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Original Research Article

EFFECT OF ADAPTIVE REPLANNING ON ORGAN AT RISK DOSES AT 40 Gy IN HEAD AND NECK CANCERS

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Abstract

Background: The effect of adaptive replanning on organs at a risk dose of 40 Gy in head and neck cancers. **Aim:** To evaluate the dose-volume histogram data of patients diagnosed with stage III/IV cancer of the nasopharynx, oropharynx, or hypopharynx. **Material and Methods**: This was a prospective study of DOSIMETRIC analysis performed at our institute between March 2017 and August 2017. We evaluated TCP and NTCP data calculated based on the equivalent uniform dose (EUD). Cone beam CT images were taken for patients at 40 Gy and organs at risk (OAR) such as the spinal cord, brainstorm, parotid gland, and mandible were contoured by the same radiation oncologist on the CBCT image set and deformed to the initial planning CT. The DVH generated for these structures from the initial clinical plan were evaluated, and NTCP and TCP were calculated. **Results**: The results showed a significant increase in parotid dose when the initial plan was continued up to 60 Gy, leading to a higher probability of normal tissue complications. Replanning at 40 Gy reduced the dose received by the parotids, lowering the probability of complications, especially xerostomia. The mean parotid dose was approximately 28-30 Gy for both glands, resulting in reduced morbidity. Comparisons of planned target volumes showed a significant reduction in gross tumour volume, highlighting the potential for minimising normal tissue complications. The dose distribution to the parotids during replanning exhibited a substantial change, indicating the importance of adapting the plan to 40 Gy. **Conclusion**: We observed a significant increase in NTCP when the same clinical plan was continued beyond 40 Gy.

INTRODUCTION

The rising incidence of head and neck cancers necessitates increased awareness among oncologists to adopt various approaches, ensuring improved quality of life for patients undergoing concurrent chemoradiation. Multidisciplinary strategies are vital for organ preservation, which is crucial in enhancing patients' quality of life after treatment. The Veteran Affairs Laryngeal study marked a significant turning point, as it highlighted the adverse consequences of surgical intervention, leading to a shift towards functional preservation. Concurrent chemoradiation emerged as a viable alternative, offering favorable outcomes and quality of life.

However, challenges still exist, particularly concerning setup uncertainties that impact dose distribution and target coverage. Inadequate delineation of target volumes and failure to account for organ motion may result in suboptimal treatment delivery, diminishing tumor control probability (TCP) while elevating normal tissue complication probability (NTCP). Adaptive radiotherapy (ART) presents a promising solution, enabling adjustments to accommodate anatomical changes during treatment. Still, its implementation involves considering factors such as cost, workload, and potential increases in radiation doses to organs at risk (OARs).

Daily online image guidance helps alleviate setup uncertainties, while CBCT imaging at specific fractions facilitates monitoring of anatomical changes. OARs, such as the parotid glands, are meticulously contoured on CBCT images, allowing for precise assessment of NTCP. The consistency between setup errors and target structure alignment is vital for optimal treatment outcomes. Replans

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based on acquired CBCT images ensure dose accuracy, especially considering the observed reduction in tumor volume over the course of treatment.

However, continuing with the initial plan without adjustment poses risks, as organs initially distant from the treatment field may migrate into it, leading to unintended overexposure and subsequent complications such as xerostomia. Therefore, ongoing evaluation and adaptation of treatment plans are essential to minimize morbidity and optimize therapeutic efficacy.

Aim

To analyse the impact of adaptive radiotherapy on organs at risk at 40 Gy before radiotherapy, and changes occurring during radiation leading to erroneous dose distribution to normal tissues, organs at risk in patients with head and neck cancers, and the need for replanning at 40 Gy. To evaluate the dose-volume histogram data in patients diagnosed with stage III/IV cancer in the nasopharynx/oropharynx/hypopharynx.

MATERIALS AND METHODS

This prospective study was conducted on 30 patients who were at risk of OAR receiving higher doses than the planned dosage due to anatomical variations in our institute between March 2017 and August 2017.

Inclusion Criteria

Age >30 years, both sexes sites included the nasopharynx, oropharynx, and hypopharynx (stage II/III) Patients planned for definitive, chemoradiation/definitive radiation were included.

Exclusion Criteria

Patients with poor performance status (PS ≥ 2), previously treated or treated outside initially upfront surgery, and palliative intent treatment/metastatic disease were excluded.

Patients were immobilised using a thermoplastic mask. CT for RT planning was performed from the orbit to the shoulder with 3 mm cuts, and marks, such as lead shots, were placed at places in the same line over the patient's surface using a laser to facilitate accurate daily positioning. For patients receiving definitive radiation, CTV was defined as GTV+1-1.5 cm margin. Guidelines for the delineation of elective nodal CTV were followed. The PTV was extended by 3 mm around the CTV, and IMRT plans were generated. The prescription dose was 54 Gy to the CTV and boosted to high-risk regions of the primary and involved lymph nodes up to a total dose of 66 Gy.

The patients were positioned on the couch according to the reference marks already maintained during planning. Online On-board imaging (2D KVCT daily and 3D CBCT at the 10th and 20th fractions) was performed and registered with digitally reconstructed radiographs from the treatment planning images. The images were compared by

correlation of bony anatomy, and differences were corrected by shifting the couch translationally before treatment with at least three reference landmarks, including visible bony landmarks: the vertebra of the cervical spine, nasal septum, and mandible profile. In CBCT, OAR image structures are outlined and registered with the planning CT, and the registered structures are evaluated for the dose delivered by the clinical plan.

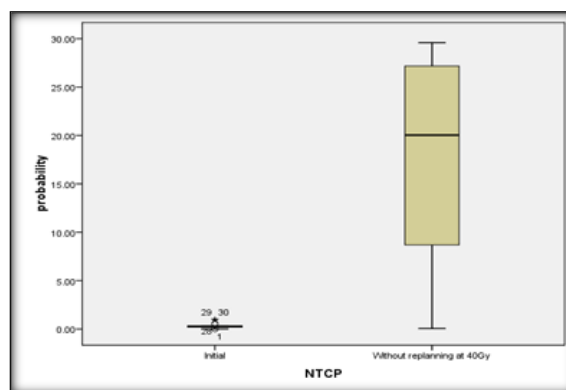**Statistical Analysis**

RESULTS

Figure 1: NTCP of parotids

Box plot analysis explains the probability of normal tissue complications in parotids without replanning at 40 Gy. There was an apparent increase in the dose received by the parotids when the same initial plan was continued until 60 Gy. The p-value in our study was <0.001, which was statistically significant. These statistically significant values were also transformed to obtain practically significant results. Therefore, we can infer that replanning at 40 Gy will reduce the dose received by the parotids and thereby reduce the probability of normal tissue complications. This means that the mean parotid dose received was only approximately 28-30 Gy for both parotids. Therefore, this is in favour of a study that aims to reduce morbidity and long-term complications, such as xerostomia which can be prevented in our patients by adaptive replanning at 40 Gy. [Figure 1]
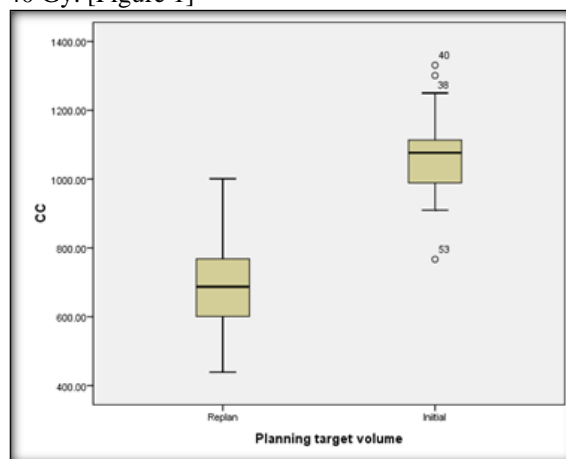

Figure 2: Planning target volume

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The planned target volume comparison between the initial planning and replanning cone beam CT (CBCT) structure sets also showed that there was a significant reduction in the gross tumour volume. From this, we can infer that at the 20th fraction of the radiation regimen, there was a significant reduction in the planning target volume which, if considered during replanning, can reduce normal tissue complications. The box plot curve of the planning target volume (PTV) showed a significant reduction in the volume of the planned target prescribed to obtain a V95% dose. When the initial planning target volume was compared with the replanning target volume, the values were statistically significant, with a p-value of <0.001. This variable also supports this study, whereby the effect of replanning at 40 Gy can bring about a significant change/reduction in the morbidity of the patient. [Figure 2]
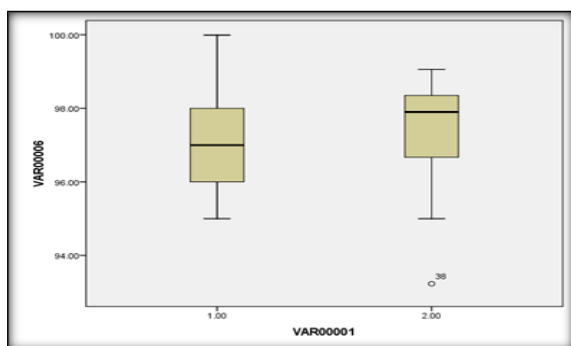

Figure 3: PTV V95% dosage

V95% is the planned target volume receiving 95% of the prescribed dose. There was no significant difference in the paired t-test compared with the initial PTV V95%. Therefore, this analysis shows that even though there is a change in the gross tumour volume, the dose that must be received by the planned target volume is not compromised, which in turn positively reflects the study. The bar diagram also indicated that the PTV V95% for the initial planning CT was 97.43%. The PTV V95% for replanning the CT was approximately 97.1%. Thus, there was not much difference in the dose received by the target. [Figure 3]
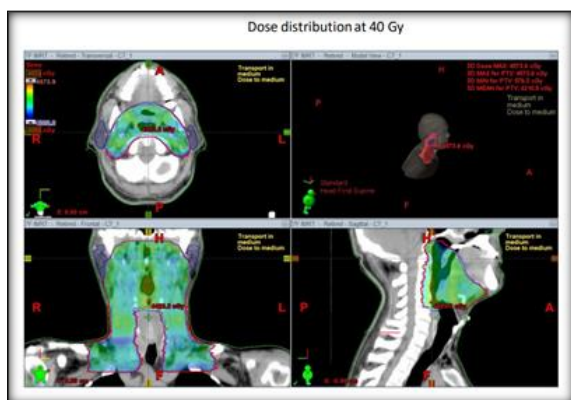

Figure 4: Dose distribution at 40 Gy

During replanning at 40 Gy, the dose distribution to the parotids showed a significant change compared with the initial planning target volume. In addition, the volume of the gross tumour also shows a significant decrease, so the shrinkage of the tumour and other body mass factors related to it shows that if the same initial plan is followed, the parotids will also receive the target/prescribed dose, leading to an increase in the dose received by the normal tissues, leading to unplanned normal tissue complications. [Figure 4]
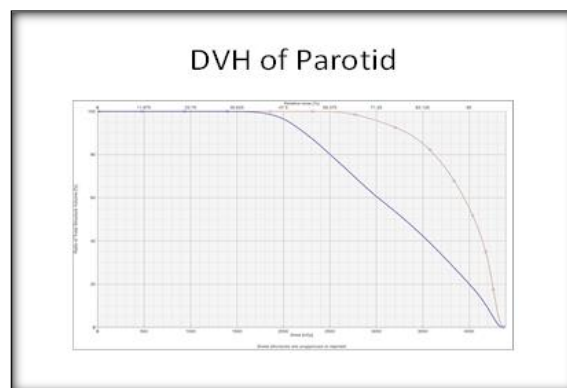

Figure 5: Dose-volume histogram of parotids

The dose-volume histogram of the parotids shows the DVH of the initial parotids with that of the DVH of the replanning CBCT image taken at 40 Gy. There was a significant increase in the dose received by the parotids when the same initial clinical plan was continued until 60 Gy. The blue line denotes the initial planning CT with the DVH of the parotid, and the red dotted line denotes the DVH of the parotids for replanning the CBCT images at 40 Gy. Thus, the dose-volume histogram depicts a clear advantage in favour of replanning CT at 40 Gy. [Figure 5]
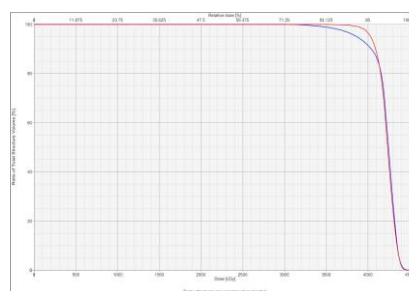

Figure 6: Dose-volume histogram of PTV

The dose-volume histogram of the initial PTV dose was compared to the replanned PTV dose. We infer that the dose received by the planned target volume always receives the maximum prescribed dose, thereby helping to achieve the planned dose while simultaneously reducing the dose received by the parotids. Parotids are the major salivary glands, and

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sparing them will help reduce late complications such as xerostomia and difficulty in swallowing. [Figure 6]

Figure 7: Fusion of CT with CBCT image

The image shows that the initial planning CT images are fused with the cone-beam CT images (CBCT) so that we can evaluate the percentage of normal tissue receiving a dose higher than the initial plan. The parotids that were away from the planned target volume in the initial CT scan moved very well into the treatment field, thereby receiving the planned target dose which in turn increased the mean volume of the parotids. The sinking of the parotids into the PTV resulted in an increased dose, leading to xerostomia. [Figure 7]

DISCUSSION

The effect of adaptive radiotherapy in head and neck cancers has long been considered to produce accurate dose delivery to the planned target volume variations in the anatomy because shrinkage of the tumour volume and positional error have an overall impact on the treatment of head and neck cancers. The effect of radiation on gross tumour volume occurs at approximately the 20th fraction of radiation /40 Gy tumour dose. Most of our patients showed a gross reduction in tumour volume.

In our study involving 30 patients, we observed that the mean PTV value of the initial planning CT was approximately 1070.58cc. The median planning target volume (PTV) for the initial plan was 1076.50 cc. The minimum PTV for the initial plan was approximately 767 cc. The maximum PTV for the initial plan was 1331 cc. After the completion of 40 Gy in 20 fractions, we observed a gross reduction in the volume of the GTV on our weekly CBCT images by assessing other morphological changes. The mean PTV in the replan CT(CBCT) was 694. 55cc.The median PTV volume in the CBCT images was 687.0, the minimum target volume in CBCT images was approximately 439.0, and the maximum target volume in CBCT images was 1001.0cc. From this observation, we found that most patients exhibited a significant reduction in the PTV after completion of 40 Gy. Thus, this study helped us to

investigate the effect of dose distribution on the PTV and close-lying OARs, namely parotids.

As the parotids are located peripheral to the tumours, any shrinkage in the tumour volume results in the parotids sinking into the treatment field. In IMRT treatment, we always limit the dose to the OARs(parotids) just at the tolerance limits, due to its anatomical location. The ability of IMRT to sculpt the dose and take shapes to avoid parotids can be greatly appreciated in the treatment plans. After approving the plan, which has already met the dose volume objectives of the OARs and PTV, we assume that the same has been delivered; however, owing to tumour regression and other factors, including morphological changes, we end up blindfolding ourselves from retrieving and correcting for the dosimetric impact of the structures. Considering the effect of parotids sinking into the treatment fields at 40 Gy owing to the various factors listed above, we studied volume regression and dose distortion based on CBCT data acquired at 40 Gy.

We analysed the PTV volumes in CBCT datasets and their effect on the OARs dose increase. We calculated the normal tissue complication probability for parotids based on a MAT LAB program which calculated the NTCP of the parotids based on the EUD obtained from the DVH data. The following results were observed in the NTCP (normal tissue complication probability) increase, in case a replan has been initiated for dose deposition on the parotids. NTCP of parotids for initial planning of CT plans. All values in the paired t-test were found to have a significant p-value of <0.001 which was statistically significant in our study.

The mean NTCP of parotids for the initial planning CT plan for the parotid was approximately 0.289%, the median NTCP of parotids for the initial planning CT plan was 0.245%, and the maximum NTCP of parotids received by the initial plan for the parotid was approximately 0.980%. When the same initial plan was continued until 40 Gy, the dose received by the parotids showed a significant difference, that is, the mean dose received by the parotids in CBCT image contoured sets is 18.39 Gy, the median dose received by the parotids in CBCT is 20.03 Gy, and the maximum dose received by the parotids if the same initial plan is continued can increase to 29.58 Gy. These values were then used to calculate the p-value which was highly significant (p < 0.001).

V95% was defined as 95% of the planned target volume that received ≥ 95% of the prescribed dose. The mean PTV V95% for the initial plan and 95% for the plan performed in the replanning CBCT image were 97.43% and 97.09%, respectively. The median volumes of PTV receiving ≥ 95% of the prescribed dose when compared between the initial plan and the replanning CBCT image were 97.90% and 97.00%, respectively. The maximum PTV V95% for an initial plan is around 99.06 and 99.99 for replanning the CBCT image set.

When these variables were calculated for the p-value using the paired t-test, there were no significant p-values. Thus, we infer that although there were changes in the volume of the planned target and the parotid moving into the field, the planning target volume V 95% dose received by the initial plan and the replanning CBCT did not show much difference. Thus, the p-value is not statistically significant in this case which means that even though replanning is performed at 40 Gy, the dose to be received by the planned target will not be significantly reduced or affected. This means that the effect of adaptive radiotherapy plays a significant role in reducing normal tissue complications, especially the dose received by the parotids (which reciprocates in terms of the reduction of xerostomia in patients who had adaptive radiotherapy). The initial plan for the spinal cord had a mean dose of 32.32 Gy and the mean dose for the spinal cord in the replanning cone-beam CT image was approximately 10.94 Gy. Thus, the total point dose of the parotid gland was not more than 45 Gy in all patients included in this study.

CONCLUSION

Adaptive replanning is necessary for head and neck cancers at 40 Gy to evaluate the dose received by the tumour area, in contrast to the dose received by the organs at risk. Continuing radiotherapy without replanning leads to dosimetric errors in dose distribution to the planning target volume, which in turn leads to inappropriately high doses to the normal structures and leads to an increase in morbidity. In addition, in high-volume centres, cone-beam computed tomography provides an efficient option for assessing the tumour response along with dose comparison to both tumour areas and organs at risk. Replanning at 40 Gy considers the tumour regression, nutritional status of the patient, and body mass index, and hence helps in replanning the dose to the planning target volume, thereby improving the treatment response and reducing treatment-related morbidity, thereby resulting in improved quality of life.

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