional plans and feasibility of dose escalation. Int J Radiat Oncol Biol Phys 2003;56:145-157.
- Scott-Brown M, Miah A, Harrington K, Nutting C. Evidence-based review:quality of life following head and neck intensity-modulated radiotherapy. Radiother Oncol 2010;97:249-257.
- 4. Chau RM, Teo PM, Kam MK et al. Dosimetric comparison between 2-dimensional radiation therapy and intensity modulated radiation therapy in the treatment of advanced T-stage nasopharyngeal carcinoma: to treat less or more in the planning organ-at-risk volume of the brainstem and spinal cord. Med Dosim 2007;32:263-270.
- Wu Q, Manning M, Schmidt-Ullrich R et al. The potential for sparing of parotids and escalation of biologically effective dose with intensity-modulated radiation treatments of head-and-neck cancers: a treatment design study. Int J Radiat Oncol Biol Phys 2000;46:195-205.
- Yu CX, Tang G. Intensity-modulated arc therapy: principles, technologies and clinical implementation. Phys Med Biol 2011;56:R31-54.
- 7. Lu SH, Chia J, Cheng H et al.Volumetric modulated arc therapy for nasopharyngeal carcinoma: A dosimetric comparison with TomoTherapy and step-andshoot IMRT. Radiother Oncol 2012;104:324-330.
- Edge SB, Byrd DR, Compton CC et al. American Joint Committee on Cancer, American Cancer Society. AJCC cancer staging manual, 7th edn, 2012. Springer, Berlin, Heidelberg, New York.
- 9. www.rtog.org/CorelLab/ContouringAtlases/ HNAtlases.
- Xiao WW, Han F, Lu TX, Chen CY, Huang Y, Zhao C. Treatment outcomes after radiotherapy alone for patients with early-stage nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys 2009;74:1070-1076.
- 11. Yi JL, Gao L, Huang XD et al. Nasopharyngeal carcinoma treated by radical radiotherapy alone: ten-year

experience of a single institution. Int J Radiat Oncol Biol Phys 2006;65:161-168.

- 12. Zhao C, Han F, Lu LX et al. Intensity modulated radiotherapy for local-regional advanced nasopharyngeal carcinoma. Ai Zheng 2004;23:1532-1537.
- Palma D, Vollans E, James K et al. Volumetric modulated arc therapy for delivery of prostate radiotherapy: comparison with intensity-modulated radiotherapy and three-dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 2008;72:996-1001.
- 14. Verbakel WF, Cuijpers JP, Hoffmans D, Bieker M, Slotman BJ, Senan S.Volumetric intensity-modulated arc therapy vs. conventional IMRT in head and neck cancer: a comparative planning and dosimetric study. Int J Radiat Oncol Biol Phys 2009;74:252-259.
- 15. Bertelsen A, Hansen CR, Johansen J, Brink C. Single arc volumetric modulated arc therapy of head and neck cancer. Radiother Oncol 2010;95:142-148.
- 16. Johnston M, Clifford S, Bromley R, Back M, Oliver L, Eade T. Volumetric modulated arc therapy in head and neck radiotherapy: a planning comparison using simultaneous integrated boost for nasopharynx and oropharynx carcinoma. Clin Oncol (R Coll Radiol) 2011;23:503-511.
- 17. Vanetti E, Clivio A, Nicolini G et al. Volumetric modulated arc radiotherapy for carcinomas of the oro-pharynx, hypo-pharynx and larynx: a treatment planning comparison with fixed field IMRT. Radiother Oncol 2009;92:111-117.
- Shibamoto Y, Ito M, Sugie C et al. Reeovery from sublethal damage during intermittent exposures in cultured tumor cells: implications for dose modification in radiosurgery and IMRT. Int J Radiat Oncol Biol Phys 2004;59:1484-90.
- Bradley JA, Paulson ES, Ahunbay E, Li XA, Schultz C, Wang D. Dynamic MRI Analysis of Tumor Motion during Deglutition and Intrafraction Margin Assessment for Radiotherapy of Head-and-Neck Cancer. Int J Radiat Oncol Biol Phys 2011;81:e803-812.
- 20. Bao-min Zheng, Xiao-xia Dong, Hao Wu, You-jia Duan, Shu-kui Han, Yan Sun. Dosimetry and Comparison between Volumetric Modulated Arc Therapy with RapidArc and Fixed Field Dynamic IMRT for Local-Regionally Advanced Nasopharyngeal Carcinoma. Chin J Cancer Res 2011;23:259-264.