Comparison of Electronic Portal Imaging and Cone Beam Computed Tomography for Position Verification in Children


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Abstract

Aim: To compare the accuracy of radiotherapy set-up using an electronic portal imaging device (EPID) versus megavoltage cone beam computed tomography (MV-CBCT) in paediatric patients.

Materials and methods: In total, 204 pairs of EPID and MV-CBCT were carried out for 72 patients in the first 3 treatment days and weekly thereafter.

Results: For the whole group, the mean systematic EPID set-up errors were 1.8 (⁺/⁻1.7), 1.6 (⁺/⁻1.3), 1.4 (⁺/⁻1.5) mm and 2.3 (⁺/⁻1.7), 1.6 (⁺/⁻1.3), 2.4 (⁺/⁻1.6) mm for MV-CBCT in the longitudinal, lateral and vertical directions, respectively, whereas the mean EPID random errors were 2.0 (⁺/⁻1.7), 1.4 (⁺/⁻1.5), 1.2 (⁺/⁻1.6) and 1.9 (⁺/⁻1.5), 1.5 (⁺/⁻1.3), 2.1 (⁺/⁻1.7) mm for MV-CBCT in the longitudinal, lateral and vertical directions, respectively. For systematic errors of head and neck patients, there was a statistically significant difference in the lateral and vertical directions (P = 0.027, 0.003), whereas in the non-head and neck patients there was a statistically significant difference in the lateral direction only (P = 0.031). In head and neck patients, the mean random errors were significantly different in the vertical and lateral directions, whereas in non-head and neck patients, they were significantly different in the vertical direction only. The larger values alternate between the two modalities. The systematic and random errors (detected by EPID and MV-CBCT) were significantly correlated in almost all direction in all tumour sites.

Conclusions: The comparison between set-up error in EPID and MV-CBCT was not in favour of any of the two modalities. However, the two modalities were strongly correlated but fairly agreed and the differences between the shifts reported were small and hardly influenced the recommended planning target volume margin.

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Key words: Cone beam CT; EPID; paediatric tumours; PTV margin; radiotherapy position verification; set-up error

Introduction

In the last two decades, paediatric patients have shown excellent treatment end-results, not only due to the multidisciplinary approach adopted, but also due to the huge advancement in each discipline. The clinical outcome of patients treated with radiation is related to the tumour control probability, which improves with multimodality imaging for accurate tumour delineation, precise planning, utmost verification and better knowledge of the normal tissue complication probability [1,2]. Patient immobilisation, improved volume delineation, organ motion control and dose delivery verification have tremendously progressed in the last two decades. These issues decrease the geographical miss to a minimum and raise the local control to a maximum and consequently markedly improve the patient outcome. Highly conformal radiation therapy aims at tailoring prescription isodoses to encompass the target volumes as possible and to minimise normal tissue toxicities. Increasing the accuracy of radiation dose delivery to the target volume improves the tumour control probability and reduces treatment-related morbidity. Many trials have shown that the proper execution of treatment ensures good coverage of the target volume with the prescription isodose and spares adjacent critical organs. The accuracy of the set-up is considered the main concern of all radiation oncologists to ensure delivery of the prescribed treatment and to gain the desired tumour control probability [3,4].

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Technical advances in radiotherapy have focused on the control of patient movement, organ motion and anatomical deformation, which limit the effectiveness of high-precision treatment [5,6]. Recently, target positioning has been inferred from surface marks on the patient’s skin or an immobilisation device, and verified using megavoltage radiographs of the treatment portal [7,8]. The accuracy of the set-up errors could not be absolutely evaluated because a reference procedure (i.e. a gold standard) was lacking.

A megavoltage electronic portal imaging device (EPID) uses X-ray beams to produce good image quality, sufficient for detecting bone structures [8,9]. Modern EPIDs offer advantages over film-based megavoltage radiography, mainly because of the ability to adjust display contrast, and to assess the target position and to adjust the patient promptly. Moreover, EPID has the potential for in vivo measurements and three-dimensional dose verification [10]. It is still difficult to assess field placement with respect to soft tissue structures by using megavoltage radiographs. The desire to further improve normal tissue sparing is driving requirements for greater accuracy in target localisation. Recently, the shift from two-dimensional detection (EPID) to three dimensions (cone beam computed tomography [CBCT]) took place in many centres, with the assumption that CBCT images offer high subject contrast compared with portal imaging. Such characters facilitate image interpretation and render automatic image matching more reliable. Moreover, some investigators assume that the CBCT system is more stable [11]. CBCT systems enable volumetric imaging on a conventional linear accelerator. In a single gantry rotation, volumetric images are reconstructed by back-projection of hundreds of two-dimensional radiographs acquired from using a large-area amorphous silicon detector in the treatment position just before treatment delivery [12].

Factors that can lead to treatment set-up uncertainties have been discussed in some studies [13,14]. Here we focus on the differences between two-dimensional (EPID) and three-dimensional (CBCT) image alignment.

The aims of the present study were to evaluate set-up variation of paediatric patients undergoing three-dimensional conformal radiotherapy using EPID and MV-CBCT in the same sitting, to assess the existence of correlation between the results of the two modalities, to compare the recorded errors for both modalities in different tumour sites and to evaluate the estimated planning target volume (PTV) margin based on each dataset.

**Patients and Methods**

**Patient Data**

All children who were treated in the Children’s Cancer Hospital, Egypt using three-dimensional conformal radiotherapy in the period from December 2008 to April 2009 were included in our study. In total there were 72 children, 48 boys and 24 girls, with ages ranging between 2 and 17 years (median 7 years; mean ± standard deviation 6.4 ± 3.8). On the basis of anatomical classification, 44 of these children were diagnosed with head and neck tumours, 16 with thoracic tumours and 12 with abdominal/pelvic tumours. The pathological diagnoses for these patients were as follow: Hodgkin’s disease (14), rhabdomyosarcoma (12), Wilms’ tumour (12), medulloblastoma (9), neuroblastoma (8), brain (7), brainstem tumours (3), germinoma (3), leukaemia and non-Hodgkin’s lymphoma (3) and nasopharyngeal carcinoma (1). Eighteen patients received their treatment under general anaesthesia.

**Immobilisation and Reference Reconstruction**

All patients were immobilised in the treatment position during planning computed tomography and during daily fractions. For head and neck sites, a thermoplastic immobilisation system with a suitable head rest was used. For non-head and neck sites, a vacuum mattress and/or a body frame and thermoplastic body mask were used.

Contrast-enhanced planning computed tomography (0.98 × 0.98 mm axial pixels, 4 mm slice thickness) was carried out. The data were transferred to the planning system (Xio, CMS, TPS) where three-dimensional conformal radiotherapy plans were created. The clinical target volume (CTV) margin to create the PTV was 5 mm in the three dimensions in all tumour sites.

The planning computed tomography scan with the isocentre position as well as two digitally reconstructed radiographs (DRRs) for the orthogonal portals was imported from the planning system to the treatment control station to be used as a reference.

**Patient Set-up**

The patients received their prescribed treatments in a range of between six and 33 treatment sessions of 180 cGy per fraction, with a median of 12 sessions. Both MV-CBCT scans and EPID images were acquired for each patient in the first 3 treatment days and weekly thereafter. Both tools were used during each verification session for comparison. Whenever, for any reason, only one tool (EPID or MV-CBCT) was used, this reading was not considered for the purpose of this study. The two verification procedures were carried out immediately before treatment execution, without special time predilection. Random choice depended mainly on machine gantry position and different radiation therapist preference. Two hundred and four pairs of assessable EPID–CBCT alignment sets were obtained. In general, set-up verification was carried out in less than 5 min before the start of the irradiation.

**Electronic Portal Imaging**

Before radiotherapy, two orthogonal EPID images (anterior—posterior and lateral) were acquired using an Optivue 1000 ST amorphous silicon flat panel detector (1024 × 1024 pixels, 41 × 41 cm² corresponding to a field size in the isocentre plane of 27.4 × 27.4 cm²), using two monitor units each. These images were acquired using coherence therapist
software. A bone template was defined on the DRR. The DRR edges were matched automatically with the portal field edges. Thereafter, manual adaptation of the bony anatomy was carried out by a radiation oncologist (MSZ, AGM or EE). The set-up error was recorded in two directions in each image and the error calculated in the three dimensions.

Cone Beam Computed Tomography

The patients underwent MV-CBCT scanning using the therapeutic X-ray beam and the Optivue flat panel detector. Using the megavoltage scan protocol, 200 projections were acquired over an arc of 200°, yielding an imaging dose of about 7 cGy at the isocentre. Image projections were acquired by the flat panel detector and reconstructed using a filtered back projection algorithm to give the three-dimensional volumetric computed tomography image set. Patient anatomy as detected in the CBCT scans was automatically registered to the planning scan using voxel-based registration for bone, air and soft tissue. The CBCT images were then matched with the planning computed tomography images to check for positional errors. The set-up error was recorded in the three directions.

Systematic Set-up Errors

Set-up shifts were recorded in the first three treatment fractions using both MV-CBCT scans and EPID images. In the first three fractions, temporary set-up correction was carried out before treatment. Average set-up shifts recorded in the first three treatment days were used to define systematic set-up errors. MV-CBCT systematic error had to be applied for the rest of the treatment fractions.

Random Set-up Errors

Set-up errors were recorded once weekly (random error) before treatment. To limit workload, only set-up errors of more than 3 mm (action level) were corrected.

Table 1

Mean systematic and random shifts (mm ± standard deviation) as measured using an electron portal imaging device (EPID) and megavoltage cone beam computed tomography (MV-CBCT)

<table>
<thead>
<tr>
<th>Error</th>
<th>Site</th>
<th>Tool</th>
<th>Longitudinal</th>
<th>Lateral</th>
<th>Vertical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic</td>
<td>Head and neck</td>
<td>EPID</td>
<td>1.5 (±1.4)</td>
<td>1.2 (±1.0)</td>
<td>1.5 (±1.3)</td>
</tr>
<tr>
<td></td>
<td>Non-head and neck</td>
<td>MV-CBCT</td>
<td>1.9 (±1.1)</td>
<td>1.4 (±1.2)</td>
<td>2.4 (±1.4)</td>
</tr>
<tr>
<td></td>
<td>EPID</td>
<td>2.3 (±2.1)</td>
<td>2.3 (±1.5)</td>
<td>1.2 (±1.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MV-CBCT</td>
<td>3.0 (±2.1)</td>
<td>2.1 (±1.2)</td>
<td>2.2 (±1.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EPID</td>
<td>1.8 (±1.7)</td>
<td>1.6 (±1.3)</td>
<td>1.4 (±1.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MV-CBCT</td>
<td>2.3 (±1.7)</td>
<td>1.6 (±1.3)</td>
<td>2.4 (±1.6)</td>
<td></td>
</tr>
<tr>
<td>Random</td>
<td>Head and neck</td>
<td>EPID</td>
<td>1.8 (±1.6)</td>
<td>1.2 (±1.4)</td>
<td>1.2 (±1.5)</td>
</tr>
<tr>
<td></td>
<td>Non-head and neck</td>
<td>MV-CBCT</td>
<td>1.6 (±1.2)</td>
<td>1.3 (±1.1)</td>
<td>2.0 (±1.6)</td>
</tr>
<tr>
<td></td>
<td>EPID</td>
<td>2.5 (±2.0)</td>
<td>1.8 (±1.7)</td>
<td>1.2 (±1.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MV-CBCT</td>
<td>2.4 (±1.8)</td>
<td>2.1 (±1.6)</td>
<td>2.3 (±1.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EPID</td>
<td>2.0 (±1.7)</td>
<td>1.4 (±1.5)</td>
<td>1.2 (±1.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MV-CBCT</td>
<td>1.9 (±1.5)</td>
<td>1.5 (±1.3)</td>
<td>2.1 (±1.7)</td>
<td></td>
</tr>
</tbody>
</table>

Systematic as well as random set-up error datasets were evaluated for different anatomical sites using both MV-CBCT and EPID. The correlation between the two datasets was tested using Pearson’s correlation coefficient, whereas the difference between the two datasets was statistically tested using the non-parametric Wilcoxon signed-rank test for two related samples. Agreement between MV-CBCT and EPID was assessed by Bland–Altman analysis [15]: bias (mean of the differences between pairs of measures) and 95% limits of agreement (±1.96 standard deviation of the difference between pairs of measures). The Bland–Altman analysis plots the individual differences between the two measurements against the mean of the measurements to test for agreement. ‘Good agreement’ was considered when the difference between the two measurements was within the limits of the ‘mean ± one standard deviation’, ‘Fair agreement’ was when the difference was within the limit of the ‘mean ± two standard deviations’, whereas ‘Poor (or bad) agreement’ was when the difference was within the limits of ‘mean ± three standard deviations or more’ [16].

Pre-study Consent

The institutional review board of the Children’s Cancer Hospital, Egypt approved the study. Written consent was given by our patients’ guardians before the patients were included in the study.

Results

For the whole study group, the mean systematic set-up errors (± standard deviation) were 1.8 (±1.7), 1.6 (±1.3) and 1.4 (±1.5) mm by EPID and 2.3 (±1.7), 1.6 (±1.3) and 2.4 (±1.6) mm as determined by MV-CBCT in the longitudinal, lateral and vertical directions, respectively. On the other hand, the mean random set-up errors (± standard deviation)
were found to be 2.0 (±1.7), 1.4 (±1.5) and 1.2 (±1.6) mm in the longitudinal, lateral and vertical directions, respectively, using EPID and 1.9 (±1.5), 1.5 (±1.3) and 2.1 (±1.7) mm via MV-CBCT.

Using both EPID and MV-CBCT, the mean systematic set-up error recorded was found to be ≤ 3 mm in all tumour sites. Moreover, none of the mean random shifts exceeded 2.5 mm in any direction using either MV-CBCT or EPID (see Table 1).

**Frequency of Set-up Error**

Systematic errors in the head and neck site exceeded 3 mm in at least one direction in 10 (22.7%) and 15 (34.1%) of the 44 patients using EPID and CBCT, respectively. Using CBCT, systematic error exceeded 5 mm in only two (4.5%) patients; it did not exceed 5 mm in any patient using EPID (Fig. 1a). On the other hand, in non-head and neck tumours, it exceeded 3 mm in 12 (42.9%) and 13 (46.4%) of the 28 patients using EPID and CBCT, respectively (Fig. 1b), whereas it exceeded 5 mm in four (14.3%) patients using either EPID or CBCT.

Random errors in the head and neck site demanded correction action (>3 mm) in 27 (26.7%) and 21 (20.8%) of the 101 set-ups using EPID and CBCT, respectively (Fig. 1c). For non-head and neck tumours, correction action (error >3 mm) was taken in 18 (39.1%) and 23 (50%) of the 46 set-ups using EPID and CBCT, respectively (Fig. 1d).
Fig. 2. Systematic error as recorded using an electronic portal imaging device (EPID) plotted against megavoltage cone beam computed tomography (MV-CBCT): (a) longitudinal direction in head and neck patients; (b) lateral direction in head and neck patients; (c) vertical direction in head and neck patients; (d) longitudinal direction in non-head and neck patients; (e) lateral direction in non-head and neck patients; (f) vertical direction in non-head and neck patients.
Comparison between Electronic Portal Imaging and Cone Beam Computed Tomography Recorded Error

Systematic error
In head and neck sites, the systematic set-up error using MV-CBCT was found to be larger than the errors detected using EPID. The mean differences were found to be 1.0 (±1.3), 1.1 (±1.2) and 1.5 (±1.2) mm in the longitudinal, lateral and vertical directions, respectively. Using the Wilcoxon signed-rank test, such differences were found to be statistically significant in the lateral and vertical directions, but not in the longitudinal direction (P = 0.027, 0.003 and 0.317, respectively).

In non-head and neck sites, the systematic set-up errors via MV-CBCT were significantly larger than the errors detected using EPID in the vertical direction only (P = 0.002). On the contrary, the systematic set-up errors via EPID were significantly larger than the errors detected through MV-CBCT in the lateral direction (P = 0.031). The difference was not statistically significant in the longitudinal direction (P = 0.757) (Fig. 2).

Random error
In head and neck sites, the random set-up errors detected by MV-CBCT were significantly larger than those detected by EPID in the vertical and lateral directions (P = 0.000 and 0.033, respectively), whereas the difference was not statistically significant in the longitudinal direction (P = 0.201).

In non-head and neck sites, the random set-up error detected via MV-CBCT was found to be significantly larger than the errors detected using EPID in the vertical direction only (P = 0.000). The difference was not statistically significant in either the longitudinal or the lateral direction (P = 0.66 and 0.415, respectively).

Effect of Anaesthesia
Eighteen children received their treatment settings with general anaesthesia (10 with head and neck tumours and eight with non-head and neck tumours). The mean systematic set-up errors for all anaesthetised patients were 2.0 (±2.1), 1.7 (±1.1) and 0.9 (±1.3) mm as detected by EPID and 2.5 (±2.3), 2.1 (±1.2) and 2.3 (±1.5) mm as determined by MV-CBCT in the longitudinal, lateral and vertical directions, respectively. There was no statistically significant difference between the 18 children treated with anaesthesia and the whole population of children. The MV-CBCT recorded errors were found to be larger than the EPID recorded errors. The differences were statistically significant in the longitudinal and vertical directions, but not in the lateral direction (P = 0.025, 0.001 and 0.185, respectively).

The mean random set-up errors were found to be 2.3 (±1.6), 1.5 (±1.6) and 1.1 (±1.6) mm in the longitudinal, lateral and vertical directions, respectively, by EPID and 2.2 (±1.5), 2.1 (±1.3) and 1.7 (±1.5) mm via MV-CBCT. The random error depicted via CBCT was found to be significantly larger than the EPID recorded error in the vertical direction (P = 0.012), but not in the longitudinal and lateral directions (P = 0.579 and 0.121, respectively).

Optimum Planning Target Volume Margin Definition

The optimal margin that should be evenly added to the CTV was calculated using the set-up error (systematic and random). The calculations were carried out twice using data obtained from both EPID and CBCT (Table 2). The Van Herk equation [17] (recommended PTV margin = 2.5 × standard deviation of systematic error + 0.7 standard deviation of random error) was applied in the three planes to ensure that the 95% isodose line covers the CTV for 90% of patients [18]. Table 2 shows the comparison between estimated PTV margins using EPID and CBCT. The maximum difference between the calculated margins in any direction was 1 mm in head and neck sites and 0.8 mm in non-head and neck sites. These differences were not statistically significant.

Correlation and Agreement between Electronic Portal Imaging and Cone Beam Computed Tomography Recorded Error

Systematic set-up error

Using the Pearson correlation test, systematic set-up errors recorded in head and neck sites using EPID were found to be correlated with those recorded using CBCT in the lateral and longitudinal directions, but not in the vertical direction (P = 0.000, 0.009 and 0.186, respectively). On the other hand, systematic set-up errors recorded in non-head and neck sites using EPID were found to be correlated with those recorded via CBCT in the longitudinal, lateral and vertical directions (P = 0.000, 0.005 and 0.000, respectively).

In spite of such good correlation, the agreement between the two modalities was fair. A Bland—Altman plot [15] of the systematic set-up errors detected via EPID and MV-CBCT is shown in Fig. 4. The mean deviation and limits of agreement (±1.96 standard deviation) of the two modalities in the head and neck group of patients were: 0.4 (−4.0 to 4.7) mm, 0.5 (−2.4 to 3.5) mm and −1.2 (−5.9 to 3.5) mm in the longitudinal, lateral and vertical directions, respectively (Fig. 4a–c). The absolute difference did not exceed 3 mm in most of the patients (Table 3). On the

Table 2
The calculated planning target volume margin using an electronic portal imaging device (EPID) and cone beam computed tomography (CBCT) datasets

<table>
<thead>
<tr>
<th>Site</th>
<th>Planning target volume (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Modality</td>
</tr>
<tr>
<td>Head and neck</td>
<td>EPID</td>
</tr>
<tr>
<td></td>
<td>CBCT</td>
</tr>
<tr>
<td>Non-head and neck</td>
<td>EPID</td>
</tr>
<tr>
<td></td>
<td>CBCT</td>
</tr>
</tbody>
</table>
other hand, the mean deviation and limits of agreement (±1.96 standard deviation) of the two modalities in the non-head and neck group of patients were: 0.2 (−5.1 to 5.6) mm, 0.9 (−3.5 to 5.3) mm and −1.0 (−4.2 to 2.1) mm in the longitudinal, lateral and vertical directions, respectively (Fig. 4d–f). In more than 80% of the patients, the absolute difference did not exceed 3 mm in any direction (Table 3).

Fig. 3. Random error as recorded using an electronic portal imaging device (EPID) plotted against megavoltage cone beam computed tomography (MV-CBCT): (a) longitudinal direction in head and neck patients; (b) lateral direction in head and neck patients; (c) vertical direction in head and neck patients; (d) longitudinal direction in non-head and neck patients; (e) lateral direction in non-head and neck patients; (f) vertical direction in non-head and neck patients.
Random set-up error

Random set-up errors recorded in head and neck sites through EPID were found to be correlated with those recorded through CBCT in the longitudinal, lateral and vertical directions ($P = 0.000, 0.001$ and 0.000, respectively). Moreover, the recorded error in non-head and neck sites using EPID were found to be correlated with those recorded via CBCT in the longitudinal, lateral and vertical directions ($P = 0.000, 0.000$ and 0.001, respectively) (Fig. 3).

The two modalities showed fair agreement both in the head and neck as well as the non-head and neck groups of patients. A Bland–Altman plot of the random set-up errors detected via EPID and MV-CBCT is shown in Fig. 5. The mean deviation and limits of agreement (±1.96 standard deviation) of the two modalities in the head and neck group of patients were: $-0.3$ (−4.9 to 4.3) mm, $0.4$ (−3.5 to 4.2) mm and $-1.1$ (−3.0 to 5.3) mm in the longitudinal, lateral and vertical directions, respectively (Fig. 5a–c). Meanwhile, the mean deviation and limits of agreement of the two modalities in the non-head and
Table 3
The differences between electron portal imaging device (EPID) and cone beam computed tomography (CBCT) mean set-up errors, the 95% agreement limits and the percentage of less than or equal to 3 mm difference between the readings via the two modalities in each directions using the Bland–Altman analysis.

<table>
<thead>
<tr>
<th>Systematic error</th>
<th>Non-head and neck</th>
<th>Head and neck</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Longitudinal</td>
<td>Lateral</td>
</tr>
<tr>
<td>Difference between EPID and CBCT averages (mm)</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>95% limits of agreement (mm)</td>
<td>−4.0 to 4.7</td>
<td>−2.4 to 3.5</td>
</tr>
<tr>
<td>% of absolute difference ≤ 3 mm</td>
<td>91%</td>
<td>91%</td>
</tr>
<tr>
<td>Random error</td>
<td>−0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Difference between EPID and CBCT averages (mm)</td>
<td>−4.9 to 4.3</td>
<td>−3.5 to 4.2</td>
</tr>
<tr>
<td>% of absolute difference ≤ 3 mm</td>
<td>85%</td>
<td>89%</td>
</tr>
</tbody>
</table>

Discussion

Set-up Errors in Electronic Portal Imaging and Cone Beam Computed Tomography

To the best of our knowledge, this is the first study focused on comparing EPID and CBCT in the paediatric age group. Using appropriate patient immobilisation tools and careful daily positioning, both systematic and random errors were found to be clinically acceptable and satisfying the needs for considerable accuracy (Table 1). Systematic and random errors were relatively smaller in head and neck compared with non-head and neck patients owing to minimal discrepancy in set-up geometry due to the rigid nature of the site. Using EPID, systematic and random set-up uncertainty analysis revealed small errors in head and neck patients (maximum standard deviation 1.4 and 1.6 mm, respectively) (Table 1). Such small systematic errors indicate no significant motion during planning computed tomography, minimal uncertainty in image registration and data transfer. Our data seem to be consistent with many studies addressing the set-up accuracy in adult head and neck patients [19–21]. In all these studies, the calculated standard deviation of the systematic and random errors ranged between 1 and 2 mm in all directions. However, larger set-up errors were reported by Weltens et al. [22], who evaluated set-up error for 43 head and neck adult patients. They reported a maximum standard deviation of 2.4 and 3.9 mm for random and systematic errors, respectively, regardless of the type of fixation device. Such larger errors may be attributed to the use of relatively primal verification films compared with the more advanced flat panel EPID used in our study. In our study, systematic errors detected via CBCT were larger (maximum 2.4 ± 1.4) than EPID-detected errors. The same finding was also reported in the study of Li et al. [23]. The minimal systematic error was tested in an ideal situation using a head phantom (a rigid body with no curvature change, interval movement or rotation). The maximum error was −0.3 mm (±0.6) for two-dimensional registration (EPID) and 0.6 mm (±0.4) for CBCT [19]. In a review of the use of EPID in head and neck patient positioning, Hurkmans et al. [24] found that a standard deviation of 2 mm or less for both the random and the systematic set-up error can be considered good clinical practice.

Relatively larger errors were recorded in non-head and neck patients owing to the less tight fixation and higher possibility for tilting and rotation compared with the head and neck sites. Our EPID data were consistent with El-Gayed et al. [25]. The calculated standard deviation for systematic and random errors in our data (Table 1) was found to be less than that reported by Creutzberg et al. [26]. Their random error standard deviations were 2.5, 4.2, 4.2 mm compared with 1.7, 2.0 and 1.7 mm in our study, for the lateral, longitudinal and vertical directions, respectively. They also reported the systematic error standard deviations to be 2.5, 3.9 and 3.7 mm compared with 1.5, 2.1 and 1.8 mm in our study in the lateral, longitudinal and vertical directions, respectively. Such relatively higher shifts may be attributed to the simple positioning technique they used in which a vertical pin (pushed against the pubic bone) was the only device determining the cranio-caudal field placement. Borst et al. [27] reported larger set-up shifts for lung cancer patients. They reported the standard deviation of the random errors as 3.7, 3.2 and 2.5 mm compared with 1.8, 1.6 and 1.8 mm in our study for the longitudinal, lateral and vertical directions, respectively, using CBCT. Hurkmans et al. [24] considered that 2.5 and 3.0 mm or less for the standard deviation of the random and systematic errors for prostate and pelvic treatment techniques, and 3.5 mm for lung patients, as ‘state of the art’.

In general, our study documented that systematic errors in head and neck sites never exceeded 5 mm using EPID, whereas it was exceeded in only 4.2% using CBCT. Random errors in head and neck sites demanded correction action
Factors that can lead to treatment set-up uncertainties have been discussed in many trials [13,14]. There are several sources of inconsistency observed between the two-dimensional (EPID) and three-dimensional (CBCT) techniques. First is the time interval between the CBCT and EPID measurements. Although this time was a few minutes, the observed set-up differences between CBCT scans and EPID images might be caused by patient and/or respiratory motion between image acquisitions. Moreover, the accuracy of the validations is limited by the resolution of couch digital readouts, which is of the order of 1 mm. Second, the variations may be attributed to the usage of different regions of interest for matching. Zhang and colleagues [13] reported shifts in 11.2 and 18.7% of set-ups using EPID and CBCT. On the other hand, correction action was needed for non-head and neck patients in 39.1 and 50% using EPID and CBCT.

**Discrepancy between Two- and Three-dimensional Techniques**

Fig. 5. The agreement between random errors recorded via EPID and MV-CBCT: (a) longitudinal direction in head and neck patients (b) lateral direction in head and neck patients (c) vertical direction in head and neck patients (d) longitudinal direction in non-head and neck patients (e) lateral direction in non-head and neck patients (f) vertical direction in non-head and neck patients.

(>3 mm) in only 26.7 and 20.8% of the 101 set-ups using EPID and CBCT. Li et al. [23] reported shifts (≥3 mm) in 11.2 and 18.7% of set-ups using EPID and CBCT. On the other hand, correction action was needed for non-head and neck patients in 39.1 and 50% using EPID and CBCT.
reported such differences for head and neck patients using different bony structures (C2, C6, and the palatine process of the maxilla) for matching. A third factor might be that EPID measures only the set-up errors in the lateral, longitudinal and vertical directions and not rotations. On the contrary, CBCT takes rotation into consideration when calculating for errors [28]. Needless to mention that three-dimensional verification using CBCT is capable of detecting changes in treatment volume, especially the soft tissue component, due to marked tumour reduction, oedema, etc., whereas EPID verification can hardly do so. Borst et al. [27] observed a correlation between the rotations and the differences between CBCT and EPID. The most important factor might be the relatively poor visibility of anatomic structures in the DRRs calculated from the planning computed tomography scan and portal images. The relative loss of detail caused by the 4 mm slice thickness does not significantly influence the computed tomography to CBCT registration accuracy because of the three-dimensional nature of this matching algorithm.

Set-up Differences and Correlation

Systematic set-up errors measured through CBCT were generally larger than those measured with EPID in head and neck sites. The largest difference was observed in the vertical direction, as also reported by Borst et al. [26]. However, the comparison between the two modalities in detecting systematic error for non-head and neck sites as well as the random error in all sites was not in favour of any, and it alternated between EPID and CBCT in the different directions. In spite of these differences, the PTV required margin was equal (4.6 mm) for head and neck sites concerning both modalities. Such estimated margins were consistent with those of Li et al. [23], who recommended the addition of 3.9 and 5.1 mm for PTV uncertainty margin creation based on EPID (using Mutual Information software) and CBCT, respectively. In non-head and neck patients, the EPID-estimated PTV margin (6.7 mm) was marginally larger than the CBCT-based margin (6.5 mm). This can be attributed to the more crude alignment of the two-dimensional EPID. The least random error standard deviation in non-head and neck patients was recorded in the lateral direction using both EPID and CBCT. This can be explained by the minimal organ motion in the lateral direction compared with the longitudinal and vertical directions [29]. Moreover, the simple daily alignment of the patient’s midline reduces lateral random errors compared with the longitudinal and vertical positions, which need a bilateral check. Such smaller standard deviations dictated a smaller (5 mm) PTV-recommended lateral margin compared with 6 mm for vertical and 7 mm for longitudinal directions. These findings strongly support the use of an anisotropic PTV margin in non-head and neck patients.

In the present study, a strong correlation has been observed between set-up errors recorded using EPID and CBCT in almost all directions in both systematic and random errors. Such a correlation denotes reliable manual matching of the EPID with the DRR that was consistent with digital fusion of the planning computed tomography scan and the CBCT. Such correlation was also reported by Li and colleagues [23]. This strong correlation, between EPID and CBCT datasets emphasizes their value in set-up verification.

From the above data, we can conclude that in paediatric patients, the use of proper immobilisation tools yields acceptable systematic and random set-up errors. Such errors seem to be less in head and neck patients compared with other sites, owing to better fixation. The comparison between the set-up errors in the two modalities was not in favour of any and it kept switching between EPID and CBCT in the different directions. Although some consider shifts depicted using CBCT as the reference shifts, they were strongly correlated with the EPID results and the differences between the shifts recorded using the two modalities were small and hardly influenced the recommended PTV margin. However, they showed fair agreement using the Bland–Altman analysis. The use of EPID to overcome the limitation in the number of MV-CBCT should be carefully adopted and clinically judged in the verification procedure, especially in paediatric patients.

References


