

Evaluation of set-up shift values detected in CBCT and kV-kV images taken on set-up day and interfraction treatment days in patients with laryngeal cancer who underwent image-guided radiotherapy

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ABSTRACT

Objectives: The aim of this study is to retrospectively analyze the first image values obtained with cone-beam computed tomography (CBCT)/kilovoltage (kV-kV) image on the set-up day, and the kV-kV image values taken on the following treatment days in the vertical (Vert), longitudinal (Long), and lateral (Lat) directions separately, and to evaluate the shift values in three axes within the framework of clinical applicability.

Patients and methods: Between March 2020 and November 2021, a total of 30 laryngeal cancer patients (18 males, 12 females; mean age: 58.2 years) planned for curative radiation therapy treatment with intensity-modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) technique were included in the study. In order to keep the patients stable on the treatment table during irradiation and to minimize set-up errors, immobilization was performed using thermoplastic masks that also included the head-shoulder area. Tomography images of cases were taken with computed tomography (CT) with a 2.5 mm slice thickness to be used in the treatment planning systems (TPS). Planning CT images were transferred to the Eclipse TPS, and target volumes and critical organs were defined on the system for each patient. Double-Arc VMAT and 7-field IMRT plans were designed with a total treatment dose of 66-70 Gray on TPS by the same medical physicist. All IMRT and VMAT treatments were performed on the Varian Trilogy device and pre-treatment and set-up images were taken using the Varian on-board imaging system. Images of each patient were collected by taking CBCT/kV-kV on the first set-up day and then kV-kV images every day or every other day until the end of the treatment. The shift value of the CBCT and kV-kV images obtained around 17/24 on average per patient was recorded and extracted the mean shift values for the Vert, Long, and Lat directions from the offline review system on TPS. Shift on the images approved by the same radiation oncologist with reference to the target volume and bone structures on CBCT/kV-kV images taken on set-up day and pre-treatment were retrospectively analyzed for each patient.

Results: The CBCT/kV-kV images taken on the set-up day and the kV-kV images taken every other day were analyzed in two different ways. The first analysis included CBCT/kV-kV images taken on the set-up day and the kV-kV images taken every other day during all treatment time. The analysis of the first group's mean shift values was found as Vert: 0.24 mm, Long: 0.27 mm, and Lat: 0.32 mm, respectively. In the second analysis, the image taken on the day of the set-up was excluded, the kV-kV images taken on during the treatment days were examined within themselves, and the mean shift value was found as Vert: 0.13 mm, Long: 0.20 mm, and Lat: 0.27 mm, respectively. Analysis revealed that the mean shift values in the Vert, Long, and Lat directions were ≤ 1 mm both in the first and second analyzed groups. The shift values are among the limit values determined for the image-guided radiotherapy (IGRT) technique to be applied to head and neck cancer patients.

Conclusion: The evaluation of the images taken on the set-up day and subsequent fractions, and the follow-up of the shifts on the images are important in terms of the quality assurance of the applied IGRT to the patients. In addition to correct positioning with CBCT/kV-kV on the day of set-up, it is recommended to take kV-kV images every other day and follow up with weekly CBCT imaging to monitor the change in the patient's anatomical structure throughout the treatment.

Keywords: Cone-beam computed tomography imaging, kV-kV imaging, laryngeal cancer, set-up shift.

Head and neck cancer (HNC) accounts for about 5% of all malignancies.^[1] Intensity-modulated radiotherapy (IMRT) and volumetric

modulated arc therapy (VMAT) techniques allow an increase in dose conformity around the target volume and reduce the dose in critical structures (spinal cord, brain stem, optic structures, parotid glands) compared to the three-dimensional (3D) conformal technique in the head and neck region radiation therapy (RT).^[2-5]

Technically speaking, since it provides a steeper dose gradient between the target volume and surrounding healthy tissue, IMRT/VMAT is particularly sensitive to uncertainties in setup positioning before irradiation (IR) and changes

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in patient anatomy (tumor-related and/or patient-related), and changes in patient treatment position.

Daily set-up errors along the 6/7 weeks of a standard radiotherapy course of HNC may result in significant deviations from the planned dose distribution treatment geometry, enhancing the risk of unnoticed local miss of the planning target volume (PTV) and/or overdosage of healthy tissues.^[6,7]

Correct immobilization at the beginning of the treatment is very important for these techniques, which are sensitive to patient positioning. For this purpose, thermoplastic masks with a 5-point pinning system and head support system are used for the immobilization of patients with HNC tumors for RT. The immobilization systematic aims to prevent major shifts during the IR of the patient.^[8]

Although all these factors are taken into account, set-up day and daily error on the images of patients taken is an inherent part of treatment processes.^[9]

In order to minimize these errors in image-guided radiotherapy (IGRT), it is aimed to provide the most accurate IR positioning conditions with the imaging to be performed within a certain protocol before each treatment. So the set-up errors and shift from the planned treatment field are detectable to be analyzed via following-up of these pre-treatment images taken according to a clinical protocol.

Mainly, set-up verification has been done with the acquisition of two-dimensional (2D) kilovoltage (kV) or megavoltage (MV) portal images, which can be compared or matched with the digitally reconstructed radiographs (DRRs) generated from the planning computed tomography (CT) scan. Computed tomography scans were obtained to be used in the treatment planning systems (TPS) on the design of the patient treatment plan.

The recent development of volumetric imaging techniques such as cone-beam computed tomography (CBCT) deeply impacted the overall quality of IGRT, moving from 2D verification of the position of bony landmarks to 3D assessment of the position of target volumes and organs at risk near the target.^[10-12]

A kilovoltage imaging system capable of radiography, fluoroscopy, and CBCT can be

mounted on the medical linear accelerator in order to perform IGRT. The combination of CBCT and image registration software makes it possible to measure the positional error in the treatment field to be irradiated directly.^[12]

Our aim was to retrospectively evaluate the first image values taken on the set-up day with CBCT/kV-kV and kV-kV image values obtained on the following treatment days in the vertical (Vert), longitudinal (Long), and lateral (Lat) directions separately, and to detect the shift on the image in three axes.

PATIENTS AND METHODS

This retrospective study was conducted at Kartal Dr. Lütfi Kırdar City Hospital, Department of Radiation Oncology between March 2020 and November 2021. A total of 30 laryngeal cancer patients (18 males, 12 females; mean age: 58.2 years) who were planned for curative RT treatment with IMRT or VMAT techniques were included in the study.

Simulation, immobilization system and treatment planning

All patients were placed in the supine position and the proper position was given for immobilization on the couch. For immobilization, the patient's head, neck, and shoulder movements were limited by using a thermoplastic head-shoulder mask.

The in-room lasers cross to define a reference point according to the volume to be treated. Tomography images of 30 cases were taken with General Electric BrightSpeed CT (General Electric-Milwaukee Wisconsin, USA) with a 2.5 mm slice thickness to be used in the TPS. Computed tomography images taken for each patient were transferred to the Eclipse (Varian Medical System, Palo Alto, CA, USA) TPS through the digital imaging and communications in medicine (DICOM) network.

The target volumes and critical organs were defined on the system for each patient by the same radiation oncologist according to ICRU62. In order to accurately localize the gross tumor volume (GTV), fusion images were created using magnetic resonance (MR), and positron emission tomography (PET)-CT images in all patients. The gross tumor volume and GTV-nodal was

contoured in all cases. The clinical target volume (CTV) was delineated around the GTV to cover areas at risk for the presence of microscopic disease. The PTV margins were 3-5 mm in all directions to the respective CTV's. Planning organ at risk volumes (PRVs) were created by the addition of 3-5 mm for the carotid arteries, brain stem, and spinal cord. A prescribed dose range of treatment of 66-70 Gray (Gy) for high-risk PTVs, 60-63 Gy for intermediate-risk PTVs, and 50-54 Gy for low-risk PTVs is planned to be IR in 30-35 fractions.

Double-Arc VMAT and 7-field IMRT plans were designed with 6MV photons and using coplanar beams on the Varian Eclipse TPS by the same medical physicist. All IMRT and VMAT treatments were applied to the Varian Trilogy device (Varian Medical Systems Trilogy™, California, USA).

On-board imaging (OBI) components

Kilovoltage X-rays are generated by a conventional X-ray tube mounted on a retractable arm at 90° to the treatment source. A 41×41 cm² flat-panel X-ray detector is mounted opposite the kV tube. The entire imaging system operates under computer control, with a single application providing calibration, image acquisition, processing, and CBCT reconstruction.

Cone-beam CT imaging involves acquiring multiple kV radiographs a while the gantry rotates through 360° of rotation. A filtered back-projection algorithm is used to reconstruct the volumetric images of the patient. Geometric nonidealities in the rotation of the gantry system are measured and corrected during reconstruction. Qualitative evaluation of imaging performance is performed using an anthropomorphic head phantom and a coronal contrast phantom. The influence of geometric nonidealities is examined.

Using the CBCT/kV-kV imaging system, consisting of an X-ray tube mounted on a linear accelerator and an amorphous silicon planar detector, orthogonal kV-kV images in 2D and kV CBCT images give the tomographic images of the patient in 3D.^[11]

Image guidance procedure

All pre-treatment images were taken using the Varian OBI. The offline view was utilized to

calculate the translation shifts and data extraction. Observed translational displacements in three axes: Vert, Long, and Lat values were recorded and always corrected online before delivering treatment.

Pre-treatment CBCT/kV-kV images in all patients:

- The first (1-3 days) of the IRs, the set-up error corrections are made before the treatment,
- If there is a shift greater than 3 mm in any direction,
- A weekly routine repeat of kV CBCT was performed throughout the entire treatment period.

Shift on the images approved by the same radiation oncologist on CBCT/kV-kV images taken before the treatment with reference to the target volume and bone structures were retrospectively analyzed for each patient. Images of each patient were collected by taking CBCT/kV-kV on the first set-up day and then kV-kV images every day or every other day until the end of the treatment as shown in Figure 1. The shift data of the CBCT/kV-kV images obtained around 17-24 CBCT/kV-kV pairs on average per patient was recorded on the system OBI for Vert, Long, and Lat directions.

Quality assurance (QA) procedures for CBCT images include a monthly check of the mechanical system and image quality, as well as weekly geometrical accuracy tests to verify that the CBCT reconstruction center is coincident with the isocenter of the linear accelerator. Also, it is very vital to perform properly these QA procedures for imaging tools in order to eliminate systematical errors.

Set-up errors assessment and analysis

We recorded the magnitude of shift for the Vert, Long, and Lat axes of the taken patient image. The total list of shift values for all images taken is obtained from the offline system as the table of 'delta between online/offline match' and is entered into SPSS to calculate mean values for every single direction. Statistical analysis was performed using the PASW version 17.0 software (SPSS Inc., Chicago, IL, USA) program to determine the mean of shift values individually at three axes.

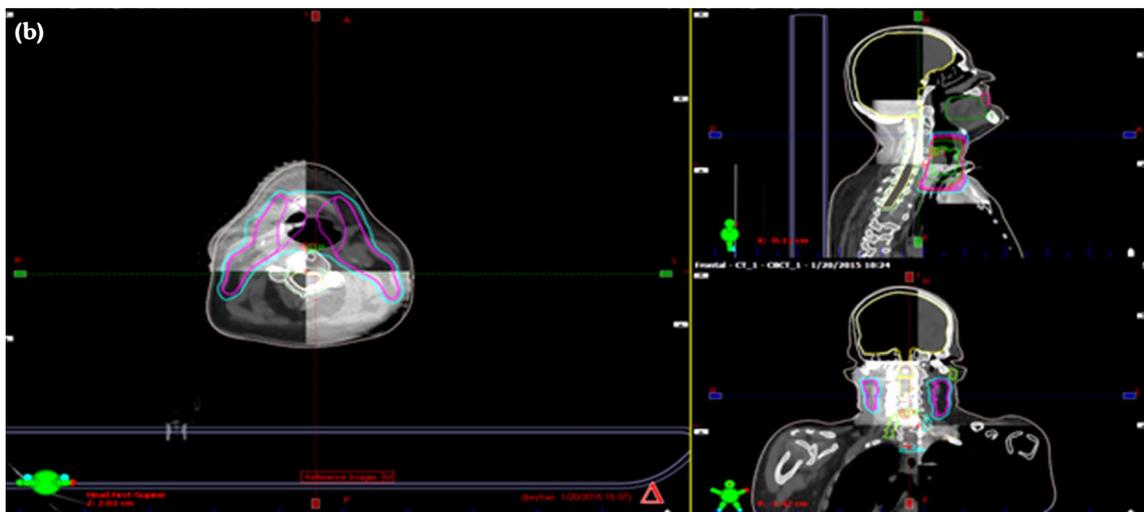


Figure 1. kV-kV images taken every other day during the treatment.

kV: Kilovoltage.

RESULTS

The CBCT/kV-kV images of the patients taken on the set-up day and the kV-kV images taken every other day were analyzed in two different ways. The first analysis included CBCT/kV-kV images taken on the set-up day and the kV-kV images taken every other day during all treatment time. The analysis of the first group's mean shift values was found as Vert: 0.24 mm, Long: 0.27 mm, and Lat: 0.32 mm, respectively. In the second analysis, the image taken on the day of the set-up was excluded, the kV-kV images taken on during the treatment days were examined within themselves, and the mean shift value was found as Vert: 0.13 mm, Long: 0.20 mm, and Lat: 0.27 mm, respectively, as shown in Table 1.

The mean shift values obtained from the first analysis are higher in all directions than the second analysis. The reason is the inclusion of first treatment day set-up day shift values in the first analyzed group. Since the shift value obtained on the first set-up day is the major shift

given pre-treatment, it is likely to be higher than the shift values obtained from the images captured interfraction. Analysis revealed that the mean shift values in the Vert, Long, and Lat directions were ≤ 1 mm both in the first and second analyzed groups. And the shift values are among the limit values determined for the IGRT technique to be applied to HNC patients.

DISCUSSION

Advanced RT techniques have better protection of critical structures in the treatment of HNC, and contributed to safely reaching the higher doses required for disease control.^[13-17]

During treatment administration, the aim is to provide and maintain the planning conditions created in the CT simulation and TPS throughout the entire treatment and to prevent positioning errors.

Multiple causes of positioning errors exist, including a systematic difference between patient immobilization at simulation and treatment,

Table 1. Mean shift values obtained from CBCT/kV-kV images on set-up day + treatment days and kV-kV images treatment days only

	Vert _{mean}	Long _{mean}	Lat _{mean}	Limit
Set-up day + treatment days (mm)	0.24	0.27	0.32	≤ 4
Treatment days (mm)	0.13	0.20	0.27	≤ 3

CBCT: Cone-beam computed tomography; kV-kV: Kilovoltage.

random daily setup errors in positioning on treatments, and alterations in patient anatomy during treatment.^[10] Therefore, it must be absolute for the treatment practice, to follow the changes in the patient treatment position via taken images between treatments, to record the determined shift values from these images, and to create their own set-up correction circumstances in-clinic.

Technological developments have enabled the use of intrafractional or interfractional imaging techniques that provide the determination of treatment accuracy. The evaluation of the images taken on the set-up day and subsequent fractions and the follow-up of the shifts on the images are important in terms of the quality of assurance of the RT treatment especially on IGRT.

The advent of treatment machines equipped with both kV radiographic and cone beam imaging capability has resulted in a choice of setup procedures.

Many in-room imaging techniques like MV, kV, and CBCT integrated into the medical linear accelerator have been evaluated and compared with designed studies. Megavoltage portal imaging was used to verify the position in HNC treatment, however, this modality was reported poor contrast imaging in studies.^[7,10,17-21]

In a study, Pisani et al.^[22] showed that pre-treatment images taken with kV reduced setup error significantly more than with MV.^[10]

In principle, 3D imaging methods like CBCT are expected to better visualize internal landmarks and lead to more accurate setups than 2D kV-kV imaging. However, the potential benefits of patient positioning techniques based on 3D over 2D imaging need to be described.

Three-dimensional imaging like CBCT increases a patient's radiation exposure and requires a longer time and more sophisticated radiation therapist skills to acquire and register images, while the patient is waiting for the IR on the treatment couch.^[23,24]

The difference between the images obtained by the 3D CBCT/kV-kV pair and the images obtained by 2D kV-kV is that the 3D CBCT/kV-kV can show rotational set-up shifts too.^[2]

In the literature, it has been expressed that the rotational shift detected to a degree of ≤ 3 mm can

be ignored.^[10] In our study, we did not record or evaluate rotational shifts. In our clinical protocol, the rotational shift is not applied and the position of the patient with this deviation is re-evaluated, the mask and patient position checked, and the pre-treatment image is taken again.

A study designed to quantify by means of CBCT the random and systematic uncertainty involved in RT with HNC and thoracic cancer patients. Aim to determine if the information obtained is possible to use for technical quality assurance, evaluation of patient immobilization, and determination of margins for the treatment planning. Revealed that the total uncertainty leads to 4 mm on the patient's position growth during the treatment course, especially in the longitudinal direction for patients receiving thoracic IR but in all directions for HNC patients. Immobilization of these patients was considered the cause of the error.^[12]

In our study for HNC patients set-up errors were ≤ 1 mm in all directions. It has been observed that the clinical practices are reliable and the shifts are compatible with other studies. The reason why the shift values are so small in all directions is associated with the CT immobilization, the patient mask design, and the treatment position that is made under a radiation oncologist control for each patient in our clinic.

Delishaj et al.'s^[13] study focused on investigating set-up errors and suggest adequate PTV margins and IGRT frequency in HNC treated with the IMRT technique assessed by CBCT/ kV. Subsequent to the systematic set-up errors correction, the adequate margin to overcome the problem of set-up errors was found to be less than 3 mm. The CBCT/kV at first three fractions and followed by weekly is useful for reducing significantly set-up errors in HNC treated with IMRT technique. Finally, 3-5 mm PTV margins appear adequate and safe to overcome the problem of set-up errors.

As revealed in our study similar to Delisahaj et al.,^[13] regular application of the CBCT/kV combination keeps the errors at limits between the set-up image and during treatment image comparison.

Another study was designed to compare the patient set-up error detection capabilities of 3D-CBCT and 2D-kV techniques with HNC

patients under IMRT. Linear set-up errors were observed for 2D-kV and 3D-CBCT image guidance techniques. Higher rotational deviations around the table's vertical axis were detected by the 3D-CBCT with respect to the 2D-kV method.^[2]

In our study highest deviations were observed on the lateral axis and the least on the vertical axis unlike Ciardo et al.^[2] In our patient group, most of the deviations were in the lateral direction and the deviation value was <1 mm. For this reason, it was thought that the errors might be related to weight loss rather than setup.

In conclusion, since the shift values of CBCT/kV-kV images of the two analyzes are very close; In addition to correct positioning with CBCT/kV-kV on the day of set-up, taking kV-kV images every other day to monitor the change in the patient's anatomical structure throughout treatment may provide the advantage of better imaging of the treatment field and lower dose administration to the patient.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

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