RESEARCH ARTICLE

Adaptive Radiotherapy in Locally Advanced Head and Neck Cancers: Impact on Target Volume Shrinkage and Organ at Risk and its Clinical Outcome

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Abstract

Positional uncertainties due to tumor shrinkage and weight loss, leads to decrease therapeutic ratio due to higher treatment toxicity and decreased local control rates. Adaptive Radiotherapy refers to changing treatment plan during the treatment sessions to account for this decreased therapeutic ratio. Total of 50 patients were treated with image-guided radiotherapy for locally advanced head and neck cancers. Replan was done at 17th fraction. The cross-comparison of dosimetric analysis of GTV 100 and PTV 95 was statistically significant. Mean volume reduction rate in ipsilateral parotid and contralateral parotid was in our study mean shrinkage in volume of right parotid 13–10.4 cc, left parotid 14–10.5 cc, respectively. Patients who had TVRR ≥20% at interim replan done after 17 fractions at 4th week had complete response at 6 months after treatment while in patients with TVRR <20%, 42% had complete response at 6 months. Out of 50 patients enrolled in the study 32 patients (64%) had complete response on clinical evaluation and follow-up CT scan.

Keywords: Adaptive, Cancer, Tumor volume.

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Introduction

The treatment of unrespectable Head and Neck Cancer (HNC) consists of chemo-radiotherapy (CRT).[1,2]

Radiotherapy (RT) has evolved from conventional to conformal techniques. Conventional radiotherapy techniques have historically used blocks based on bony landmarks and sometimes under dosing.[3] The target and higher doses to normal tissue with high incidence of adverse reactions. To reduce toxicity and improve therapeutic ratio is better target delineation and sparing of normal tissue. This can be achieved by conformal RT technique like three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT) using off-line and online computed tomography (CT) and rescanning to identify visible tumor and organ at Risk.[4-8]

One of the unique aspects of head and neck radiation therapy is that noticeable changes in the anatomy occur during the treatment course.[9] This is mostly result of the response to the radiation and often combined chemotherapy and positioning uncertainties and weight loss.[10] Positional changes include shrinkage of the tumor and normal tissue volumes as parotid gland (PG) and other structures.[11,12]

Therefore, there is speculation that the plan created on the initial planning CT may no longer be optimal for changing anatomy during the treatment, and the actual radiation dose delivered to the patient may be significantly different from that in the plan.[13,14]

Adaptive Radiotherapy (ART) refers to changing the radiation treatment plan delivered to a patient during a treatment session to account for change in anatomy like tumor shrinkage, weight loss, change in clinical/palpable tumor volume, ill-fitting mask, or prolonged treatment breaks. Decreased appetite and reduced oral intake contribute to weight loss in cancer patients. Tumor volume may shrink after chemoradiation. The distance between OAR (organ at risk) and PTV (Planning target Volume) decrease. These lead to change in dose distribution to normal surrounding tissues (organ at risk) and toxicities.

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Materials and Methods

Patient history and physical examination were done thoroughly for clinical evaluation and performance status will be measured by Karnofsky Performance scale.[15]

All selected patient were underwent basic set of investigations-hematological investigations, X-ray chest, contrast-enhanced computed tomography neck.

All biopsy proven cases stating squamous cell carcinoma were included in the study.

Total 50 patients were treated with image-guided radiotherapy with concurrent chemotherapy (CCRT) [total dose 70Gy/35# (in 7 weeks)] for locally advanced head and neck carcinomas [T3–T4a, N0–2]

Planning CT (CT simulation) scans were acquired pretreatment and interfractional (Replanning) [at 17# completion].

In 1st session treatment was delivered on the basis of pretreatment CT planning after generating optimal plan (P1).

In 2nd session [at completion of 17#] another CT Simulation was done and replanning done on the basis of new images (P2).

Comparing both plan, target volume shrinkage and dose distribution to target volume and normal tissues (OAR) was recalculated.

Outcome was assessed by clinical examination at every month till 6 months and radiologically by CT scan neck at 3 and 6 months.

Dosimetric Analysis

The dosimetric effects were quantified by comparing dose-volume histograms of P1 and P2. The target coverage in these plans was clinically assessed using GTV (Gross tumor volume) V100 and PTV (Planning target volume) V95 (volume receiving 100% and 95% of the prescription dose, respectively).[16,17]

Tumor Volume Reduction Rate (TVRR)

Total gross tumor volume (GTVt) changes between the original and rescan CT were analyzed. Pre-RT GTVt and rescan GTVt values were used to calculate TVRR, which defined as: [pre-RT GTVt–rescan GTVt]/pre-RT GTVt[18,19]

Volume Reduction in OARs:

Pre-RT Volume (V1) – rescan Volume (V2)/ pre-RT Volume (V1)

Result and Discussion

Intensity-modulated radiation therapy (IMRT)/Image-guided radiation therapy (IGRT) is treatment modality technique of choice for management of head and neck cancers. As we know radiation has biological and structural effect on tumor and normal tissue in patients; further patients has weight loss during treatment. And treatment would be delivered on the plan made on the basis of pre-treatment CT scan only, then normal tissue would get higher radiation dose than expected which can result in unexpected high-grade toxicities. So, replan after 17 fractions can evaluate tumor volume reduction rate (TVRR) which has prognostic significance and reduce dose to normal tissue which leads to decrease in late toxicities.

We observed that the mean pair-wise distribution of GTV 100 Plan 1 vs PTV 95 Plan 1 was −0.524cc and GTV 100 Replans vs PTV 95 Replan was −0.446cc. The cross-comparison of dosimetric analysis of GTV 100 and PTV 95 was statistically significant (*p* value 0.001).

As effect of radiation, tumor shrinks, in this study change in volume of GTV range from 0.90–136.50 cc. The mean p-GTV was 28.71cc with standard deviation (SD) 25.18cc. The replan-GTV volume of r-GTV was ranging from 0.80–119.30cc; mean 24.79cc with SD 22.05cc. The decrease in GTV was ranging from 135.60cc and 118.50cc, respectively. The decrease in GTV was not statistically significant (*p* value = 0.409).

Hyebin Lee et al. had documented the patients who achieved locoregional control had a higher TVRR than those with loco-regional failure ($p = 0.010$), and those with the tumor VRR > 35% achieved significantly higher loco-regional control at 3 years (94.4% vs 72.4%; p = 0.018). In our study, we observed that the mean pair-wise distribution of GTV 100 Plan 1 vs PTV 95 Plan 1 was −0.524cc and GTV 100 Replans PTV 95 Replan was −0.446cc. Patients who had TVRR ≥20% at interim replan done after 17 fractions at 4th week had complete response at 6 months after treatment while in patients with TVRR <20%, 42% has complete response at 6 months.

Kataria et al. has investigated efficacy and toxicities of adaptive radiotherapy and documented median reductions in gross primary disease volumes on midtreatment scans was 34%; 16 patients experienced grade three acute mucositis; four patients developed local recurrences, all within the RT field. In our study reduction in GTV was 0.90–136.50cc; 20 patients had grade three acute mucositis; 10 patient had local recurrence and eight had distant metastasis in lung during follow-up.

Castadot et al. also quantified volumetric and positional changes of gross tumor volumes (GTV), clinical target volumes (CTV), and organs at risk (OAR) and documented decrease in GTV at a mean rate of 3.2% and 3.9%/treatment day (td), respectively; nodal GTVs decreased at a mean rate of 2.2%/td. The ipsilateral and contralateral parotid glands showed a mean decrease of 0.9% and 1.0%/td, respectively. In our study, mean shrinkage in volume of right parotid- 13–10.4cc, left parotid- 14–10.5cc.

Ryota Bando et al. observed a marked reduction of GTV by 28% of the initial volume was seen by the third week during RT (*p*-value 0.01).

Shih-Neng Yang et al. has shown primary tumor volume and T staging as a prognostic factors for primary tumor relapse-free survival for OPC (Oropharyngial Carcinoma): T4 tumor ($p = 0.0001$, hazard ratio 7.38), pGTV ≥20 mL ($p = 0.01$, hazard ratio 10.61).[13] In our study, stage III has 85.7% complete response and 14.3% partial response whereas stage IV has 36.3% complete response and 63.7% has partial response. But we didn't find significant corelation between pretreatment GTV and clinical response.

Joel Castelli et al. showed that the main goal of definitive chemo-radiotherapy in locally advanced HNC (Head and Neck Cancers) is to improve locoregional control, while keeping a high quality of life by reducing the dose in the parotid gland during the whole course of IMRT and therefore xerostomia is a major challenge. Indeed, they found the majority of the parotid gland (59%) was being over irradiated by a mean dose of 4Gy (up to 10 Gy), resulting to an absolute increase risk of xerostomia of 8% (up to 24%). The Adaptive Radiotherapy strategy appears to benefit not only to the overirradiated parotid gland patients, reducing the mean dose of 5 Gy (up to 12 Gy) and the xerostomia risk of 11% (up to 30%), but also to the non-over-irradiated parotid gland. These results suggest thus a large use of adaptive radiotherapy for the majority of locally advanced HNC patients.

Qiuwen Wu, et al. stated that multiple factors affect the parotid glands doses. If no replanning is done, then the actual dose (D mean) delivered to the patient will be 10% higher than those shown in the initial plan. Reducing margins from 5–0 mm, improve the sparing of the parotid gland by 22%. Therefore, the main benefit of replanning is to preserve the sparing of the parotid show in the initial plan.

Murat Surucu, et al. furthermore correlated TVRR with clinical outcomes and were able to show statistically significant differences in DFS and OS for patients with TVRR 35.2% and TVRR >35.2% control. Thus, by identifying patients with low TVRR with the use of ART, physicians can potentially consider change in therapeutic strategy for this group of patients. This study has identified numerous benefits to ART for patients with HNC, including improvement in tumor coverage, decrease in dose to OARs, and measurement of tumor volume regression rate to potentially tailor therapy for individual patients.

Conclusion

The cross-comparison of dosimetric analysis of GTV 100 and PTV 95 was statistically significant.

The decrease in GTV was ranging from 135.60cc and 118.50cc, respectively. The decrease in GTV was not statistically significant.

Volumetric change was seen in OARs except mandible and spinal cord. All organ at risk have decrease in volume during replan except mandible and spinal cord which was statistically significant.

As we have done only one replan therefore it will be inappropriate to conclude ideal time period for adaptive replan. But this study has concluded that interim replan at 4 weeks (after 17 fractions) appear to be beneficial. Out of 50 patients enrolled in study 32 patients (64%) had complete response on clinical evaluation and follow-up CT scan after 6 months.

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