Volumetric variations and the effects of these differences on dosimetry during the course of volumetric modulated arc therapy for head and neck cancer

S Ozdemir1, Y Coban1, A Bakır1, O Uzel1

Abstract

Introduction

To observe the changes in the patients’ anatomy and the effects of these differences on dose distribution throughout the treatment in order to design an optimal adaptive plan and to find the optimal time for replanning in head and neck cancer patients who receive primary radiotherapy or chemoradiotherapy.

Materials and Methods

Fifteen head and neck cancer patients were evaluated prospectively. VMAT plan with simultaneous integrated boost or sequential technique was performed. The last CBCT of the 3rd and 5th week were fusioned deformably with planning CT. Initial plans were adapted to these CBCT images. An adaptive plan was generated during the week when normal tissues overdosed more than 5% or the target volume underdosed more than 5%. The volumetric changes and dosimetric differences in target volumes, parotid glands and spinal cord were compared between planning CT and CBCT images. Also adaptive plan doses were compared with delivered doses in terms of target volumes, parotid glands and spinal cord.

Results

While there was no significance at the comparison of the volumes in GTV and PTV70 between the planning CT and 3rd week CBCT, it became significant at the 5th week. Primary and lymph node GTVs reduced by 44.8% and 70.9% respectively. Parotid glands and spinal cord doses increased in the 3rd week as well as; it rose a significant level for the ipsilateral parotid and spinal cord in the 5th week. Adaptive plan was needed in 10 patients. Adaptive plan provided a 1 Gy dose reduction in contralateral parotid glands, 1.4 Gy in ipsilateral parotid glands and 1 Gy in the spinal cord.

Conclusion

Significant changes were observed in the volume of target and parotid glands despite it not being reflected much in dosimetry. A new CT scan can be recommended to evaluate for an adaptive plan in 5th week in the absence of clinically usable online correction methods.

Introduction

During the utilization of IMRT, sharp dose decline may allow dose reduction to target volume and dose escalation to surrounding normal tissues1.2.3.4. Modifications of daily anatomy and changes in the shape and position of the target volume may cause significant differences between the planned and delivered dose. Therefore, adaptive radiotherapy (ART) requirement which means creation of a new plan during radiotherapy occurs. Head and neck cancers can benefit from ART because of weight loss, organ deformation, volume reduction, shrinkage of the tumour and/or involved lymph nodes depending on dose response in the course of the treatment.

This study aimed to observe the changes in the patients’ anatomy and the effects of these differences on dose distribution throughout the treatment in order to design an optimal adaptive plan in head and neck cancer patients who receive primary radiotherapy or chemoradiotherapy. In addition, to find the optimal time for an adaptive plan.

Materials and Methods

Istanbul University Faculty of Medicine Clinical Research Ethics Review Board approval was obtained before the study. This prospective study included 15 nonmetastatic head and neck cancer patients who received radical radiotherapy or chemoradiotherapy between January 2012 and September 2012. Inclusion and exclusion criteria are shown in Table 1. Pretreatment evaluation included medical history, physical examination, panendoscopy, complete blood count and serum chemistry panel. GFR was measured in patients who received chemoradiotherapy. All cases were asked to undergo PET-CT in treatment position with treatment mask and a contrast enhanced MRI of the head and neck. Patients were evaluated by a dentist, if there was a need for dental treatment, it was performed before radiotherapy.

Table 1: Inclusion / Exclusion criteria.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newly diagnosed</td>
<td>Radiotherapy and/or chemotherapy received previously</td>
</tr>
<tr>
<td>Between 18-70 years old</td>
<td>&lt; 18 years old</td>
</tr>
<tr>
<td>Patients with radiologically visible mass</td>
<td>Patients with severe malnutrition</td>
</tr>
<tr>
<td>Karnofsky Performance Scale (KPS) ≥70</td>
<td>KPS &lt;70</td>
</tr>
<tr>
<td>T1 ve T2 glottic tumor</td>
<td>Patients with recurrence, metastasis</td>
</tr>
</tbody>
</table>

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Competing interests: None declared.

All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript. All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

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Patient immobilization

Immobilization of patients was provided with a thermoplastic head and neck mask. An appropriate pillow was used to support the patients’ neck during the treatment.

Planning CT

Imaging was performed from the top of the head to the lower part of the sternoclavicular joint with 2.5 mm sliced images.

Contouring

PET-CT and MRI images were fusioned with planning CT for all patients. Target volumes and critical organs were delineated on 2.5 mm sliced planning CT according to RTOG atlas by a single physician. The gross tumour volume (GTV70) was defined as primary tumour and involved lymph nodes considering physical examination, endoscopic findings, CT, PET-CT, and magnetic resonance imaging (MRI). The clinical target volumes (CTVs) were created as; CTV70: GTV+ 5mm margin, CTV60: high risk area and GTV54: low risk area. Planning target volumes (PTV) was used to support the thermoplastic head and neck mask. An appropriate pillow was used to support the patients’ neck during the treatment.


<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Localization</th>
<th>Stage</th>
<th>Concurrent Chemotherapy</th>
<th>Weight Loss (%)</th>
<th>Adaptive plan</th>
<th>Adaptive fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>63</td>
<td>H</td>
<td>4a</td>
<td>+</td>
<td>10</td>
<td>+</td>
<td>23</td>
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<tr>
<td>2</td>
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<td>62</td>
<td>B.T</td>
<td>4a</td>
<td>+</td>
<td>8.2</td>
<td>+</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>60</td>
<td>B.T</td>
<td>4a</td>
<td>+</td>
<td>12.5</td>
<td>+</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>67</td>
<td>H</td>
<td>4a</td>
<td>+</td>
<td>9.6</td>
<td>+</td>
<td>25</td>
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<tr>
<td>5</td>
<td>M</td>
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<td>N</td>
<td>3</td>
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<td>+</td>
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<td>M</td>
<td>50</td>
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<td>+</td>
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</tbody>
</table>

Figure 1: The change of the GTV volume during the treatment course for patient 10 (fusion of adaptive CT and planning CT).

Planning

All of the treatments were planned with the Eclipse (ver. 8.6) treatment planning system by using VMAT plans. IMRT was administered using the simultaneous integrated boost (SIB) technique in 14 patients. The doses to the planning target volumes of the primary tumour and involved lymph nodes (PTV70), high risk (PTV60), and low risk (PTV54) lymph node regions were 70 Gy, 60 Gy, and 54 Gy delivered simultaneously over 33 fractions for 11 patients. PTV 70 and PTV 54 volume have been identified for 3 other patients with the SIB technique over 33 fractions. One patient was treated sequentially; 70 Gy in 35 fractions, to gross tumour and lymphadenopathy, and 50 Gy in 25 fractions to electively irradiated neck nodes.

Treatment

Treatment was implemented with Varian DHX OBI linear accelerator. Patients were treated with IGRT and treatment positions were confirmed by daily kV-CBCT imaging (Varian On-Board Imaging version 1.5, Varian Medical Systems, Palo Alto, CA) according to the clinical protocol.

Follow up during the treatment

Weight of the patients was measured and recorded per week throughout the treatment. Oral nutritional support was provided to patients. Supportive care was applied for acute side effects.

Plan adaptation

The last CBCT of the 3rd and 5th week were fusioned deformably with planning CT in the Velocity AI (version 2.8.1) device. Initial plans were adapted to these CBCT images. An adaptive plan was generated during the week when normal tissues overdosed more than 5% or the target volume underdosed more than 5%. The volumetric changes and dosimetric differences in target volume, parotid glands and spinal cord were compared between planning CT and CBCT images. Also adaptive plan doses...
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## Discussion

In the treatment of head and neck cancer, treatment planning and implementation of radiotherapy must be optimal due to the adjacent important structures such as the spinal cord, eyes, optic nerve, optic chiasm, brain stem, temporomandibular joint, salivary glands, thyroid gland, pituitary gland, larynx, oral and oropharyngeal mucosa in terms of late morbidity. Weight loss, tumour shrinkage, deformation and modification of shape in normal tissues may be observed during radiotherapy. These changes are dose-dependent and specific to the patient. And they may lead to clinically significant changes in dosimetry. Thus, 'Image Guided Radiotherapy' (IGRT) methods were developed which evaluated the accuracy of radiotherapy with 2 or 3-dimensional imaging during treatment. However, IGRT do not include treatment planning and it is not capable of correcting dosimetric errors and potential changes in delivered dose. The aim of ART is to equalize planned dose distribution with delivered dose distribution, by measuring changes during treatment.

Barker and colleagues examined GTV changes in head and neck cancer patients treated with IMRT. GTV decreased median 0.2 cc (0.01-1.95 cc) per day and the last day of treatment median reduction was 70% (10% - 92%). Castadot and colleagues reported significant volumetric and positional changes in 10 locally advanced pharyngolaryngeal cancer patients treated with concurrent chemoradiotherapy. They have detected 3.2% and 2.2% average daily reduction in primary tumour volume and in nodal GTV respectively. In our study, average 16.87 cc (44.5%) reduction in GTV was observed between planning CT, adaptive plan in terms of dose distribution. However, no increased 61% and 65% of patients benefited from homogenity increased from CT1 to CT4. PTV coverage was found between second and 4th week. Ahn et al. planned the first prospective adaptive plan in head and neck cancer patients. They generated a new plan after 11, 22 and 33 fractions to 23 CT and adaptive CT. In the first year, salivary secretion will be recovered and xerostomia will be prevented. Minimum parotid gland dysfunction was seen at doses less than 10-15 Gy. Hypofunction was seen dramatically after 40 Gy and increased at 20 to 40 Gy gradually. In the first year, salivary secretion has been reduced by 25% and 15% after an average of 35 Gy and 20-Gy parotid gland irradiation respectively. In the PARSPORT study which was a multicentre phase 3 randomised studies with locally advanced cancers of the oropharynx and hypopharynx; conventional RT was compared with IMRT. IMRT reduced the ratio of ≥ grade 2 xerostomia (p < 0.01). Average contralateral parotid gland doses (25.4 Gy in IMRT and 60.0 Gy in conventional RT group) were found to be consistent in the reduction of salivary secretion. Toledeno et al. (2004-03 GORTEC) indicated that, the rate of grade ≥ 2 xerostomia increased by 3% and 7% per 1 Gy if the parotid gland mean dose exceeded 28 Gy and 33 Gy respectively. All of these results showed that; 1 Gy dose fall off on parotid gland tolerance dose; may be clinically effective on xerostomia. In a study, which was included in 11 head and neck cancer patients treated with IMRT, a significant enhancement was
observed in the parotid gland doses without an adaptive plan. The authors stated that, 3% reduction of the parotid gland dose with an adaptive plan, 5% reduction with two plans and 8% reduction with six plans25.

O’Daniel et al. investigated the differences between the planned and delivered doses in the parotid gland and target volume in head and neck cancer patients treated with IMRT. IMRT plan was calculated on the repeated CT images. Parotid gland doses were found 5-7 Gy higher in 45% of patients. Parotid gland doses fell (median 2 Gy) in 91% of patients with IGRT. The delivered dose to the parotid gland was higher than the planned dose due to the displacement and contraction of parotid volume26. Lee et al. found that, daily parotid gland average dose was 15% different from the original plan, in patients performed a deformable fusion13. They observed an escalation of more than 102% per parotid gland dose in 3 of 10 patients at the end of the treatment. A prospective study from M.D. Anderson Cancer Center with locally advanced cancers of the oropharynx, a dose reduction of 0.6 Gy was observed in the contralateral parotid gland and 1.3 Gy in the ipsilateral parotid gland, in the IGRT group27. In the current study, while delivered doses to the ipsilateral and contralateral parotid glands were increased 12.6 Gy and 3.6 Gy, this difference decreased 11.2 Gy and 2.6 Gy thus with an adaptive plan. Therefore 1.4 Gy and 1 Gy dose reduction were found respectively. Also, an escalation of 1.4 Gy was observed in the ipsilateral parotid gland and 2.9 Gy in the contralateral parotid gland dose in the 3rd week. It may be imported for the function of the parotid glands. And when we consider the spinal cord, 1 Gy dose reduction was provided by an adaptive plan.

Weight loss has been reported in most of the patients during treatment10. Median 7.1% (+5.2%, -13.0%) weight loss was observed during treatment in a Barker and colleagues study10. It has been suggested that reduction in body contour was associated with weight loss. However we had a deficiency in our study. We could not compare the group of patients who had an adaptive plan and who did not, due to insufficient number of patients. Therefore we could not show an exact association between weight loss and requirement of an adaptive process.

Conclusion
Significant changes were observed in the volume of target and parotid gland despite it’s not reflected much in dosimetry. Adaptive radiotherapy may be helpful in improving the dose to the parotid glands and spinal cord. A new CT scan can be recommended to evaluate for an adaptive plan in the 5th week in the absence of clinically usable online correction methods.

References


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