Volumetric and dosimetric changes to salivary glands during radiotherapy for head and neck cancer

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To the Editor,

Intensity modulated radiotherapy (IMRT) has become the standard of care in treating head and neck (HN) cancers because of its ability to deliver a highly conformal dose to a well defined target volume and with a rapid dose gradient, allowing relative dose sparing of critical structures [1]. The delivery of IMRT relies on effective immobilization devices and the main factor contributing to the interfractional variability is treatment-related volume changes. The reasons for this are multifactorial and include tumor shrinkage, weight loss and volumetric and positional changes in organs at risk (OARs). Previous studies have documented shrinkage of the parotid gland (PG) with medial displacement, and associated increase in mean dose. Hansen et al. demonstrated a mean reduction in PG volume by 15–21.5% [2]. Castadot et al. reported the mean shrinkage of the PG was 0.9–1.0% per day, with the PG moving medially by a mean distance of 3.4 mm [3]. These minor shifts can have significant dosimetric effects as shown by Wu et al. with a mean increase in the PG dose by 10% [4]. A single set of planning data obtained prior to commencing RT does not account for these dynamic treatment-related anatomical changes which may be further contributing to treatment-related toxicity and negate the benefits of IMRT.

The purpose of this study was to document volumetric and positional changes in organs at risk during IMRT and to determine whether these anatomical changes affect the cumulative dose to these structures. We also aim to document when these changes are most likely to occur and determine the optimal time for a replan.

Material and methods

Twenty patients who underwent radical comprehensive IMRT for locally advanced HN cancer between 2013 and 2014 were identified. Prescribed dose was 66–70 Gy/33–35#. Contrast-enhanced computed tomography (CT) scans were performed at 2.5 mm intervals. Gross tumor volume (GTV) was based on visible tumor and information from diagnostic imaging. Clinical target volume (CTV) was obtained with an 8–10 mm expansion to the GTV. Planning target volume (PTV) was obtained with a 3 mm expansion to the CTV. The OARs were manually contoured on an initial planning CT (pCT) and a subsequent weekly cone beam CT (CBCT) by a single radiation oncologist (RO). A total of 151 scans were contoured. OARs included the pharyngeal constrictors (SPC, MPC, IFC), submandibular glands (SMG), and PG. Volume of the OAR was determined on each scan (ml). GTV was assessed on pCT and on prospective scan. Positional change of the OAR was calculated using the centre of mass (COM) of C2 vertebra as a reference point. The average of the x, y, and z coordinates for each OAR was calculated.

Results

A total of 20 patients were enrolled. The majority were male, with a median age of 61years (Supplementary Table I, available online at http://www.informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068951). The mean weight loss was -4.7% (2.8—15.5%) despite 17/20 patients having a prophylactic feeding tube. There was no relationship found between weight loss and volume or positional change in OAR. The mean

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reduction in GTV was -9% (38—54%). There was no relationship between initial GTV and rate of GTV reduction, or volumetric or positional changes in OAR. Volume change to most OAR was not markedly different to that on the initial pCT scan, except for the salivary structures. The mean PG volume, at initial RT, was 32.1 ml, and 23.6 ml at the end of RT. The mean reduction in PG volume during RT was 24.4% (0–53.6%). This reduction was seen in 80% of the ipsilateral, and 90% of the contralateral PG. The volume reduction was most pronounced in the contralateral PG (27% vs. 22%) (Supplementary Tables II–III, available online at http://www.informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068951). The mean parotid volume loss was 4.9% per week (0–10.5%). Figure 1 illustrates the mean change in PG volume against treatment fraction. Volume loss was most pronounced from fraction 5–15. PG shifted medially by a mean distance of 3.4 mm, posteriorly by 2.7 mm and superiorly by 1 mm.

These volumetric and positional changes corresponded to an increase in dose to the PG (Supplementary Figure 1, available online at http://www.informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068951). The mean increase in PG dose was 19.5% (-6.7–61%) and was more pronounced in the contralateral PG (23.4% vs. 15.7%). Only four patients had the ipsilateral PG initially planned to a mean of 24 Gy, with the remaining 16 patients (80%), the ipsilateral PG dose was high (ranging from 30 to 63 Gy) due to PTV coverage. However, on the contralateral side, 18 patients had an initial PG dose to 24 Gy or less. At completion of RT, for 12 of these patients (67%) the dose to the contralateral PG had increased to 27–50 Gy (mean dose 33 Gy).

Mean volume of the SMG was 8.8 ml initially, and 7.1 ml at completion of treatment, with a mean reduction in volume of 19.3%. However, this was not associated with a change in cumulative dose to the SMG (mean initial dose of 65.5 Gy, and 65.4 Gy cumulative dose).

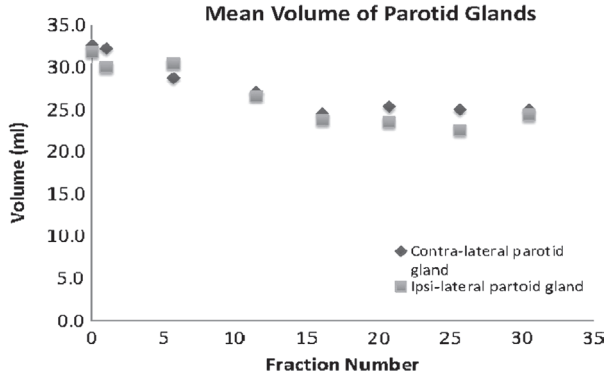

Figure 1. Mean PG volume against treatment fraction.

Discussion

Daily image guidance used to verify patient set-up based on bony landmarks is effective but does not take into account anatomical changes that occur during RT. These anatomical changes can have potentially significant dosimetric and clinical implications by underdosing the tumor volumes, or overdosing OAR [2,5].

In our study, we aimed to quantify the volumetric and dosimetric changes in OAR during a course of RT for HN cancer. The only marked changes observed were in the PG. There was a mean reduction in the PG volume of 24.4%. The PG moved medially during RT by a mean distance of 3.4 mm. These changes corresponded to a mean increase in PG dose of 19.5%. These findings were in keeping with previously published data [2,4–7]. Elstrom et al. demonstrated a reduction in the PG volume by 30% by the end of RT, with a corresponding daily mean dose increase to 115% during the last half of RT [8]. O'Daniel et al. reported the dose to the PG increased by 5–7 Gy in 45% of patients [6]. These changes were most pronounced in the ipsilateral PG. Our results were conflicting to these findings. We demonstrated the volumetric changes to be most pronounced in the contralateral PG (27% vs. 22%), and similarly the dosimetric changes to be more pronounced in the contralateral PG (23.4% vs. 15.7%. This is of particular significance as a number of patients with advanced HN cancer will have the initial planned dose to the ipsialteral PG higher than ideal due to optimizing PTV coverage, as the PG lies in close proximity. It is therefore important to keep the contralateral PG dose as low as possible in order to spare the toxicity of xerostomia. Beetz et al. recently published data on normal tissue complication probability (NTCP) for patient-related xerostomia using the QUANTEC criteria and showed that the contralateral PG was the most significant OAR for patient-related xerostomia at six months [9]. Lee et al. also published data based on the Lyman-Kutcher-Burman (LKB) model to derive NTCP for xerostomia based on scintigraphy and quality of life (QOL) questionnaires (QLQ-HN35 and QLQ-C30). They reported that at the three- and 12-month time point, the dose to the contralateral PG significantly correlated with xerostomia. Severe xerostomia could be avoided if at least one PG received a mean dose of ≤ 20 Gy, or if both PG received a dose of ≤ 25 Gy [10]. These results support the importance of the changes observed in the contralateral PG, and may be an indicator for a replan, or adapting treatment

to maintain these tolerances in order to reduce the incidence of xerostomia. The PG volume reduction was observed by fraction 15, and then stabilized at which point there was a corresponding increase in cumulative dose to the PG by fraction 20 which suggests the ideal time to replan is during this period.

Declaration of interest: The 5authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Supplementary material available online

Supplementary Figure 1 and Table I to III online at: http://informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068951