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Dosimetric evaluation of a three-phase adaptive radiotherapy for nasopharyngeal carcinoma using helical tomotherapy

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ABSTRACT

Adaptive radiotherapy (ART) has been introduced to correct the radiation-induced anatomic changes in head and neck cases during a treatment course. This study evaluated the potential dosimetric benefits of applying a 3-phase adaptive radiotherapy protocol in nasopharyngeal carcinoma (NPC) patients compared with the nonadaptive single-phase treatment protocol. Ten NPC patients previously treated with this 3-phase radiation protocol using Hi-Art Tomotherapy were recruited. Two new plans, PII-ART and PIII-ART, were generated based on the up-to-date computed tomography (CT) images and contours and were used for treatment in phase two (PII; after 25th fraction) and phase three (PIII; after 35th fraction), respectively. To simulate the situation of no replanning, 2 hybrid plans denoted as PII-NART and PIII-NART were generated using the original contours pasted on the PII- and PIII-CT sets by CT-CT fusion. Dosimetric comparisons were made between the NART plans and the corresponding ART plans. In both PII- and PIII-NART plans, the doses to 95% of all the target volumes (D_{95}) were increased with better dose uniformity, whereas the organs at risk (OARs) received higher doses compared with the corresponding ART plans. Without replanning, the total dose to 1% of brainstem and spinal cord (D_1) significantly increased 7.87 ± 7.26% and 10.69 ± 6.72%, respectively ($P = 0.011$ and 0.001, respectively), in which 3 patients would have these structures overdosed when compared with those with two replannings. The total maximum doses to the optic chiasm and pituitary gland and the mean doses to the left and right parotid glands were increased by 10.50 ± 10.51%, 8.59 ± 6.10%, 3.03 ± 4.48%, and 2.24 ± 3.11%, respectively ($P = 0.014$, 0.003, 0.053, and 0.046, respectively). The 3-phase radiotherapy protocol showed improved dosimetric results to the critical structures while keeping satisfactory target dose coverage, which demonstrated the advantages of ART in helical tomotherapy of NPC.

Introduction

Radiotherapy is the treatment of choice in treating nasopharyngeal carcinoma (NPC). Recently, image-guided radiotherapy using computed tomography (CT), such as CT on rails,[1] cone-beam CT,[2,3] and megavoltage (MV) CT,[4] is widely used because they provide volumetric images for treatment verification. Compared with conventional portal vision, the more superior soft tissue visualization from volumetric images allows direct measurement of organ or target variation instead of using bony structures as surrogates.[3,5] Precise correction of setup errors can be performed by assessing the coordinate changes to make corresponding couch translation and rotation. Nevertheless, most head and neck cancer patients experience tumor, involved lymph nodes, or parotid gland shrinkage and displacement throughout the 6- to 8-week radiotherapy course.[6–9] These patients may also have weight loss, which can lead to an ill-fitting immobilization mask. These nonrigid anatomic deformations cannot be corrected solely by geometrical couch offset calculated by the image guidance system. Furthermore, because the initial CT image set acquired before the start of treatment for planning no longer reflects the true appearance of the targets and the organs at risk (OARs), the treatment plan may no longer be valid. For intensity-modulated radiotherapy (IMRT), the sharp dose gradient at boundaries between targets and OARs increases the treatment sensitivity to these anatomic changes, in which a small deviation may greatly alter the actual dose delivered. The potential consequences are insufficient dose coverage to tumors and/or overdose to adjacent OARs.[10–12]

To restore the planned dose distribution, adaptive radiotherapy (ART) has been introduced. ART refers to the modification of treatment plan based on tumor response and normal tissue anatomic changes.[13–15] Basically, ART involves (1) rescanning of the patient, (2)

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recontouring of targets and OARs, and (3) replanning. ART is accomplished by the use of the CT image set acquired at specific times during a treatment course. The targets and OARs are contoured according to their changes on each set of CT scans. Any deviation from the original plan is assessed and a new treatment plan is generated for subsequent fractions whenever necessary. Several studies[6,7,10,11] tried to quantify the anatomic changes and potential dosimetric benefit of ART in head and neck cancers. Hansen *et al.*[10] repeated CT scan after 19 (mean ± 6) fractions of treatment for replanning purposes and showed improvement in target coverage and OAR dose reduction. Kuo *et al.*[11] carried out replanning after 25 fractions for patients with enlarged neck lymph nodes and showed that replanning according to the parotid medial shift caused by lymph node regression (>50%) could provide the dosimetric benefit of more than 3-Gy reduction in the mean dose.

NPC is prevalent in Southern China. It was the fifth and twelfth most common cancer in men and women, respectively, in 2007 in Hong Kong.[16] Nevertheless, few ART studies have been carried out specifically on NPC, but 2 studies to evaluate the potential benefit of replanning in midstage of treatment were recently conducted.[17,18] It is observed that only 1 replan was used and the day for plan modification varied among these studies. The issue of when and how many times the replanning should be performed is still controversial because of lack of clinical data. Considering the fact that the tumor and OARs have substantial anatomic changes, adaptive planning on different stages of a treatment course may be more beneficial.

In our center, a three-phase radiotherapy protocol for NPC treated with helical tomotherapy has been adopted since 2005. Helical tomotherapy is a specialized technique of delivering IMRT. The machine generates a modulatable fan beam from a 6-MV radiation source that is rotated around the patient in a helical manner. The beam intensity is modulated by sliding the leaves into and out of the path of the fan beam across its width, at the same time as the radiation beam rotates around the patient and the treatment table, advancing toward the gantry along the patient's craniocaudal direction.[19,20] The objective of this study is to evaluate the potential dosimetric benefits of applying the current 3-phase protocol in NPC patients treated by helical tomotherapy compared with the single-phase treatment protocol.

Methods and Materials

Patient characteristics

This was a retrospective study recruiting 10 NPC cases treated with Hi-Art tomotherapy (TomoTherapy Inc., Madison, WI) at the Radiotherapy Department of Hong Kong Sanatorium and hospital in 2005 through 2008. Among the patients, 7 had stage III disease, 2 had stage I disease, and 1 had stage IIb according to AJCC's staging system.[21] All patients except those with stage I disease were treated with concurrent chemotomotherapy. The three-phase radiotherapy protocol, which consists of 25 fractions in phase one (PI), 10 fractions in phase two (PII), and 2–3 fractions in phase three (PIII), was applied. Among the 10 patients, 7 received a total of 38 fractions of treatment and 3 received 37 fractions. All patients underwent repeat kilovoltage (kV) CT scans and replanning for PII and PIII.

Treatment planning and delivery

During kVCT simulation, all patients were immobilized with T-VacLok (Med-Tec Inc., Orange City, IA) at the head and neck region and covered with thermoplastic cast (Med-Tec Inc.). CT slices with thickness of 3 mm were acquired from the vertex down to upper chest. The CT image sets were first sent to the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) for manual contouring. The gross tumor volume of the nasopharyngeal region (NP-GTV) included all gross disease determined by CT, magnetic resonance imaging, positron emission tomography, and endoscopic findings. The clinical target volume of this region (NP-CTV) included the parapharyngeal space, uvula, pterygo-maxillary fissure, outer table of clivus, basisphenoid, petrous tip, foremen ovale, foremen rotundum, inferior half of the sphenoid sinus, anterior arc of atlas (C1), and prevertebral muscle/fascia, posterior 1–2 cm of maxillary antrum and nasal septum. In case of stage III disease, the inner table of the skull was included in the NP-CTV.[21] For stage IV disease, the para-caverous sinus and the orbits would be included in the NP-CTV depending on the location and the extension of NP-GTV involvement. The planning target volume of the nasopharyngeal tumor (NP-PTV) was generated automatically by the planning software by adding a 3-mm margin to the NP-CTV to account for setup errors. This margin was decreased to 1 mm in posterior aspect if the NP-CTV was within 3 mm from the spinal cord and brainstem. For the neck region, the GTV of involved lymph nodes (LN-GTV) included any nodes >1 cm and the nodes with necrotic centers. The lymph nodes CTV (LN-CTV) in PI covered the whole neck bilaterally, which included lymph nodes of surgical levels II–V. For PII, the LN-CTV included the nodes at surgical level II–III, the upper portion of level IV, and the mid portion of level V. The LN-CTV in PIII included any residual lymph nodes plus 3-mm margin. Another 3-mm margin was added to the LN-CTV without extending beyond the body surface to generate the lymph nodes PTV (LN-PTV). The target volumes were defined separately for the left and right side in the neck region. The same oncologist conducted the target delineation for all patients and the OARs were contoured by radiation therapists. The contoured OARs included the brainstem, spinal cord, optic chiasm, pituitary gland, and bilateral parotid glands. After contouring, the CT data with the structures were transferred to the TomoTherapy Planning Station (Version 2.2.1) for helical tomotherapy treatment planning. The optimization parameters, including the pitch, field width, calculation grid size, and modulation factor, were set during the planning process and kept constant in all plans for the same patient.

Table 1
Standard dose prescription for NPC case

Target Volumes	Dose Prescription		
	PI	PII	PIII
NP-CTV	52.5 Gy/25 Fr.	21.0 Gy/10 Fr.	7.4 Gy/2 Fr. or 10.5 Gy/3 Fr.
NP-PTV	51.5 Gy/25 Fr.	20.6 Gy/10 Fr.	7.0 Gy/2 Fr. or 10.5 Gy/3 Fr.
LN-PTV (I/R)	50.0 Gy/25 Fr.	20.0 Gy/10 Fr.	7.0 Gy/2 Fr. or 10.5 Gy/3 Fr.

Repeat kVCT scans for PII and PIII treatments were scheduled within 1 week before the beginning of the corresponding phase. The same immobilization shell with original isocenter was used to set up the patient for image acquisition and subsequent treatment. In these repeated scans, the targets and OARs were recontoured based on their up-to-date anatomic changes. The target delineation was performed by the same oncologist. Two new treatment plans, denoted as PII-ART and PIII-ART, were optimized based on the modified contours on these CTs for subsequent PII and PIII treatments, respectively. Table 1 shows the standard prescriptions for the target volumes in NPC case. All target doses were prescribed at 95% isodose level.

To simulate the dosimetric effect as if no replanning were applied in PII and PIII, 2 more plans, denoted as PII-NART and PIII-NART, were optimized for each patient. The original contours from the initial CT sets were pasted on the PII and PIII CT sets by CT-CT fusion and were used for PII- and PIII-NART plan optimization. In this way, these plans would visualize the isodose distribution when no modification was done and the dose delivered to the actual target volumes and OARs in these 2 phases could be obtained. During optimization, the planning objectives of the PII- and PIII-NART plans were made consistent with the initial plan to ensure that the dosimetric differences between NART and ART, if any, would be mainly a result of the anatomic changes of the structures in these phases.

Dosimetric comparison

Dose-volume histograms (DVHs) were generated for all target volumes and OARs in all plans. For both PII and PIII, dosimetric comparison was performed between the NART plans and the corresponding ART plans to investigate the dose effect caused by anatomic changes in these 2 phases. Dose evaluation was done on all target volumes and selective OARs that were close to target sites (bilateral parotid glands, brainstem, spinal cord, optic chiasm, and pituitary gland). Other than the maximum (D_{max}), mean (D_{mean}), and minimum (D_{min}) doses of the target volumes and the D_{max} of the OARs, the dose received by 95% of the target volumes (D_{95}) and the dose received by 1% (D_1) of the brainstem and spinal cord were also recorded.

To assess the target dose homogeneity in each plan, the homogeneity index (HI) was calculated. The HI was calculated by dividing the difference of the maximum dose and the minimum dose by the mean dose.[22] The value of HI decreases with increasing target homogeneity and ultimately reaching 0 when the target dose is perfectly uniform.

To demonstrate the resultant dosimetric outcome after the 37–38 fractions of radiotherapy course, the recorded doses were summed from the 3 phases under the same stream and compared between "replanning twice" and "without replanning." For example, the total maximum dose received by the brainstem after the whole course of treatment with adaptive measures would equal the sum of its maximum doses from PI, PII-ART, and PIII-ART. All data comparisons were also statistical analyzed by two-tailed paired *t*-test or Wilcoxon matched-pairs test.

Results

Dosimetric comparison

In general, the mean D_{95} of all targets for the NART plans were higher, with smaller mean HIs. The mean endpoint doses of all OARs in the NART plans were higher when compared with the ART plans.