

TIMING OF REPLANNING IN HEAD AND NECK CANCERS ON RADIATION BY IMRT AND ITS SIGNIFICANCE IN TUMOUR VOLUME AND CRITICAL STRUCTURE VOLUME AND DOSE

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ABSTRACT

BACKGROUND

Radiation to head and neck cancers by Intensity Modulated Radiotherapy (IMRT) is associated with high-dose conformity to target volume, which results in reduced dose to the critical normal tissues. Average duration of radiation will be 6 to 7 weeks. During the course of treatment, anatomical variations like loss of weight or tumour shrinkage may lead to interfractional variation. This variation might result in inadequate coverage of target volume or over dosage of critical structures. Adaptive radiotherapy using replanning in between treatment is one of the ways to reduce such uncertainty. In this study, timing of replanning was analysed with respect to tumour and critical structure (parotid), volume change and dose received by parotids.

The aim of the study is to determine the timing of replanning in head and neck cancer treated by IMRT and its significance to parotid volume and mean dose and tumour volume and Planned Target Volume (PTV).

MATERIALS AND METHODS

From October 2014 to January 2016, 40 patients of head and neck squamous cell carcinoma treated in our institution by IMRT were grouped into ARM1 (A1) replanning at 15 fractions and ARM2 (A2) replanning at 20 fractions of radiation. Paired t-test was applied to analyse the difference and level of significance between initial scan and repeat scan. The difference was considered significant, if p-value was less than 0.05.

RESULTS

In A1 group, volume comparison showed statistically significant difference in target volume- PTV 703.05 cm³ vs. 554.71 cm³ (p=0.0005), GTV T (tumour) 52.86 cm³ vs. 36.47 cm³ (p=0.0001), and GTV N (node) 106.28 cm³ vs. 62.95 cm³ (p=0.0124) and left parotid volume 22.97 cm³ vs. 17.61 cm³ (p=0.0001) and right parotid volume 21.02 cm³ vs. 17.27 cm³ (p=0.0000). Mean dose to left parotid 38.57 Gy vs. 37.92 Gy (p=0.6776), mean dose to right parotid 40.60 Gy vs. 41.49 Gy (p=0.5733). In A2 PTV (cm³) 751.03 vs. 645.98, p=0.0000; GTV T (cm³) 52.51 vs. 28.01, p=0.0005; GTV N (cm³) 44.38 vs. 23.03, p=0.0001; left parotid volume 23.04 cm³ vs. 15.94 cm³ (p=0.0000); and right parotid volume 25.21 cm³ vs. 16.22 cm³ (p=0.0000). Mean dose to left parotid 37.18 Gy vs. 35.86 Gy (p=0.5930) and mean dose to right parotid 34.89 Gy vs. 36.15 Gy (p=0.6558).

CONCLUSION

Both treatment arms showed significant difference in volume though did not have benefit in dose to critical structures. Concluding mid treatment replanning is beneficial in all cases of head and neck cancers treated by IMRT.

KEYWORDS

Adaptive Radiotherapy, Parotid Volume, Head and Neck Cancers, Radiation, IMRT.

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BACKGROUND

Intensity-Modulated Radiation Therapy (IMRT) in Head and Neck (H and N) cancer has interfractional variations that occur because of setup error and anatomical modifications. Multiple factors like shrinkage of primary tumour and nodal disease, alterations in normal tissues, weight loss and

resolution of postoperative soft tissue changes result in treatment response. It is recognised that the primary tumours can shrink volumetrically by up to 90% and parotid glands involute and shift medially by up to a centimetre during treatment course. Therefore, the accuracy of IMRT delivery for H and N cancer may be compromised during the treatment course.¹⁻⁵ Adaptive radiotherapy technique aims to customise each patient's treatment plan to patient-specific variation. In case of head and neck, most anatomic changes take place gradually over the first few weeks of treatment. Thus, there is no need for real-time intervention unless an acute, unforeseen event such as rapid disease progression occurs. Therefore, offline ART appears to be a more practical approach for head and neck cancers in majority cases.⁴ It helps in avoiding unintended toxicity to the normal tissues, while maintaining adequate coverage of

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tumour volumes by modifying the original plan according to the changes that have occurred during the course of RT.^{4,5} In the present study, timing of replanning and its relation to volume variations in tumour and parotid shrinkage was analysed.

MATERIALS AND METHODS

A hospital-based prospective trial enrolling 40 patients with histopathological-proven head and neck cancers receiving radical radiotherapy by IMRT from October 2014 to January 2016. The study was approved by the Hospital Ethics and Scientific Review Board. Patients were immobilised by a head rest and thermoplastic mask and underwent simulation CT scan with IV contrast with 3-mm slice thickness from base of skull to the upper mediastinum. Radiation was planned and delivered using IMRT with a prescription dose of 66-70 Gy to the gross primary tumour and involved lymph nodes, 60 Gy to high-risk nodal regions and the anatomical compartments around the gross tumour volumes and 50 Gy to low-risk nodal regions in 33-35 fractions treatment will be delivered once daily 5 fractions per week over 7 weeks. Concurrent chemotherapy using Cisplatin 40 mg/m² IV weekly once was administered.

Study Intervention- A repeat CT scan was taken for each patient in ARM1 after 15th fraction and ARM2 after 20th fractions. A new mask was made for immobilisation before getting a repeat CT scan in patients for whom the initial mould could not be fit properly as a result of weight loss and tumour shrinkage. The volumes drawn on coronal, axial and sagittal views of the repeated CT scans were fused with the primary CT used for planning and compared accordingly for analysis. New IMRT plans were generated and approved for each patient.

Statistics- Paired t-test was applied to analyse the difference and level of significance between initial scan and repeat scan. The difference was considered significant, if p value was less than 0.05.

RESULTS

Median age was 56 years (55 years - A1 and 62 years - A2). Sex wise distribution showed 32 (A1 - 15; A2 - 17) male and 8 (A2 - 5 and A2 - 3) female patients. Squamous cell carcinoma was seen in 32 patients and rest of them was with poorly differentiated or undifferentiated carcinoma. Subsite-wise distribution of head and neck cancer seen was 12 in oropharynx (30%), 10 in hypopharynx (25%), 8 in nasopharynx (20%), 5 in larynx (12%) and 5 in oral cavity (13%). Stage-IVA disease was seen in 18 (45%); stage-III in 12 (30%); stage-IVB in 9 (23%); and stage-I in 1 (2%) patient. Stage-III disease was seen in 50% of the patient in A1, whereas 60% of patients in A2 had stage IVA disease.

Results of comparison in ARM1 and ARM2 (initial, IMRT vs. repeat CT IMRT)- ARM1- Target volume- PTV (cm³) 703.05 vs. 554.71 and 297.18 vs. 204.64 with a Mean Standard Deviation (MSD) of 66.45 vs. 45.76 and significant p=0.0005. GTV T (tumour) (cm³) was 52.86 vs.36.47

and 31.07 vs. 25.04 with MSD of 6.94 vs. 5.60 with significant p value 0.0001. GTV N (node) (cm³) was 106.28 vs. 62.95 and 94.43 vs. 58.52 with MSD of 24.38 vs. 15.11 with p-value 0.0124. Left parotid volume (cm³) was 22.97 vs. 17.61 and 8.02 vs. 6.86 with MSD of 1.79 vs. 1.53 with p-value 0.0001. Right parotid volume (cm³) was 21.02 vs. 17.27 and 5.95 vs. 6.04 with MSD of 1.36 vs. 1.37 with p-value 0.0000. Mean dose (GY) delivered to left parotid was 38.57 vs. 37.92 and 8.67 vs. 9.52 with MSD of 2.04 vs. 2.22 with p-value 0.6776. Whereas, mean dose delivered to right parotid was 40.60 vs. 40.60 and 7.31 vs. 10.17 with MSD of 1.67 vs. 2.33 with p-value 0.5733.

ARM2- Target volume - PTV (cm³) 751.03 vs. 645.98 and 161.1 vs. 122.32 with a Mean Standard Deviation (MSD) of 36.03 vs. 27.35 with p=0.0000. GTV T (tumour) (cm³) was 52.51 vs. 28.01 and 39.06 vs. 20.42 with MSD of 8.73 vs. 4.56 with significant p value 0.0005. GTV N (node) (cm³) was 44.38 vs. 23.03 and 42.29 vs. 27.51 with MSD of 9.96 vs. 6.48 with p-value 0.0001. Left parotid volume (cm³) was 23.04 vs. 15.94 and 5.95 vs. 6.04 with MSD of 2.12 vs. 1.53 with p-value 0.0000. Right parotid volume (cm³) was 25.21 vs. 16.22 and 8.4 vs. 6.64 with MSD of 1.94 vs.1.52 with p-value 0.0000. Mean dose (GY) delivered to left parotid was 37.18 vs. 37.18 and 10.27 vs. 9.18 with MSD of 2.49 vs. 2.22 with p-value 0.5930. Whereas, mean dose delivered to right parotid was 34.89 vs. 36.15 and 9.76 vs. 9.28 with MSD of 2.60 vs. 2.48 with p-value 0, p=0.6558.

DISCUSSION

Adaptive radiotherapy is conceptually an attractive approach to compensate for tumour and normal tissue variations during treatment, but limited work exists currently to guide its clinical application in day-to-day practice. Little practical evidence exists regarding issues like the timing of rescan, the dose at which adaptive planning to be executed, the basis of patient selection for adaptive planning and the volumes and margins to be considered.

Volume Comparison- In literature, few studies have reported volumetric changes during adaptive planning. In a study by Barker et al,⁶ the median GTV decreased at a rate of 0.2 cc per day corresponding to 70% reduction on last day of RT. In this study, both primary tumour and involved nodes lost volume at approximately same rate of 1.6% per day. The same study showed that parotid glands decreased in volume (median, 0.19 cm³/d range, 0.04-0.84 cm³/d) and generally shifted medially (median, 3.1 mm; range, 0-9.9 mm) with time. This medial displacement of the parotid glands correlated highly with the weight loss that occurred during treatment. Vasquez Osorio et al⁷ looked at the 3D anatomical changes of tumours irradiated or spared parotids and submandibular glands by performing CT scan analysis at 0 and 46 Gy. They showed that the primary tumour volume shrunk by 25% ± 15% compared with its original volume. Regarding normal tissue changes, Lee et al⁸ acquired data using mega voltage CT imaging. Parotid volumes decreased with a median loss of 21.3% volume or 0.7% per day. Parotids migrated medially with a median

distance of 5.26 mm (0.00-16.35 mm) or 0.22 mm per day. Hansen et al⁹ performed a study on 13 head and neck cancer patients treated with IMRT. Planned CT scans were performed before treatment and after an average dose of 36 Gy. A mean reduction in the parotid volume of 21.5% and 15.6% was observed for the left and right gland, respectively. No changes were observed for the GTV. Vasquez Osorio et al⁷ looked at the 3D anatomical changes of tumours, irradiated or spared parotid and submandibular glands by performing CT scan analysis at 0 and 46Gy. Irradiated and spared parotid glands had a volume loss of $17\% \pm 7\%$ and $5\% \pm 4\%$, respectively.

Dose Comparison- Using daily MV imaging in 10 tomotherapy patients, Lee et al analysed changes in parotid gland dose using a deformable image registration method.⁸ They found that the daily parotid mean dose of the 10 patients differed from the plan dose by an average of 15%. Tamaki Nishi et al¹⁰ in a study proved that the volumes of primary tumours and parotid glands on CT-2 regressed significantly. Parotid glands shifted medially an average of 4.2 mm on CT-2. The mean doses of the parotid glands in the initial and transferred plans were 25.2 Gy and 30.5 Gy, respectively.

Timing of Replanning- In the past, studies have been done to find out the optimum timing of adaptive replanning. Wu et al¹¹ performed such a study where 11 patients underwent weekly helical CTs during routine IMRT. The authors reported that one adaptive replanning during midcourse improved parotid mean dose sparing by 3%, two replanning by 5% and six replanning by 6% assuming that adaptive replanning transpires one week prior to actual treatment delivery. If six weekly replans were used immediately, parotid dose sparing improved by 8%. Ahn et al¹² reported that 65% patients benefited from adaptive planning in terms of reduced dose to normal structures by using rescanning at 11, 22 and 33 fractions. Schwartz et al¹³ in their study concluded that ART can provide dosimetric benefit with only one or two mid-treatment replanning events and this seems a more practical and resource effective strategy.

In the present study, we see similar volume changes and dose comparison in parotid glands. Mean volume reduction of GTV T is 16.388 cm^3 (0.78 cm^3 per day) and 24.80 cm^3 (0.87 cm^3 day) corresponding to 1.47% per day and 1.6% per day in A1 and A2, respectively. Mean volume reduction of GTV N is 43.380 cm^3 (2.06 cm^3 per day) and 21.346 cm^3 (0.76 cm^3 per day) corresponding to 1.9% per day and 1.71% per day in A1 and A2, respectively. Significant difference in nodal volume was due to more N0 cases in A1 compared to A2. The rate of volume loss of left parotid per day is 0.25 cm^3 (1.11%) and 0.338 cm^3 (0.81%) in A1 and A2, respectively. The rate of volume loss of right parotid per day is 0.133 cm^3 (0.63%) and 0.32 cm^3 (1.27%) in A1 and A2, respectively.

The present study showed benefit with replanning of patients in both arms in terms of volume difference.

Between groups, there is no significant difference in terms of volume comparisons. Dosimetric comparisons between two plans did not show any difference mean doses to parotid.

Limitations of the Study- Small sample size, short follow-up to assess the outcome of replanning. Dosimetric comparison of repeat CT volume with respect to initial IMRT plan not addressed. This comparison will be necessary to indicate accurate dose received by the tumour and critical structure, if the replanning was not done. This will depict the tumour underdosing or critical structure overdosing. In this study, replanning done by inverse planning IMRT, but forward IMRT keeping the same beam configuration as the initial IMRT plan would have been the ideal plan to compare dose.

CONCLUSION

The initial and repeat CT scans done for planning showed statistically significant difference in tumour volumes and in parotids volume in both arms. No difference in the mean dose to parotids observed. Patients in all subgroup of head and neck cancers treated have benefit from mid treatment replanning. This benefit was more evident in patients with large nodal mass. Significant volume changes were noticed in patients with large tumour and nodal volume with replanning done in between treatment. No difference was seen between two arms.

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