



Setup verification

Measuring radiotherapy setup errors at multiple neck levels in nasopharyngeal cancer (NPC): A case for differential PTV expansion



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ABSTRACT

Background and purpose: We aim to quantify the magnitude of the systematic and random setup errors at three different anatomical levels of the neck in Nasopharyngeal Carcinoma (NPC) when clivus matching is used, and recommend appropriate PTV margins for each level.

Material and methods: Thirty-six patients undergoing image-guided radiotherapy (IGRT) each with 9 scheduled CBCTs were reviewed. The magnitude of setup errors were measured at the level of the clivus, C4 and C7 vertebrae, before and after CBCT correction. The 3D displacements, systematic and random errors were calculated for each level. The appropriate PTV expansion was determined using Van Herk's formula.

Results: Mean 3D displacement was 1.88, 2.66 and 3.35 mm at the clivus, C4 and C7 before correction. The differences were statistically significant ($p < 0.05$). The PTV margin required without correction was 2.33, 4.33 and 6.52 mm respectively. These were reduced to 1.20, 3.72 and 6.08 mm after CBCT corrections.

Conclusions: Variability is seen in setup errors at the clivus, C4 and C7 vertebral levels. A variable planning margin approach with reduced margin at the clivus is recommended. Use of daily CBCT allows the PTV expansion to be reduced to 1.2 mm.

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NPC is commonly seen in endemic populations from Southern China, Hong Kong, Taiwan and Singapore [1]. The main curative treatment modality is radiation therapy (RT), with or without chemotherapy [2]. Intensity modulated radiation therapy (IMRT) has been shown to improve outcomes [3], and has been adopted as standard of care in Singapore for the past decade.

With the steep dose drop-offs seen in IMRT plans, set-up accuracy is imperative to avoid geographical misses. The advent of cone-beam computed tomography (CBCT) has improved set-up accuracy such that PTV expansion margin can be safely dropped from a uniform 5 mm to 3 mm [4,5]. When CBCTs are performed prior to treatment, priority is given to matching at the clivus over the neck because of its proximity to the primary tumor as well as critical organs such as the brainstem and optic chiasm. This approach to matching at the clivus may impact on the setup errors and adequacy of Planning Target Volume (PTV) margins at the lower neck.

We aim to establish the magnitude of the systematic and random setup errors at the clivus, mid-neck and supraclavicular (SCF) region, and thus suggest an appropriate PTV margin at each level.

Method and materials

Patient selection

Patients with tumors arising from the nasopharynx or paranasal sinuses treated with high dose radiotherapy (>60 Gy) at our center from Oct 2013 to Oct 2014 with 3D image verification via CBCT were enrolled. Patients who required re-simulation and re-planning mid-treatment were excluded.

CT simulation

Immobilization was achieved with a thermoplastic shell with 5-point fixation (Civco, IA, USA) with the patient placed on a neck rest that provided the most appropriate fit. CT images with intravenous contrast were obtained from the vertex to the mediastinum, in 3 mm cuts within the volume of interest.

Treatment planning

Tumor volumes were designed using our previously described protocol [6]. Typically, there were three dose levels at 69.96 Gy, 59.4 Gy and 54 Gy, delivered over 33 fractions using the simultaneous integrated boost (SIB) technique. Dose calculations were performed by the Monaco treatment planning system (ver-

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sion 3.20.02, Elekta Medical Systems, Sweden) using a Monte Carlo algorithm.

Daily setup and image guidance

Before daily radiotherapy, patients are first set up by aligning the treatment lasers to the respective shell markings. The necessary couch shifts were applied as determined at planning for the first 3 sessions. Kilovoltage (kV) CBCTs are performed prior to each of these sessions and reviewed by the radiotherapist-in-charge. When bony alignment could not be achieved uniformly throughout the entire length of the neck, priority would be given to matching at the clivus over the lower neck. If there was rotation of $>3^\circ$ in any axis, the patient will be re-setup. The average shifts in the Medio-Lateral (ML), Superior-Inferior (SI) and Anterior-Posterior (AP) axes over the 3 days were determined, and these are then added to the original couch shifts applied to constitute the new couch shift to be used for all the remaining 30 treatment setups. Subsequently, a confirmatory CBCT is done on day 4 of treatment after setting up with the newly determined couch shifts. If the setup error before CBCT correction is less than 2 mm, this new couch shift will be adopted for all subsequent treatments.

Thus a total of nine scheduled CBCTs were performed for each patient: four consecutive daily CBCTs for the first 4 days, followed by 5 weekly CBCTs thereafter. Additional CBCTs may be performed as clinically indicated, but these were not included in the analysis.

The IGRT platform used was the Elekta XVI R4.5, a kV CBCT system which acquires the image through a 200 degree arc traversed in 1.2 min.

Analysis

Each of the nine CBCTs for the 36 patients was retrospectively reviewed to determine the setup error at the clivus, C4 and C7 vertebral levels. The C4 and C7 vertebral levels were selected as representative of the mid-neck and SCF regions due to their anatomical correlation with the hyoid body and inferior cricoid cartilage [7], which also bears clinical significance as the landmarks dividing the neck nodes into levels II, III and IV [8].

The setup errors consisted of the initial error prior to CBCT correction as well as residual error post CBCT correction. As the CBCT resulted in a translational shift that impacted all 3 anatomical levels to the same extent, residual error at each level is essentially the addition of the translational shift to the initial error at each level. For each patient, the initial error in all 3 dimensions (ML, SI and AP) at each of the anatomic levels (Clivus, C4 and C7) was recorded for all 9 CBCTs through the treatment.

The 3-dimensional (3D) displacement was calculated as the square root of the quadratic sum of the errors on each of the 3 axes. At each of the anatomical levels, this 3D displacement was calculated at each of the 9 CBCTs for every one of the 36 patients (324 data points in total) both before and after CBCT correction. The 2-tailed unpaired *T*-test was used to analyze for differences in 3D displacement between the clivus and C4, and between C4 and C7, except for instances of non-parametric distribution, where the Mann-Whitney *U* test was used.

For every patient and at each anatomic level, the errors in the 3 dimensions were analyzed separately for the mean and standard deviation (SD). The average of all individual patient means was calculated as the overall mean (*M*), which was taken to be the group systematic error. The systematic setup error (Σ), was calculated as the SD of the individual means. The random setup error (σ), was calculated as the root mean square of the SD of all patients. The van Herk formula was used to arrive at the PTV margin, stated as $[2.5\Sigma + 0.7\sigma]$, which ensures the 95% isodose line covers the CTV for 90% of the patients [9].

The same calculations were performed for the residual error to arrive at the systematic, random setup errors and the PTV margin required after CBCT shifts.

Analyses were performed using MS Excel 2007 and STATA.

Results

Patient characteristics

324 CBCTs of 36 patients were analyzed. The patient characteristics are summarized in Table 1. Of the 36 patients 26 were male. Their ages ranged from 15 to 81 years, with a median of 58.5 years. Thirty-four of 36 patients had undifferentiated carcinoma arising from the nasopharynx, while the remaining two patients had Sinonasal Undifferentiated Carcinoma (SNUC) and mucoepidermoid CA arising in the nasopharynx. Of the 34 NPC patients, nine (26%) had T4 disease, and six had N3 disease.

Magnitude of 3D displacement at clivus, C4 and C7

The mean 3D displacement at the clivus, C4 and C7 were 1.88, 2.66 and 3.35 mm respectively before CBCT correction. The difference between the 3D displacement at clivus and C4 was statistically significant ($p < 0.001$), as was the difference between C4 and C7 ($p = 0.002$).

The respective mean 3D displacements were reduced to 0.30, 1.74 and 2.62mm after CBCT correction.

These differences remained significant even after CBCT correction, when comparing clivus with C4 ($p < 0.001$, Mann-Whitney *U* Test), and C4 with C7 ($p < 0.001$).

Figs. 1 and 2 Distribution of 3D displacements before and after CBCT correction.

Setup errors and required PTV margin

Table 2 shows the setup errors (systematic and random) and required PTV margins in each axis at the 3 anatomical levels, both before CBCT correction (Initial Error) and after CBCT correction (Residual Error).

When the results are compared by anatomical levels, the systematic and random setup error showed an increase from the cranial to caudal direction, along all 3 axes. This was true for both

Table 1
Characteristics of patients.

Characteristic	Number of patients
Gender	
M	26
F	10
Age	
Median	58.5
Range	15–81
Histology	
NPC (undifferentiated carcinoma)	34
Others	2
AJCC (7th Edition) stage(10) (NPC)	
1	3
2	6
3	9
4A	9
4B	6
4C	1
Not applicable	2
Chemotherapy	
Concurrent	14
Induction and concurrent	14
Radiotherapy alone	8

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