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Quantitative Analysis of Parotid Sparing and Reducing Xerostomia Using Volumetric Modulated Arc Therapy in Oral Cancer Patients

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ABSTRACT

Introduction: In head and neck cancer (HNC) radiotherapy, parotid, submandibular, and minor salivary glands are often incidentally irradiated. Hence, Xerostomia is the most significant disabling side-effect, to improve the quality of life, it should be reduced. The study was to evaluate the parotid dose and PTV coverage in post operated Oral cancer patients using Volumetric Modulated Arc Therapy (VMAT) technique.
Material and Methods: The authors generated VMAT plans for 14 post operated oral cancer patients, where primary disease crossed midline or nodal stage ≥ 2. The doses to the moderate high-risk volume of the clinical target volume (CTV) and planning target volume (PTV) were 60Gy in 30 fractions. The low-risk volume received a dose to the CTV and PTV of 54Gy in 30 fractions. Plans were made for each patient, and the dose to D95 and D98 of target volumes was analyzed. The mean dose of the parotid and parotid minus PTV volumes were analyzed and compared with target doses (D98 & D95).
Results: Median dose to the ipsilateral parotid gland was 54.45Gy and to the ipsilateral parotid gland minus PTV was 45.60Gy while to the contralateral parotid gland median dose was 16.31Gy, (mean is ranging from 14.01 to 17.06Gy) and to the contralateral parotid gland minus PTV was 14.92 (mean is ranging from 12.42 to 15.18Gy) after achieving the 95% coverage of PTV.
Conclusion: Better sparing of contralateral parotid glands with the help of VMAT technique in post-operative HNC patients is possible, which can prevent xerostomia in most patients.

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Introduction

A reduction in salivary function is a common toxicity of Head & Neck Cancer (HNC) patients, leading to xerostomia. Xerostomia is the most extensive late side effect of radiotherapy for head and neck malignancies and is one of the factors associated with poor quality of life. In addition, it can cause diminished saliva production, alterations in speech and taste, and difficulties chewing and swallowing. This can even lead to dental caries [1-2]. Many critical structures close to the target are located in the head and neck region. The lack of movement of internal structures in the head and neck region makes it consummate for better conformity of the radiation dose around the tumor and enhancing the normal tissue conserving, as well as the parotid glands by Volumetric-Modulated Arc Therapy (VMAT) [2]. The functional modifications in the parotid glands and the impact on the oral structures depend on the radiation dose and the volume irradiated. In accordance with the literature, xerostomia may be prevented until a mean dose of 26Gy is reached [2-3].

High precision radiation therapy plans are generally designed to cover the planning target volume (PTV) with a homogeneous dose concurrently minimizing dose to nearby organs-at-risk (OARs) [4]. This is especially difficult to achieve with multiple PTVs and OARs in the vicinity. Treatment planning aims to create plans with an optimal trade-off between PTV dose coverage and OAR sparing.

In treatment planning, the planned dose should be as homogeneous as possible over the PTV, non-uniform dose will probably either underdose some of the treatment areas or deliver a higher dose than necessary to normal tissues outside the PTV [5]. In practice, dose distributions cannot be made entirely homogeneous due to inhomogeneity in the radiation

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beams, the patient's shape, and tissue density, or because of the desire to avoid specific organs at risk. The dose gradient across the tumor should be minimized.VMAT gives better conformal dose and reducing dose to the critical organs which is nearby target without compromising the PTV coverage when compared with the 3DCRT.Treatment delivery time and monitor unit (MU) is reduced as compare to IMRT with achieving better plan quality such as PTV coverage, conformity, homogeneity and sparing of OARs [5-8].Our present study is an institutional study that is focused on parotid sparing. The purpose of this study is a quantitative analysis of parotid sparing and reducing xerostomia using VMAT in oral cancer patients.

Materials and Methods

In this study, 14 patients of non-metastatic histologically have proven oral squamous cell carcinoma, where primary disease crossed midline / nodal stage ≥ 2, were operated on and excluded the laryngeal, pharyngeal and metastatic cases. All plans were done in Elekta Monaco® treatment planning system (TPS) for Elekta (Stockholm, Sweden) Versa HD™ linear accelerator, as shown in figure 1. The dose to the moderate high-risk volume of clinical target volume (CTV) and planning target volume (PTV) was 60Gy in 30fractions while Low-risk CTV and PTV volume received a dose of 54Gy in 30 fractions. For each patient, specific plans were made, and the dose to D95 and D98 of target volumes was analyzed with parotid glands' sparing. The mean dose of the whole parotid and Parotid minus PTV were analyzed and compared with the target dose (D98 & D95).

The patient in supine position was immobilized with thermoplastic cast and indexed carbon fibre board for patient positioning. Computed tomography (CT) scans were carried out with slice thickness of 2.5mm from vertex to fourth dorsal vertebra (D4), and the images were transferred to the contouring workstation for delineation of target and normal structures (OARs). In accordance with the primary location of the tumor, the CTV was contoured. The PTV was determined to have a 3 mm margin around the CTV for setup uncertainty. Treatment plans were generated with inverse planning in the VMAT technique (Monaco 5.11.02) of full arc with increments of 20°, calculation grid spacing and statistical uncertainty of each plans were 3mm and 1% respectively. Target and avoidance margin of PTV were 3-4 mm and 8mm.Maximum number of arc were chosen in the range of 2-3, maximum number of control points per arc was in the range of 180-220 and minimum segments width was 7 to 10mm. Monaco Treatment planning system uses two calculation algorithm namely pencil beam and Monte Carlo. Two stage processes for dose calculation, in stage one ideal dose fluence distribution is optimized by pencil beam algorithm and stage two includes segmentation by Monte Carlo algorithm. Dose constraints were given to the normal structures like the spinal cord, brainstem, mandible, parotid glands, eye, optic nerve, lens, cochlea, pharyngeal constrictor, larynx, lips, nasal cavity, thyroid, trachea, oesophagus, TM joint, temporal lobe, and humeral heads. Tight constraints to the contralateral parotid gland were given without compromising PTV coverage. And the dose distribution was seen in each axial slice. Both parotids were assessed separately for the mean dose. CTV, PTV, and OARs were analyzed using dose-volume histograms (DVH). It was the dose that covered 95% of the PTV that was prescribed.

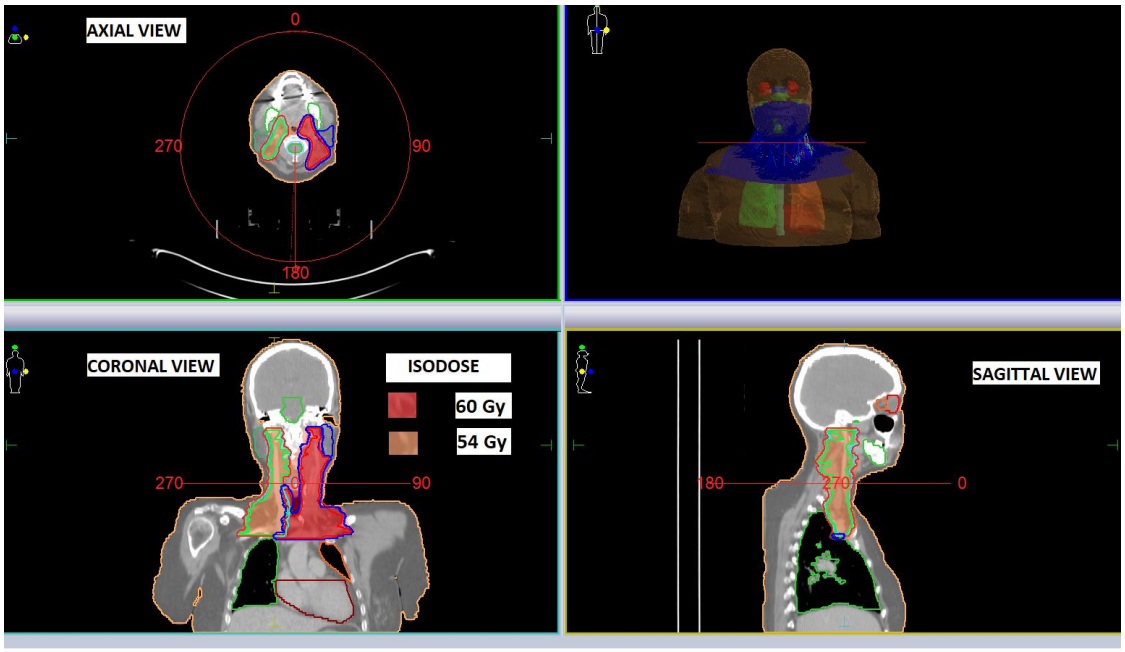

Figure 1. Sparing of Parotid gland with achieving PTV Coverage in VMAT technique

Results

The age of the study population ranged from 40-59 years (median 55), with male preponderance (93%). All the subjects had oral cavity cancers (Buccal mucosa 50%, alveolus 21%, and anterior tongue 29%). Stage IV is commonly observed in 36% of cases, followed by stage I (29%), stage III (21%), and stage II (14%), as mentioned in (Table 1).

Table 1. Patient and tumour characteristics.

Characteristics	No. (%)
Gender	
Male	13 (93%)
Female	1 (7%)
Tumour site	
Buccal Mucosa	7 (50%)
Alveolus	3 (21%)
Anterior Tongue	4 (29%)
Tumour stage (TNM staging system)	
I	4 (29%)
II	2 (14%)
III	3 (21%)
IV	5 (36%)

Table 2. Dose and Volume Parameter for Targets were both parotid glands are involved partially in the target area

Patient No.	PTV 60		PTV 54	
	98% (cGy)	95% (cGy)	98% (cGy)	95% (cGy)
1	5771.8	5895.0	4887.9	5140.0
2	5854.5	5948.9	4945.5	5182.7
3	5813.5	5898.4	4948.6	5190.7
4	5765.4	5866.0	4878.1	5139.3
5	5765.8	5850.6	4922.3	5180.8
6	5829.9	5946.6	5315.5	5412.9
7	5741.7	5836.7	4998.3	5167.5

Table 3. Dose and Volume Parameter for parotid glands were both parotid glands are involved partially in the target area

Patient No.	Ipslat Parotid		Ipslat Parotid-Ptv	Contrlatparotid		Contrlat Parotid-Ptv
	Mean (cGy)	Involved Parotid volume (%)	Mean (cGy)	Mean (cGy)	Involved Parotid volume (%)	Mean (cGy)
1	2364.00	0.43	2358.4	1487.5	2.00	1445.5
2	4669.10	46.91	3438.3	1542.0	4.76	1406.3
3	5150.70	59.87	4269.9	1548.4	1.56	1516.9
4	5516.70	30.05	4770.3	1401.2	3.34	1323.0
5	5445.20	60.02	5161.0	1541.1	1.67	1242.8
6	5556.80	50.00	4560.6	1654.6	7.97	1418.1
7	5976.80	67.00	5830.0	1501.7	3.80	1369.5

In 50% of the subjects, both parotid glands were partially involved in the PTV area. The median dose of the ipsilateral parotid gland is 54.45Gy (mean ranges from 23.6Gy to 59.7Gy), and for the ipsilateral parotid minus PTV was 45.6Gy (mean is ranging from 23.5Gy to 58.3Gy). In the contralateral parotid gland, the median dose was 15.41Gy (mean is ranging from 14Gy to 16.5Gy), and for the contralateral parotid minus PTV was 14.06Gy (mean is ranging from 12.4Gy to 15.16Gy) is shown in (Table 2). The PTV coverage was also achieved as per standard guidelines. For high-risk PTV60, D98 was more than 96 percent, and for low-risk PTV54, D95 was more than 95 percent (Table 3).

In the remaining 50% of the subjects, one parotid gland was fully involved in the target area, and hence we have collected the data for the contralateral parotid. The median dose to the contralateral parotid gland was 16.28 (mean dose in the range of 14.04Gy to 17.06Gy) and for parotid minus PTV was 14.92 (mean dose in the range of 12.72Gy to 15.18Gy), given in (Table 4). The PTV coverage was also achieved as per standard guidelines. For high-risk PTV60, D98 was more than 96 percent, and for low-risk PTV54, D95 was more than 95 percent (Table 5).

Table 4. Dose and Volume Parameter for contralateral parotid glands were one parotid gland fully involved in the target area.

Patient No.	Contrlatparotid		Contrlatparotid-Ptv
	Mean (cGy)	Volume of Involved Parotid (%)	Mean (cGy)
1	1567.2	0.00	0.000
2	1404.1	0.97	1272.3
3	1685.1	7.90	1481.3
4	1635.2	3.60	1503.9
5	1706.7	5.55	1518.0
6	1442.9	0.96	1409.9
7	1628.5	1.22	1511.9

Table 5. Dose and volume parameter for targets were one parotid gland fully involved and other parotid gland partially involved in the target area

Patient No.	PTV60		PTV54	
	98% (cGy)	95% (cGy)	98% (cGy)	95% (cGy)
1	5882.0	5952.7	4989.3	5198.5
2	5868.6	5931.5	4987.1	5192.4
3	5647.0	5769.3	5116.7	5230.4
4	5777.4	5857.1	4876.2	5136.2
5	5888.0	5945.5	4901.4	5143.7
6	5846.5	5897.4	5101.5	5293.4
7	5703.7	5819.0	5015.2	5315.9

Discussion

VMAT is a highly conformal technique in radiotherapy. The advantage of VMAT in head and neck cancer is achieving better dose distribution and uniformity with better sparing of normal structures with less treatment delivery time [6-7].

In order to maintain the parotid volume after target delineation, the parotid gland had to be delineated correctly before target delineation [1-2]. Parotid glands with the closest proximity to the target volume receive a high dose while those farthest from the target volume receive a low dose. Often, it is difficult to achieve a mean dose less than 26 Gy for the ipsilateral parotid gland. Contralateral parotid gland doses were usually kept below the threshold level of 26Gy in many cases [2, 9].

The literature says that the parotid gland shrank during radiotherapy, and little change in position decreased the sparing of the parotid gland [10-11]. Parotid gland will receive more dose than predicted during radiotherapy treatment due to weight loss and tumor shrinkage in head and neck cases [3].

Several studies suggest that the mean dose to the parotid dose should not be more than 26 Gy; QUANTEC guideline asserts that to avoid xerostomia, at least one parotid gland should receive the mean dose less than 20Gy or both glands should be less than 25Gy [12-15].

In our study, we have achieved the mean dose to the contralateral parotid gland in the range of 14.01Gy to 17.06Gy, and for the contralateral parotid minus PTV, a mean dose in the range of 12.42Gy to 15.18Gy was achieved. Blanco et al. reported that a mean dose less than 26Gy to one parotid gland in conventional fractionation could significantly reduce the xerostomia [16-18]. Jeremias Hey et al. observed that after 36 months of radiotherapy, the salivary flow reached again 74% from an initial value of pre-treatment if the mean dose to the parotid gland received less than 26Gy and there is no significant recovery for more than 40Gy and a mean dose less than 26Gy to at least one parotid gland would be sufficient to reach complete recovery of saliva flow rate and good sparing of the parotid gland [3, 17-18]. Li et al. reported that for mean doses <25Gy, the average stimulated saliva recovers to pre-treatment levels in 12 to 24 months, and for mean doses >30Gy, the stimulated saliva does not return to original levels after two years. If the mean dose to the parotid gland is less than 25–30Gy, recovery is substantial and returns to pre-treatment levels 2 years after RT [19-20]. In our study, for all patients, contralateral parotid gland mean dose achieved less than 26Gy, and we were achieved in the range of 14.01Gy to 17.06Gy.

Roesink J et al. reported the partial recovery of parotid gland function over 6weeks, 6 months, and one year after radiation with a mean dose of 31Gy, 35Gy, and 39, respectively [21]. In this study, 100% of the subjects achieved the mean dose to the contralateral parotid gland less than 31Gy (14.01Gy to17.06Gy). Franzén, L et al. reported that a mean dose to the parotid gland of about 40-50Gy causes reversible change and almost restores the function of salivary secretion within 6-18 months following the end of radiotherapy. The dose exceeds 65Gy irreversible alteration in the parotid gland [22]. In our study, all the subjects of the contralateral parotid gland achieved less than 50Gy (14.01Gy to17.06Gy). Ipsilateral parotid minus PTV, 70% of subjects less than 50Gy (23.58Gy to 47.7Gy) and 30% of the subjects more than 50Gy, because of more than 60% volume of parotid gland involvement in the target area.

Conclusion

Xerostomia is the most common and prominent complication during and after radiotherapy for most head-neck cancer patients. The VMAT technique is capable of achieving a better dose distribution in delineated targets, as well as OAR constraints. Thus, the prevention of xerostomia in most head and neck cancer patients can be achieved by better sparing the contralateral and ipsilateral parotid gland without compromising the target coverage. The severity of the damage to the parotid glands depends on the parotid volume receiving the dose. It is important to contour the target volume and relevant normal structure volume accurately and generate an optimum plan for treatment and its implementation. However, sparing of the parotid glands also depends on the tumour location, the extension of disease, and overlapping of parotid gland volume to the target area. The limitation of this study is the sample size. We need a larger sample size for better validation of results.

References

1. Eisbruch A, Ship JA, Martel MK, Ten Haken RK, Marsh LH, Wolf GT, et al. Parotid gland sparing in patients undergoing bilateral head and neck irradiation: techniques and early results. International journal of radiation oncology, biology, physics. 1996 Sep 1;36(2):469-80.
2. Anand AK, Jain J, Negi PS, Chaudhoory AR, Sinha SN, Choudhury PS, et al. Can dose reduction to one parotid gland prevent xerostomia?—A feasibility study for locally advanced head and neck cancer patients treated with intensity-modulated radiotherapy. Clinical Oncology. 2006 Aug 1;18(6):497-504.
3. Hey J, Setz J, Gerlach R, Janich M, Hildebrandt G, Vordermark D, et al. Parotid gland-recovery after radiotherapy in the head and neck region-36 months follow-up of a prospective clinical study. Radiation oncology. 2011 Dec;6(1):1-8.
4. Marks LB, Yorke ED, Jackson A, Ten Haken RK, Constine LS, Eisbruch A, Bentzen SM, et al. Use of normal tissue complication probability models in the clinic. International Journal of Radiation Oncology* Biology* Physics. 2010 Mar 1;76(3):S10-9.
5. Ali DR, Amin AE, Sallam AM, El-Sayed ES. Comparison Between VMAT and IMRT in Remaining Volume at Risk for Large Volume Head and Neck Cancer Patients. 2021.
6. Holt A, Van Gestel D, Arends MP, Korevaar EW, Schuring D, Kunze-Busch MC, Louwe RJ, van Vliet-Vroegindeweij C. Multi-institutional comparison of volumetric modulated arc therapy vs. intensity-modulated radiation therapy for head-and-neck cancer: a planning study. Radiation oncology. 2013 Dec;8:1-11.
7. Chen BB, Huang SM, Xiao WW, Sun WZ, Liu MZ, Lu TX, et al. Prospective matched study on comparison of volumetric-modulated arc therapy and intensity-modulated radiotherapy for nasopharyngeal carcinoma: dosimetry, delivery efficiency and outcomes. Journal of Cancer. 2018;9(6):978.
8. Afrin KT, Ahmad S. 3D conformal, IMRT and VMAT for the treatment of head and neck cancer: a brief literature review. Journal of Radiotherapy in Practice. 2022 Jun;21(2):259-62. DOI:10.1017/S1460396920001053.
9. Amosson CM, Teh BS, Van TJ, Uy N, Huang E, Mai WY, et al. Dosimetric predictors of xerostomia for head-and-neck cancer patients treated with the smart (simultaneous modulated accelerated radiation therapy) boost technique. International Journal of Radiation Oncology* Biology* Physics. 2003 May 1;56(1):136-44.
10. Barker Jr JL, Garden AS, Ang KK, O'Daniel JC, Wang H, Court LE, et al. Quantification of volumetric and geometric changes occurring during fractionated radiotherapy for head-and-neck cancer using an integrated CT/linear accelerator system. International Journal of Radiation Oncology* Biology* Physics. 2004 Jul 15;59(4):960-70.
11. Robar JL, Day A, Clancey J, Kelly R, Yewondwossen M, Hollenhorst H, et al. Spatial and dosimetric variability of organs at risk in head-and-neck intensity-modulated radiotherapy. International Journal of Radiation Oncology* Biology* Physics. 2007 Jul 15;68(4):1121-30.
12. Deasy JO, Moiseenko V, Marks L, Chao KC, Nam J, Eisbruch A. Radiotherapy dose–volume effects on salivary gland function. International Journal of Radiation Oncology* Biology* Physics. 2010 Mar 1;76(3):S58-63.
13. Chen AM, Yoshizaki T, Wang PC, Veruttipong D, Beron PJ, Chin R, et al. Hazards of sparing the ipsilateral parotid gland in the node-positive neck with intensity modulated radiation therapy: Spatial analysis of regional recurrence risk. Advances in radiation oncology. 2018 Apr 1;3(2):111-20.
14. Chen AM, Farwell DG, Luu Q, Vazquez EG, Lau DH, Purdy JA. Intensity-modulated radiotherapy is associated with improved global quality of life among long-term survivors of head-and-neck cancer. International Journal of Radiation Oncology* Biology* Physics. 2012 Sep 1;84(1):170-5.
15. Marks LB, Yorke ED, Jackson A, Ten Haken RK, Constine LS, Eisbruch A, et al. Use of normal tissue complication probability models in the clinic. International Journal of Radiation Oncology* Biology* Physics. 2010 Mar 1;76(3):S10-9.
16. Blanco AI, Chao KC, El Naqa I, Franklin GE, Zakarian K, Vicic M, et al. Dose–volume modeling of salivary function in patients with head-and-neck cancer receiving radiotherapy. International Journal of Radiation Oncology* Biology* Physics. 2005 Jul 15;62(4):1055-69.
17. Eisbruch A, Ship JA, Dawson LA, Kim HM, Bradford CR, Terrell JE, et al. Salivary gland sparing and improved target irradiation by conformal and intensity modulated irradiation of head and neck cancer. World journal of surgery. 2003 Jul;27:832-7.
18. Chao KC, Majhail N, Huang CJ, Simpson JR, Perez CA, Haughey B, et al. Intensity-modulated radiation therapy reduces late salivary toxicity without compromising tumor control in patients with oropharyngeal carcinoma: a comparison with conventional techniques. Radiotherapy and oncology. 2001 Dec 1;61(3):275-80.

19. Li Y, Taylor JM, Ten Haken RK, Eisbruch A. The impact of dose on parotid salivary recovery in head and neck cancer patients treated with radiation therapy. International Journal of Radiation Oncology* Biology* Physics. 2007 Mar 1;67(3):660-9.
20. Marsh L, Eisbruch A, Watson B, Martel MK. Treatment planning for parotid sparing in the patient requiring bilateral neck irradiation. Medical Dosimetry. 1996 Mar 1;21(1):7-13.
21. Roesink JM, Moerland MA, Battermann JJ, Hordijk GJ, Terhaard CH. Qantitative dose-volume response analysis of changes in parotid gland function after radiotheraphy in the head-and-neck region. International Journal of Radiation Oncology* Biology* Physics. 2001 Nov 15;51(4):938-46.
22. Marsh L, Eisbruch A, Watson B, Martel MK. Treatment planning for parotid sparing in the patient requiring bilateral neck irradiation. Medical Dosimetry. 1996 Mar 1;21(1):7-13.