Original Article

Prospective comparative evaluation of planning target volume margin for brain intensity modulated radiotherapy utilizing hybrid online imaging modalities

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ABSTRACT

Background: A new advancement in daily monitoring of patient positioning is the use of hybrid technologies where two separate online imaging modalities are integrated to achieve precise treatment delivery. Our center has a set-up that integrates Elekta Linear accelerator device (EPID) with BrainLAB ExacTrac imaging for the first time in the world. We calculated planning target volume (PTV) margin for brain radiotherapy with thermoplastic mask immobilization with conventional EPID and BrainLAB ExacTrac image guidance system. **Materials and Methods:** EPID (iViewGT) and ExacTrac verification images of 32 patients in total 784 radiotherapy sessions were acquired and analyzed. Systematic (Σ) and random errors (σ) were calculated in cranio-caudal, lateral and anteroposterior directions. PTV margins calculated using van Herk ($2.5\ \Sigma + 0.7\ \sigma$) formula for each imaging system. **Result:** Of total 784 sessions EPID image were obtained in 723 sessions, ExacTrac obtained in 431 sessions. In cranio-caudal direction, the systematic error, random error, and the calculated PTV margin were 0.09 cm, 0.12 cm, and 0.31 cm, respectively, with EPID image and 0.17 cm, 0.13 cm, and 0.51 cm, respectively, with ExacTrac. The corresponding values in lateral direction were 0.11 cm, 0.15 cm, and 0.40 cm with EPID and 0.16 cm, 0.10 cm, and 0.47 cm, respectively, with ExacTrac image. The same parameters for anteroposterior were 0.10 cm, 0.13 cm, 0.37 cm with EPID and 0.144 cm, 0.10 cm, and 0.43 cm with ExacTrac image. Pearson's correlation coefficient was found to be 0.66, 0.67, 0.62 in these three directions. **Conclusion:** With dual imaging modalities, our calculated adequate PTV margin for brain radiotherapy cases are 0.51 cm, 0.47 cm, is 0.43 cm in cranio-caudal, right-left, and anteroposterior directions, respectively.

Key words: Brain radiotherapy, on board imaging, planning target volume margin

INTRODUCTION

Margins are used in conformal radiation therapy to account for geometrical uncertainties. The margins are expansions to the shape of a treatment beam, to ensure that dosimetric planning criteria are met in the presence of inter- and intra-fraction set-up variations.[1,2] With the help of new imaging technologies, target volume position errors have become easier to measure, and their accuracy has increased. Set-up margins should be optimized to prevent inadvertent irradiation of adjacent normal structures without compromising adequate dose coverage of target volume tissues.[3,4] Planning target volume (PTV) that encompasses the clinical target volume (CTV) with some margins is generated to account

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for uncertainties in patient positioning, organ motion, and beam geometry.[1-3]

This CTV to PTV margin is much more important for intensity modulated radiation therapy (IMRT) plans, as they usually have high dose gradients between tumor volume and adjacent normal tissue.[3] Set-up uncertainties in patient positioning can lead to undertreatment of some part of the tumor, thereby increasing the possibility of local tumor recurrence, while some nontarget tissues may be over-irradiated causing increased normal tissue toxicity.[3]

Set-up margins need to be measured at each center depending on the set-up and the imaging techniques available. Portal imaging (PI) or electronic portal imaging device (EPID) was one of the first modalities used for getting image verification of patient set-up just before treatment. It has been used to measure and correct set-up errors as a standard practice.[4]

PI allows for easily repeatable imaging and image processing and rapid quantitative assessment of treatment set-up errors. Several publications on PI guided set-up corrections for conformal and IMRT have been reported,[5-14] however, these studies have included either small patient groups or did not use daily PI, making difficult to draw conclusions on set-up margins. It is generally recommended that every institution generates its own data on set-up accuracy. It is in this context, this study was planned at a newly commissioned Radiotherapy Department of a Comprehensive Cancer Centre, a novel image guidance system (ExacTrac, BrainLAB, Germany) has been incorporated with conventional PI (iViewGT, Elekta, Crawley, UK).

This unique assembly enables us to acquire set-up error data by two independent imaging modality in four different planes; these planes are anteroposterior, lateral, and two oblique's (right oblique and left oblique).

With conventional PI, anteroposterior and lateral portal image with corresponding digitally reconstructed radiographs (DRR) are matched whereas with ExacTrac, two oblique images (right oblique and left oblique) are matched with corresponding DRR (DRR is generated in oblique planes by ExacTrac software system). The purpose of the current study was to analyze the set-up corrections data obtained by daily PI and the corresponding set-up corrections obtained by ExacTrac imaging. The final aim was to generate appropriate PTV margins for the brain IMRT treatments in our department using this hybrid imaging system. As this imaging assembly (iViewGT and ExacTrac) is unique and installed in our center for the first time, we have also evaluated the correlation between the margins calculated independently by these two systems.

MATERIALS AND METHODS

ExacTrac system

The ExacTrac X-ray six-dimensional (6D) system is primarily composed of an infrared-based optical positioning system (ExacTrac) for initial set-up and precise control of couch movement, and a kilovoltage (kV) X-ray imaging system (X-ray 6D) for position verification based on internal anatomy. The X-ray component consists of two floor-mounted kV X-ray tubes, projecting medial, anterior, and inferior oblique beams onto two corresponding flat panel detectors mounted on the ceiling, which record two-dimensional X-ray images. The 6D fusion software generates various sets of DRRs in 3 translational and 3 rotational directions for the CT images, which can be compared with the corresponding X-ray images until maximal superposition is achieved. The best match is thus determined, and the 6D offsets are computed. Within 10 s, it completes the image acquisition and computation and provides the translational shifts.

In this prospective study, a total of 32 brain tumor patients were immobilized using a three clamp thermoplastic cast. Write about the process of computed tomography (CT) simulation.

A CT-based IMRT plan was generated, and patients were set-up in the following sequence:

1. Proper laser alignment
2. Source to skin distance matching in anterior-posterior (AP) and on each side
3. A measured table top (surface) to lateral LASER height matching. This height is routinely measured using a rigid scale holding it perpendicular to the couch top during planning CT scan and on the treatment couch. This is an additional parameter to ensure accurate patient positioning by surface marking.

For ExacTrac

1. Infrared markers placed with a couch array for ExacTrac image guidance
2. ExacTrac image matching done with automatic fusion and checked for proper matching by an experienced radiation oncologist.

For portal image

3. Portal image taken and is matched manually by the same experienced radiation oncologist
4. Shift calculated by PI is applied before treatment (the final executed shift for the patient).

Both the set-up error data that is shifts in all the tree dimensions were noted and entered in Microsoft Excel sheet. This whole procedure was done in the presence of one experienced and trained Medical Physicist and Radiation Oncologist. The entire sequence was repeated every day for all the patients before treatment execution to allow capture of imaging data for all the fractions. The data acquisition protocol has been explained in Figure 1.

Evaluation of systematic and random errors

The shifts required in each direction to match the reference DRR images with the corresponding images taken during every treatment session represent the error in that direction in patient positioning for that treatment session under consideration. These shifts are due to the combined effect of both systemic and random errors involved in the patient set-up process. The mean values of the shifts in each direction were tabulated for the 32 patients, and the standard deviation (SD) of these values gave the systematic error involved in the process. Random errors are represented by the dispersion of individual data around the mean. For each patient, the random displacement was assessed by subtraction of the systematic displacement from the daily displacements. Systematic and random errors were calculated for each patient, and PTV margins were derived using van Herk formula for both the PI shifts as well as the ExacTrac shifts.[15]

For the whole population, the distribution of random errors is represented by the SD from all individual random values

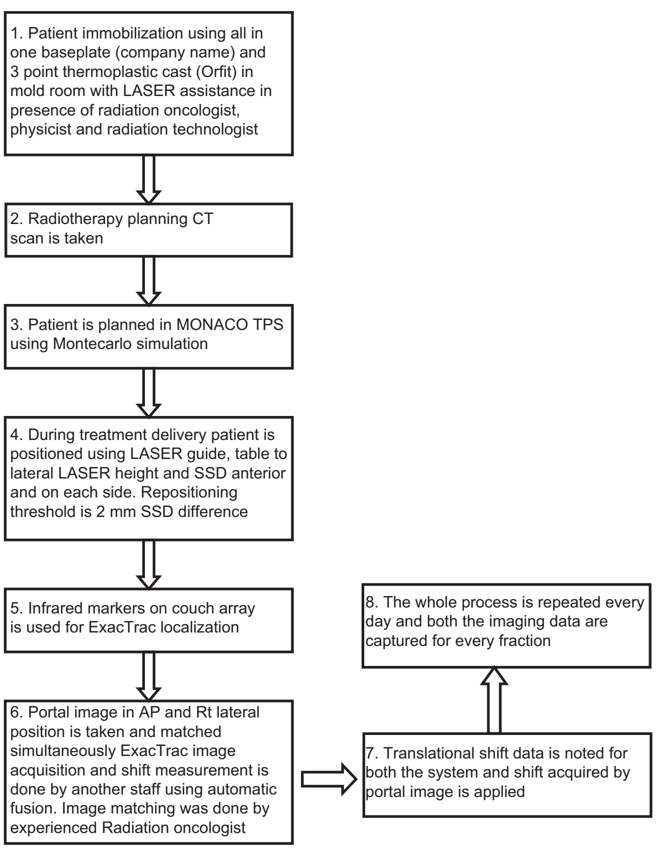

Figure 1: Protocol of patient set-up and data acquisition

and was calculated as the root mean square of the SD values. Systematic and random errors were calculated for both iViewGT and ExacTrac data sets separately. Shifts in each direction for both the data sets were plotted graphically, and difference of shifts between the datasets for each patient were also plotted.

RESULTS

This study evaluated the data related to 32 patients and corresponding 784 imaging sessions. We recorded 723 iViewGT and 431 ExacTrac translational shift data.

Mean shifts detected for each patient in all three directions by both imaging modalities were plotted. The direction of shifts (i.e. positive or negative) detected by two systems in all directions was in concurrence for every individual patient. Mean shift of each patients when plotted it is seen that maximum dispersion of in right-left direction from the isocenter determined was between + 0.2 cm/–0.2 cm and + 0.3 cm/0.3 cm by PI and by ExacTrac, respectively [Figure 2]. For vertical shifts, the corresponding values were between + 0.25 cm and – 0.25 cm by PI and between + 0.35 cm and –0.35 cm by ExacTrac [Figure 3]. The shifts in the cranio-caudal direction by PI were between + 0.25 cm and –0.15 cm and by ExacTrac between + 0.25 cm to –0.35 cm [Figure 4].

To analyze the correlation between the two imaging systems, Pearson's correlation coefficient was determined for the shifts calculated in each direction and correlation found between the two systems has been elaborated in Figure 5 and Table 1.

From these shifts, PTV margins were calculated separately for PI and ExacTrac.

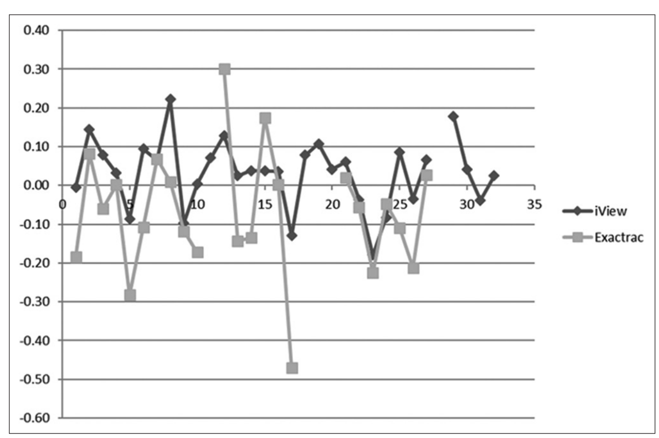

Figure 2: iViewGT and ExacTrac translational shift in right-left directions, minimum and maximum for each patient: X axis patients, Y axis shifts in cm, positive sign denotes shift in right side and negative denotes in left side

Table 1: PTV margin calculated for each direction by Iview-GT and ExacTrac data using Van Herk Formulae .Also showing the Pearson's correlation coefficient between the margins calculated by the two imaging systems. Vector margin calculated by the two systems and their correlation has also been shown

Site	Total no. of sessions	iView GT sessions	Exactrac sessions	Direction	iView GT			Exactrac			Correlation coeffitient
					Systematic (s)	Random (s)	Margin	Systematic (s)	Random (s)	Margin	
Cranium 32 patients	784	723	431	Sup/Inf	0.09	0.12	0.31	0.17	0.13	0.51	0.666
				Right/Left	0.11	0.15	0.4	0.16	0.1	0.47	0.673
				Ant/Post	0.1	0.13	0.37	0.14	0.1	0.43	0.624
				Vector margin			0.36			0.46	0.56

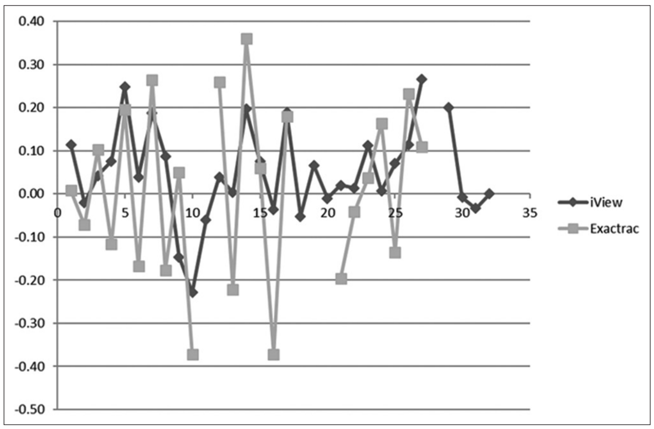

Figure 3: iViewGT and ExacTrac translational shift in vertical (anteroposterior) directions, minimum and maximum for each patient: X axis patients, Y axis shifts in cm, positive sign denotes shift in anterior direction and negative denotes in posterior direction

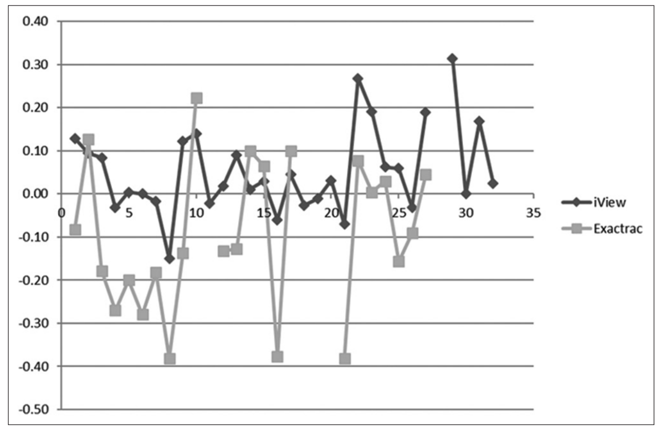

Figure 4: iViewGT and ExacTrac translational shift in cranio-caudal directions, minimum and maximum for each patient: X axis patients, Y axis shifts in cm, positive sign denotes shift in cranial direction and negative denotes in caudal direction

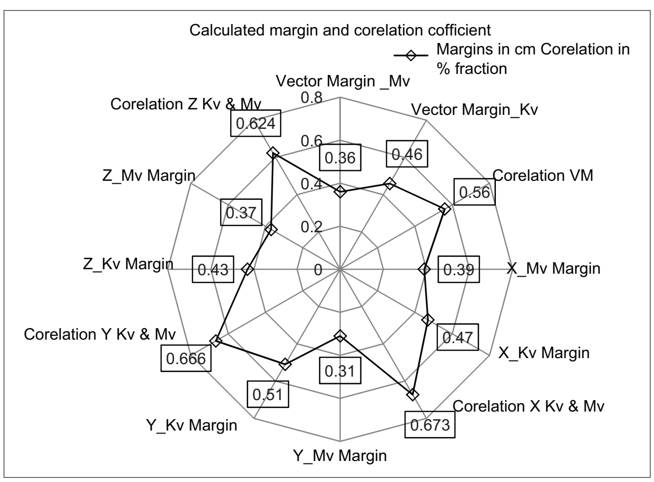

Figure 5: Web plot showing calculated margins by the two systems and Pearson's correlation coefficient

DISCUSSION

Our study in determining the CTV to PTV margin is distinctive and different from similar studies reported in the literature because of the following reasons: (i) We have used two different image guidance systems simultaneously and independently; (ii) We have collected set-up error data for all the fractions and for all the patients; (iii) Use of PI and ExacTrac enabled us matching images in four different planes: Anteroposterior, lateral, and two oblique planes.

Two types of set-up uncertainties are identified: systematic and random. Systematic error is the deviation between the planned patient position and the average patient position over the whole course of radiation therapy. It is largely attributed to the machine-related errors and target delineation uncertainties. The random error, on the other hand, is the day-to-day deviation from the average target position, introduced mainly due to internal motion and patient-related or mask-related factors. It is universally accepted that systematic setup errors influence more the physical dose distribution than the random set-up errors.[15] Li *et al*. published their data of set up error using CT for 19 brain patients. The PTV margin calculated by them using the same van Herk formula came to be 0.28 cm. While deriving this value, they have concluded that it should be treated as the lower limit, as the maximal shifts in the three translational directions observed by them were significantly larger than the margin calculated.[16]

It is evident from our results that the error as determined from ExacTrac data is larger than that determined by iViewGT [Table 1]. This can be explained by the fact that the cortical margin of bone can be better-appreciated in a kV image than in a megavoltage (MV) image where the margins are blurred. It is obvious that bony anatomy can be matched better in ExacTrac. It is our postulation that the improved accuracy in anatomy matching manifests as larger set-up margin observed with ExacTrac. In addition, the fact that ExacTrac matching is an automated process helps in reducing the subjective bias compared to that present in PI. Numerous reports have indicated that the set-up verification is more accurate with better resolution of the image while using image guidance and as a consequence more accurate patient positioning can be obtained.[17-19]

ExacTrac stereoscopic image matching accuracy has already been published by Ackerly *et al*. based on a data set having more than 10,000 images.[20] Several other researchers have also published their data on both phantom and in an actual clinical situation using stereoscopic oblique image data sets of ExacTrac.[21] These research works establish ExacTrac as an efficient tool for image guidance. Comparisons with MV EPIDs images suggest a localization accuracy of 1 mm.[21] There are reasons other than direct verification to expect that the ExacTrac system is spatially accurate. Theoretical criticisms of the ExacTrac 6D image fusion algorithm have been discredited.[22]

It is to be noticed that the systematic error calculated by ExaxTrac is more than iViewGT in all three directions. Though the magnitude of difference is only around 1 mm, the difference in the magnitude of set-up margin is large since the systematic error is dominant in PTV margin calculation. This should be attributed to the improved image quality and automated image matching algorithms. Xing *et al*. observed that 3 mm error of the couch location in the AP direction resulted in a 38% decrease of the minimal target dose or in a 41% increase of the minimal spinal cord dose. Hence, it is worthwhile to quantify, and if possible to reduce set-up margin.[6] Hence, every clinic should make an effort to scientifically determine set-up margins for every site and where possible to reduce their magnitude.

Drabik *et al*. in their study mentioned that in Glioblastoma multiforme, brain tumor patients' margin in X, Y, and Z directions are 3–4 mm, 2 mm, and 2–4 mm, respectively.[23] Shaleen Kumar *et al*. have recommended in their study using Gill–Thomas-Cosman relocatable frame in brain fractionated stereotactic radiotherapy that 4 mm CTV to PTV margin is adequate for dose coverage of CTV.[10]

However, results from our study show that margins of at least –0.43 cm in vertical, 0.51 cm in cranio-caudal and 0.47 cm in right-left directions are necessary in cranial IMRT if daily online correction protocol is not followed. The vector margin of all the three directions calculated by ExacTrac is 0.46 cm.

ExacTrac and iViewGT collaboration is a unique assembly which has been installed first 1st time in the world, so we tried to find out the correlation between the margins calculated by these two systems independently. The Pearson's correlation coefficient between the two imaging system also shows the correlation of 0.67, 0.66, and 0.62 in X, Y, and Z direction, respectively [Figure 5]. Though the correlation is not very strong enough but the direction of shifts calculated by the two systems are in each coordinate (X, Y, Z) are in concurrence [Figures 2-4].

Our study data and calculated PTV margins can be used as a reference for other radiation oncology departments practicing image guided techniques although in ideal practice PTV margins should be estimated locally on the basis of the institutional facilities and practices.

There are some limitations of this study we should mention. First of all, we have not compared ExacTrac data with cone beam CT (CBCT) data set rather than we have used PI. The probable counter argument may be that in brain radiotherapy bone matching is sufficient as it has a stable bony structure that is, skull and X-ray matching is fair enough for that. In our ongoing research, we have indeed incorporated CBCT as well. Many centers who practice IMRT without CBCT facility may use ExacTrac kV imaging as a betted tool for image matching rather than EPID MV image matching.

Finally, we want to emphasize that as evident from our analysis that a kV-kV image matching with ExacTrac is detecting more error in set-up which is attributed by better resolution, accuracy of image matching, and avoidance of subjective error (we should keep in mind that the actual set-up error remains same for a particular set-up event, only the accuracy of detecting it changes with different imaging modality). On the basis of the finding, we should rethink of changing our PTV margin to avoid any geographic miss. Incorporating the knowledge of better image matching can improve the local control which is the long-term goal. The magnitude of this improvement is not easy to determine as clinical and dosimetric study with large sample size is required and it will also have ethical issues as by virtue of its good quality kV-kV image matching is no doubt superior that Mv-kV image matching. So on, the basis of our study our recommendation is to calculate institutional PTV margin using best available imaging modality and if available to use kV-kV matching for the obvious reason of its better quality. As the technology advances and easy and quick method of kV-kV image matching is being available, we should try to adopt this new technology to improve our clinical outcome.

It can be concluded from our study that PTV margin of at least –0.43 cm in vertical, 0.51 cm in cranio-caudal, and 0.47 cm in right-left directions are necessary in cranial IMRT if daily online correction protocol is not followed.

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Conflicts of interest

There are no conflicts of interest.

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