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RESEARCH ARTICLE

EPID VS EXACTRAC IN DETERMINING TREATMENT UNCERTANITIES

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ABSTRACT

Background: The use of IMRT treatment delivery has caused dramatic change in aspects of the treatment delivery process. The importance of correcting systematic setup uncertainty has led to use of sophisticated offline or online repositioning scheme. Daily Image Guided Radiation Therapy provides detailed information about the positioning and make the adaptive treatment changes possible and allow for individualisation of the margin and setup techniques. The aim of the study was to compare the setup errors as detected by Electronic Portal Imaging Device (EPID) and ExacTrac systems.

Materials and Methods: 30 patients were taken up for the study, 20 cases of head and neck cancer and 10 cases of pelvic cancer. Electronic portal images were taken in the anterior and lateral views during the first 5 fractions of treatment and day 1 of every subsequent week till completion of treatment. Each portal image was compared with ExacTrac and the setup error was calculated.

Results: In the head and neck patients the mean systematic error were found to be 0.84, 1.21 and 0.77 in the lateral, longitudinal and vertical coordinates by ExacTrac. By EPID the mean systematic error was 0.12, 0.17 and 0.16 in lateral, longitudinal and vertical directions. The random errors by ExacTrac were 1.58, 1.24, 1.58 in the lateral, longitudinal and vertical directions respectively, and by EPID it was 0.25, 0.24 and 0.26 respectively. The differences were statistically significant. Stroom's margin recipe was used to calculate the PTV margin which was about 0.5 mm in all the directions by EPID and 2.9 mm by ExacTrac. By van Herk margin recipe the PTV margin was 0.6 mm by EPID and 3.4 mm by ExacTrac. Similarly in pelvic cancer the systematic and random errors were higher by ExacTrac when compared to EPID. The PTV margins were about 0.8 mm and 3.8 mm by EPID and ExacTrac using Stroom's margin recipe and 0.8 mm and 4.2 mm respectively by van Herk Margin recipe.

Conclusion: The setup errors estimated by Exac Trac are significantly higher than that with EPID. CTV to PTV margin of 4 mm in head and neck cancers and 5 mm in pelvic cancers may be considered to account for most of the setup errors.

INTRODUCTION

Radiation therapy has been used as a treatment for cancer for more than 100 years, with its earliest roots dating back to the discovery of X-rays in 1895. Approximately 60% of cancer patients currently receive radiation therapy at some stage during their illness with 75% of these treated with curative intent. As advances in radiation oncology has enabled higher precision in treatment delivery, it has become important to understand the factors that contribute to treatment uncertainty. The goal of conformal radiotherapy is to increase the likelihood of tumor control while minimizing irradiation of normal surrounding tissues by precise confirming the dose distribution to the target volume shape. The treatment process of external beam radiotherapy inherently introduces geometrical uncertainties referred to as errors. It is normally calculated as a shift in treatment field position when a treatment image is compared against its corresponding reference (Bijhold J *et al*, 1992; van Herk 2004). The main sources of uncertainty are tumor delineation inaccuracies of the gross tumor volume (GTV), unknown extent of microscopic tumor, organ positional variation within the patient, and setup variations (van Herk, 2004). The errors in radiotherapy can be classified as

- Systematic or preparation error,
- Random or the execution error.

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The systematic component of any error is a deviation that occurs in the same direction and is of a similar magnitude for each fraction throughout the treatment course. The random component of any error refers to the deviation that can vary in direction and magnitude for each delivered treatment fraction and in radiotherapy used to refer the individual patient or to the treatment population. An off-line correction strategy cannot predict the random error component in subsequent fractions and so treatment margins must be calculated to include these variations. Online correction strategies are used to control random errors.

At present, one expands the Clinical Target Volume (CTV) with a safety margin to obtain the Planning Target Volume (PTV). The PTV is given a high dose to ensure that the CTV receives adequate dose despite "small" geometrical errors. The development and implementation of electronic portal imaging devices for megavoltage imaging, diagnostic x-ray images (Bourland JD, 2008), and megavoltage or diagnostic Cone-based computed tomography (CBCT) scanning using accelerator-based systems have revolutionized the setup and localization process. The use of Intensity Modulated Radiation Therapy (IMRT) treatment delivery has also caused a dramatic change in aspects of the delivery process. The importance of correcting the systematic setup uncertainty, if possible, has also led many institutions to convert their positioning verification procedure from the use of weekly port films, with position correction if a large-enough error is seen, to a more sophisticated offline or online repositioning scheme, and to more sophisticated setup, localization, and imaging strategies that are now called Image Guided Radiation Therapy (IGRT). Use of daily IGRT setup correction based on imaging is the most accurate method for daily patient positioning (Bourland JD, 2008, Jaffaray DA *et al*, 2002). Daily IGRT also provides detailed information about the stability of patients and their positioning, and can make possible adaptive treatment changes that can allow individualization of the margins and setup techniques used for individual patients. This is a rapidly developing area, and promises improvements in patient treatment precision, as well as in improving our ability to image (Jaffaray DA, 2007).

Hurkmans *et al*, 2001 published a comprehensive review on set-up verification using portal imaging for several anatomic sites. For HN-RT it was concluded that set-up errors (systematic and random) should be less than 2 mm (1 S.D.), using currently unavailable immobilisation equipment. It was stated that additional set-up correction strategies could reduce these errors even more. Huizenga *et al*, 1988, measured the set-up errors in the cranio-caudal and ventro-dorsal directions by comparing megavolt portal films to simulation film. Patients were immobilised using plastic cast. For both directions, both the systematic and random deviations were 2.1 mm (1 S.D.).

They found that position variation within the cast was a source of error, which might be explained by the use of a standard, non-customised HN-support. Weltens C *et al*, 1995, used EPID and megavolt portal films and measured the set-up errors in the cranio-caudal and ventro-dorsal directions. The systematic errors were 3.4 and 3.6 mm (1 S.D.) and the random errors 2.1 mm (1S.D.).

Reduction of the systematic set-up error has a major influence on the CTV–PTV margins required. For high precision radiotherapy, especially in the HN-region where the tumour is often in close proximity to radio-sensitive organs and tissues, reduction of these margins is very important. As a result of the improved patient set-up, CTV–PTV margins can be reduced to 3–4 mm.

In pelvic cancers the predominance of set-up errors in the anterior -posterior direction found in some studies is mainly due to the use of skin marks to determine the isocentre height in combination with the use of the pelvic bones as a match structure. The movement of the skin marks used for patient positioning relative to the pelvic bones, results in a set-up error. The skin movement might be due to respiration, weight loss or relaxation of the patient (Kitamura K *et al*, 2002). This movement is expected to be small in the cranial caudal and medial lateral direction and more pronounced in the anterior-posterior direction. There is no clear predominance of set-up errors in one direction when all pelvic studies are taken together. There is little detailed information about set-up errors comparing prone versus supine patient position (van Herk *et al* 2002; Huddart RA *et al*, 1996; Stroom *et al*, 1998). Tinger *et al*, 1996, found that the standard deviation of the random error was at least three times as large as the standard deviation of the intra-fraction errors for all translations. In general, intra-fraction errors were around 2 mm (1 SD).Study by Luchka *et al*, 1996, reported setup errors for an obese patient which was much larger than for normal patients. They concluded that daily on-line imaging and positioning corrections are valuable for this sub-group.

MATERIALS AND METHODS

This study was conducted on 30 patients who presented to the department of Radiotherapy for receiving radical radiation therapy with the IMRT technique, for specific sub-sites at Father Muller Medical College Hospital, Mangalore, between May 2012and September 2014. For purpose of simulation and subsequent treatment, patient's were immobilized in supine position with thermoplastic mould using appropriate neck rest. During simulation, infrared spheres were placed and the mould was marked with reference lines, using wall mounted laser beams to indicate isocentre. Electronic Portal images were taken in anterior and lateral views during the first 5 fractions (days 1-5) of treatment course, and day 1 of every subsequent week till completion of treatment. Eachportal image were compared with DRR generated from CT scan and ExacTrac images and set up errors were calculated. CTV to PTV margin is calculated based on van Herk and Stroom *et al* formula:

1. Stroom's margin recipe
2.

$2\Sigma + 0.7\sigma$, where Σ is the systematic error and σ is the random error.

This recipe sees to it that on an average, 99% of the CTV receives more than orequal to 95% of the prescribed dose.

van Herk margin recipe
$\Sigma + 0.7\sigma$

This recipe sees to it that on an average 90% of patients in the population receive a minimum cumulative CTV dose of at least 95% of the prescribed dose.

Inclusion Criteria

Patients of head and neck, and pelvis planned for radical radiotherapy with IMRT technique.

Exclusion Criteria

- Metastatic patients
- Plans changed during radiotherapy

The images were digitally reconstructed and there was a comparison made of the corresponding images with the ExacTrac and DRR respectively. In our study we used the ExacTrac IGRT system (Brain LAB) with system software version 5, consisting of infrared tracking and x-ray components. The infrared tracking component include

- The passive IR reflecting spheres which are placed on the patient or on the immobilization device and a thermoplastic mould moulded to the patient's contour.
- The active IR cameras are rigidly mounted to the ceiling which emits a low IR signal that is reflected and analysed for positional information.

Patient setup is then achieved by moving the couch to match the marker's position with those recorded in a CT image. The software has the ability to provide rotational of fsets along three primary axis. The external markers are positioned in a relatively stable location to achieve accurate setup. The x-ray component used in our study consists of two floor-mounted kV x-ray tubes that project in an oblique angle medially, anteriorly, and inferiorly corresponding to flat panel detectors mounted on the ceiling .Two stereoscopic images produced by the two kV x-ray tubes are obtained after the patient is initially setup with the ExacTrac. The images thus obtained are then compared with the corresponding CT simulation images in the form of DRRs. The set up error is then calculated. In our institute the tolerance level for the set up error was taken to be less than 3mm in head and neck patients and less than 5mm in patients with pelvic malignancy. If the setup were incorrect the patient position was corrected and the Portal images were performed to recheck the positioning.

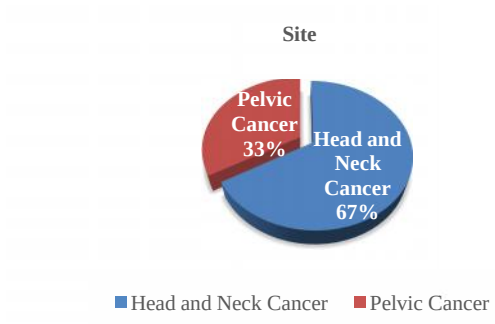

Figure 1 Site of cancer

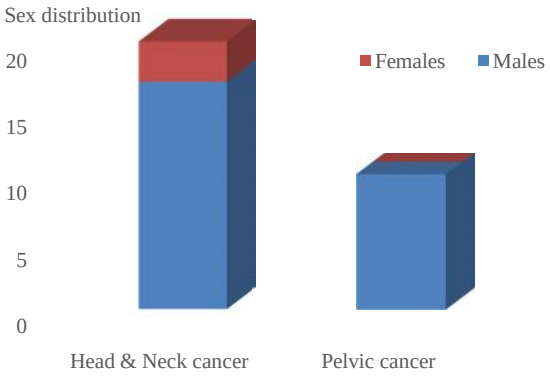

Figure 2 Sex Distribution

Table 1 Age Distribution

Age Group (years)	Number of patients (%)	
	Head and neck cancer	Pelvic cancer
< 40	3 (15%)	0 (0%)
41 – 50	5 (25%)	1 (10%)
51 – 60	5 (25%)	4 (40%)
61- 70	6 (30%)	4 (40%)
71 – 80	1 (5%)	1 (10%)
>80	0 (0%)	0 (0%)

RESULTS

In our study 30 patients were included; they were further sub-grouped based on the site of cancer into those with diagnosed with head and neck cancer and pelvic cancer with 20 and 10 patients in the subsets respectively. A total of 500 portal images, 262 anterior posterior portal images and 238 lateral images were matched in head and neck patients. In the pelvic group 295 portal images, 161 in AP portal images and 134 lateral images were matched.

Age Distribution

In our study most cases belonged to the age group 61-70 years

Sex Distribution

In those diagnosed with head and neck cancer 17 were males and 3 females. In the pelvic subsets all ten were males.

Setup errors

The systematic and random errors were estimated using both EPID and ExacTrac. The systematic error in head and neck cancers as calculated using EPID was 0.129 mm, 0.17 mm and 0.158 mm in the lateral, longitudinal and vertical directions respectively. By ExacTrac the systematic error was 0.837mm, 1.207 mm and 0.773 mm respectively. The difference observed between the two methods was statistically significant ($p < 0.0001$, 95% CI ± 0.1478).

The random error in head and neck cancers by EPID was 0.253 mm, 0.243 mm and 0.263 mm in the lateral, longitudinal and vertical directions respectively and by ExacTrac was 1.578 mm, 1.236 mm and 1.582 mm respectively ($p < 0.0001$, 95% CI ± 0.1405).

Similarly in pelvic cancers, the systematic error by EPID was 0.145 mm, 0.356 mm and 0.128 mm in the lateral, longitudinal and vertical directions respectively and 1.081 mm, 0.824 mm and 0.737 mm respectively by ExacTrac ($p < 0.0001$, 95% CI ± 0.3159). The random error in pelvic cancer by EPID was 0.456 mm, 0.652 mm and 0.325 mm in the lateral, longitudinal and vertical directions respectively and by ExacTrac was 2.588 mm, 3.678 mm and 2.408 mm respectively ($p < 0.0001$, 95% CI ± 0.4994).

Stroom's margin recipe and van Herk margin recipe were used to calculate the PTV margins. In head and neck cancers by Stroom's margin recipe the PTV margins were 0.43 mm, 0.51 mm and 0.50 mm respectively in the lateral, longitudinal and vertical directions respectively when the errors calculated by EPID were considered. Similarly by using the van Herk margin recipe the PTV margins were 0.50 mm, 0.59 mm and 0.58 mm respectively in the 3 directions. The PTV margins were greater in all the directions when the errors calculated using ExacTrac were considered. By Stroom's margin recipe the margins were 2.78 mm, 3.28 mm and 2.66 mm respectively and by van Herk margin recipe the margins were 3.20 mm, 3.88 mm and 3.04 mm respectively.

In pelvic cancers by Stroom's margin recipe the PTV margins were 0.61 mm, 1.17 mm and 0.48 mm respectively in the lateral, longitudinal and vertical directions respectively when the errors calculated by EPID were considered. Similarly by using the van Herk margin recipe the PTV margins were 0.58 mm, 1.35 mm and 0.55 mm respectively in the 3 directions.

Similar to the head and neck cancers the PTV margins were greater in all the directions when the errors calculated using ExacTrac were considered. By Stroom's margin recipe the margins were 3.97 mm, 4.22 mm and 3.16 mm respectively and by van Herk margin recipe the margins were 4.51 mm, 4.63 mm and 3.53 mm respectively.

DISCUSSION

This was a study to analyse the differences in setup errors estimated by EPID and by ExacTrac and further to determine the PTV margins. 20 head and neck cancer patients and 10 pelvic cancer patients were included in the study. Significant differences were noted in the systematic and random errors calculated by the two methods. Suzuki M *et al*, 2006, analysed 10 patients with a total of 170 images, in our study we analysed 262 AP images and 238 lateral images as online protocol. The reported SE (Σ) and RE (σ) ranged from 0.6 to 1.3 mm and 0.8 to 1.6 mm respectively. In our study it ranges from 0.77 to 1.2 mm and 1.2 to 1.6 mm. The calculated CTV to PTV margin ranges from 1.7 to 3.5mm. In our study the CTV to PTV margin ranges from 3.0 to 3.88 mm. de Boer *et al*, 1998, reviewed 3 reports analysing set up errors in small groups with head and neck tumors and reported that SE (Σ) and RE(σ) ranged from 1.6 to 2.1mm and 1.0 to 2.0mm respectively. Hurkmans CW *et al*, 2001 reviewed some of the publications for head and neck region treated with conformal radiotherapy. In this study the Standard deviation of systematic and random errors were 1.6 to 4.6mm and 1.1 to 2.5mm respectively. In our study of 10 pelvis patients the mean systematic error (SE) for various coordinates were calculated and found to be 1.08 mm, 0.82 mm and 0.74 mm in the lateral, longitudinal and vertical coordinates. The mean random error was 2.58 mm, 3.68 mm and 2.41 mm.

The CTV to PTV margin were calculated using the standard recommended formula Stroom *et al* and van Herk *et al* formula. The calculated margins based on van Herk *et al* are 4.51 mm, 4.63 mm and 3.53 mm in lateral, longitudinal, vertical coordinates. The calculated margins based on Stroom *et al* formula the calculated margins are 3.97 mm, 4.22 mm and 3.16 mm. Ueda S *et al*, 2006, in the study for Evaluation of Prostate Motion and Optimum PTV Margin in Prostate Intensity Modulated Radiation Therapy (IMRT) Based on Fiducial Markers Using X-ray IGRT system, and the pre- and post-treatment CBCT images were obtained using the CBCT IGRT.

On the X-ray IGRT system, the calculated PTV margins in this study were: vertical, 2.8 mm; longitudinal, 2.6 mm; and lateral, 2.5 mm. The results showed that a minimum of at least 4 mm is needed as the optimum PTV margin for prostate IMRT, even using fiducial settings.

CONCLUSIONS

The setup errors estimated by ExacTrac are significantly higher than that with EPID. CTV to PTV margin of 4 mm in head and neck cancers and 5 mm in pelvic cancers may be considered to account for most of the setup errors.

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