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Evaluation of Carotid Artery and Carotid Sinus doses in Early stage Carcinoma Glottis with and without bolus

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Abstract
Objective: *To evaluate the doses received by Carotid artery and Carotid sinus in Early stage Carcinoma Glottis by 3DCRT and IMRT plans with and without bolus.*
Materials and Methods: *20 patients of Early stage Carcinoma Glottis (T1/T2 N0 M0) were evaluated in this study. CT simulation was done using 3mm cuts. Target Volumes and OARs were contoured. Carotid artery and Carotid sinus were also contoured as Organs At Risk (OARs). 3DCRT & IMRT plans were generated for these patients. All patients were treated by 2D technique using 6MV photons to a total dose of 66Gy in 30fr. PTV coverage with and without bolus, V36, dose to Carotid artery and Carotid sinus were evaluated.*
Results:*: PTV coverage with and without bolus by 3DCRT plan was 96% and 93.5% and by IMRT plan was 97.3% and 93.91% respectively. Average volume of Carotid artery and Carotid sinus was 7.2cc and 0.67cc. The mean dose received by Carotid artery with and without bolus by 3DCRT was 39.97Gy and 38.93Gy and by IMRT technique was 33.94Gy and 29.05Gy. The mean dose received by Carotid sinus with and without bolus in 3DCRT was 53.4Gy and 53.18Gy and by IMRT technique was 38.52Gy and 37.97Gy respectively. The V36 of Carotid artery with and without bolus by 3DCRT was 57.72% and 57.5% and by IMRT was 50.6% and 49.8%.*
Conclusion: *By using Conformal technique, adequate coverage of PTV is achieved. Irrespective of the technique used in Radiation therapy treatment delivery, there is always better target volume coverage with the use of bolus. Conformal techniques of treatment delivery have the advantage of delivering very minimal dose to Carotid artery and Carotid sinus. The Carotid artery and Carotid sinus must also be contoured as Organs At Risk in all cases of Head and Neck carcinomas and hence has a vital role in re-irradiation cases.*
Keywords: *Early stage Carcinoma Glottis, Carotid artery, Carotid sinus, 3-Dimensional Conformal Radiation Therapy (3DCRT), Intensity Modulated Radiotherapy (IMRT), Stereotactic Body Radiation Therapy (SBRT).*

Introduction

Early stage Glottic Carcinoma is a curable disease. In conventional radiation therapy planning, a simple parallel opposed small field (4-6 sq.cm) is followed. IMRT is becoming the standard treatment in Head and Neck malignancies because of better target volume coverage and very minimal dose to normal structures [(1)].

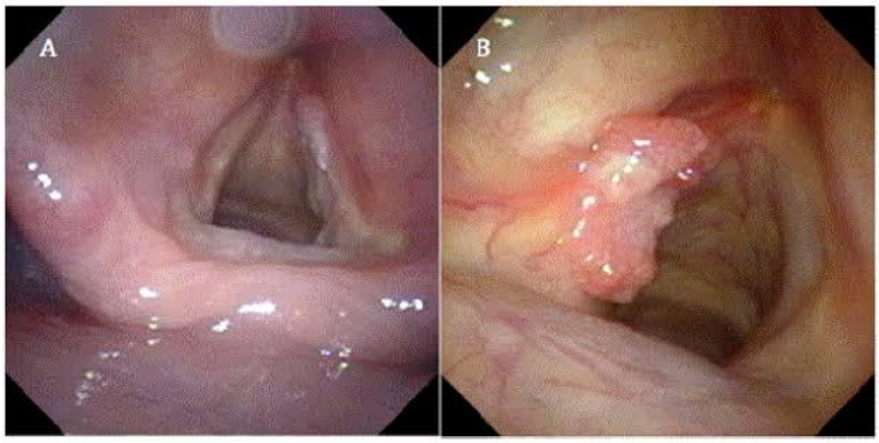

Figure 1: (A) Right T1 Glottic Carcinoma (B) Left T2 Glottic Carcinoma

Carotid artery and Carotid sinus are also the structures in treatment field which receives a substantially higher dose. Recent studies have demonstrated that there is an increased risk of Carotid stenosis in Head and Neck Carcinoma patients receiving radiotherapy. Dose more than 36Gy to Carotid artery causes stenosis and haemorrhage. The acute and late treatment effects to the neck reported is minimal[(2)].The vascular effects of radiation therapy are observed only after a long duration[(3)]. Lam et al in his study on Nasopharyngeal Carcinoma patients has reported that 75% of patients previously treated with radiation showed some degree of Carotid stenosis versus 19% of patients in the control group who have not yet received Radiation therapy[(4)].

There is an accelerated progression of Carotid stenosis in patients who are previously irradiated to the neck [(5)]. The relative risk of stroke is slightly increased in the general population of patients who have received Head and Neck radiation. A very high precision Radiation therapy delivery to the target volumes with minimal doses to adjacent tissues is possible with IMRT technique and hence is required to minimise the adverse effects. In the race to achieve higher target volume coverage, homogeneity of dose is compromised. There is a concern of higher mean dose by IMRT planning because of higher volumetric dose. Multiple target volumes can be treated within single treatment delivery using Simultaneous Integrated Boost (SIB) technique, resulting in heterogeneity inside the different target volumes and adjacent critical normal structures.

Doses to the Carotid artery and Carotid sinus are very significant and are crucial because they constitute the medial boundary for jugulodigastric nodes which are usually in the high-risk target volumes. By two parallel opposed Radiation therapy treatment delivery, the Carotid artery doses might be higher than the target volumes. There are very limited number of studies comparing the radiation dose delivered to Carotid artery and its clinical outcome.

Carotid irradiation results in direct potential injury which may accentuate the chances of stroke in patients with co-morbid conditions like Diabetes mellitus, hypertension and old age. It also limits the role of Radiation therapy in second primary malignancies of Head and Neck Carcinoma. The complications of re-radiation in Head and Neck Carcinoma are increased risk of carotid injury, stenosis, blowout syndrome [(6, 7)].

Stereotactic Body Radiation Therapy (SBRT) has shown promising results for re-radiation of Head and Neck Carcinomas. Carotid Blowout Syndrome is very minimal in Head and Neck Carcinoma patients treated by SBRT technique

when the maximum Carotid artery radiation dose is less than 34Gy [8].Smith et al, analysed SEER dataset for older patients and found that cerebrovascular events within 10 years of diagnosis was 33% for those treated with Radiation therapy alone compared to 25% for those treated with surgery (p value is equal to 0.001) [9].

Materials and Methods

In this study, 20 patients of Early stage Carcinoma Glottis (T1/T2 N0 M0) in the age group of 35 to 65 years were selected. After strict immobilization using thermoplastic device, planning CT scan with a 3 mm slice thickness was obtained. Target volume was contoured using the additional information from the previously done imaging (CT scan or MRI scan) and the Radiation Therapy Oncology Group (RTOG) target delineation guidelines in Head and Neck Carcinoma was followed.

The right and left Common Carotid artery, the Internal and External Carotid arteries, Carotid sinus, spinal cord and thyroid were contoured for each patient as OARS. The Common Carotid artery was contoured from the aortic arch, including the brachiocephalic trunk, up to the carotid bulb. The Internal Carotid artery was contoured from carotid bulb to the base of skull and the External Carotid artery was contoured from carotid bulb to the parotid gland.

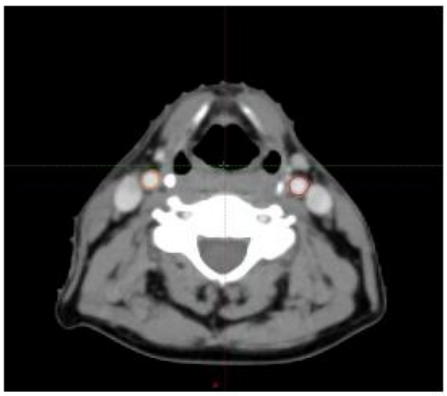

Figure 2: Carotid artery contouring

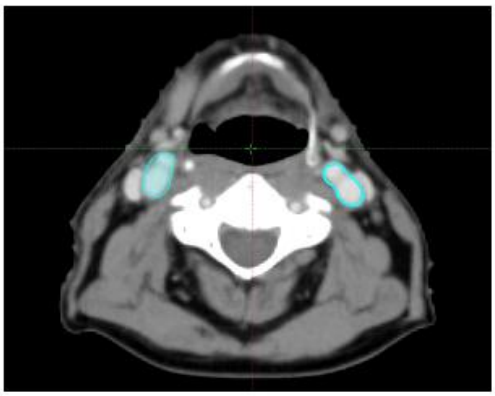

Figure 3: Carotid sinus contouring

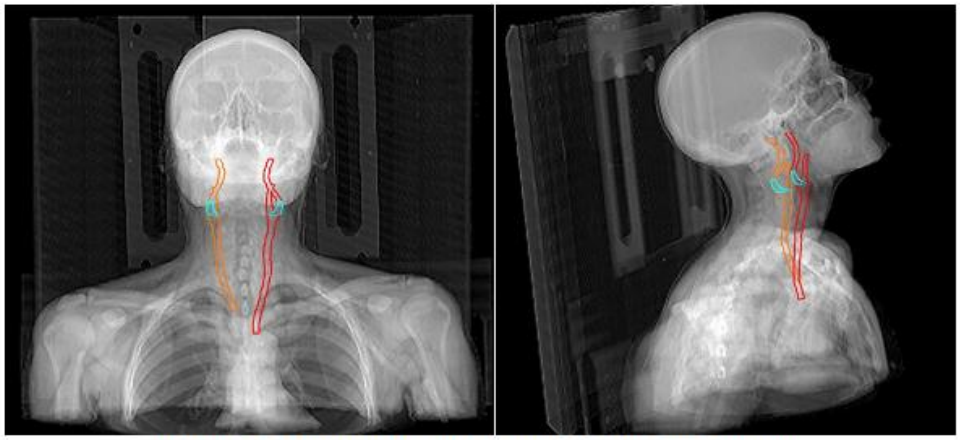

Figure 4: Carotid artery and Carotid sinus contouring

3DCRT and IMRT plans were generated with and without bolus for all 20 patients using Eclipse software. All the patients received treatment by two parallel opposed fields using 6 MV photons.

The Carotid artery and Carotid sinus doses in each plan were calculated and DVH was obtained for all patients. Planning dose constraints to Carotid artery was limited to 55Gy to 80% of the volume with desirable maximum dose of 59.4Gy.

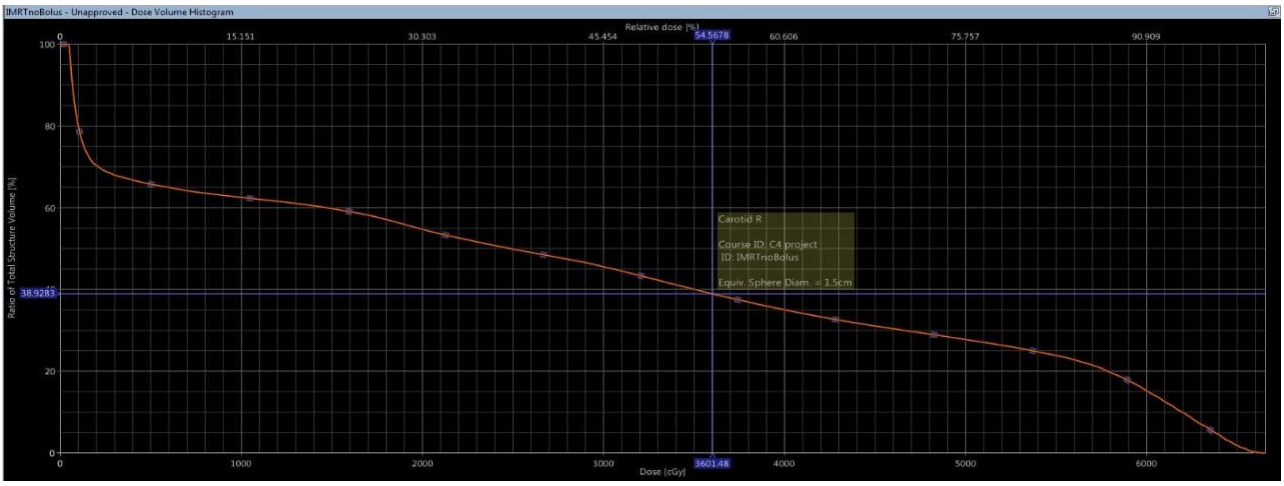

Figure 5: DVH of Carotid Artery

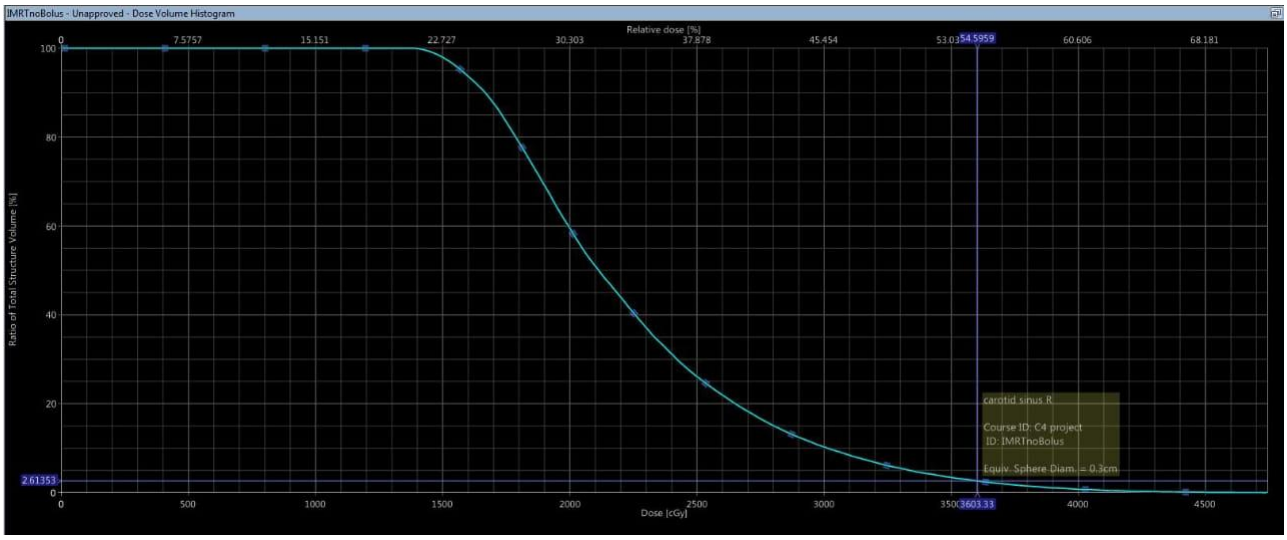

Figure 6: DVH of Carotid Sinus

Result

Statistical analysis was done using "R" software. Independent t-test was done to correlate significance within the subgroup for treatment with bolus and without bolus. ANOVA was done for the 2 techniques (3DCRT, IMRT) for treatment with bolus (40 Plans) and without bolus (40 plans) separately and also combined analysis of total 80 plans was done.

Patients were in the age group of 35-65 years, of which 19 patients were male and 1 was female.

Table 1: Gender distribution of Carcinoma Glottis

GENDER		
Sex	**Number**	**Percentage (%)**
Male	19	95.0
Female	1	5.0
Total	**20**	**100**

Table 2: TNM Staging of Carcinoma Glottis cases

TNM Staging	Number
Stage I	14
Stage II	6

14 patients (70%) belong to stage I and 6 patients (30%) belong to stage II according to TNM Staging 8th Edition.

Average volume of Carotid artery and Carotid sinus was 7.2cc & 0.67cc. The PTV coverage with and without bolus in 3DCRT was 96% and 93.5% and in IMRT it was 97.3% and 93.91%. This chart demonstrates that IMRT has an advantage over 3DCRT in terms of PTV coverage.

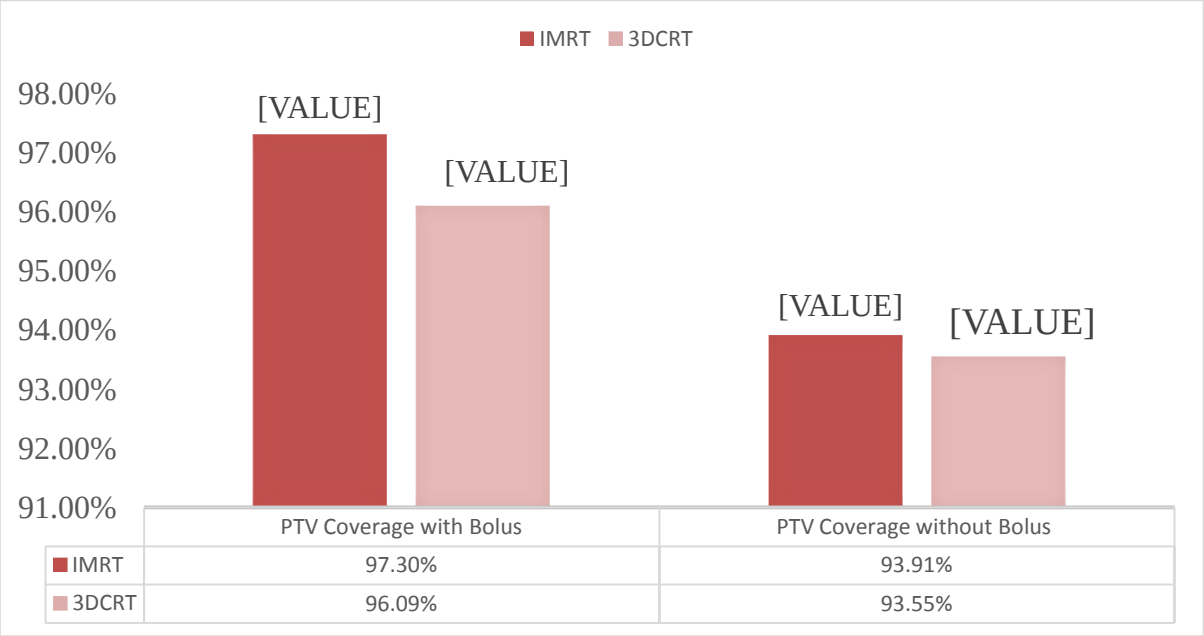

Figure 7: Bar Diagram of PTV coverage of 3DCRT and IMRT

The mean dose received by Right Carotid Artery with and without bolus in 3DCRT was 38.7Gy and 39Gy and in IMRT was 34.1Gy and 33.5Gy respectively. The mean dose received by Left Carotid Artery with and without bolus in 3DCRT was 32.1Gy and 33.1Gy and in IMRT was 29.8Gy and 29.1Gy respectively. With IMRT, mean dose to Carotid artery is less and also there is slightly higher dose to Right Carotid artery than Left Carotid artery.

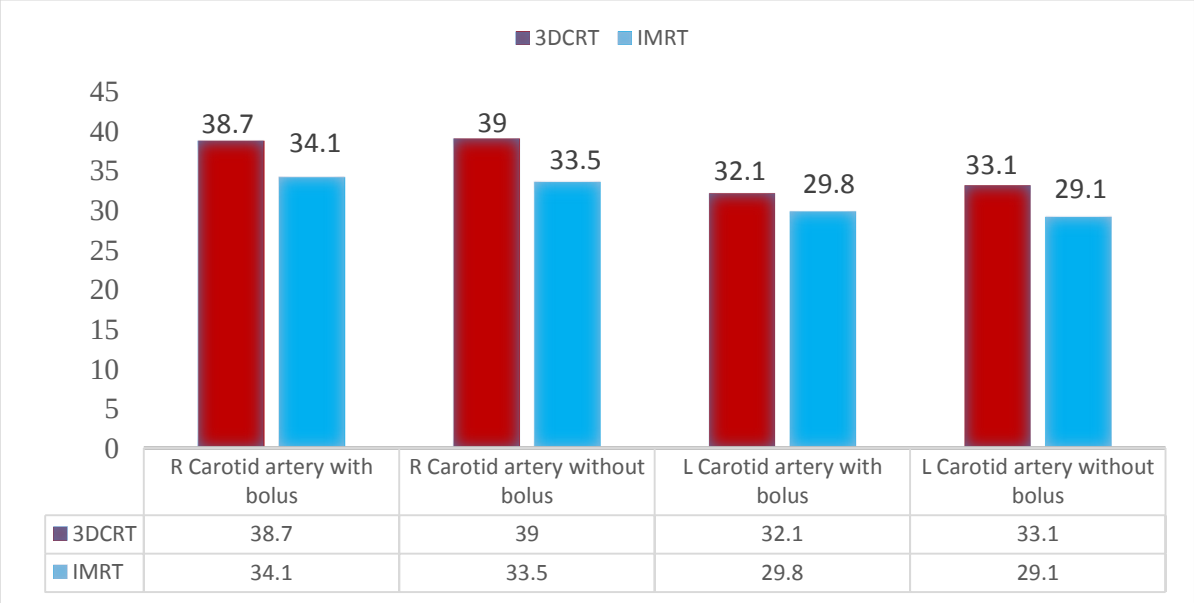

Figure 8: Bar Diagram of mean doses of Right and Left Carotid Artery with and without bolus in 3DCRT and IMRT

The mean dose received by Right Carotid Sinus with and without bolus in 3DCRT was 54.5Gy and 55.8Gy and in IMRT was 38.5Gy and 38Gy respectively. The mean dose received by Left Carotid Sinus with and without bolus in 3DCRT was 53.2Gy and 52.4Gy and in IMRT was 34.8Gy and 34.2Gy respectively. With IMRT, mean dose to Carotid Sinus is less and also there is slightly higher dose to Right Carotid sinus than Left Carotid Sinus with these techniques.

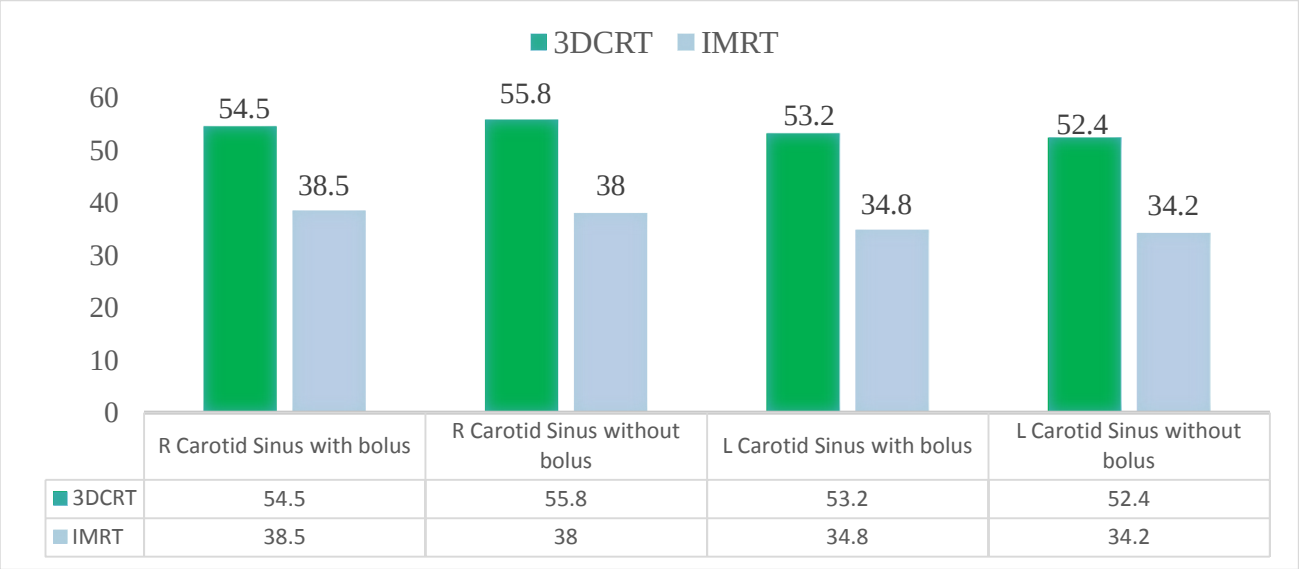

Figure 9: Bar Diagram of mean doses of Right and Left Carotid Sinus with and without bolus in 3DCRT and IMRT

The V36 received by Right Carotid Artery with and without bolus in 3DCRT was 54.1% and 57.2% and in IMRT was 50.7% and 49.8% respectively. The V36 received by Left Carotid artery with and without bolus in 3DCRT was 49% and 47.7% and in IMRT was 49.1% and 45.2% respectively. IMRT has lower V36 of Carotid artery and also there is slightly higher dose to Right carotid artery than Left carotid artery with these techniques.

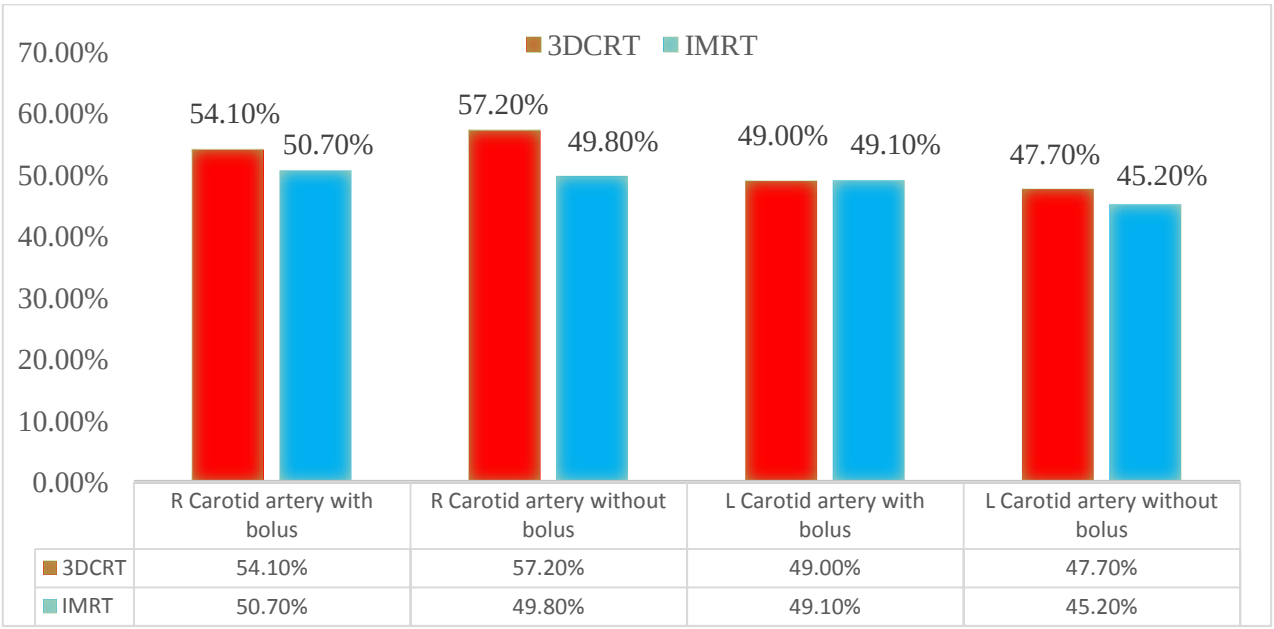

Figure 9: Bar Diagram of V36 of Right and Left Carotid Artery with and without bolus in 3DCRT and IMRT

Conclusion

IMRT with bolus has better target coverage and reduced dose to Carotid artery and it was found to be the best plan amongst the plans generated for each patient. IMRT planning gives the advantage of limiting dose to the Carotid artery and gains significance in patients with co-morbid conditions. Dose response relationship for carotid artery necessitates the use of IMRT technique whenever feasible and results

in the avoidance of complications and side effects of Radiation Therapy delivery. By Conformal techniques (IMRT), adequate coverage of PTV can be achieved and irrespective of technique there is always better coverage with addition of bolus. Conformal techniques scores over conventional technique by delivering minimal dose to Carotid artery and Carotid sinus and thus reducing the late effects.

All the patients treated, have clinically complete response and there was no incidence of symptoms associated with Carotid blowout or stenosis. Also, future re-irradiation can be kept as an option in Recurrences or second malignancies without much severe adverse effects.

Discussion

In the target volume delineation of Head and Neck Carcinomas, Carotid artery has been included in the CTV to address the neck. By Conformal techniques like 3DCRT and IMRT, the target volume coverage is always superior as compared to conventional radiation treatment delivery. IMRT plans have more high dose regions in the target volumes. This might result in better local control. Dose heterogeneity in the CTV, which contains normal tissues, might result in complications which must be analysed.

Dose to carotid artery by IMRT technique is increased because of dose in homogeneity. SIB technique results in differential dosing to different target volumes and the BED (Biological Equivalent Dose) doses in conventional techniques cannot be compared with the same. It is further complicated in previously irradiated patients for second primary or recurrent carcinomas, as they might receive a very high dose of greater than 100Gy to carotid artery[(10)]. Carotid Blowout Syndrome is the life-threatening complication associated with re-irradiation in these cases.

Cheng et al observed that annualised progression rate from <50% to >50% stenosis in irradiated arteries was 15.4% as compared to 4.8% in non - irradiated vessels. He also noted time from radiation therapy (>years) as a significant risk factor [(5)]. The ideal head and neck carcinoma patients for carotid artery sparing are patients with minimal nodal disease who have high risk factors for stroke, older patients and previously irradiated patients. Reduced complication rates without compromising the loco-regional control in IMRT (SIB), fraction size per day needs to be evaluated.

Dorresteijn et al did a study in patients irradiated to cervical region and found that they had increased risk of stroke [(11)]. Stereotactic Body Radiation Therapy (SBRT) is the new radiation therapy technique for re-irradiation in Recurrent Head and Neck Carcinoma patients. The role of chemotherapy resulting in stroke in head and neck carcinoma patients was evaluated in Hodgkin's lymphoma patients and it was found to be inconclusive [(12)].

Yazici et al analysed Carotid Blowout Syndrome after SBRT and found that Carotid Blowout Syndrome did not occur in any of the patients who received a maximum carotid artery dose of <34Gy and also that every other day SBRT treatment is better in decreasing Carotid Blowout Syndrome. The BED formula has not been validated for the large doses per fraction.

Yamazaki et al studied the frequency, outcome and the prognostic factors of Carotid Blowout Syndrome in re-irradiation of head and neck carcinoma using cyber knife. It was found that an angle of carotid invasion $>180^0$, ulceration, PTV and irradiation to lymph node areas were all statistically significant risk factors for Carotid Blowout Syndrome [(13)].

References

1. Gregoire V, De Neve W, Eisbruch A, Lee N, Van den Weyngaert D, Van Gestel D. Intensity-modulated radiation therapy for head and neck carcinoma. *Oncologist*. 2007; 12: 555–564.
2. Mendenhall WM, Amdur RJ, Morris CG, et al. T1-T2N0 squamous cell carcinoma of the glottic larynx treated with radiation

therapy. J Clin Oncol. 2001; 19:4029–4036.
3. Haynes JC, Machtay M, Weber RS, et al. Relative risk of stroke in head and neck carcinoma patients treated with external cervical irradiation. Laryngoscope. 2002; 112:1883–1887.
4. Lam WW, Yuen HY, Wong KS, et al. Clinically under-detected asymptomatic and symptomatic carotid stenosis as a late complication of radiotherapy in Chinese nasopharyngeal carcinoma patients. Head Neck 2001;23:780–4.
5. Cheng SW, Ting AC, Ho P, et al. Accelerated progression of carotid stenosis in patients with previous external neck irradiation. J Vasc Surg. 2004; 39:409–415.
6. De Crevoisier R, Bourhis J, Domenge C, et al. Full-dose reirradiation for unresectable head and neck carcinoma: experience at the Gustave-Roussy Institute in a series of 169 patients. J Clin Oncol. 1998; 16:3556–3562.
7. Salama JK, Vokes EE, Chmura SJ, et al. Long-term outcome of concurrent chemotherapy and reirradiation for recurrent and second primary head-and-neck squamous cell carcinoma. Int J Radiat Oncol Biol Phys. 2006; 64:382–391.
8. Johansen LV, Grau C, Overgaard J: Supraglottic carcinoma: patterns of failure and salvage treatment after curatively intended radiotherapy in 410 consecutive patients. Int J Radiat Oncol Biol Phys. 2002, 53:948–958.
9. Smith GL, Smith BD, Buchholz TA, et al. Cerebrovascular disease risk in older head and neck cancer patients after radiotherapy. J Clin Oncol. 2008; 26:5119–5125.
10. Luo CB, Teng MM, Chang FC, et al. Radiation carotid blowout syndrome in nasopharyngeal carcinoma: Angiographic features and endovascular management. Otolaryngol Head Neck Surg. 2008;138: 86–91
11. Dorresteijn LD, Kappelle AC, Boogerd W, et al. Increased risk of ischemic stroke after radiotherapy on the neck in patients younger than 60 years. J Clin Oncol. 2002;20:282-288.
12. De Bruin ML, Dorresteijn LD, van't Veer MB, et al. Increased risk of stroke and transient ischemic attack in 5-year survivors of Hodgkin lymphoma. J Natl Cancer Inst. 2009;101:928-937.
13. Yamazaki H, Ogita M, Kodani N, Nakamura S, Inoue H, Himei K, Kotsuma T, Yoshida K, Yoshioka Y, Yamashita K, Udono H: Frequency, outcome and prognostic factors of carotid blowout syndrome after hypofractionated re-irradiation of head and neck cancer using CyberKnife: a multi-institutional study. Radiother Oncol. 2013; 107:305–309.