Geometrical uncertainty margins in 3D conformal radiotherapy in the pediatric age group

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Purpose: To evaluate set-up variation of pediatric patients undergoing 3D conformal radiotherapy (3DCRT) using electronic portal image device (EPID), in an effort to evaluate the adequacy of the planning target volume (PTV) margin employed for the 3DCRT treatment of pediatric patients.

Materials and methods: Set-up data was collected from 48 pediatric patients treated with 3DCRT for head and neck (31 patients), abdomino-pelvic (9 patients) and chest (8 patients) sites during the period between September 2008 and February 2009. A total of 358 images obtained by EPID were analyzed. The mean ($M$) and standard deviation (SD) for systematic and random errors were calculated and the results were analyzed.

Results: All images were studied in anterior and lateral portals. The systematic errors along longitudinal, lateral and vertical directions in all patients showed an $M$ equal to 1.9, 1.6, and 1.6 mm with SD of 1.8, 1.4, and 1.8 mm, respectively; (head and neck cases: $M$ equal to 1.5, 1.2, and 1.6 mm with SD 1.4, 1.2, and 1.8 mm; chest cases: $M$ equal to 2.5, 1.8, and 0.8 mm with SD 2.7, 1.7, and 1.2 mm, abdomino-pelvic cases: $M$ equal to 2.9, 2.8 and 2.3 mm with SD 1.6, 1.2, and 2.3 mm). Similarly, the random errors for all patients showed SD of 1.9, 1.6, and 1.8 mm, respectively (head and neck cases: SD 1.7, 1.3, and 1.5 mm; chest cases: SD 1.2, 1.9, and 2.5 mm; abdomino-pelvic cases SD 2.5, 2, and...
Introduction

A critical requirement in radiation therapy is the accurate daily treatment set-up. Early studies based on port films indicated the benefits of portal verification to this end [1,2]. Subsequent studies have characterized the magnitude and nature of set-up errors for a variety of clinical conditions with a reported random and systematic error of up to 6 mm [3]. The planning target volume (PTV) is defined as the clinical target volume CTV plus a setup margin and an internal margin. The setup margin is defined to account for uncertainties in the setup of the patient. An effective means to reduce set-up uncertainties would be to increase the frequency of treatment verification with portal imaging [4]. Electronic portal imaging devices (EPID) have become standard in radiotherapy practice and are convenient and efficient for the acquisition and analysis of planar portal images [5]. Set-up uncertainties can be evaluated using pretreatment imaging by using electronic portal imaging devices. The ability to measure set-up errors, in combination with the demand to reduce set-up errors in order to reduce planning target volume (PTV) margins, has led to a growing number of studies on this topic [6–10]. EPID verification systems attached to treatment machines are also able to study the accuracy and reproducibility of treatment delivery and document the delivered radiation dose in terms of pretreatment verification [6,7]. Pre-treatment patient positioning constitutes one important element in determining treatment accuracy. In 1990s, weekly port films were a standard method for assessing patient positioning accuracy [8]. Several studies have emphasized the need for field electronic portal verification with online or off-line imaging review [9,10], and much of the advancements in radiation therapy have concentrated on image guided radiation therapy (IGRT) and imaging modalities with volumetric soft tissue imaging capabilities such as cone beam computed tomography, megavoltage computed tomography, as well as other planar radiographic methods.

Notwithstanding the advances in IGRT, EPID imaging remains the standard for the majority of radiotherapy practice. The aim of our study was to evaluate set-up variation of pediatric patients undergoing 3D conformal radiotherapy (3DCRT) using EPID, in an effort to evaluate the adequacy of the imperial PTV margin employed for the 3DCRT treatment of pediatric patients.

Materials and methods

Forty-eight pediatric patients with cancer treated with 3DCRT at Children’s Cancer Hospital, Egypt (CCHE) between September 2008 and February 2009 were considered in this study. Thirty one had head and neck tumor, 9 had abdominal and pelvic tumor and 8 patients had chest malignancies. The median age of the patients was 8 years (range 2–16 years). The diagnosis of these patients were Hodgkin’s disease (15 patients), brain tumor (14 patients), Wilms’ tumor, rhabdomyosarcoma (5 patients each), neuroblastoma (4 patients), germ cell tumor, leukemia (2 patients each) and one patient with nasopharyngeal carcinoma. 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 where three-dimensional conformal radiotherapy plans were created.

CTV margin to create the PTV was 5 mm in the three dimensions in all tumor sites as an empirical margin. Patients received 180cGy daily treatments ranging from 6 (Wilms’ tumor) to 36 fractions (nasopharyngeal carcinoma), with a median of 12 fractions. Only 6 patients were treated under general anesthesia.

Head and neck patients – at our institution – are immobilized using head–neck–shoulder thermoplastic immobilization system with a suitable headrest. The other patients were immobilized using Vac–Lock cushions or hemi-body Orfit cast. Contrast enhanced CT simulation scans with a 4 mm slice thickness were performed for each patient. The data was transferred to the treatment planning system in order to plan the 3D CRT treatment. Digitally reconstructed radiographs (DRRs) were created for the orthogonal portals (0° and 90°) with fixed field sizes of 10 × 10 cm² taken at the isocenter.

Prior to treatment, patients were setup in the appropriate immobilization device, moved to the treatment isocenter, and orthogonal portal images were acquired using an amorphous silicon digital portal imaging device (OPTIVUE) with a resolution of 1024 × 1024 pixel. The portal images were compared to the DRRs, which were obtained from the treatment planning system (TPS) (CMS, Xio release 4.4), using Viewstation (Therapist Workstation, Siemens Healthcare Oncology, Erlangen, Germany) to view the images. Matching DRR and EPID images were performed using the anatomy matching software (PRIMEVIEW, Siemens). The displacements in two dimensions were noted for each treated field to study the set-up errors. The match structures along with the field formed the match template with automatic image matching software, then manually adjusted to the visible bony anatomy of the portal image. The resulting difference between the planned and delivered field was then given by the image matching software.

Full control over image display contrast, window level, image filter (smoothing filters, etc.), and magnification is available on the workstation. The DRRs and portal images were displayed adjacent to each other on the same screen. On the basis of the comparison of anterior and lateral views of both DRRs and portal images, isocenter misalignments greater than 3 mm were corrected by the therapist using a couch shifts or by correcting the patient position.

The protocol in CCHE department of radiation oncology is to perform set-up verification prior to the first three sessions and derive the average (though correcting for the deviation in each day). The new corrected isocenter after considering the average shift is marked. Weekly setup verification is performed thereafter. Deviation from this new corrected isocenter...
is calculated and any necessary shift (above the tolerance of 3 mm) is routinely performed. Set-up errors were divided into two main classes:

(a) **Random or inter-fraction errors**: Which are deviations between different fractions taken weekly during a treatment series.

(b) **Systematic errors**: Which are deviations between the planned patient position and the average patient position of a course of fractioned therapy taken in the first three settings.

The mean (M) and standard deviation (SD) of the systematic error and SD of random errors were analyzed. To represent true magnitude of errors, the absolute value of the deviations was also considered.

**Results**

The deviations recorded from the verification of 358 EPID (248, 54 and 56 for head-and-neck, chest and abdomino-pelvis cases, respectively) in anterior and lateral portals were analyzed through usual statistical methods (mean M and standard deviation SD). The calculated SD of systematic and random errors for head and neck, chest and abdomino-pelvic cases, along with the study details are shown in Table 1.

In order to minimize subjective errors, electronic portal images (EPIs) were analyzed independently by two observers and the deviations was noted. Deviations smaller than 1 mm between readings of the two observers were ignored while those more than 1 mm were corrected by taking the average of the two sets of readings.

We evaluated set-up errors separately in three dimensions (longitudinal, lateral and vertical). The two radiation oncologists agreed (within 1 mm) in 276 (77.1%) readings out of the 358. The differences ranged between 2 and 4 mm in the remaining 82 recorded reading that was averaged (Table 2).

In head and neck cases, the shift from isocenter ranged from 0 to 7 mm in any of the three directions. The percentage of EPID images in which the errors exceed 3 mm along longitudinal, lateral and vertical directions were equal to 16%, 3%, and 12.9%, for systematic errors and 16%, 6.5%, and 7.5%, respectively, for random errors.

The percentage of images in which errors exceeded 5 mm was 3.2% in vertical direction for systematic errors, while that for random errors were 2.2% in both longitudinal and vertical directions. The maximum error was never higher than 6 mm for systematic and 7 mm for random errors, respectively. The histograms of frequency (percentage of EPIs) of systematic and random errors for head and neck cases in longitudinal, lateral and vertical directions are shown in Figs. 1 and 2.

The calculated PTV margin for head and neck, chest and abdomino-pelvis cases, along with the study details are shown in Table 1.

![Figure 1](https://via.placeholder.com/150)

**Table 1** Calculated SD of systematic errors and SD of random errors along longitudinal, lateral and vertical directions.

<table>
<thead>
<tr>
<th>Site</th>
<th>SD of systematic errors (mm)</th>
<th>SD of random errors (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Longitudinal</td>
<td>Lateral</td>
</tr>
<tr>
<td>Head and neck</td>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Chest</td>
<td>2.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Abdomino-pelvis</td>
<td>1.6</td>
<td>1.2</td>
</tr>
<tr>
<td>All patients</td>
<td>1.8</td>
<td>1.4</td>
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</tbody>
</table>

Applying the equation of Van Herk [11] (2.5 times the SD of systematic errors plus 0.7 times the SD of random errors) to develop PTV margins, a proper plane-dependent margin to clinical target volume (CTV) was estimated to ensure that the dose to the CTV was 95% in 90% of the treated patients. The calculated PTV margin for head and neck, chest and
abdomino-pelvic cases in longitudinal, lateral and vertical directions are shown in Table 3. Only six patients (12.5%) were treated under general anesthesia with no difference of statistical significance in either systematic or random errors, between the anesthetized and nonanesthetized patients.

Discussion

To the best of our knowledge, this is the second study to report on the effect of tumor site on the uncertainty margins in the pediatric population. The first one was reported also by our group in Children’s Cancer Hospital, Egypt (CCHE). We classified patients into head and neck and non-head and neck tumors without further site specification [12]. Another two recent publications from St. Jude Children’s Hospital, Memphis, studied the uncertainty margin restricted to head and neck pediatric patients (including brain tumor) [13,14]. These four studies represent the whole published pediatric experience on setup uncertainty till now. Using appropriate patients’ immobilization 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 tumors compared to non-head and neck patients owing to minimal discrepancy in setup geometry due to the rigid nature of the site. Several studies on adult head
and neck patients had been performed to determine setup accuracy, they showed similar conclusions. Furthermore, our previous study on pediatric patients reached the same conclusion [12]. Hunt et al. immobilized six nasopharynx patients with a customized aquaplast head restrainer [15]. Bel et al. investigating the set-up of ten patients immobilized by individual transparent polyvinyl chloride (PVC) mask [16]. And Yan et al. obtained set-up data for 12 patients immobilized by thermoplastic masks [17]. For each study, the calculated SD of random errors were in the range of 1–2 mm and 2 mm in longitudinal and vertical directions, respectively. These values are fully consistent with our results. Weltens et al. performed a set-up study on 43 head and neck patients positioned in either PVC or thermoplastic masks. Independently from fixation device, they found that SD of random errors was 2.1 mm in both longitudinal and vertical directions [18]. In their presentation, the SD of systematic errors in the three set-up directions cannot be uniquely distinguished. Their values were approximately equal to 3.5 mm. These values were significantly larger than the SD of the systematic errors obtained in the present study [18]. Furthermore larger systematic set-up errors were found by Mitine et al. for 27 head and neck patients immobilized in plastic masks. They measured SD of systematic errors as 4.3 and 4.6 mm in longitudinal and vertical directions, respectively, and much smaller values of the SD of random errors (2.5 and 2 mm, respectively) [19].

Numerous set-up errors studies have been performed for pelvic treatments in adult patients. El-Gayed et al. performed a set-up analysis of 10 prostate cancer patients. They found SD of random errors of 2.4, 2.5, and 2.6 mm in lateral, longitudinal and vertical directions, and 1.8, 1.7, and 2.8 mm for systematic errors, respectively [20]. These values are in good agreement with our results. Moreover Creutzberg et al. investigated the set-up errors of 16 pelvic patients. The calculated SD of random errors was equal to 2.5, 4.2, and 4.2 mm for lateral, longitudinal and vertical directions, and 2.5, 3.9, and 3.7 mm, respectively for systematic errors [21]. These values were larger than the errors obtained in the pediatric patients as evident in the present study, as well as our previous study comparing portal imaging and cone-beam CT in determining the set-up errors [12].

It is worth noting that the amount of data concerning set-up errors for chest irradiation techniques is limited. Yan et al. reported set up data for 27 chest patients. They found that the SD of random errors of 2.5 and 3.5 mm in lateral and longitudinal directions, and 2.3 and 2.7 mm, for systematic errors respectively. These values were larger than the values for our pediatric patient who has tumors in the chest [17].

Various tumor sites, treatment techniques, patient’s age, possible weight loss, different materials for fixation devices, were the factors affecting the set up errors in various adults’ studies. The magnitude of systematic and random errors that were reported in these studies was comparable to or sometimes larger than the reported values in the present study for pediatric patients. The interobserver difference between the two radiation oncologists in the presented study was minimal. Around 93% of the cases the difference was within 2 mm. In 99.5% of cases the difference were within the action level 3 mm (Table 2).

Van Herk et al. defined the PTV margin as the margin needed to ensure, in the presence of set-up and other uncertainties, that the dose to the CTV was 95% in 90% of the treated patients [11]. Many centers use an empirical PTV expansion of 5–10 mm based on historical practice and clinical experience. There are several published formulations for calculating the necessary PTV [22–25]. In the present study the calculated PTV was obtained using Van Herk formulation.

In head and neck sites, PTV required margin was equal to 4 mm in lateral, 4.5 mm in longitudinal and 5.5 mm in vertical direction. Such estimated margin in head and neck cases was nearly different from Li et al. who recommended a uniform addition of 3.9 mm for the PTV uncertainty margin creation based on EPID on head and neck adult patients [26]. In children, an unisometric margin is needed in various directions.

The estimated PTV margin was relatively larger in chest, abdomen and pelvis sites compared to head and neck patients owing to the less tight fixation and higher possibility for tilting and rotation in non head and neck sites. The least PTV margin in all patients was recorded in the lateral direction. This can be explained by the minimal organ motion in the lateral direction compared to the longitudinal and vertical directions [27]. Moreover, the simple daily alignment of the patient’s midline reduces lateral random errors compared to the longitudinal and vertical position that needs bilateral check. Hence, the use of unisometric PTV margin can be implemented in pediatric patients.

Conclusion

This study showed the range of systematic and random set-up errors during the course of radiotherapy treatment for pediatric patients. Our results revealed that the ranges of set-up errors are site specific. Non-isometric PTV margins may be considered.

References


