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Original Article

Comparison of geometric uncertainties between alpha cradle and thermoplastic ray cast immobilisation in abdominopelvic radiotherapy: a prospective study

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Abstract

Context: Setup error significantly affects the accuracy of treatment and outcome in high precision radiotherapy.

Aims: To determine total, systematic, random error and clinical target volume (CTV) to planning target volume (PTV) margin with alpha cradle (VL) and ray cast (RC) immobilisation in abdominopelvic region.

Methods and material: Setup error was compared by using digitally reconstructed radiograph (DRR) as reference image with electronic portal image (EPI) taken during the treatment. *Statistical analysis used*: The total errors in mediolateral (ML), craniocaudal (CC) and anteroposterior (AP) directions were compared by *t*-test. For systematic and random errors variance ratio test (F-statistics) was used. Margins were calculated using International Commission of Radiation Units (ICRU), Stroom's and van Herk's formula.

Results: A total number of 306 portal images were analysed with 144 images in RC group and 162 images in VL group. For VL, in ML, CC, AP directions systematic errors were, in cm, (0.45, 0.29, 0.41), random errors (0.48, 0.32, 0.58), CTV to PTV margins (1.24, 0.80, 1.25), respectively. For RC, systematic errors were (0.25, 0.37, 0.80), random error (0.46, 0.80, 0.33), CTV to PTV margins (0.82, 1.30, 1.08), respectively. The difference of random error in CC and AP directions were statistically significant.

Conclusions: Geometric errors and CTV to PTV margins are different in different directions. For abdomen and pelvis in VL immobilisation, the margin ranged from 8 mm to 12.4 mm and for RC it was 8.2 mm to 13 mm. Therefore, a margin of 10 mm with online correction would be adequate.

Keywords

CTV to PTV margin; pelvic radiotherapy; precision radiotherapy; random error; systematic error

INTRODUCTION

External beam radiotherapy aims to enhance the therapeutic index by maximising the ratio of the probability of tumour control to the normal

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tissue complications. With the advent of high precision radiotherapy, like conformal radiotherapy, intensity modulated radiotherapy (IMRT) with image guidance (IGRT), it is feasible to reduce the margin given to the clinical target volume minimising the dose to normal structures. To achieve this objective, reduction of the geometric uncertainties associated with planning and treatment execution is important. Errors can be introduced during imaging, volume delineation and during positioning the patient.[1–4] Setup errors, like systematic and random errors, cause failure to achieve desired dose to the target volume. Several authors have used systematic and random errors in deriving the CTV to PTV margin.[5–7] When allowing a fixed reduction of the minimum cumulative dose (i.e. to 95%), the effect of the random error on margin is small (i.e. 0.7 σ) compared to the systematic error.[8] Many published margin recipes ignore systematic errors or fail to differentiate between systematic and random errors.

Immobilisation of the region of treatment is important in high precision radiotherapy. Alpha cradle and thermoplastic ray cast are two commonly used immobilisation devices for abdominopelvic radiotherapy. Any centre practicing high precision radiotherapy must follow strict quality assurance protocols. The analysis and quantification of the errors during treatment execution should be an integral part of quality assurance. This helps to derive patient-specific clinical target volume (CTV) margins based on the immobilisation device. The aims of the present work were (1) Comparison of Alpha Cradle (also called Vaclock, henceforth shortened as VL) and Thermoplastic Ray Cast (henceforth shorted as RC) as immobilisation devices in terms of setup errors and positional accuracy for abdominopelvic radiotherapy based on bony landmark matching using electronic portal imaging (EPI); (2) Quantification and comparison of total, systematic and random errors in mediolateral (ML), craniocaudal (CC) and anteroposterior (AP) directions; (3) To derive the CTV to planning target volume (PTV) margin based on the systematic and random error measurements.

MATERIALS AND METHODS

All participants were explained about the study and were included after they had signed the informed consent form. The study was approved by the Institutional Review Board. Twenty participants were randomised by block randomisation either to immobilisation with VL or thermoplastic RC (Figure 1). All patients had contrast-enhanced CT scan which was used for contouring the volumes of interest (Gross Tumour Volume or GTV, Clinical target Volume or CTV, Planning Target Volume or PTV, Organs at risk or OAR) as per International Commission of Radiation Units (ICRU)-50 and 62 guidelines.[3] Planning was done using the Plato IRIX version 6.5 treatment planning system and 5 mm margin was given to the PTV while carrying out the treatment planning. Digitally reconstructed radiographs (DRR) were generated for referencing. Patients were treated on dual energy Primus Linear Accelerator (Siemens, USA) capable of delivering 6 and 15 MV photons and a range of electron energies and fitted with a Si-based EPID system (Siemens, Germany). The EPID had a sensitive area of 41×41 cm^2 (pixel matrix size 512×512).

During the course of radiotherapy treatment orthogonal (AP and lateral), double exposure EPI were acquired for set-up verification. These images were compared with the DRR in reference to several fixed bony points like, ischial spine, symphysis pubis and pelvic brim, etc. The EPIs were taken on first 3 days and once weekly, thereafter. If values were not acceptable and required online correction, imaging was continued till three acceptable values were obtained. The total errors in ML, CC and AP directions were measured.

Displacements were compiled and arithmetic mean was calculated (individual systematic error). Individual systematic error was subtracted from total error to obtain random error for each treatment episode. The standard deviation of individual systematic error gave the population systematic error (Σ) and standard deviation of individual random errors gave the

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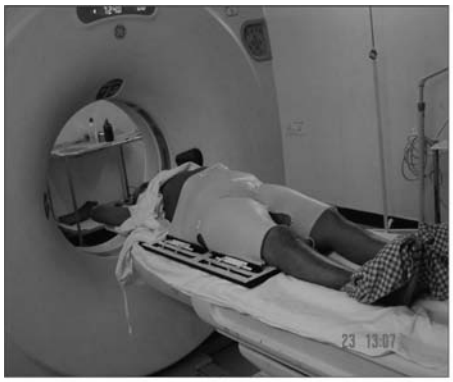
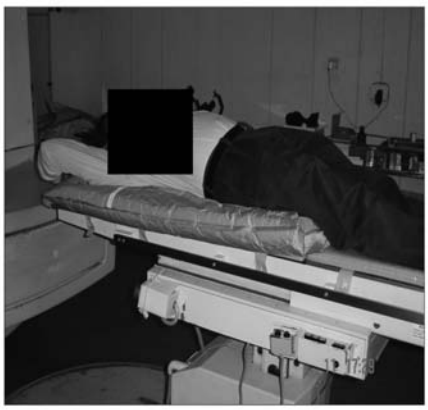


(a)



b (i)

b(ii)

Figure 1. Immobilisation of patients with thermoplastic ray cast and alpha cradle.

population random error (σ,). The CTV to PTV margin was calculated using ICRU 62 ($\Sigma + 0.7\ \sigma$) Stroom's ($2\ \Sigma + 0.7\ \sigma$) and Van Herk's ($2.5\ \Sigma + 0.7\ \sigma$) formula.[8] Statistical significance was calculated using *t*-test and variance ratio test (F-statistics). For statistical significance, $p \leq 0.05$ was considered significant. For each immobilisation, average total error for all patients in ML, CC and AP directions were plotted against time to assess the time trend of displacement.

RESULTS

A total of 20 participants were randomised to two immobilisation devices with 10 in each group. The two groups were comparable in terms of age, sex, average number of treatment fractions and number of portal images analysed. This data is shown in Table 1. We compared the bony anatomy of the region of treatment with the DRR. Bony anatomy was used as a surrogate marker of the anatomic region treated. The bony anatomy compared involved pelvic region and spinal anatomy, and the number of pelvic and spinal anatomy analysed in each group were comparable among the groups. A total number of 306 portal images (153 lateral and 153 AP) were analysed with 144 images in RC group (72 anterior and 72 lateral) and 162 images (81 anterior and 81 lateral images) in VL group.

All patients (VL and RC groups combined)

Translational shifts were measured in all 306 images. The mean displacements in ML, CC and AP directions were 0.11 cm (SD 0.58),

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Table 1. *Patient characteristics: VL group and RC group*

Patient no.	Age	Sex	Diagnosis	Bony anatomy	Tele-therapy Dose (Gy)	Fraction	Portal imaging
VL group							
1	67	M	Carcinoma prostate	Pelvis	74	37	10
2	70	M	Carcinoma prostate	Pelvis	74	37	11
3	64	M	Carcinoma rectum	Pelvis	50	25	7
4	53	M	Lumbosacral sarcoma	Spine	60	30	7
5	51	M	Anorectum adenocarcinoma	Pelvis	66	33	9
6	60	F	Carcinoma cervix	Pelvis	50	25	8
7	53	M	Carcinoma bulbar urethra	Pelvis	66	33	8
8	65	M	Carcinoma oesophagus	Spine	54	27	8
9	63	F	Abdominal fibromatosis	Spine	59.4	33	7
10	60	M	DLBCL Lymphoma (D10)	Spine	40	20	6
Total							81
RC group							
1	58	M	Spinal glioma (T12-L1)	Spine	54	27	7
2	68	F	Carcinoma endometrium	Pelvis	65.2	36	8
3	45	M	Carcinoma oesophagus	Spine	62	31	6
4	35	M	Carcinoma oesophagus	Spine	46	23	6
5	47	F	Carcinoma cervix	Pelvis	50	25	9
6	48	M	Carcinoma oesophagus	Spine	50	25	6
7	58	M	Spindle cell sarcoma of presacral region	Pelvis	66	33	8
8	48	F	Carcinoma cervix	Pelvis	50	25	7
9	46	M	Carcinoma oesophagus	Spine	45	25	7
10	47	F	Carcinoma cervix	Pelvis	50	25	8
Total							72

0.09 cm (SD 0.67) and 0.03 cm (SD 0.60), respectively. The systematic errors were 0.35 cm, 0.32 cm and 0.41 cm and random errors were 0.47 cm, 0.59 cm and 0.48 cm in ML, CC and AP directions. The PTV margins calculated by Stroom's formula were 1.04 cm, 1.07 cm and 1.16 cm, respectively, in ML, CC and AP directions (Table 2). In 70 to 80% of the measurements, total translational error was within 5 mm (Table 3). The total errors in ML, CC and AP directions were normally distributed (Figure 2).

Alpha cradle immobilisation (VL group)

Mean total displacements in ML, CC and AP directions were 0.07 cm (SD 0.63), 0.15 cm (SD 0.40) and 0.006 cm (SD 0.708), respectively, and it was normally distributed. The systematic errors were 0.45 cm, 0.29 cm and 0.42 cm and random errors were 0.49 cm, 0.32 cm and 0.59 cm respectively, in ML, CC and AP directions. The PTV margins calculated by Stroom's formula were 1.24 cm, 0.804 cm and 1.25 cm, respectively, in ML, CC and AP directions.

Immobilisation with thermoplastic ray cast (RC group)

Mean total displacements in ML, CC and AP directions were 0.16 cm (SD 0.53), 0.02 cm (SD 0.88) and 0.06 cm (SD 0.47), and it was normally distributed. The systematic errors were 0.25 cm, 0.37 cm and 0.42 cm and random errors were 0.46 cm, 0.80 cm and 0.34 cm respectively, in ML, CC and AP directions. The PTV margins calculated by Stroom's formula were 0.82 cm, 1.3 cm and 1.08 cm, respectively, in ML, CC and AP directions.

PTV margin calculations in all patients and in different subgroups

The CTV to PTV margins were calculated using ICRU, Stroom's and Van Herk's formula. The CTV to PTV margins were 0.69 cm, 0.74 cm and 0.75 cm, respectively, in ML, CC and AP directions by ICRU formula. Margins

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Table 2. *Mean, standard deviation, systematic and random error, PTV margin using ICRU, Stroom's and van Herk formula Immobilisation—Alpha cradle (VL) and ray cast (RC) in cm*

		All patients	VL	RC
ML	Mean	0.1143	0.076	0.1574
	SD	0.58633	0.631	0.532
	Systematic error	0.355	0.451	0.25
	Random error	0.478	0.489	0.46
	PTV margin ICRU	0.6896	0.7933	0.572
	PTV margin (Stroom)	1.04	1.244	0.822
	PTV margin (van Herk)	1.22	1.47	0.947
CC	Mean	0.086	0.15	0.0157
	SD	0.674	0.40	0.881
	Systematic error	0.329	0.29	0.371
	Random error	0.595	0.32	0.801
	PTV margin ICRU	0.7455	0.514	0.9317
	PTV margin (Stroom)	1.07	0.804	1.302
	PTV margin (van Herk)	1.239	0.949	1.488
AP	Mean	0.0324	0.0067	0.0612
	SD	0.607	0.708	0.471
	Systematic error	0.410	0.418	0.421
	Random error	0.484	0.586	0.338
	PTV margin ICRU	0.748	0.828	0.658
	PTV margin (Stroom)	1.16	1.25	1.08
	PTV margin (van Herk)	1.36	1.45	1.29

Table 3. *Distribution of error*

	Mediolateral						Craniocaudal						Anteroposterior					
	VL		RC		All		VL		RC		All		VL		RC		All	
Range	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
5 mm or less	60	74.1	61	84.8	121	79.1	66	81.5	52	72.3	118	77.1	64	79.0	42	58.4	106	69.3
5 mm to 1 cm	12	14.8	9	12.5	21	13.7	10	12.3	18	25	28	18.3	14	17.3	16	22.2	30	19.6
More than 1 cm	9	11.1	2	2.7	11	7.2	5	6.2	2	2.7	7	4.6	3	3.7	14	19.4	17	11.1
Total	81		72		153		81		72		153		81		72		153	

Note: (Denominator is total number of EPIs analysed, VL = alpha cradle, RC = ray cast).

calculated by Stroom's formula were 1.04, 1.07 and 1.16 cm in ML, CC and AP directions and 1.22 cm, 1.24 cm and 1.36 cm, respectively, by Van Herk's formula. The results show that largest margin is required in AP directions (Table 4). In ML direction, systematic error (0.25 cm versus 0.45 cm), random error (0.46 cm versus 0.48 cm) and CTV to PTV margin (0.82 cm versus 1.2 cm) were less for RC compared to VL but this difference was not statistically significant. In CC direction, total error was more in VL than RC (1.5 mm versus 0.15 mm, $p =$ NS). However, VL had less systematic error (0.29 cm versus 0.37 cm, $p =$ NS) and significantly less random error than RC (0.32 cm versus 0.80 cm, $p < 0.05$). The CTV to PTV margin was also significantly less in VL than RC in the CC direction (0.8 cm versus 1.3 cm, $p = 0.03$). In AP direction, total error was less with VL than RC (0.067 mm versus 0.61 mm). Systematic errors were almost same (4.1 mm versus 4.2 mm), but RC had less random error than VL (3.3 mm versus 5.8 mm, $p = 0.03$). The CTV to PTV margin calculated was less in RC than VL (1.08 cm versus 1.25 cm) though this difference was not statistically significant (Table 5).

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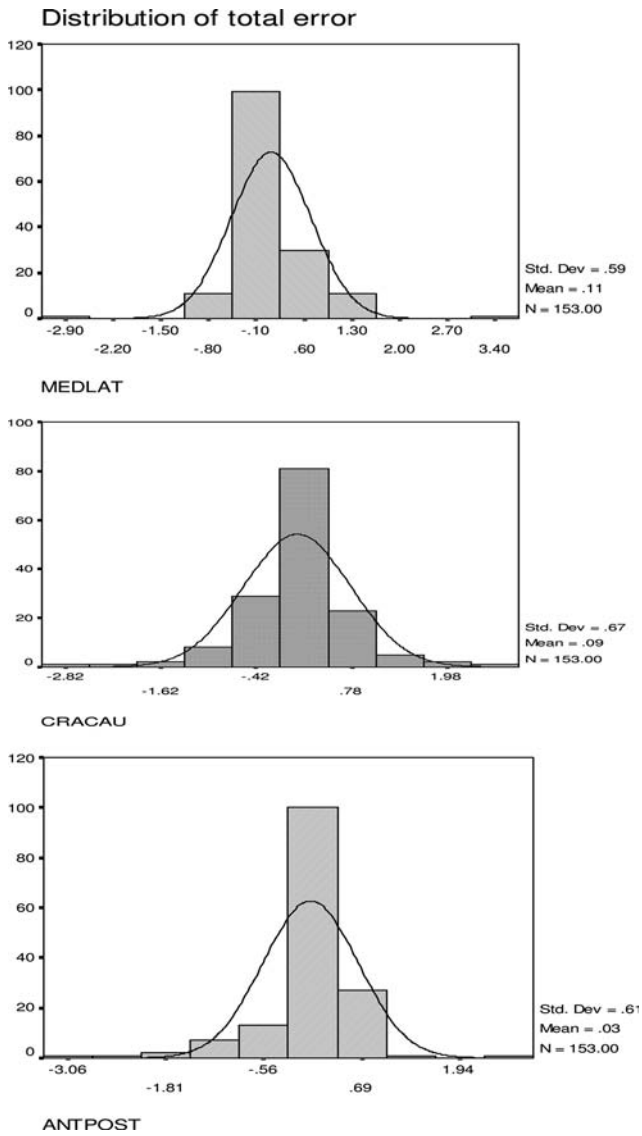

Figure 2. Distribution of total error in ML, CC and AP directions (immobilisation with VL and RC).

Time trend analysis

Average of total error every week in each direction for 20 patients was compared. This provided an idea of behaviour of total error across time and also was an indicator to the consistency of the immobilisation device over a period of time. Similar comparison between VL and thermoplastic RC showed the range of shift in VL to be (+0.75 to −0.25 cm), whereas for thermoplastic RC it was between ± 0.5 cm. The VL appeared to be a better immobilisation device than RC as per time trend analysis though in both cases the errors were within acceptable limits (Figure 3). All patients were monitored for radiation-induced reactions and weight changes weekly. There was no clinically significant change of body weight during the course of treatment.

DISCUSSION

A significant reduction in local disease control can result from even small (7−15%) changes in dose. The ICRU report recommends accuracy

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Table 4. Shift CTV–PTV margin: VL and RC

		CTV–PTV margin (cm) Systematic Error (Σ)	Random Error (σ)	ICRU 62*	Stroom's**	van Herk's***
All patients						
	ML	0.355	0.478	0.689	1.044	1.22
	CC	0.329	0.595	0.745	1.074	1.24
	AP	0.410	0.484	0.748	1.159	1.36
VL only						
	ML	0.451	0.489	0.793	1.244	1.47
	CC	0.290	0.321	0.514	0.804	0.95
	AP	0.418	0.586	0.828	1.25	1.45
RC only						
	ML	0.250	0.469	0.572	0.822	0.947
	CC	0.371	0.801	0.931	1.303	1.49
	AP	0.421	0.338	0.657	1.08	1.29

Note: CTV–PTV margin: *ICRU ($\Sigma + 0.7 \times \sigma$), **Stroom's formula ($2 \times \Sigma + 0.7 \times \sigma$), ***van Herk's formula ($2.5 \times \Sigma + 0.7 \times \sigma$).

Table 5. Comparison of total error, systematic error, random error and PTV margin (Stroom's formula) between VL and RC

Parameter	Levene's test for equality of variance		*t*-test for equality of means				
			Mean difference	Std. error of difference	*p* value	95% confidence interval of the difference	
	F	Sig				Lower	Upper
Total error in ML direction	2.33	0.129	−0.081	0.094	0.389	−0.267	0.104
Total error in CC direction	16.595	<0.001	0.1343	0.1133	0.239	−0.906	0.359
Total error in AP direction	0.550	0.459	−0.0546	0.0963	0.572	−0.245	0.135
Systematic error in ML direction	0.807	0.381	−0.0278	0.1632	0.867	−0.377	0.322
Systematic error in CC direction	1.208	0.286	0.1151	0.1489	0.450	−0.199	0.429
Systematic error in AP direction	0.082	0.778	−0.0579	0.1879	0.762	−0.452	0.336
Random error in ML direction	1.02	0.314	0.001	0.077	0.990	−0.152	0.154
Random error in CC direction	28.49	<0.001	0.0011	0.101	0.991	−0.199	0.201
Random error in AP direction	4.40	0.037	−0.374	0.0763	0.626	−0.188	0.113
PTV margin ML	3.68	0.05	−0.1604	0.119	0.183	−0.397	0.076
PTV margin CC	16.71	<0.001	0.2638	0.124	0.037	0.167	0.511
PTV margin AP	0.001	0.981	−0.1082	0.135	0.424	−0.374	0.158

in dose delivery, which should be within ± 5%.[9] An ideal immobilisation should not only immobilise the region of interest but should also be easy to set up and comfortable.[10] In treatment set up without immobilisation, the proportion of fractions with set-up errors greater than the 5 mm ranges from 17% to 57% and greater than 10 mm are observed in up to 15% of fractions.[11] Several reports comparing immobilisation devices to a free set-up have demonstrated a reduction in positioning errors with immobilisation.[12] The EPI provides an effective tool to verify positional accuracy of the immobilisation devices.

Malone et al. compared HipFix, which is a thermoplastic RC-based immobilisation, VL and leg cushion as in terms of accuracy of immobilisation. The study revealed HipFix to be significantly superior to the other two devices in reducing mean set-up errors in all axes ($p < 0.005$). In this study, the average field-positioning error with the HipFix ranged from 1.9 to 2.6 mm for all axes, whereas the

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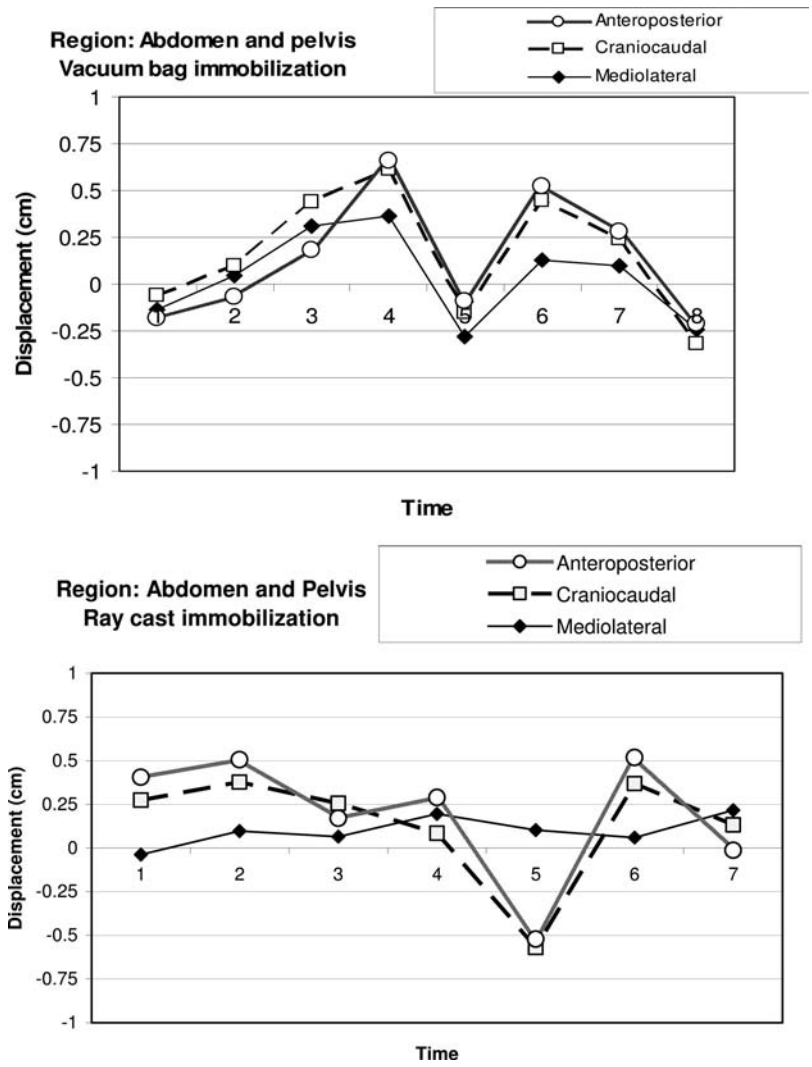

Figure 3. Time trend analysis of total error in abdomen and pelvis. Upper panel: VL immobilisation; Lower panel: RC immobilisation.

deviation for the other two systems ranged from 2.7 to 3.4 mm.[13] Systematic and random errors have different effects on dose distribution. In case of systematic errors, all fractions are equally affected leading to a very serious problem due to the shifting of the dose distribution as the CTV may shift out of the high dose region. Random error can occur every day and small dose variation will lead to blurring, causing decrease of the dose at high dose regions near the edge.[14]

In the literature simulator film, DRR, and portal image taken on first treatment day have been used as reference image to compare with daily treatment. The advantage of the simulator film is high quality, better delineation of the bony landmarks. However, the disadvantage is that it does not take into account the processes like CT scan, volume delineation, data transfer, and planning, which are important contributory factors to the systematic error.[15] Similarly the use of portal image taken at the first day of treatment as reference can also exclude all systematic errors involved in planning process. The DRR gives an excellent reference for comparison of treatment variation, since it is generated during treatment planning.

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Several offline strategies of detection and correction of systematic error have been proposed. Bijhold et al., suggested two-dimensional shrinking confidence ellipse model based on portal images acquired every third fraction.[16] Bel et al., developed a shrinking action level (SAL) method that rectifies patient position based on each measurement if the action level is exceeded.[17] Correction of position smaller than the measured mean was introduced by Pouliot and Lirette.[18] Denham et al., developed a two-dimensional 95% confidence ellipse model based on Hotelling's T2 statistics.[19] Yan et al., developed an 'accept or reject model' based on a 95% confidence level. A no action level (NAL) offline protocol has also been proposed where all patients have their set-ups corrected based on average thrice measurement.[20]

An optimal offline correction protocol would use minimum number of images required to detect the systematic error early and find the random treatment execution error. Denham et al., suggested 7–8 images in their protocol.[19] Yan et al., predicted for a group of 25 patients (pelvic radiotherapy) random and systematic errors in SI, ML and AP directions within ± 0.5 mm, ± 0.5 mm and 1 mm with 95% confidence limit using ≤ 9 portal images.[20] In NAL, protocol 3–4 images for set-up verification have been suggested.[21,22] Ludbrook et al., suggested an optimum number of images in pelvic radiotherapy to be five for accurately determining systematic and random error.[23]

In the present protocol, portal images were acquired on first 3 days and then every week and an about 7–8 images were obtained per patient. In ML direction, the error and calculated margin were less with RC compared to VL, but there was no statistically significant difference in total error (0.76 mm versus 1.57 mm, $p =$ NS), systematic error (0.45 cm versus 0.25 cm), random error (0.48 cm versus 0.46 cm) and CTV to PTV margin (0.82 cm versus 1.2 cm). In CC direction, total error was more in VL than RC (1.5 mm versus 0.15 mm, $p =$ NS). However, VL had less systematic error (0.29 cm versus 0.37 cm, $p =$ NS) and significantly less random error than RC (0.32 cm versus 0.80 cm, $p < 0.05$). The CTV to PTV margin was also significantly less in VL than RC in the CC direction (0.8 cm versus 1.3 cm, $p = 0.03$). In AP direction, total error was less with VL than RC (0.067 mm versus 0.61 mm). Systematic error was almost same (4.1 mm versus 4.2 mm), but RC had less random error than VL (3.3 mm versus 5.8 mm, $p = 0.03$). The CTV to PTV margin calculated was less in RC than VL (1.08 cm versus 1.25 cm) but this difference was not statistically significant. Time trend analysis shows that VL had a narrower range of total error than RC, but both are within acceptable limits.

This data will be useful for selection of appropriate immobilisation device based on cost and availability in the centres where EPI and bony anatomy-based comparison are incorporated as a routine method during the process of treatment delivery. The data could be used to calculate CTV to PTV margin. There are several limitations in this study. Since it was a bony anatomy-based comparison, organ motion and soft tissue movement were not quantified; hence, this component of error was out of the scope of the study. There is some heterogeneity in the group as far as the disease and stage of the disease is concerned, but the groups were comparable in terms of number of treatment fractions, average number of portal images compared or bony anatomy which was taken as a surrogate marker of the region of treatment.

CONCLUSIONS

The EPI is an effective tool for determination of total, systematic and random errors in abdomino-pelvic radiotherapy. Total, systematic, random errors and CTV to PTV margin, for VL and RC immobilisation, set-up errors vary with direction and both were within acceptable limits. The VL has a statistically significant lower CTV to PTV margin in CC direction and narrower range of errors in time trend analysis. In case of VL immobilisation, the margins ranged from 8 mm to 12.4 mm and for RC it was 8.2 mm to 13 mm. Therefore, a margin of 5–10 mm with online correction would be adequate.

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