

Research Article

Clinical Outcomes and Dosimetric Analysis of 3D Conformal, Intensity-Modulated and Volumetric Arc Radiation Therapy in Post-operative Oral cavity Cancers – A Single Institution Retrospective Audit.

Dr Siddhesh Tryambake¹ M.D, R Vikram² M.Sc, Akash Dhavale² M.Sc, Santosh Mali² M.Sc

1. Department of Radiation Oncology, Onco-Life Cancer Centre, Shendre, Satara, Maharashtra, India.
2. Department of Medical Physics, Onco-Life Cancer Centre, Shendre, Satara, Maharashtra, India

***Corresponding Author: Dr Siddhesh Tryambake, M.D** Radiation Oncology, Oncolife Cancer Centre, Satara, Maharashtra, India

Received Date: May 22, 2021

Publication Date: June 01, 2021

Abstract

Background: With cases of carcinoma oral cavity on the rise in developing countries and challenges associated with radiation planning in such cases owing to a large number of OARs in close proximity, distorted post-operative anatomy, and pre-existing surgical morbidities, choice of radiation delivery technique has become of prime importance. This study aims at a broad comparison of radiotherapy treatment planning of 3DCRT, IMRT, and VMAT for post-operative oral cavity carcinomas treated at our centre.

Patients and Methodology: A retrospective analysis of 15 averagely built adult patients with post-operative status of carcinoma oral cavity divided into three groups (3DCRT, IMRT, and VMAT) of 5 patients each based on the technique used for delivery of post-operative radiation therapy (PORT) between July 2019 to December 2019 in the Onco-Life Cancer Centre, Satara was done. Treatment planning was done within 6 weeks of surgery for the standard PORT dose of 60 Gy/30 # to be delivered over 6 weeks on the treatment planning system (MONACO Ver 5.11) with a planning CT scan of the face and neck with 5 mm slices after delineation of various target volumes such as



clinical target volume (CTV), planning target volume (PTV), and organs at risk (spinal cord, both the parotid, eyes, brain stem, larynx, and thyroid) contoured on each slice. An isotropic margin of 5 mm provided to the CTV for final PTV and 2 mm to organs at risk for planning organ at risk volume. The comparison between 3DCRT, IMRT, and VMAT was done with respect to target coverage, OAR doses, toxicity profile, and beam-on time (BOT) estimated from the MUs delivered.

Results: On the evaluation of target dose coverage amongst all three techniques, the 3D-CRT plan achieved a mean coverage of 86.37% of PTV volume, IMRT achieved 98.26% while the VMAT plan achieved 97.44% of PTV volume. Keeping OAR dose as constant, VMAT target dose coverage was comparatively better than the IMRT plan. The mean target dose for 3DCRT, IMRT, and VMAT plans were 59.38Gy, 60.34Gy, and 60.40 Gy respectively. Mean OAR doses were maximum with 3DCRT and comparable in IMRT and VMAT techniques which reflected upon the toxicity profile with toxicity rate of dermatitis, mucositis, dysphagia, subcutaneous fibrosis, and xerostomia being grade III and above with 3DCRT plan and grades I and II with IMRT and VMAT plans. VMAT plans were associated with better target dose coverage and comparatively better OAR doses as compared to IMRT. On analysis of beam-on time (BOT), a 3D-CRT plan had the least BOT with a mean delivery of 221.12 MUs and mean BOT 0.36 minutes as compared to IMRT and VMAT which may be attributed to the lack of optimization. IMRT plan had the longest BOT with a mean delivery of 952.61 MUs and mean BOT of 1.58 minutes while VMAT plans had relatively lesser BOT with the mean delivery of 765.11 MUs and mean BOT of 1.27 minutes. Based on these results, with VMAT, the delivery times can be expected to be reduced by ~ 20% compared to IMRT ignoring the time gap for beam-off gantry motion. VMAT was associated with better target dose coverage and comparatively better OAR doses as compared to IMRT.

Conclusion: Our limited sample-sized study depicts our own experience to suggest that the toxicity profile in patients treated with 3D-CRT is high and is associated with a compromised target coverage as compared to those with IMRT and VMAT treatment planning techniques. IMRT and VMAT are better and more efficient methods with regards to treatment outcome in this particular set of patients having pre-existent surgical morbidities, for they allow for better sparing of normal tissue, thereby causing lesser normal tissue toxicity, leading eventually to a better quality of life vis-a-vis 3D-CRT. 3DCRT had the least beam-on time which may be attributed to lack of optimization while VMAT fared better than IMRT with 20 percent lesser beam-on time as compared to the later. VMAT appears to be the best treatment modality with a better target dose coverage, minimal doses to OARs, and relatively lesser beam-on time vis-à-vis IMRT and may be warranted wherever feasible.

Keywords:

Carcinoma oral cavity, post-operative radiation therapy, 3D conformal radiation therapy (3DCRT), Intensity-modulated radiation therapy (IMRT), Volumetric modulated arc therapy (VMAT), toxicity, quality of life, beam-on time, single-institution study



Abbreviations –

HNC - head-and-neck cancer,

CTV - clinical target volume,

PTV - planning target volume,

BOT - beam-on time,

MUs – Monitor Units,

- fractions,

Gy – Gray,

MV – Megavolt,

AJCC – American Joint Committee on Cancer,

CT - Computed tomography,

MLCs – Multileaf Collimators,

DVHs – Dose Volume Histograms,

OARs - Organs at Risk,

3D-CRT - 3D-Conformal Radiation Therapy,

IMRT - Intensity-Modulated Radiation Therapy,

VMAT – Volumetric Modulated Arc Therapy,

RTOG - Radiation Therapy Oncology Group,

EORTC – European Organisation for Research and Treatment of Cancer,

PORT - post-operative radiation therapy,

LVI – Lymphovascular invasion,

PNI – Peri Neural Invasion,

SC – Spinal Cord,

BS – Brain Stem,

SCF – subcutaneous Fibrosis,

CTh – Chemotherapy,

I/L – Ipsilateral,

C/L – Contralateral,

CI – Conformality Index



Introduction

As per GLOBOCAN 2020, there were 1,35,929 new cases and 75,290 deaths from carcinoma oral cavity in India making it the most common malignancy in Indian males and second common considering both the sexes. [1] Adjuvant postoperative radiation therapy is indicated in presence of adverse pathological features like T3-T4 tumors, close/positive cut margins, LVI, PNI, or node-positive status with or without ENE. Advances in reconstructive surgery have led to better functional outcomes following primary surgical resection [2]. RT and concurrent, radio-sensitizing chemotherapy continue to be integral components of the treatment paradigm to improve both locoregional control and survival; Radiation Therapy Oncology Group (RTOG) [3] and EORTC [4] trials showed 10% improvement in locoregional control in head and neck cancer patients treated with concurrent postoperative chemotherapy and radiotherapy relative to radiation therapy alone. These improvements in locoregional control, however, come at the expense of increased toxicities. In RTOG 9501 and EORTC 22931 trials, the incidence of grade ≥ 3 acute toxicity is approximately twice as high with concurrent treatment; however, grade 3 or higher late toxicities were similar among the groups in RTOG and EORTC trials, at approximately 30–40%. These facts make these patients, who have been going through various surgical morbidities related to infections and cosmetic issues, very much vulnerable at the stage of radiation planning. This vulnerability may even at times result into patients having poor compliance adding to the drop-out rates or in a worst case scenario even leading to complete avoidance of the much needed adjuvant treatment. The only way to reduce these maladies is to use high-end conformal radiation delivery techniques than the conventional modality. A notable difficulty with irradiation of head-and-neck cancer (HNC) is a large number of organs at risk (OARs) in close proximity to regions with a disease, including the salivary glands, spinal cord, and brainstem, larynx, and thyroid. Introduction of intensity-modulated radiation therapy (IMRT) techniques for the treatment of HNC replaced conventional 3D-conformal radiation therapy (3D-CRT) techniques, which resulted in much better dose conformity and sparing of the OARs and, therefore, less radiation-induced toxicity [5-6].

So also, as per the literature available, compared to static beam 3D Conformal Radiation Therapy and Intensity-Modulated Radiation Therapy (IMRT), the main advantage of Volumetric Modulated Arc Therapy (VMAT) is a shortened delivery time with better dose coverage, which leads to improved patient comfort and possibly smaller intra-fraction movements. However, no real-world data from remote and peripherally based institutions like ours comparing 3DCRT, IMRT, and VMAT techniques in postoperative patients of carcinoma oral cavity has been reported so far. The small study presented here is the result to share our own experience related to the same. We intend to evaluate the potential of VMAT by retrieving the data with uniformity in the patient population with respect to their built and disease status. Different treatment plans with three different techniques were not raised in the same



patient so as to assess the toxicity profile. Single clinician, a single physicist with standard departmental policies, and single TPS-based planning was chosen so as to maintain the uniformity in the data analysis related to differences in optimization strategies and different preferences for sparing of OARs.

Methods

A retrospective dosimetric analysis of 15 adult averagely built patients with post-op status of carcinoma oral cavity staged using AJCC guidelines, and divided into three groups of 5 patients each for 3D-CRT, IMRT, and VMAT, treated between July 2019 to December 2019 in Onco-Life Cancer Center, Satara was done. Computed tomography (CT) data including contouring of these 15 patients with operated oral cavity cancer were selected in each group. According to the standard guidelines, the patient data was properly anonymized and no informed consent of the patient was required. The planning target volumes (PTVs) and organs at risk (OARs) like the spinal cord, both the parotid, eyes, lens, optic nerve, brain stem, larynx, and thyroid were delineated by an experienced clinician using standard guidelines. All of the contouring was done by a single physician to maintain uniformity. Treatment planning was done in the treatment planning system (MONACO Ver 5.11). An isometric margin of 5 mm provided to the CTV for final PTV and 2 mm to organs at risk for planning organ at risk volume. The comparison between IMRT, VMAT, and 3D-CRT was done with respect to beam-on time, OAR doses, target coverage, and toxicity profile. Beam-on time was extrapolated from the monitor units (MUs) calculated using the constant dose rate of 600 MUs/min for 6MV photons used for all the patients in all three techniques.

Patient selection and contouring

For this retrospective treatment planning study, computed tomography (CT) data including contouring of fifteen averagely built patients with post-op status of oral cancer were selected (patient characteristics listed in Table 1). These patients were previously treated with the standard clinical protocols. Each group had few patients treated concurrently with cisplatin to a dose of 40 mg/m² so as to enhance the radiosensitivity. The planning target volumes (PTVs) and organs at risk (OARs) like the spinal cord, both the parotid, eyes, lens, optic nerve, brain stem, larynx, and thyroid were delineated by an experienced clinician using standard guidelines. (See Table 1 for patient characteristics and MUs required)



| Reg.no | Sex | Age | Diagnosis | Stage | Stage Group | Radiation Technique | (MUs/BOT in min) |
|--------|--------|-----|------------------------|---------|-------------|---------------------|------------------|
| 4436 | Female | 45 | Ca Left RMT | pT4pN1 | IV A | 3D-CRT | 227.58/0.38 |
| 168 | Male | 37 | Ca Left Buccal Mucosa | pT1pN2 | IV A | 3D-CRT | 238.22/0.39 |
| 121 | Female | 48 | Ca Left Buccal Mucosa | pT4pN1 | IV A | 3D-CRT | 214.47/0.35 |
| 141 | Male | 54 | Ca Left Alveolus | pT4pN1 | IV A | 3D-CRT | 228.94/0.38 |
| 5682 | Male | 49 | Ca Left Buccal Mucosa | pT2pN0 | II | 3D-CRT | 196.43/0.32 |
| | | | | | | | Mean BOT - 0.36 |
| 9524 | Female | 42 | Ca Right GBS | pT2 PN0 | II | IMRT | 1086.54/1.8 |
| 9392 | Female | 53 | Ca Right GBS | pT2pN1 | III | IMRT | 988.19/1.64 |
| 9429 | Male | 39 | Ca left buccal Mucosa | pT2pN0 | II | IMRT | 848.54/1.41 |
| 9422 | Male | 58 | Ca Left Buccal Mucosa | pT1pN1 | III | IMRT | 842.67/1.4 |
| 9476 | Male | 45 | Ca Right Buccal Mucosa | pT1pN2 | IV A | IMRT | 997.11/1.66 |
| | | | | | | | Mean BOT – 1.58 |
| 9200 | Male | 43 | Ca left Buccal Mucosa | pT2pN1 | III | VMAT | 788.43/1.31 |
| 9169 | Male | 44 | Ca Left GBS | pT2pN1 | III | VMAT | 743.22/1.23 |
| 8271 | Male | 54 | Ca Left Buccal Mucosa | pT4pN1 | IV A | VMAT | 771.25/1.28 |
| 8614 | Male | 40 | Ca Left GBS | pT3pN3 | IV B | VMAT | 678.99/1.13 |
| 9129 | Male | 42 | Ca Right Buccal Mucosa | pT2pN1 | III | VMAT | 843.66/1.4 |
| | | | | | | | Mean BOT – 1.27 |

Table 1**Dose prescription and plan acceptance parameters**

All the plans were generated for treatment in 30 fractions, to deliver a total dose of 60 Gy to the PTV (i.e. a fraction dose of 2 Gy). Primary goal of treatment planning was to cover at least 99% of the volume of PTV with 95% of the prescribed dose (57 Gy), and to restrict the volume receiving more than 107% in the PTV of the prescribed dose (64.2 Gy). The maximal allowed point dose to OARs was 54 Gy for the brainstem and 46 Gy for the spinal cord. In addition, the mean dose was tried to be limited below 25 Gy for the parotid glands (for at least one parotid), and below 45 Gy for the larynx.

Treatment planning

The CT data sets of all the patients were used for 3DCRT, IMRT and VMAT plans in the respective groups using Elekta Synergy Linear Accelerator equipped with Agility MLC having leaf width of 0.5 cm at the isocentre. For VMAT and IMRT treatment planning, each optimization was started with the generation



of fluence maps. After typically 10–15 iterations, at the so-called conversion iteration, segments were produced. Following an intermediate Monte Carlo dose calculation, optimization was continued using Segment Shape Optimization up to a total of 30–50 iterations.

3DCRT planning parameters

Two field wedge-based anterolateral plans were generated for all the patients using 6 MV photon beams baring the dose constraints to critical structures like spinal cord.

IMRT planning parameters

Dynamic IMRT plans were generated using typically 5–9 coplanar beams with a total of 50–70 segments. The lower limit for the segment size ranged from 4 to 9 cm², with a minimum of 2 to 5 monitor units (MUs) per segment.

VMAT planning parameters

VMAT plans were generated using one dual arc (i.e a double arc generated from a single beam at the segmentation step) with an arc length close to 360°. Before starting the study, we had tested different arc setups. It was concluded that the use of a dual arc with single beam over the full range would yield the most promising, clinically acceptable results. The final resolution of control points within the arc was set to 4°, which was found to allow sufficient modulation at a still acceptable duration of the optimization. The collimator angle was typically set to a value between 10° and 30° (or alternatively between 330° and 350°) to avoid tongue-and-groove effects. All IMRT and VMAT plans were generated using 6 MV photons.

VMAT plan optimization was restarted typically three to five times after the initial run without prior resetting of the earlier optimization result including segments and dose rate along the arcs (so-called “warm re-starts”). At the end of each of these optimization steps, the Monte Carlo dose calculation algorithm was used to calculate the dose distribution. After a restart of the optimization altered dose distributions after adaptation of segments are calculated as a small perturbation on the previously calculated dose distribution using Monte Carlo dose calculation based approach. This approximation leads to an accumulation of errors in the dose distribution during the optimization process, which is then “repaired” by the forced intermediate-dose calculation after a fixed number of iterations. This procedure greatly improves in accordance with the planning objectives in each step since dose distribution after full dose calculation including inhomogeneity corrections will be close to the altered



dose distribution found during the optimization process. If necessary and desirable, target doses and/or objective weights were adapted during the optimization process and in-between re-starts to further lower dose to OARs and/or improve PTV coverage. However, in case of large changes in the objectives the optimization was repeated including the segmentation step, i.e. re-started from scratch.

Planning objectives –

Were uniform in all the patients in all three subgroups.

Determination of effective delivery times –

All plans were made using 6 MV photons. Delivery times for all three techniques were extrapolated using Monitor Units (MUs) delivered which reflected upon the beam-on times considering the constant machine dose rate of 600 MU/min the energy used. It should be noted, however, that our timings neglect possible delays during beam-off gantry motion and interaction with the patient in-between the delivery for any cause. (See Table 1 for MUs calculated)

Data retrieval and statistical analysis –

All the data was pooled and DVHs and dose parameters were retrieved for each plan using automated procedures. The data from all fifteen patients were analyzed in version 25 and Rstudio version 1.2.1335. as a whole.

Results –

Clinically acceptable 3DCRT, IMRT, and VMAT plans for all the patients as per set objectives were produced. We had aimed to limit dose to OARs as much as possible and tightened the objectives accordingly as long as the primary goals of the treatment planning protocol were still fulfilled (see Table 2.1-Table 2.4 for various observations)



| Radiation Technique | Target Dose Coverage in % | Target Mean Dose in Gy | CI |
|---------------------|---------------------------|------------------------|------|
| 3D-CRT | 78.11 | 57.93 | - |
| | 85.02 | 59.35 | - |
| | 88.86 | 59.52 | - |
| | 91.01 | 59.57 | - |
| | 88.87 | 60.53 | - |
| IMRT | 97.70 | 60.36 | 0.71 |
| | 99.00 | 60.82 | 0.82 |
| | 98.12 | 60.17 | 0.68 |
| | 97.81 | 59.92 | 0.48 |
| | 98.58 | 60.47 | 0.71 |
| VMAT | 98.16 | 60.35 | 0.68 |
| | 96.74 | 59.84 | 0.50 |
| | 96.81 | 60.55 | 0.80 |
| | 97.21 | 60.50 | 0.76 |
| | 98.30 | 60.39 | 0.68 |

Table 2.1

| Radiation Technique | SC (Gy) | BS (Gy) | I/L Parotid (Gy) | C/L Parotid (Gy) | I/L Eye (Gy) | C/L Eye (Gy) | Larynx (Gy) | Thyroid (Gy) |
|---------------------|---------|---------|------------------|------------------|--------------|--------------|-------------|--------------|
| 3D-CRT | 44.38 | 12.31 | 59.16 | 1.60 | 50.07 | 21.19 | 44.05 | 23.22 |
| | 45.19 | 47.89 | 60.48 | 2.28 | 13.54 | 16.26 | 53.99 | 29.65 |
| | 38.38 | 18.16 | 58.17 | 2.19 | 7.29 | 5.86 | 33.29 | 44.79 |
| | 2.28 | 17.20 | 61.93 | 1.76 | 31.68 | 5.22 | 44.04 | 31.72 |
| | 45.38 | 24.63 | 59.59 | 19.14 | 6.47 | 6.49 | 47.40 | 1.88 |
| IMRT | 35.61 | 35.76 | 56.89 | 6.90 | 28.71 | 11.56 | 42.42 | 41.25 |
| | 32.90 | 29.67 | 59.27 | 5.80 | 27.78 | 12.08 | 45.95 | 33.69 |
| | 35.41 | 36.74 | 57.09 | 6.94 | 3.09 | 4.30 | 43.12 | 39.63 |
| | 36.00 | 36.18 | 35.72 | 7.20 | 24.34 | 9.22 | 44.98 | 37.55 |
| | 36.58 | 22.39 | 44.31 | 5.64 | 5.56 | 11.45 | 40.63 | 37.80 |
| VMAT | 33.47 | 27.79 | 60.51 | 5.15 | 33.56 | 14.56 | 35.05 | 36.63 |
| | 32.44 | 21.68 | 59.33 | 5.96 | 7.08 | 7.93 | 35.15 | 32.41 |
| | 30.12 | 31.46 | 61.39 | 4.19 | 49.48 | 15.11 | 49.79 | 40.99 |
| | 38.61 | 25.45 | 53.96 | 4.85 | 7.81 | 7.83 | 50.24 | 43.49 |
| | 36.78 | 36.12 | 58.87 | 7.09 | 23.45 | 13.89 | 42.77 | 40.01 |

Table 2.2



| Radiation Technique | Dermatitis | Mucositis | Dysphagia | SCF | Xerostomia | CTh |
|---------------------|------------|-----------|-----------|-----|------------|-----|
| 3D-CRT | II | II | II | II | III | Yes |
| | IV | III | III | III | III | Yes |
| | III | III | I | III | II | No |
| | IV | IV | II | III | III | Yes |
| | III | III | III | III | III | No |
| IMRT | II | II | I | II | II | No |
| | II | I | II | II | II | Yes |
| | II | II | II | II | II | Yes |
| | II | I | II | I | I | No |
| | II | II | I | I | II | Yes |
| VMAT | II | I | I | II | II | No |
| | II | I | I | II | II | No |
| | II | II | II | II | II | Yes |
| | I | II | II | I | II | Yes |
| | I | II | I | I | II | Yes |

Table 2.3

| Objectives (Mean) | 3D-CRT | IMRT | VMAT |
|---------------------------|--------|--------|--------|
| Target Coverage (%) | 86.37 | 98.26 | 97.44 |
| Treatment Time(MU) | 221.12 | 952.61 | 765.11 |
| Mean Target Dose (Gy) | 59.38 | 60.34 | 60.32 |
| Conformity Index | - | 0.68 | 0.68 |
| Homogeneity Index | 1.13 | 1.06 | 1.07 |
| Mean OAR Dose (Gy) | | | |
| Spinal Cord | 36.12 | 35.30 | 34.28 |
| Brain Stem | 24.03 | 32.15 | 28.50 |
| Ipsilateral parotid | 59.86 | 50.66 | 58.81 |
| Contralateral Parotid | 5.39 | 6.49 | 5.45 |
| Ipsilateral Lens | 6.85 | 2.71 | 3.26 |
| Contralateral lens | 5.34 | 2.50 | 2.92 |
| Ipsilateral Eye | 21.81 | 13.15 | 24.28 |



| | | | |
|-------------------------|-------|-------|-------|
| Contralateral Eye | 11.00 | 9.72 | 11.86 |
| Larynx | 44.55 | 42.42 | 42.60 |
| Thyroid | 26.25 | 37.96 | 38.31 |
| Maximum Toxicity | | | |
| Dermatitis | IV | II | II |
| Mucositis | IV | II | II |
| Dysphagia | III | II | II |
| Subcutaneous fibrosis | III | II | II |
| Xerostomia | III | II | II |

Results – Summary Table 2.4

Dose distributions of 3DCRT, IMRT and VMAT plans for respective typical cases are shown in **Figure 1**.

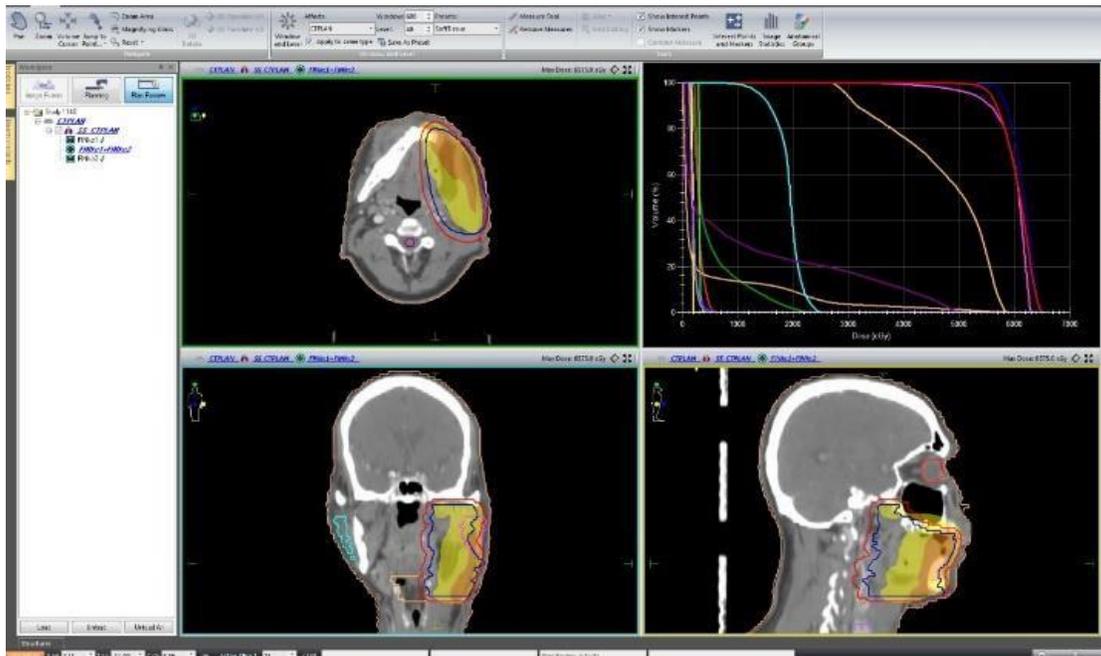


Figure 1.1 – 3DCRT Dose Distribution (Orange – 95% isodose, Yellow – 90 % isodose)

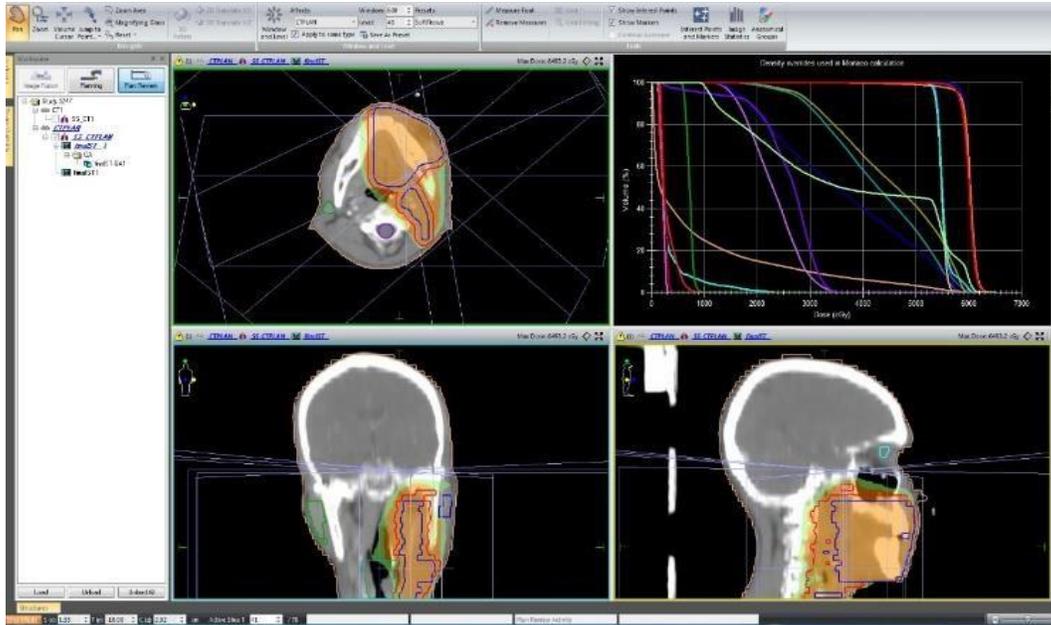


Figure 1.2 - IMRT Dose Distribution (Orange – 95% isodose, Green – 90 % isodose)

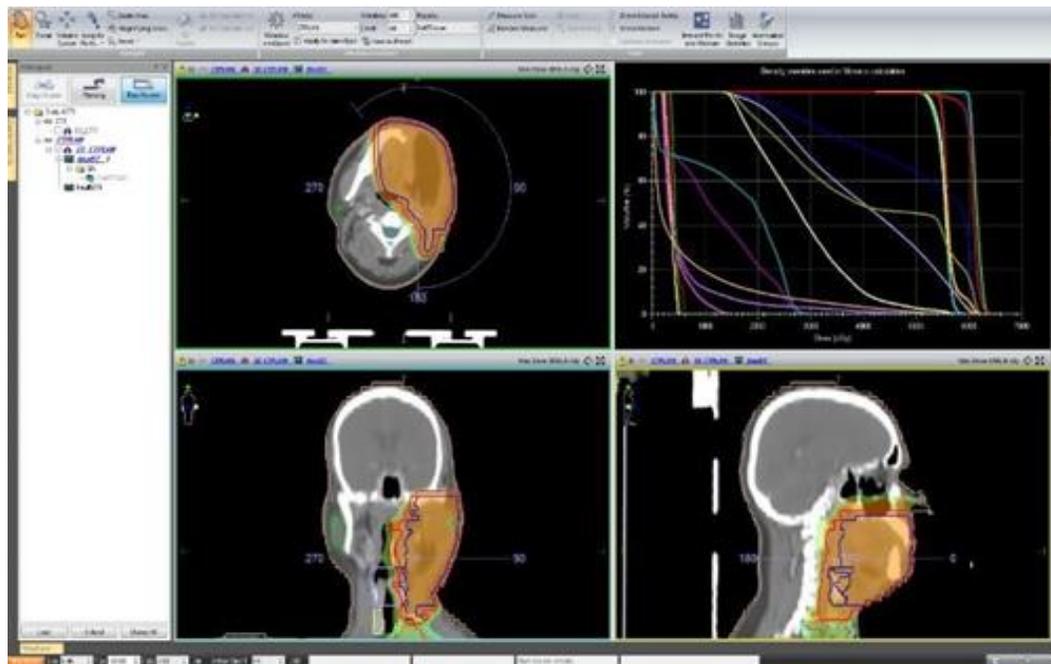


Figure 1.3 - VMAT Dose Distribution (Orange – 95% isodose, Green – 90 % isodose)



Dose volume histograms (DVH) of 3DCRT, IMRT and VMAT plans for respective typical cases are shown in **Figure 2**.

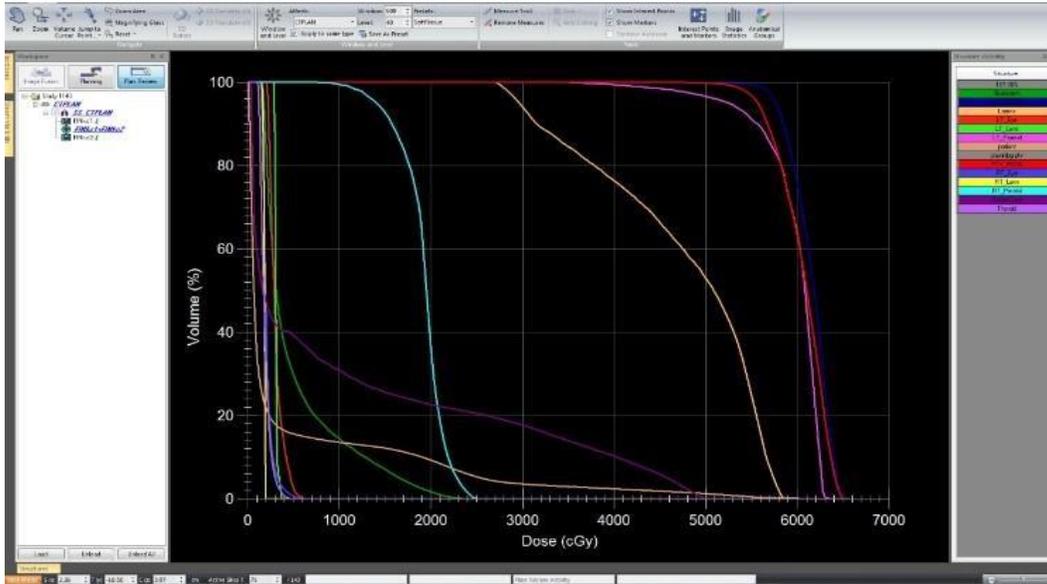


Figure 2.1 - DVH for 3DCRT

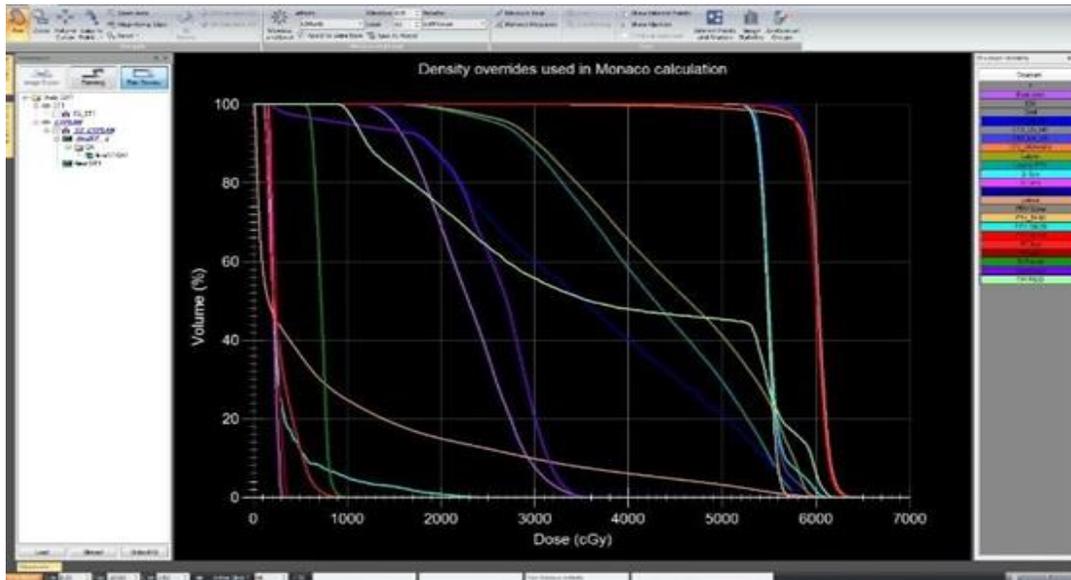


Figure 2.2 - DVH for IMRT



the isodose surfaces encompassed the PTVs more smoothly (i.e. less occurrence of high dose bulges reaching far outside the PTVs) and fewer hot spots outside the PTVs were observed (see Figure 1 for a typical example). On analysis of beam-on time (BOT), 3D-CRT plan had the least BOT with a mean of 221.12 MUs and mean BOT 0.36 minutes as compared to IMRT and VMAT which may be attributed to the lack of optimization. IMRT plan had the longest of BOT with a mean of 952.61 MUs and mean BOT of 1.58 minutes while VMAT plans had relatively lesser BOT with the mean of 765.11 MUs and mean BOT of 1.27 minutes. VMAT was associated with better target dose coverage and comparatively better OAR doses as compared to IMRT. Based on these results, with VMAT for PORT in Ca oral cavity the delivery times can be expected to be reduced by ~ 20% compared to IMRT excluding the time gap for beam-off gantry motion.

Discussion

A notable difficulty with irradiation of head-and-neck cancer (HNC) is the large number of organs at risk (OARs) in close proximity to regions with disease, including the salivary glands, spinal cord and brainstem, larynx and thyroid. The challenging task for the treatment planner is to find the most optimal trade-off in sparing the different OARs for each individual patient. Often better sparing of one OAR implies sacrificing another OAR, and in most patients high-grade radiation-induced toxicity is unavoidable while ensuring sufficient dose coverage of the planning target volume (PTV). Post-operative status in cases like Ca oral cavity worsen the scenario even further owing to the distorted anatomy and pre-existing surgical morbidities like tracheostomy, flaps, local infections and dysphagia. This may result in severe consequences on the quality of life of these patients. Addition of concurrent chemotherapy as indicated worsens the toxicity profile even further. In RTOG 9501 and EORTC 22931 trials, the incidence of grade ≥ 3 acute toxicity was approximately twice as high with concurrent treatment; however, grade 3 or higher late toxicities were similar among the groups in RTOG and EORTC trials, at approximately 30–40%.

This vulnerability may even at times lead to patients defaulting the much needed adjuvant treatment. The only way to reduce these maladies is to use better conformal radiation delivery techniques. Confining the radiation dose to the planning target volume (PTV) with minimum spillage of radiation dose outside the PTV is the main aim of radiotherapy treatment planning. 3- dimensional conformal radiotherapy (3DCRT) [5-7] is used to confine the radiation dose to PTV but intensity modulated radiotherapy (IMRT) [8-12] have an additional advantage of sparing the organs at risk (OAR). Many a times with 3DCRT, it is difficult to spare the OAR without compromising the PTV coverage. IMRT has the ability to produce the desired dose distributions shaped to the planned target volume with sparing of OARs. It is always desirable in conformal radiation treatment to shape the prescribed isodose volume perfectly around the



PTV to achieve the CI of 1.0, but because of irregular shapes of PTV, close proximity of critical organs and inadequacy of field shaping devices such as MLC leaf width and MLC transmission, make it difficult to be achieved practically. When using IMRT for irradiation of oropharyngeal cancer salivary function was less impaired, but the majority of the patients still suffered from some degree of xerostomia. [13-15] Braam et al. showed that the normal tissue complication probability (NTCP) at several time points after radiation therapy was less than 20% only if the mean dose to the parotid glands was lower than 25 Gy [16], a dose level that even with IMRT is often not achieved. Recently, the next generation of IMRT techniques, volumetric modulated arc therapy (VMAT) has become widely available. Compared to static beam 3D Conformal Radiation Therapy and Intensity-Modulated Radiation Therapy (IMRT), the main advantage of Volumetric Modulated Arc Therapy (VMAT) is a shortened delivery time with better dose coverage, which leads to improved patient comfort and possibly smaller intra-fraction movements. [17]

A number of single-institution studies have been published for VMAT for HNC [18-24]. The authors of these studies observed comparable or better PTV coverage and conformity as well as better sparing of OARs for VMAT compared to IMRT, while delivery times were shortened by 35-60 %. Recently, a multi-institutional study comparing different treatment technologies planned in different institutes has been reported [25]. The decreased treatment delivery time obtained with VMAT will improve patient comfort and result in a smaller impact of intra-fraction movements, as described by Hoogeman et al. [26]. Several single-institution studies comparing VMAT and IMRT for HNC have been reported in literature, most based on Rapid Arc [18,19] and on Smart Arc [20-24]. 3DCRT and IMRT has been the standard for radiation therapy of advanced HNC in most of the Institutes however, target coverage at the cost of high OAR doses in case of 3DCRT and increased treatment time leading more patient discomfort and intrafraction motion in case of IMRT have limited their maximum therapeutic gains. Already in 1996, Eisbruch et al. reported on a 3D-CRT technique to spare the contralateral parotid gland, while deliberately accepting underdosage in the surrounding target volume with supposedly “lower” risk to contain disease. [27] With the introduction of IMRT, this technique was refined and the contralateral gland could be spared without hazarding underdosage in the target volume; however, often at the price of still sacrificing the ipsilateral gland. [28]

It seems that the paradigm “sacrificing one parotid gland to achieve better sparing of the contralateral gland” often applied with advanced HNC can be revisited with the advent of VMAT. Our study aimed at a simplified comparison of radiotherapy treatment planning of 3DCRT, IMRT and VMAT for post-operative oral cavity carcinomas with respect to target coverage, OAR doses, toxicity profile and beam-on time (BOT). Analysis of the data resulting from this small sample sized single institution study shows that VMAT plans have an improved plan quality compared to 3DCRT and IMRT plans. Based on the effective delivery times we expect a minimum reduction in the effective delivery times of ~20% with VMAT



compared to IMRT which was excluding the time gap for beam-off gantry motion and patient related intrafraction gaps if any. This is in concordance with the literature available till date. From Table 2.4 we could see dosimetric parameters with significant difference between 3DCRT, IMRT and VMAT.

The conclusions of the presented study with VMAT leading to better dosimetric results are more striking. Limitations of the here presented study mainly include the limited sample size. However our cause with this limited sample size study was to share our own experience with these three techniques in this particular primary which accounts for more than half of our on-couch cases. The data presented in this planning study comparing static 3DCRT, dynamic IMRT and rotational VMAT aimed at a safe and fast clinical introduction of VMAT for these patients. With better target dose coverage, better OAR sparing and lesser treatment time, VMAT as a treatment modality can efficiently help to achieve a high quality of treatment planning within a short time leading eventually to better compliance and quality of life for this set of operated cases of carcinoma oral cavity.

Conclusion

Our limited sample sized study depicts our own experience to suggest that the toxicity profile in patients treated with 3D-CRT is high and is associated with a compromised target coverage as compared to those with IMRT and VMAT treatment planning techniques. IMRT and VMAT are better and more efficient methods with regards to treatment outcome in this particular set of patients having pre-existent surgical morbidities, for they allow for better sparing of normal tissue, thereby causing lesser normal tissue toxicity, eventually leading to a better quality of life vis-a-vis 3D-CRT. 3DCRT had the least beam-on time which may be attributed to lack of optimization while VMAT fared better than IMRT with 20 percent lesser beam-on time as compared to the later. VMAT appears to be the best treatment modality with a better target dose coverage, minimal doses to OARs and relatively lesser beam-on time vis-à-vis IMRT and may be warranted where-ever feasible.

Acknowledgement

Our patients, Chairman Mr Uday Deshmukh and entire Team Management of Onco-Life Cancer Centre, Satara, Maharashtra

References

1. GLOBOCAN 2020
2. Sakuraba M, Miyamoto S, Kimata Y, Nakatsuka T, Harii K, Ebihara S, et al. "Recent advances in reconstructive surgery: head and neck reconstruction". *Int J Clin Oncol* (2013) 18(4):561



5.10.1007/s10147-012-0513-6 [PubMed] [CrossRef] [Google Scholar]

3. Cooper JS, Pajak TF, Forastiere AA, Jacobs J, Campbell BH, Saxman SB, et al. "Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck". *N Engl J Med* (2004) 350(19):1937–44.10.1056/NEJMoa032646 [PubMed] [CrossRef] [Google Scholar]
4. Bernier J, Dommene C, Ozsahin M, Matuszewska K, Lefebvre JL, Greiner RH, et al. "Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer". *N Engl J Med* (2004) 350(19):1945–52.10.1056/NEJMoa032641 [PubMed] [CrossRef] [Google Scholar]
5. Powlis WD, Smith AR, Cheng E, et al. (1993) "Initiation of multileaf collimator conformal radiation therapy". *Int J Radiat Oncol Biol Phys*, 25: 171-179.
6. LoSasso T, Chui CS, Kutcher GJ, Leibel SA, Fuks Z, Ling C (1993) "The use of multileaf collimator for conformal radiotherapy of carcinomas of the prostate and nasopharynx". *Int J Radiat Oncol Biol Phys*, 25: 161-170.
7. Boyer AL, Biggs P, Galvin J, et al. (2001) "Basic applications of multileaf collimators. Report of the AAPM Radiation Therapy Committee Task Group" No. 50, *Med Phys*.
8. Boyer AL and Yu CX (1999) "Intensity modulated radiation therapy with dynamic multileaf collimator. *Semin Radiat Oncol*", 9: 48-59.
9. Wu VW, Kwong DL, Sham JS (2004) "Target dose conformity in 3-dimensional conformal radiotherapy and intensity modulated radiotherapy". *Radiother Oncol*, 71: 201-206.
10. Boethmer D, Bohsung J, Eichwurz I, Moys A, Budach V (2004) "Clinical and physical quality assurance for intensity modulated radiotherapy of prostate cancer". *Radiother Oncol*, 71: 319-325.
11. Boyer AL and Yu CX (1999) "Intensity-modulated radiation therapy with dynamic multileaf collimators. *Semin Radiat Oncol*", 9: 48-59.
12. Burman C, Chui CS, Kutcher G, et al. (1997) "planning, delivery, and quality assurance of intensity-modulated radiotherapy using dynamic multileaf collimator: A strategy for large-scale implementation for the treatment of carcinoma of the prostate". *Int J Radiat Oncol Biol Phys*, 39: 863-



873.

13. Braam PM, Terhaard CH, Roesink JM, Raaijmakers CP: “Intensity-modulated radiotherapy significantly reduces xerostomia compared with conventional radiotherapy”. *Int J Radiat Oncol Biol Phys* 2006, 66:975–980.

14. Chao KS, Majhail N, Huang CJ, Simpson JR, Perez CA, Haughey B, Spector G: “Intensity-modulated radiation therapy reduces late salivary toxicity without compromising tumor control in patients with oropharyngeal carcinoma: a comparison with conventional techniques”. *Radiother Oncol* 2001, 61:275–280.

15. Dijkema T, Terhaard CH, Roesink JM, Braam PM, van Gils CH, Moerland MA, Raaijmakers CP: “Large cohort dose-volume response analysis of parotid gland function after radiotherapy: intensity-modulated versus conventional radiotherapy”. *Int J Radiat Oncol Biol Phys* 2008, 72:1101–1109.

16. Braam PM, Roesink JM, Moerland MA, Raaijmakers CP, Schipper M, Terhaard CH: “Long-term parotid gland function after radiotherapy”. *Int J Radiat Oncol Biol Phys* 2005, 62:659–664.

17. Bedford JL: “Treatment planning for volumetric modulated arc therapy”. *Med Phys* 2009, 36:5128–5138.

18. 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.

19. Vanetti E, Clivio A, Nicolini G, Fogliata A, Ghosh-Laskar S, Agarwal JP, Upreti RR, Budrukkar A, Murthy V, Deshpande DD, Shrivastava SK, Dinshaw KA, Cozzi L: “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.

20. 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.

21. Rao M, Yang W, Chen F, Sheng K, Ye J, Mehta V, Shepard D, Cao D: “Comparison of Elekta VMAT with helical tomotherapy and fixed field IMRT: plan quality, delivery efficiency and accuracy”. *Med Phys* 2010, 37:1350–1359.



22. Clemente S, Wu B, Sanguineti G, Fusco V, Ricchetti F, Wong J, McNutt T: “SmartArc-based volumetric modulated arc therapy for oropharyngeal cancer: a dosimetric comparison with both intensity-modulated radiation therapy and helical tomotherapy”. *Int J Radiat Oncol Biol Phys* 2011, 80:1248–1255.
23. Lee TF, Chao PJ, Ting HM, Lo SH, Wang YW, Tuan CC, Fang FM, Su TJ: “Comparative analysis of SmartArc-based dual arc volumetric-modulated arc radiotherapy (VMAT) versus intensity-modulated radiotherapy (IMRT) for nasopharyngeal carcinoma”. *J Appl Clin Med Phys* 2011, 12:3587.
24. Lu SH, Cheng JC, Kuo SH, Lee JJ, Chen LH, Wu JK, Chen YH, Chen WY, Wen SY, Chong FC, Wu CJ, Wang CW: “Volumetric modulated arc therapy for nasopharyngeal carcinoma”: A dosimetric comparison with TomoTherapy and step-and-shoot IMRT. *Radiother Oncol* 2012, 104:324-330.
25. Wiezorek T, Brachwitz T, Georg D, Blank E, Fotina I, Habl G, Kretschmer M, Lutters G, Salz H, Schubert K, Wagner D, Wendt TG: “Rotational IMRT techniques compared to fixed gantry IMRT and tomotherapy: multi institutional planning study for head-and-neck cases”. *Radiat Oncol* 2011, 6:20.
26. Hoogeman MS, Nuyttens JJ, Levendag PC, Heijmen BJ: “Time dependence of intrafraction patient motion assessed by repeat stereoscopic imaging”. *Int J Radiat Oncol Biol Phys* 2008, 70:609–618.
27. Eisbruch A, Ship JA, Martel MK, Ten Haken RK, Marsh LH, Wolf GT, Esclamado RM, Bradford CR, Terrell JE, Gebarski SS, Lichter AS: “Parotid gland sparing in patients undergoing bilateral head and neck irradiation: techniques and early results”. *Int J Radiat Oncol Biol Phys* 1996, 36:469–480.
28. Anand AK, Jain J, Negi PS, Chaudhoory AR, Sinha SN, Choudhury PS, Kumar R, Munjal RK: “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”. *Clin Oncol (R Coll Radiol)* 2006, 18:497–504.

Volume 1 Issue 5 June 2021

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