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Is Exactrac X-Ray System an Alternative to CBCT for Positioning Patients Head and Neck Cancers?

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Abstract

Purpose: To evaluate the usefulness of a 6-degrees-of freedom (6D) correction using ExacTrac Robotics system in patients with head-and-neck (HN) cancer receiving radiation therapy.

Methods: Local setup accuracy was analyzed for 12 patients undergoing intensity-modulated radiation therapy (IMRT). Patient position was imaged daily upon two different protocols, cone-beam computed tomography (CBCT) and ExacTrac (ET) images correction. Setup data from either approach were compared in terms of both residual errors after correction and punctual displacement of selected regions of interest (Mandible, C2 and C6 vertebral bodies).

Results: On average, both protocols achieved reasonably low residual errors after initial correction. The observed differences in shift vectors between the two protocols showed that CBCT tends to weight more C2 and C6 at the expense of the mandible, while ET tends to average more differences among the different ROIs.

Conclusions: CBCT, even without 6D correction capabilities, seems preferable to ET for better consistent alignment and the capability to see soft tissues. Therefore, in our experience, CBTC represents a benchmark for positioning head and neck cancer patients.

Keywords: CBCT; ExacTrac; Head and neck positioning

Introduction

Proper daily patient alignment is one fundamental pre-requisite for patients with head and neck (HN) cancer undergoing intensity modulated radiotherapy (IMRT) due to the high conformality of the dose distribution.

Set-up uncertainties and anatomic variations represent critical points for HN cancer because of the complexity of the HN anatomy, proximity of cancer to several normal structures, different relative motion among HN structures (i.e. mandible, upper neck region, lower neck region). Several studies have shown a different displacement among different bony structures in the HN region [1-3].

Patient position accuracy has been assessed with megavolt (MV) X-rays, a two-dimensional (2D) radiographs projection technique after traditional immobilization with standard thermoplastic face masks, bite blocks or vacuum bags [4,5]. Determination of setup errors have been performed off-line using anatomic bony landmarks due to poor visualization of soft tissues in the planar projection X-ray images [6]. Therefore, patient's position was adjusted at a subsequent treatment fraction. However, while off-line correction ameliorates the systematic component of set-up errors, it is less effective than on-line correction to minimize both systematic and random setup errors [7].

.Nowadays several systems are available in clinical practice for daily Image Guided RT (IGRT). Daily pre-treatment acquisition of a cone-beam computed tomography (CBCT) represents a widely adopted option for set up verification of patients undergoing IMRT for HN cancers [8]. CBCT offers a three-dimensional (3D) view with a better visualization of anatomical structures and soft tissues than 2D imaging options. However, its application is limited by a relatively long image acquisition time [9], a relatively high radiation dose to the patient [10] and the lack, at least at present, of 3D rotational correction capability.

A potential alternative to CBCT is offered by the ExacTrac (ET) Robotics IGRT system (Brain LAB AG, Feldkirchen, Germany). The 6D ET is composed of an Infrared (IR) tracking system, an X-ray system (consisting of two diagnostic kV X-ray tubes and aSi detectors) and a robotic couch capable of 6D correction positioning including pitch, roll and yaw. It offers potential clinical benefits over CBCT including faster patient positioning, an alignment using 6D degree of freedom, the ability to monitoring patient motion during the treatment and a reduction in image-based radiation delivered to the patient [11]. However, to our knowledge, ExacTrac has not been directly compared to CBCT for set up of patients with head and neck cancers. The purpose of the present paper is to clarify this issue.

Materials and Methods

Patient selection

Twelve patients with HN cancer (Table 1) treated by IMRT at IRCCS CROB from January 2012 to July 2012 were selected for the present study. A 3 dose level IMRT (66, 60, 54 Gy) by means of a simultaneously integrated boost (SIB) approach was used for all patients. All doses were given in 30 fractions over 6 weeks, one fraction

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Case	Subside	TN Stage	Neck levels involved
1	Larynx	T4N0	I-V
2	Tonsil	T4N2c	I-V
3	Larynx	T4N1	I-V
4	Base of tongue	T2N0	I-IV
5	Hypopharynx	T3N0	I-V
6	Nasopharynx	T2N0	I-IV
7	Larynx	T3N1	I-IV
8	Tonsil	T1N2b	II
9	Base of tongue	T2N2b	II-III
10	Base of tongue	T1N2b	III-V
11	Tonsil	T3N2a	II
12	Pharyngeal wall	T3N0	none

Table 1: Selected patients and tumor characteristics.

per day. Each CTV was expanded to its corresponding PTV with a 5-mm margin. The routine IMRT approach at our institute involves a 7-field sliding window technique. Plans were optimized using the clinical version 8.6 of Eclipse (Varian Inc.) Treatment Planning System (TPS) with 6MV photon beams for a Varian Trilogy Linac modeled by the MLC with interdigitating capabilities for its 60 leaf-pairs of 10 and 5mm leaf-width at the isocenter. The fluence optimization was performed using the inverse planning module Helios, within the Eclipse TPS, once appropriate dose-volume constraints were assessed [12].

In order to verify the accuracy of patient positioning, our Trilogy Linac is equipped, with both a Varian KV on-board-imager (OBI) and a BrainLAB 6D ExacTrac (ET) system.

The OBI can perform 2D radiographic/fluoroscopic images and 3D cone-beam computed tomography acquisitions. The volumetric images, used for the study, were scanned in Low-Dose Head mode with "full-fan" acquisition (360 projections acquired over a gantry rotation of 200 degrees), while the detector is centered about the rotational axis. The thickness of all the slides was selected to 1 mm (as the CT simulation scan thickness).

The 6D ET system is composed of an Infrared (IR) tracking system (consisting of two infrared cameras and one video detector), an X-ray system (consisting of two diagnostic kV X-ray tubes and aSi detectors) and a robotic couch that can be used to verify the patient's position in 6D including pitch, roll and yaw.

Isocenter localization accuracy and quality assurance: The isocenter localization accuracy of both the ET and the CBCT systems, were previously evaluated using the radiation isocenter of the linear accelerator as the benchmark. Discrepancies between the two systems were compensated as described elsewhere [13]. However, the geometric calibration prior to the study showed that the isocenter of these two systems was within 0.3 mm in either of the three translational directions. The geometric linkage among the KV isocenter, the room lasers, and the ET system was checked each day before treatment [14].

Imaging correction protocols: All patients were positioned on the treatment table using a thermoplastic face mask extended to the shoulders, in combination with bite blocks and foot brace devices. Patient position was imaged daily upon two different protocols: CBCT and ET protocol as shown in figure 1. A total of 149 fractions in 6 patients and 130 fractions in 6 patients were analyzed for the CBCT and ET protocols, respectively. The former approach was used until April 2012, afterwards, ET has been used. The present study aims at comparing the performance of both methods, in terms of 6D residual setup errors. All registrations were performed by one physician (C.C.) to eliminate inter-observer variability of the process.

3D setup protocol (CBCT): After isocenter alignment using in-room lasers, a CBCT had been obtained. Positioning images were aligned to the corresponding planning CT using a 3D automatic bony anatomy-based registration targeting an extensive region of interest (ROI) that included the cervical vertebrae (C2), the jugular notch and the mandible [15]. Once the match had been optimized, the shift parameters were used to move the couch remotely to correct the rigid setup errors.

6D setup protocol (ET): After IR patient pre-position, two oblique high-quality X ray images of the patient were acquired and fused (using the bone matching automatic 6D algorithm) to digitally reconstructed radiographs (DRR) obtained from the corresponding planning CT. Exclusion of potentially deviated structures from the fusion ROI (sensitive area of 10×10cm^2 around the isocenter): e.g., IR reflectors, were also performed. Once the match was optimized, the correct couch parameters were transferred to the 6D robotic couch [11].

Evaluation methods: CBCT scans after ET and CBCT protocols: Before treatment and after each set-up correction protocol, a CBCT was obtained. The CBCT was then reviewed off-line with 6 degrees of freedom enabling rotations in addition to translations. The comparison between the two correction strategies (CBCT versus ET) was done in terms of residual errors at this CBCT.

Furthermore, we also estimated patient positioning after correction at selected points ('bony landmarks') according to each protocol. Therefore, the relative position of the center of mass of three bony landmarks (C2, C6 and the mandible) identified both on the planning CT and the post-correction CBCT images was also assessed. For each ROIs the mean vector and standard deviations (SDs) of alignment differences (bone CBCT position –bone CT reference position) along the 3 axes (LR: left to right; CC: craniocaudal; AP: anteroposterior) calculated as $\sqrt{(LR\ CBCT\text{-}LR\ CT)^2 + (CC\ CBCT\text{-}CC\ CT)^2 + (AP\ CBCT\text{-}AP\ CT)^2}$, were analyzed and compared between the two strategies [16].

Statistical analysis: Box and whisker plots (BWPs) were used to represent the distribution of residual errors. In the BWP, the whiskers represent 2.5 and 97.5 percentile, "plus" symbol the mean of variables and single points indicate the individual outliers. Statistical analysis was performed using STATA package version 11.0 (Stata Corp.). Comparison of two variables was performed using the Mann-Whitney U test and the quality of standard deviations (variances) was analyzed using Levene's test. We decided to use Mann-Whitney U test for all comparisons after that the hypothesis of a normal distribution was rejected for the majority of variables [17]. We used Shapito-Wilk test to assess normality of variable distribution. Numerical variables were described as mean and standard deviation (vector shift differences). All p-values were calculated with two-tailed tests, and statistical significance was defined as $p < 0.05$.

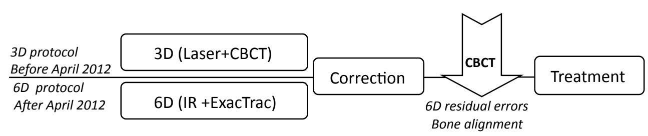

Figure 1: Correction set-up protocols adopted in the study.

Results

Figure 2 shows an example of image registration for each correction strategy: a) matched image: planning CT with CBCT; b) matched image: digitally reconstructed radiographs (DRRs) with X-ray images (ET).

6D residual error evaluation

Figure 3 shows the box-and-whisker plots representing differences in the distribution of residual errors for each protocol, for the overall treatment duration time a) and each half b) c). We chose this representation as most of the variables showed a low skewness values as departed from a normal distributions ([a] in figure 3). After CBCT or ET corrections, the 6D residual errors were small for both protocols (on average ± 1 mm, 1°). In a few cases the mean value departed slightly from zero: *Pitch* and *Roll* directions (by about +0.5 mm and up to -0.8 mm respectively) for protocols and the *CC* direction (+0.6 mm) for the ET protocol. Compared to ET protocol, CBCT correction generally showed reduced residual errors in translations, but not in rotations; a significant shift in the Pitch direction was observed for the CBCT protocol ($p<0.001$), on the overall treatment duration and specifically in the first half of the treatment. The median values and variances statistically significant are showed in figures 3 in boldface ([b]p, [c]p values).

A control quality analysis on bone alignment

The mean vector shifts and standard deviations (SDs) for each ROIs, for the overall treatment duration and each half, are summarized in figure 4. Comparing both protocols, the magnitude of vector shifts related to C2 and C6 ROIs were lower than the magnitude of vector shifts related to mandible ROI. ET correction generally showed a poorer consistency at C2-C6 compared to CBTC protocol. Specifically, the mean (SD) vector shifts for each protocols and ROIs (Mandible, C2, C6) were: 4.1 (2.7), 3.1 (1.8); 1.2 (0.5), 1.6 (0.8); 1.1 (0.7), 1.9 (1.1) for CBCT and ET on the overall treatment time, respectively. Similarly, for the first half of the treatment period, mean (SD) vector shift were: 3.8 (2.8), 2.8 (2.0); 1.2 (0.6), 1.4 (0.6); 1.1 (0.9), 1.9 (1.2) for CBCT and ET, respectively. For the second half of the treatment period, mean (SD) vector shift were: 4.1 (2.6), 3.0 (1.2); 1.1 (0.6), 1.8 (0.9); 1.0 (0.6), 1.9 (1.0) for CBCT and ET, respectively. Differences in distribution statistically significant are showed in figure 4 in asterisks (*$p<0.05$, **$p<0.01$).

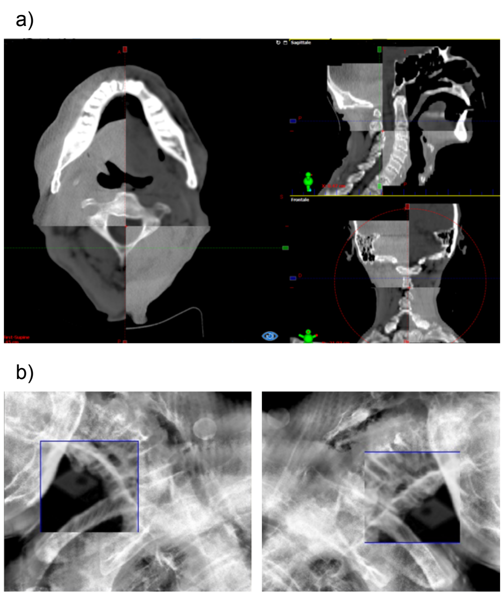

Figure 2: Example of two patients image registration: a) matched image: planning CT with CBCT; b) matched image: digitally reconstructed radiographs (DRRs) with ET X-ray images.

Discussion

The present paper compares the set-up accuracy of two strategies, CBCT and ET. Both correction protocols have distinctive features and, without knowing ahead the performance of each one in routine daily practice, they were both implemented at our institution to verify the set up of HN cancer patients undergoing IMRT.

Data from 12 consecutive patients imaged with either approach in two non-overlapping periods were compared in terms of both residual errors after correction and punctual displacement of selected regions of interest. On average, both protocols showed small residual errors and their magnitude were comparable. The observed differences in shift vectors between the two protocols (describing the deviation of the treatment position from the reference position at simulation time), showed that the anisotropic relative movement (or the flexibility) between different ROIs of HN bony structures introduces extra setup errors that seems to be corrected by either strategy in a different way. CBCT tends to weight more C2 and C6 at the expense of the mandible, while ET tends to average more differences among the different ROIs.

Zhang et al. [2], using CBCT, showed local setup variations of HN using three bony regions, C2, C6 and the palatine process of the maxilla (PPM) in 14 patients. Similarly to our findings, C2 showed the smallest setup variations indicating that C2 is the most stable region in AP and CC directions (an anatomic pivot for head motion). Of note, our experience shows that the vector displacement of C2 is significantly lower with CBCT over ET. Conversely, PPM was found to have the largest CC motion, which in turn impacted Pitch rotation. Our data are consistent with these findings. With CBCT, the (whole) mandible showed the largest vector displacements from the simulation position and, consistently, the residual error for Pitch rotation was extremely variable (figure 3a). With ET, the average displacement of the mandible was smaller and the residual Pitch rotation was less variable than with CBCT.

We hypothesize that ET, compared to CBCT, provides a more averaged interpretation of shifts, that may derive from both a more comprehensive 'view' of the ROI and the possibility to correct also for rotations over CBCT. We believe that the more consistent C2 alignment on CBCT comes from being reconstructed as a 3D structure as opposed to ET that uses, within each projected radiograph, a region with the best visible bony landmark, which may not be consistently the same throughout the two radiographs and may be different from the ROI reconstructed by CBCT.

CBCT system allowed only corrections in translations and thus we were unable to perform them in rotations. On the other hand, the ET system registers the acquired 2D planar X-ray images with DRR and achieves best match by tuning the image registration with both translations and rotations, but acquired images may not always be optimal for image registration due to substantial overlapping bony structures. Again CBCT and ET alignment use different ROIs, 3D versus 6D couch movement correction and different images quality.

On the other hand, the volumetric reconstruction (3D) of structures along with a better visualization of anatomical structures

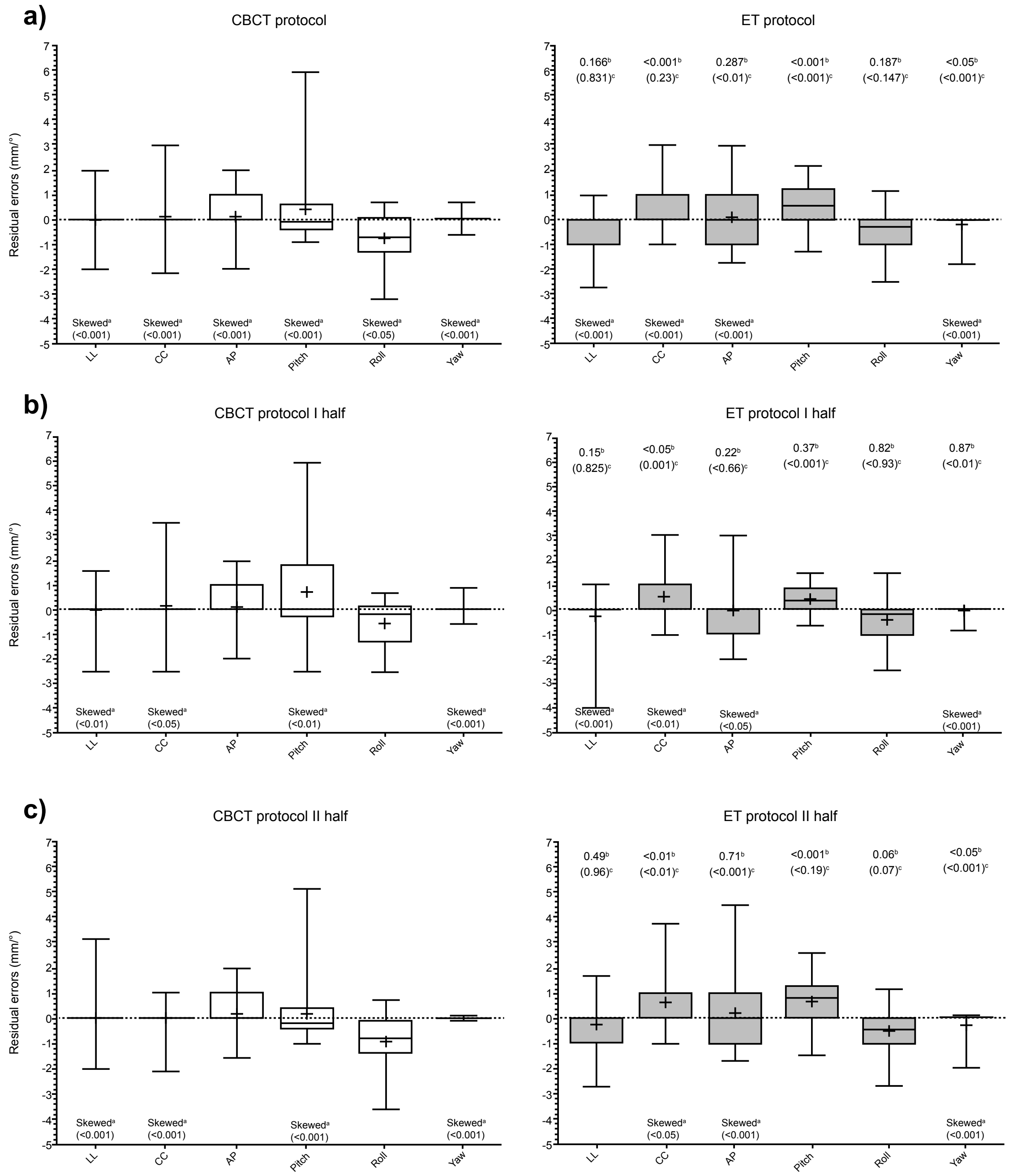

Figure 3: Comparison of CBCT and ET protocols with respect to 6D residual errors post correction, for the overall treatment duration a) and each half b) c). [a]Variables departing from a normal distribution based on Shapiro-Wilk test (p values in parenthesis). [b]p values by Mann-Whitney U-test. [c]p values by Leven's test. Significant results are shown in boldface.

and soft tissues by CBCT outweighed the disadvantage of not being able to perform 6D corrections.

Overall, CBCT seems more reliable than ET on both C2 and C6, but somewhat less performing on the mandible. Therefore, CBCT may be better indicated when, within a comprehensive treatment of the whole neck, the high dose target volume is in close proximity to the vertebral bodies (pharyngeal and laryngeal cancers) as opposed to the oral cavity. Obviously, these considerations do not take into account the fact that CBCT is able to 'see' soft tissues and their deformation, providing additional advantages in situations where this is clinically relevant.

This study has some limitations. The observed differences could reflect not just the intrinsic differences between the two approaches, but also the level of confidence of the radiotherapy staff with either method. Of note, our CBCT and ET approaches had been implemented for HN cancers about one year later after becoming available and being extensively used in other districts (prostate and brain). Therefore, we do not think that this was a relevant point. Moreover, of note, all images (both CBCT and ET) had been fused and registered by a single observer minimizing the impact of observer variability on results.

In conclusion, while both protocols achieved reasonably low residual errors after initial correction, CBCT, even without 6D correction capabilities, seems preferable to ET for better C2 and C6 alignment and the capability to see soft tissues. Therefore, in our experience, CBTC represents a benchmark for positioning head and neck cancer patients. Further clinical investigations are needed to validate the adequacy of these findings and to determine whether ET is a legitimate alternative or a complement to CBCT.

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