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THE EFFECT OF SIGNIFICANT TUMOR REDUCTION ON THE DOSE DISTRIBUTION IN INTENSITY MODULATED RADIATION THERAPY FOR HEAD-AND-NECK CANCER: A CASE STUDY

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Abstract

We present a unique case in which a patient with significant tissue loss was monitored for dosimetric changes using weekly cone beam computed tomography (CBCT) scans. A previously treated nasopharynx patient presented with a large, exophytic, recurrent left neck mass. The patient underwent re-irradiation to 70 Gy using intensity modulated radiation therapy (IMRT) with shielding blocks over the spinal cord and brain stem. Weekly CBCT scans were acquired during treatment. Target contours and treatment fields were then transferred from the original treatment planning computed tomography (CT) to the CBCT scans and dose calculations were performed on all CBCT scans and compared to the planning doses. In addition, a “research” treatment plan was created that assumed the patient had not been previously treated, and the above analysis was repeated. Finally, to remove the effects of setup error, the outer contours of 2 CBCT scans with significant tumor reductions were transferred to the planning scan and dose in the planning scan was recalculated. Planning treatment volume (PTV) decreased 45% during treatment. Spinal cord D05 differed from the planned value by $3.5 \pm 9.8\%$ (average + standard deviation). Mean dose to the oral cavity and D05 of the mandible differed from the planned value by $0.9 \pm 2.1\%$ and $0.6 \pm 1.5\%$, respectively. Results for the research plan were comparable. Target coverage did not change appreciably ($-0.2 \pm 2.5\%$). When the planning scan was recalculated with the reduced outer contour from the CBCT, spinal cord D05 decreased slightly due to the reduction in scattered dose. Weekly imaging provided us the unique opportunity to use different methods to examine the dosimetric effects of an unusually large loss of tissue. We did not see that tissue loss alone resulted in a significant effect on the dose delivered to the spinal cord for this case, as most fluctuation was due to setup error. In the IGRT era, delivered dose distributions can be more readily determined during treatment, and this information can be useful in deciding whether replanning is necessary.

Keywords

IMRT; IGRT; head and neck; planning

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INTRODUCTION

The treatment of head-and-neck cancer with external beam radiation therapy presents a number of challenges to the radiation oncologist and medical physicist. The intermingling of tumor volume requiring treatment with the healthy nearby critical structures, *i.e.*, spinal cord and salivary glands, requires a balance between delivering enough radiation to kill the tumor while sparing the critical structures.

At our institution, head-and-neck cancers are routinely treated with intensity modulated radiation therapy (IMRT), which sculpts the dose distributions to deliver prescription dose to the target while minimizing the dose to surrounding healthy tissues.^{1–3} The use of IMRT leads to steep dose gradients, especially around the spinal cord. Therefore, it is crucial that the treatment of head-and-neck cancer patients incur the minimally achievable variation between what is intended and what is delivered. There are 2 major sources of variation between the treatment plan and what actually occurs during treatment; patient setup error and anatomical variation. Setup error refers to the day-to-day variation in head-and-neck position of the patient compared to the position at simulation on which the plan is based. We use a special custom mask for patient immobilization, which extends from the top of the head to the shoulders (Orfit Industries, Belgium). The setup error associated with this mask has been previously studied.⁴ Anatomical variations refer not only to organ motion but also to tumor reduction.

Changes in a patient's anatomy during a treatment course can potentially alter the dose distribution originally planned. Such changes may lead to increased doses to the healthy tissues and increased risk of complications. The study by Barker *et al.* of 14 patients irradiated for head-and-neck cancers with a maximal diameter of 4 cm or larger, reported a median gross tumor volume (GTV) decrease of 69.5% and a median displacement in the center of mass of 3 mm.⁵ Parotid gland volumes decreased at a median rate of 0.19 cm³/day and shifted medially in correlation with weight loss.⁵ A recent paper by Kuo *et al.* reported the effects of regression of enlarged neck lymph nodes on parotid dose in IMRT head-and-neck radiotherapy. They found that node enlargement pushed the parotid glands distally, and their regression during treatment caused the parotids to move medially, often into a high-dose region.⁶ Other studies have reported similar findings.^{7–16}

Image-guided radiotherapy (IGRT) is a technology in which advanced imaging techniques may be used during a treatment session to fine-tune the daily setup of the patient, as well as visualize soft tissue structures. A common practice in radiotherapy is to use orthogonal megavoltage (MV) beams to check the setup weekly. This allows the visualization of most bony structures (with low contrast), but seldom of soft tissues. The incorporation of kilovoltage (kV) imaging devices in the treatment gantry enables the acquisition of the so-called cone-beam CT (CBCT) images with the patient setup on the patient support assembly and during a treatment session. This method involves simultaneous kV projection imaging and gantry rotation (usually 360°), followed by image reconstruction to produce a 3-dimensional image of the patient in the treatment position. This is a valuable tool for patient setup verification where visualization of soft tissue is essential, such as for high-dose, single fraction radiotherapy.

Periodic CBCT imaging is ideal for the study of anatomical changes in the head and neck during treatment. The low dose delivered per scan allows for more frequent imaging without excessive radiation dose to the patient. These data can then be used to determine delivered dose and possibly alert the clinician that replanning may be necessary.

This case study describes the analysis of weekly CBCT scans for a head-and-neck patient who had an unusually large reduction in tumor volume during treatment. Emphasis is on the effect on the dose to the spinal cord, which is the most important of the critical structures considered in head-and-neck radiotherapy. We use this unique case to illustrate a process of obtaining

dosimetric information from IGRT data, as well as illustrate some of the issues that may be relevant when considering replanning, such as the separation of the effects of setup error from the effects of missing tissue.

METHODS AND MATERIALS

A patient with a large exophytic recurrent nasopharyngeal mass was presented to our clinic for treatment with IMRT. The patient was fitted with a custom immobilization mask and a treatment planning CT scan was acquired on a Philips PQ-5000 scanner (Philips Medical Systems, Andover, MA). Target and critical structures were delineated by the physician, and a dose of 70 Gy was prescribed to the recurrent tumor with a 5-mm margin to allow for setup variation and organ motion. Because this patient had received prior radiation therapy, cerrobend shielding blocks were fabricated to block irradiation of the spinal canal plus a 5-mm margin for all but one beam, which could not fit the block due to collision issues. For this beam, the multileaf collimator (MLC) leaves covered the cord and brain stem. These 2 structures therefore primarily received dose from scattered radiation. Rapid shrinkage of the tumor necessitated the creation of a new mask approximately halfway through the treatment course. A new treatment plan was created as a result.

The patient was imaged weekly with CBCT and the acquired CBCT data sets were analyzed off-line to monitor tumor reduction and assess the effect of tumor reduction on dose delivered. A total of 8 CBCT scans were acquired using the Varian On-Board Imager (OBI, Varian Medical Systems, Palo Alto, CA). Each CBCT scan was first registered with the treatment planning CT scan using bony anatomy. The physician-drawn contours of the target volume were then transferred from the planning CT to the CBCT. There was a small nodal PTV measuring approximately 7 cc in volume inferior to the main PTV. This volume was beyond the extent of the CBCT and was not included in this analysis. Critical structures, which consisted of the spinal cord, brain stem, oral cavity, and mandible, were drawn on the CBCT by a physicist. In this case, as with all typical head-and-neck cases at our institution, the spinal cord contours included the entire spinal canal and not just the visible cord. The parotid glands were not spared for this treatment because the ipsilateral gland was involved and had to be treated, while the contralateral gland was sufficiently far from the treatment area that dose to this was not of concern. Optical structures and brachial plexus were not monitored for this case because of the limited superior-inferior extent of the CBCT scan (approximately 14 cm). The beams from the treatment plan were then transferred to the CBCT. The treatment isocenter was located by comparing digitally reconstructed radiographs (DRRs) created from the CBCT scan to 2D OBI kV images taken that day. Once the beams and contours were transferred to the CBCT scan, a dose calculation was performed. The dose received by the tumor and critical structures from the CBCT dose calculation was compared to the planning scans. CBCT scans acquired during the first phase of treatment were compared to the first planning scan and CBCT scans acquired during the second half of treatment with the new mask were compared to the second planning scan. For structures with maximum dose constraints such as the spinal cord and the brain stem, D05, or dose to 5% of the volume was reported instead of maximum dose because maximum dose refers to a single point and tends to fluctuate, especially for the spinal cord. The maximum dose was given for the spinal cord for comparison purposes. The accuracy of CT number to electron density conversion for CBCT scans is still under study.^{17,18} Therefore, no inhomogeneity corrections were made for our CBCT calculations. The effect on calculated dose is small (on the order of 5%) for this case. For the purposes of consistency, the original treatment plan was recalculated without inhomogeneity corrections for comparison. PTV contours were not modified after transfer from the planning scan to the CBCT; however, the portion of these contours outside of the patient's skin were excluded when calculating the dose-volume histogram (DVH). Therefore, even though the contours of the PTV were not changed, the PTV volume decreased from scan to scan due to the shrinking outer contour.

Research plan

Most IMRT head-and-neck patients are treated without spinal cord blocks because IMRT can adequately lower the dose in that region. Because this case is not typical in that respect, we created an alternate “research” treatment plan for this patient without spinal cord blocks, which assumed that the patient had no previous treatments and repeated the above analysis for this alternate plan.

Effects on dose distribution with setup error removed

The analysis described above included the effects of setup error and deformation as well as missing tissue. To examine changes due to missing tissue alone without the presence of setup error, we transferred the outer contours of the final CBCT scan of the first phase to the first planning scan and the final CBCT scan of the second phase to the second planning scan, after which we recalculated the planning scan dose distribution for each. We then compared this recalculated distribution to the original planning scan distribution, thereby eliminating the effects of setup error and considering tissue loss alone.

RESULTS

As shown in Fig. 1, the volume of the PTV changed from 606 to 336 cm³ over treatment, a decrease of 45%. This is solely due to the reduction of the outer contour of the patient, shown in Fig. 2.

Results are summarized in Table 1, which shows doses of interest in cGy (normalized to 70-Gy prescription dose or 35 fractions), as well as the average difference between the dose from the CBCT scans and dose from the treatment plan in percent. Results are given for both the clinical plan and the research plan. For the clinical plan, dose to 5% (D05) of the spinal cord from the CBCT scans differed from the planned value (approximately 520 cGy) by $3.5 \pm 9.8\%$ (average $\pm$ standard deviation). The difference between D05 of the spinal cord from the CBCT scan vs. the treatment plan is plotted in Fig. 3.

For the clinical plan, in which blocks were used over the spinal cord, the maximum cord dose measured from the CBCT scans was on the average $39 \pm 40\%$ higher than the treatment plan dose (approximately 712 cGy for phase 1 and 806 cGy for phase 2). This reflects the changing proximity of the spinal cord contours to the block edge, outside of which is the 70-Gy PTV. Variation of the maximum cord dose was much smaller in the research plan ($1.2 \pm 5.4\%$), in which the maximum planned cord dose was much higher (4320 phase 1, 3663 phase 2, from Table 1) and, consequently, the dose gradient in the region of the spinal cord was much less steep.

D05 of the brainstem was, on the average, significantly lower than the planned value ($-10.9 \pm 3.4\%$). The brain stem was at the superior edge of the field and behind shielding blocks, as was the spinal cord. The lower brain stem dose may be due to the neck being slightly overextended during the treatment, as illustrated in Fig. 4. For the 8 days on which CBCT scans were taken, the head was found to be overextended by an average of 2.6 ± 1.2 degrees according to measurements taken on the sagittal 2D OBI images. This tended to displace the brain stem posteriorly relative to the treatment field.

Mean dose to the oral cavity differed by $0.9 \pm 2.1\%$ relative to the planned value on the average and D05 of the mandible differed by $0.6 \pm 1.5\%$. In addition, D05 of the mandible increased linearly an average of $0.6\%/week$ during the first half of treatment ($R^2 = 0.985$) and $1.3\%/week$ during the second half ($R^2 = 0.976$), as shown in Fig. 5.

Target coverage, measured by dose to 95% of the target volume (D95) in the CBCT scans, differed by an average of $-0.2 \pm 2.5\%$ relative to the planned value. D05 of the target differed by $0.6 \pm 0.8\%$ from the planned value. In addition, the D05 of the target volume increased linearly the first half of treatment by $0.7\%/week$ ($R^2 = 0.982$). A weak correlation was seen during the second half of treatment ($R^2 = 0.339$), with a change of $0.2\%/week$, as shown in Fig. 6. The minimum dose to the PTV given by Table 1 changed more dramatically in the clinical plan vs. the research plan due to the interaction of the PTV contours with the block.

When the outer contours from 2 CBCT scans were transferred to their respective planning scans (either phase 1 or phase 2) and recalculated, the dose to the spinal cord *decreased* by 3.4% for the first phase of treatment and by 4.6% for the second phase, even though there was less tissue for the calculation due to the smaller outer contour. This is explained by the fact that the blocked spinal cord primarily received scatter dose (in addition to approximately 4% transmission) and when tissue is removed, there is less scatter. When the same exercise was repeated with the alternate research treatment plan, the spinal cord dose increased by 0.1% for the first half of treatment and 0.6% for the second half. This illustrates that in the absence of setup error, the effect of lost tissue on the spinal cord dose was not large for this case, even given the large volume of missing tissue.

DISCUSSION

The increasing conformality of the dose distribution associated with IMRT of the head and neck brings with it a demand for a more precise setup. The use of IGRT is therefore beneficial in cases like these both as a setup tool and as a way of monitoring the progress of the treatment. Our institution routinely uses 2D IGRT in head-and-neck cases that have received prior radiation to the same area. In this case, it was further decided to use CBCT to monitor the effects of tumor reduction during the treatment. This case was exceptional in that a very significant tumor reduction was observed. It is therefore an ideal case in which to pose the question of whether replanning is necessary, and why.

Repeated cone beam CT studies of this head-and-neck patient with an unusually large tumor reduction have shown a larger fluctuation in spinal cord dose in this case than for other structures. Because the spinal cord region is blocked and the margin between the block edge and the spinal cord contours is 5 mm, this structure sits close to a large dose gradient. One would expect the dose to fluctuate as the daily setup is varied. This can come about due to slight changes in neck flexion, which cannot be corrected by simply translating the patient, but require setting up the patient again. We have shown that when the setup is “perfect,” *i.e.*, when only the outer contour is modified, the effect of lost tissue on the spinal cord dose was small for this isolated case. If the cord is blocked and receives primarily scatter dose, the calculated dose can decrease.

The dose to structures close to the skin such as the target, mandible, and oral cavity did increase for this patient. High mandibular dose can lead to osteoradionecrosis; therefore, the clinician will need to decide the course of action should the mandibular dose increase beyond some acceptable tolerance. Typical tolerance for the mandible at our institution is a maximum dose of 70 Gy except for portions within the high-dose PTV, in which case, an attempt is made to avoid “hot spots.”

Given the availability of anatomical information during treatment, the question arises as to whether this will lead to more replanning for these patients. Generation of typical IMRT plans for the head and neck involve a considerable amount of time for the physician and treatment planning physicist due to the copious contouring required, the complex optimization involving many structures, and the patient-specific QA, *i.e.*, monitor unit checking, any necessary

measurements, exporting to the record-and-verify system, etc. Until the planning process is more streamlined, it may not be practical to replan patients unless a compelling need arises. The fluctuation in spinal cord dose seen for this patient represents an issue with the setup more than an anatomical issue, and should be addressed as a random setup deviation. Replanning this patient without addressing the setup fluctuations would not, on the average, mitigate these problems because they were not systematic in this case. We did replan this patient approximately halfway through treatment, but due to setup issues and not changes in the dose distribution. Had the immobilization remained firm, we would have continued treatment with the original plan.

A case in which anatomical variation may lead to replanning is one where an internal structure that was displaced by tumor moves into the high-dose region as the tumor regresses. One patient at our institution presented with such a tumor quite visibly impinging on the brain stem (Fig. 7). As the treatment progressed, there was concern that that tumor reduction would relax the position of the brain stem, such that it moved into the high-dose region formerly occupied by the tumor. Unfortunately, this patient discontinued treatment shortly after beginning and went to hospice. Until that time, no visible change in brain stem position had occurred. Another case is one in which the physician decides to draw a smaller PTV, thereby altering the geometric relationship between the PTV and the critical structures. In our case study, the only changes to the PTV studied were due to tissue loss and internal contours were not modified.

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Fig. 1. Target volume as a function of time since simulation, as measured from the 8 CBCT scans and the 2 simulation scans. Treatment began on day 10.

Fig. 2.
Corresponding axial CT slices from the beginning and the end of treatment. The original target volume is delineated by the yellow contour.

Fig. 3. Variation of spinal cord D05 between CBCT and plan for the clinical plan and research plan. The curves are separated at approximately 40 days since the patient was replanned at that time due to a loose mask.

Fig. 4. Comparison of a right lateral beam's-eye view as seen in the planning scan and a CBCT scan. The C1–C2 region was used for the setup registration and matches well; however, it can be seen that the head rotation is slightly different in the 2 images. Superiorly, the brain stem appears farther from the field edge in the CBCT scan. Inferiorly, the cord is closer to the field edge in the CBCT scan.

Fig. 5.
Variation of D05 to the mandible vs. time for the clinical plan and research plan.

Fig. 6.
Variation of D05 of the target volume vs. time for the clinical plan and research plan.

Fig. 7.
A patient in whom tumor regression may potentially move the brain stem into the high-dose region. The gross tumor is delineated by the blue contour and the brain stem is delineated by the yellow contour.

Table 1

Summary of results for the clinical plan, which had shielding blocks over the spinal cord and brainstem, and the research plan, in which the spinal cord and brainstem received full dose

Quantity	Clinical Plan		Research Plan	
	Planned Value (cGy)	Avg Δ (CBCT) $\pm$ SD (%)	Planned Value (cGy)	Avg Δ (CBCT) $\pm$ SD (%)
	Phase 1/Phase 2	Both Phases	Phase 1/Phase 2	Both Phases
Spinal Cord D05	525/517	3.5 $\pm$ 9.8	3836/2329	4.5 $\pm$ 9.1
Spinal Cord D _{max}	712/806	39.4 $\pm$ 40.1	4320/3663	1.2 $\pm$ 5.4
Brainstem D05	543/517	-10.9 $\pm$ 3.4	3919/3689	-11.2 $\pm$ 5.2
Oral Cavity Mean	3613/4193	0.9 $\pm$ 2.1	3596/4083	2.3 $\pm$ 2.2
Oral Cavity D05	5789/7242	-2.7 $\pm$ 2.6	6404/7152	-1.5 $\pm$ 2.6
Mandible Mean	5385/4463	-1.9 $\pm$ 4.8	5149/4381	-0.7 $\pm$ 3.4
Mandible D05	7852/7786	0.6 $\pm$ 1.5	7655/7478	0.8 $\pm$ 1.5
PTV D95	5925/6127	-0.2 $\pm$ 2.5	6021/6087	1.3 $\pm$ 2.3
PTV D05	7879/8005	0.6 $\pm$ 0.8	7637/7723	0.8 $\pm$ 0.8
PTV D _{min}	1588/777	-30.6 $\pm$ 19.6	3709/4318	-4.1 $\pm$ 19.1

Shown are the planned values in cGy for both phase 1 and phase 2 (normalized to 70-Gy Rx dose or 35 fractions), as well as the percent difference between the CBCT values and the planned value Δ (CBCT), averaged over the whole treatment. Note that the spinal cord contours include the entire spinal canal.