

Evaluation of Six-Dimensional Cranial Target Positioning Accuracy in Two Different Immobilization Methods Using ExacTrac System

Tamil Selvan Kasirajan^{1, 2}, Padma Ganesan¹, Revathy Murugesan Kesavan¹, N. Arunai Nambi Raj³, K.Senthilnathan², P. Ramesh Babu^{2*}

1. Department of Oncology, Apollo Cancer Hospital, Hyderabad, Telangana, India
2. Department of Physics, School of Advanced Sciences, Vellore Institute of Technology, Vellore, Tamil Nadu, India
3. Centre for Biomaterials, Cellular and Molecular Theranostics, Vellore Institute of Technology, Vellore, Tamil Nadu, India

ARTICLE INFO	ABSTRACT
Article type: Original Article	Introduction: The aim of this study was to determine the accuracy of two different immobilization methods in patient positioning in cranial radiotherapy. The six-dimensional (6D) target localization accuracy of using a dedicated stereotactic mask was compared with that of a conventional head mask by the ExacTrac system.
Article history: Received: Mar 18, 2019 Accepted: Sep 11, 2019	Material and Methods: A total of 56 patients with cranial lesions were included in this study (26 patients with a dedicated stereotactic mask and 30 subjects with a conventional head mask). The ExacTrac image-guided positioning system was utilized to obtain daily translational and rotational patient positioning displacement from the intended position. The 6D setup data was analyzed to obtain population mean, systematic and random errors, and three-dimensional (3D) vector shifts in all the patients.
Keywords: Radiotherapy Patient Positioning Radiosurgery Radiotherapy Setup Errors Immobilization	Results: The population mean values of setup errors were comparable with both immobilization systems; however, the spread as indicated by population systematic and population random errors was more in the use of a conventional head mask. The mean values of the 3D vector shifts were 2.09 ± 1.00 and 4.51 ± 3.38 mm with the use of a dedicated stereotactic mask and conventional head mask, respectively. The frequency distribution of maximum rotational deviation and statistical analysis demonstrated a significant difference in immobilization accuracy between stereotactic immobilization and 3-clamp immobilization ($P < 0.05$). Conclusion: The results revealed that there was a significant reduction in target positioning errors with a dedicated stereotactic mask, compared to that with a conventional cranial mask. Furthermore, a dedicated stereotactic mask is required to keep rotational deviations within system correctable limits.

► Please cite this article as:

Kasirajan TS, Ganesan P, Murugesan Kesavan R, Arunai Nambi Raj N, Senthilnathan K, Ramesh Babu P. Evaluation of Six-Dimensional Cranial Target Positioning Accuracy in Two Different Immobilization Methods Using ExacTrac System. Iran J Med Phys 2020; 17: 308-315. 10.22038/ijmp.2019.35652.1448.

Introduction

The aim of radiotherapy is to design a treatment solution that gives the organs at risk lower doses than the target; therefore, a curative dose can be given without producing unacceptable side effects. The ratio of tumor control probability to normal tissue complication probability is called therapeutic ratio, and most of the developments in radiotherapy aim at increasing this therapeutic ratio. The reduction of geometric uncertainties helps in increasing the therapeutic ratio.

In advanced radiation treatment technologies with tighter margins, for better local control of a tumor and minimal damage to healthy normal tissue, it is vital to have precise repositioning and localizing with the help of an efficient immobilization system. The patient setup errors can be obtained by comparing the images acquired during the treatment delivery with those in the planned position. Patient setup inaccuracies

defined by systematic and random errors can be estimated by the daily imaging of numerous patients in a particular patient group, and clinical target volume (CTV) to planning target volume (PTV) margin can be calculated based on the obtained uncertainties [1,2].

The precision and accuracy of the intracranial stereotactic positioning systems are critical for the success and safety of the treatment [3]. The accuracy of relocation systems in stereotactic radiotherapy has been investigated by various studies [4,5], and image guidance has aided in more precise quantification of the setup accuracy [6,7]. Furthermore, six-dimensional (6D) imaging techniques (e.g., cone-beam computed tomography and stereotactic X-ray imaging) have also helped in the quantification of the rotational deviations [8-10].

*Corresponding Author: Tel: +914162243091; Email: prameshbabu@vit.ac.in

Various studies have demonstrated that the correction of rotational error increased the plan quality and organ at risk sparing [11-14]. The results of these studies showed that the effect of rotational errors on target volume varies significantly based on a number of parameters, such as target shape, target size, proximity to a critical structure, and distance of the target from isocenter if multiple targets are simultaneously treated. Moreover, the effect is more pronounced if translational deviations are considered in tandem.

In the present study, the 6D cranial target localization accuracy with two different mask-based immobilization systems was analyzed using the ExacTrac 6D positioning system. Systematic and random variations and three-dimensional (3D) vector shifts were obtained from the daily ExacTrac positioning data. Obtained rotational errors were utilized to derive PTV margin requirements for rotational positional errors in the initial setup with the immobilization system.

Materials and Methods

Study Design

The objective of this study was to determine the accuracy of immobilization in patient positioning during cranial radiotherapy. A total of 56 patients with cranial lesions were included in this study. Dedicated stereotactic masks were used for 26 patients, and conventional head masks were employed for 30 subjects. The patients with dedicated stereotactic masks had 7-30 fractions, with the mean and median PTV volumes reported as 65.43 (5.5-222.7 cc) and 47.9 cc, respectively. The subjects with conventional head masks had 16-30 fractions, with the mean and median PTV volumes obtained at 244.1 (19.52-608.6 cc) and 218.4 cc, respectively. The ExacTrac 6D image guidance system of the Novalis Tx linear accelerator was used for

the pretreatment verification and correction of setup errors for both the immobilization systems.

ExacTrac Six-dimensional Image Guidance System

The ExacTrac positioning and correction system (BrainLAB AG, Feldkirchen, Germany) utilizes optical infrared tracking, stereoscopic X-ray imaging, and robotic couch for the evaluation and correction of rotational and translational deviations. Stereoscopic X-ray imaging is performed with the two X-ray tubes recessed in the treatment room floor, which project the patient anatomic images onto the amorphous silicon flat-panel detectors hooked up on the ceiling. Two infrared cameras attached to the ceiling help in the tracking of the optically guided fiducial markers over the patient. Infrared tracking is used for the prepositioning of the patient to the treatment isocenter and executing the 6D positional corrections obtained in X-ray imaging by the accurate control of the treatment table. Reference star is utilized to control the couch movements when infrared positioning array is not employed for localization. The robotic couch can correct rotational deviations (i.e., pitch, yaw, and roll) in addition to the translational deviations.

Immobilization system and patient positioning

Patient immobilization for subjects with dedicated stereotactic masks was conducted with a three-layer noninvasive thermoplastic mask. Figure 1 (a) shows this immobilization device, along with infrared positioning array. The lower layer supports the back of the head, and the middle layer of the mask consists of three reinforcing straps over the forehead, below the nose, and over the chin. Above the middle layer, a nose bridge that is shaped to take the patient's nose features helps in reducing patient rotation. Finally, a forehead and facial mask attached to the middle layer and nasal bridge forms the upper layer.

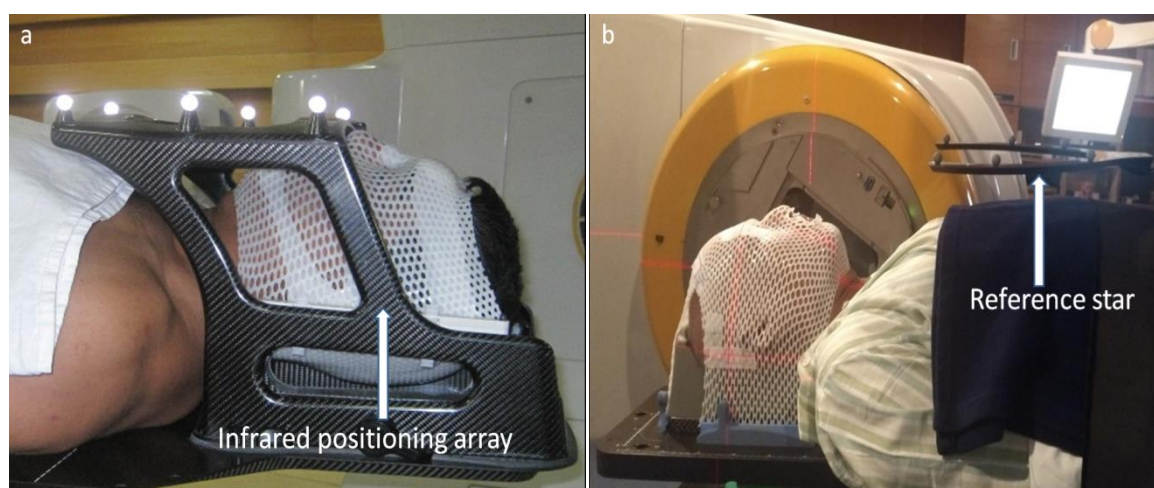


Figure 1. Cranial immobilization devices under investigation in this study; a) stereotactic immobilization with infrared positioning array; b) 3-clamp immobilization with reference star

A 2-mm spacer is initially used while preparing the mask and can be adjusted to compensate for mask loosening or tightening during the course of the treatment. Computed tomography (CT) images were obtained with a slice thickness of 1 mm, along with a localizer box. The localizer box helps in the identification of the patient isocenter in the stereotactic reference coordinate system. Infrared positioning array is attached to the delivery couch to facilitate the automatic positioning of the patient in isocenter.

For all other subjects with cranial lesions, three clamp head mask was utilized for immobilization. Figure 1 (b) depicts this immobilization device, along with a reference star. Three external radio-opaque fiducial markers placed in the mask on the anterior and lateral sides of the patient help in localizing the treatment isocenter in the treatment planning system. The CT scanning of the patient was carried out with 1 mm slice thickness. The patient was aligned with the treatment isocenter with the help of external fiducial markers and shift details obtained from the treatment planning system. The infrared reflective reference star was attached to the treatment couch to guide the ExacTrac system in correcting patient shifts in six dimensions.

Setup uncertainty analysis for immobilization system

The ExacTrac 6D image-guided positioning system was utilized to obtain daily translational and rotational setup deviations. The arithmetic mean of daily setup deviations over the course of treatment was calculated to obtain individual mean setup error. The overall population mean values of setup error is the average of the individual mean setup errors. The standard deviation of the individual mean setup error gives the population systematic error (Σ_{pop}). The individual random error is the standard deviation of the individual setup error during several fractions, and population random error (σ_{pop}) is the root mean square of the standard deviation of all patients [15].

The 3D vector shift was calculated using the following formula: $(x^2+y^2+z^2)^{1/2}$

where x , y , and z represent the lateral, longitudinal, and vertical setup deviations, respectively. The frequencies of the 3D vector shifts were determined and graphically plotted. Data analysis was carried out using Analysis ToolPak of Microsoft Office Excel 2007. Statistical analysis was performed using F-test to determine if a statistically significant difference was observed in the positioning errors between the two immobilization systems. The null hypothesis was the equality of the variances in the two immobilization devices. P-value less than 0.05 was considered statistically significant.

Estimation of rotational margins for immobilization system

Systematic and random errors were used to calculate the rotational PTV margin for each of the immobilization systems. Van Herk ($m_{ptv}=2.5\Sigma+0.7\sigma$) [2]

and Stroom ($m_{ptv}=2\Sigma+0.7\sigma$) [1] margin recipes were utilized in obtaining the margins. Van Herk formula is for a 90% confidence level and a 95% dose level with a standard deviation of penumbra at 3.2 mm. In addition, Stroom formula is for at least 95% dose to (on average) cover 99% of CTV.

These margin recipes were employed for both of the immobilization systems to compare the margin requirements in the initial position without rotational corrections. This would be helpful in assessing the additional benefits of correcting rotational deviations and provides an estimation of PTV margins if rotational deviations are left uncorrected. Mathematically the required margin for various points in the target is different based on the distance from isocenter and is obtained by the following equation:

$$m=d.\tan\theta_p$$

where d is the distance of the point from isocenter, and θ_p is the magnitude of rotation below which a fraction p of all rotational errors falls below, assuming a Gaussian distribution [16].

Factors influencing target positional accuracy

The setup uncertainty of each mask includes other factors, such as the misalignment of room lasers with the radiation isocenter, accuracy of the infrared positioning system, and positioning difference between the treatment machine isocenter and ExacTrac isocenter. Institutional quality assurance protocol was established to keep the accuracy of all these parameters within the tolerance limit. The accuracy of the laser alignment to the radiation isocenter is ensured using the Winston-Lutz test [17] with a tolerance level of 0.5 mm. The accuracy of infrared positioning is ensured with daily verification using the ExacTrac isocenter calibration phantom.

According to the evidence, it was demonstrated that the position of each infrared-reflecting sphere in the positioning array and reference star can be determined at less than 0.3 mm by the infrared camera [8]. The accuracy of ExacTrac isocenter to the laser is ensured using the Winston-Lutz test module with a tolerance setting of 0.7 mm. The results of phantom studies have revealed that the Brainlab 6D ExacTrac system is capable of high detection accuracy and sub-degree positioning accuracy [18]. Daily online imaging correction with the ExacTrac system can reduce both systematic and random deviations to negligible values, thereby reducing the clinical margin requirements.

For stereotactic immobilization, the tolerance value for the setup accuracy in the ExacTrac system can be set to the minimum assignable value of 0.2 mm for translation and 0.2° for rotations; however, with a conventional mask, it is 1 mm for translation and 0.2° for rotations. This leads to higher residual error in the conventional mask. Clinically a PTV margin of 0-2 mm was utilized for the patients with a dedicated stereotactic mask, and a PTV margin of 3-5 mm was employed for a conventional cranial mask.

Results

Evaluation of geometric uncertainties in immobilization systems

For 26 patients treated with a dedicated stereotactic mask, the fractionation (7-30 fractions) led to 574 initial setup corrections. The population mean values of setup errors were 0.14 ± 0.85 , 0.62 ± 1.31 , and -0.98 ± 0.65 mm in the lateral, longitudinal, and vertical translational dimensions, as well as $-0.12 \pm 0.81^\circ$, $0.43 \pm 0.93^\circ$, and $-$

$0.02 \pm 0.81^\circ$ in the roll, pitch, and yaw rotational dimensions, respectively. Figure 2 shows the mean translational and rotational shifts for each patient, and the error bars indicate one standard deviation of the mean during treatment fractions. Table 1 tabulates the geometric uncertainties in six dimensions for patients with dedicated stereotactic immobilization. The mean 3D vector shift was reported as 2.09 ± 1.00 mm.

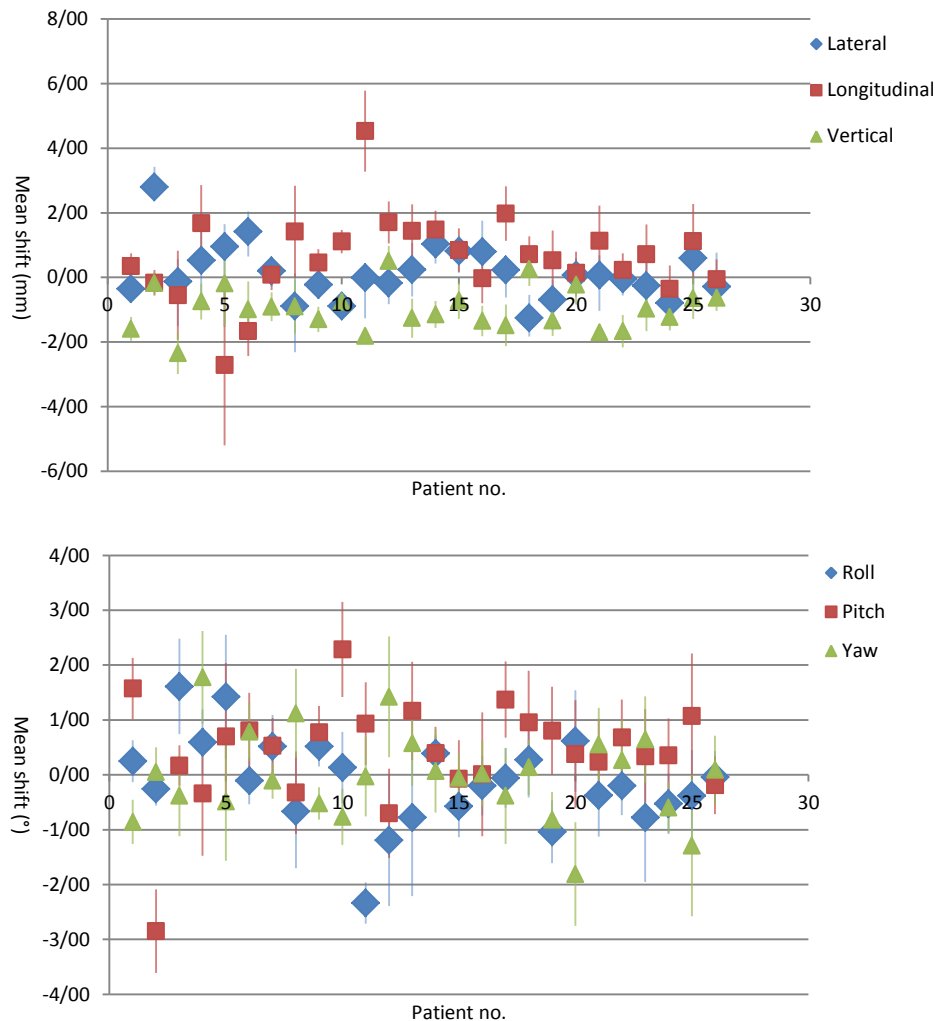


Figure 2. Mean translational and rotational shifts for patients with dedicated stereotactic masks and error bars indicative of one standard deviation of mean

Table 1. Geometric uncertainties in dedicated stereotactic immobilization and 3-clamp immobilization systems for cranial patients

			Translational deviation (mm)			Rotational Deviation (°)		
			Lateral (x)	Longitudinal (y)	Vertical (z)	Lateral (Roll)	Longitudinal (Pitch)	Vertical (Yaw)
Population setup error	Dedicated		0.14	0.62	-0.98	-0.12	0.43	-0.02
	3-clamp		-0.63	0.12	-0.91	-0.50	0.17	0.04
Population systematic error	Dedicated		0.85	1.31	0.65	0.81	0.93	0.81
	3-clamp		2.02	1.68	1.59	1.35	1.43	1.22
Population random error	Dedicated		0.68	0.94	0.57	0.73	0.80	0.71
	3-clamp		1.80	2.00	1.93	1.03	1.20	1.00

Table 2. Rotational margins in dedicated stereotactic immobilization and 3-clamp immobilization systems for cranial patients

				Rotational margin (°)	Lateral (Roll)	Longitudinal (Pitch)	Vertical (Yaw)
Planning target volume margin (Van Herk)				Dedicated	2.5	2.9	2.5
				3-clamp	4.1	4.4	3.8
Planning target volume margin (Stroom)				Dedicated	2.1	2.4	2.1
				3-clamp	3.4	3.7	3.1

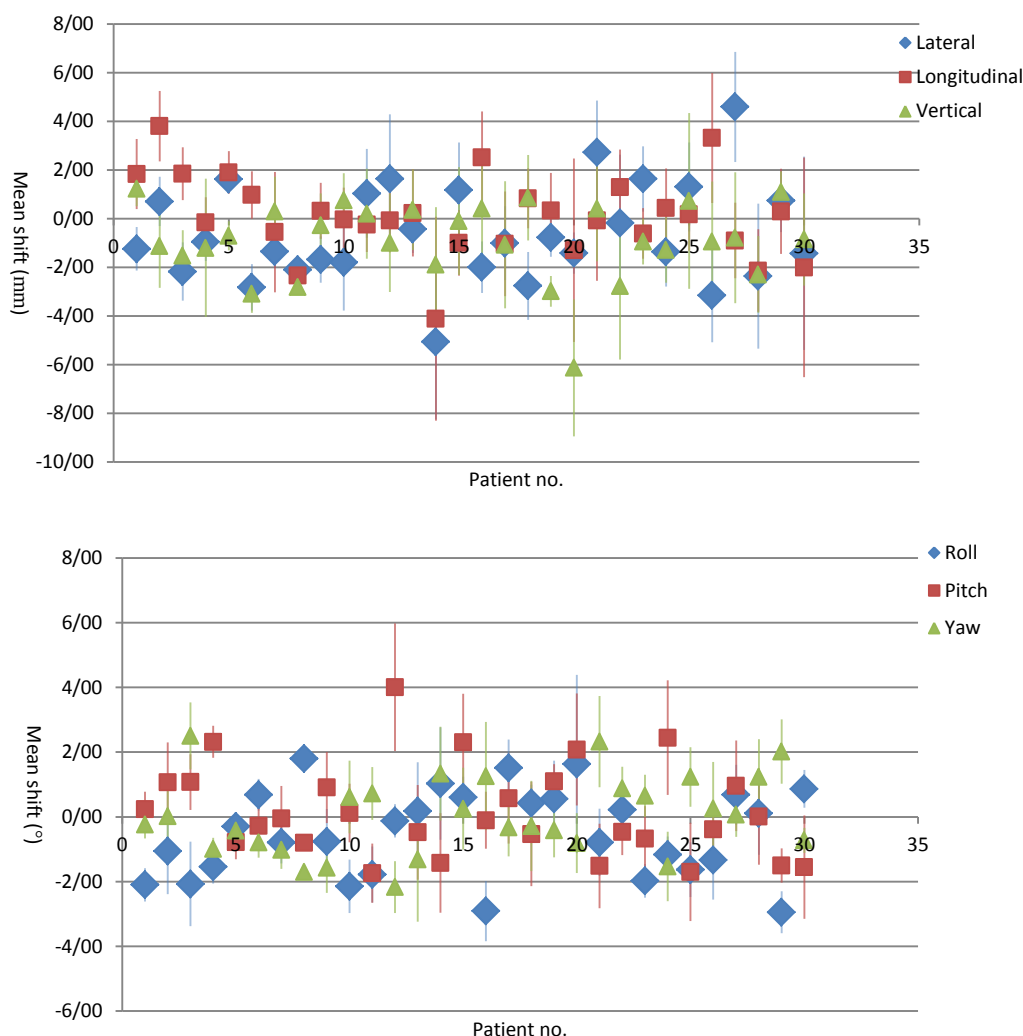


Figure 3. Mean translational and rotational shifts for patients with conventional masks and error bars indicative of one standard deviation of mean

Table 3. Statistical analysis of geometric uncertainties in stereotactic immobilization and 3-clamp immobilization systems for cranial patients

F-test results						
Deviation	Lateral	Longitudinal	Vertical	Roll	Pitch	Yaw
P-value	<0.01	0.02	<0.01	<0.01	<0.01	0.02

The population systematic and random errors were less than 1 mm and 1° in all translational and rotational deviations except for longitudinal systematic error where it was slightly higher at 1.31 mm. The margin requirements in rotational dimensions were within the range of 2.1° to 2.9° based on Van Herk and Stroom margin recipes as shown in Table 2. For 30 patients treated with the 3-clamp immobilization system, the

fractionation (16-30 fractions) led to 713 initial setup corrections. The population means values of setup errors were -0.63 ± 2.02 , 0.12 ± 1.68 , and -0.91 ± 1.59 mm in the lateral, longitudinal, and vertical translational dimensions, as well as $-0.50 \pm 1.35^\circ$, $0.17 \pm 1.43^\circ$, and $0.04 \pm 1.22^\circ$ in the roll, pitch, and yaw rotational dimensions, respectively.

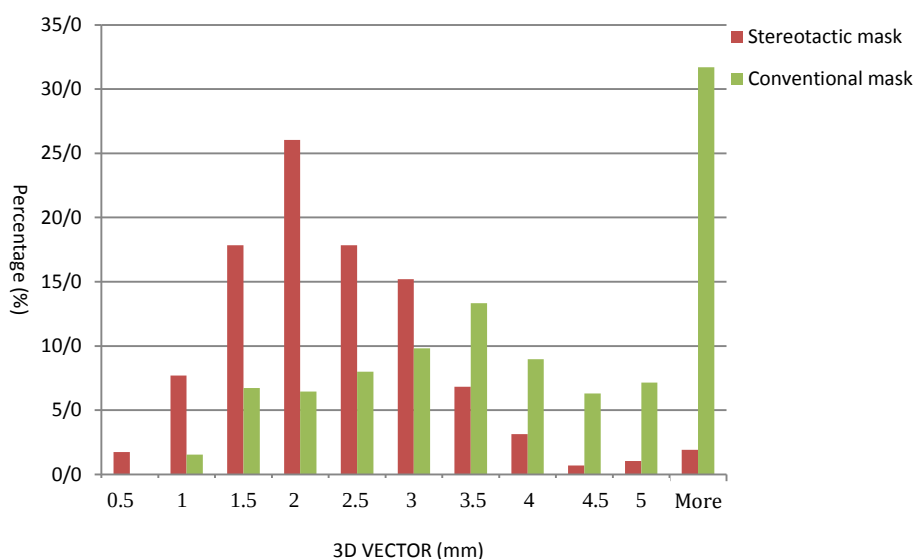


Figure 4. Frequency distribution of three-dimensional vector shift between the two immobilization systems

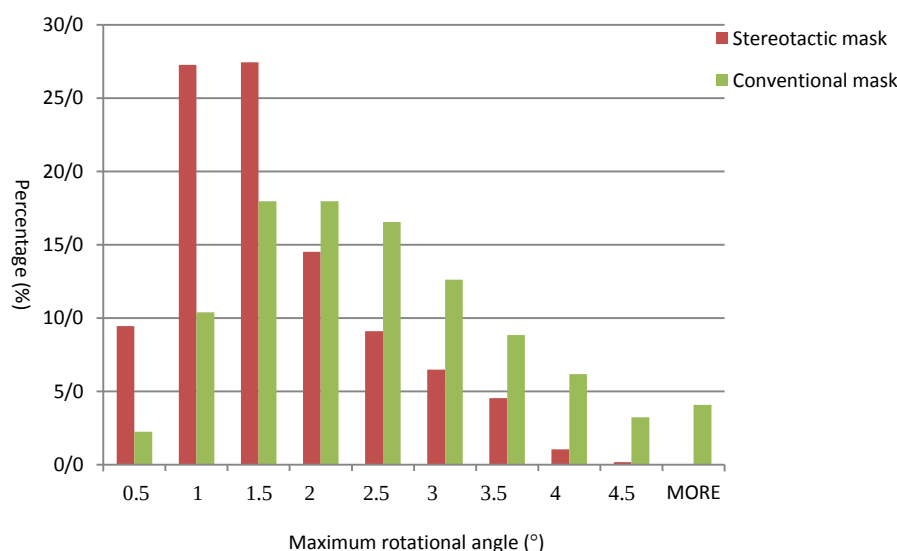


Figure 5. Frequency distribution of maximum rotational angle shift between the two immobilization systems

Figure 3 depicts the mean translational and rotational shifts for each patient, and the error bars indicate the standard deviation of the mean. Table 1 shows the geometric uncertainties in all six dimensions for patients with a 3-clamp mask. The mean 3D vector shift was reported as 4.51 ± 3.38 mm.

The population systematic and random errors were less than 2 mm and 2° in almost all translational and rotational deviations. The margin requirements in rotational dimensions ranged from 3.1° to 4.4° based on Van Herk and Stroom margin recipes as shown in Table 2. Statistical analysis using the F-test showed that there was a significant difference between the immobilization accuracy in the 3-clamp immobilization, compared to that in dedicated stereotactic immobilization in all six dimensions ($P < 0.05$) as presented in Table 3. The frequency distributions of 3D vector and maximum

rotational deviations were higher in the 3-clamp immobilization as illustrated in figures 4 and 5, respectively.

Discussion

Modern radiotherapy techniques require a high degree of geometric accuracy and precision to deliver the planned dose correctly. American Association of Physicists in Medicine (AAPM) report 54 specifies that the benefit of stereotactic localization and treatment is the ability to plan and treat a target with reduced position uncertainty [19]. Several studies have reported the accuracy of the frameless radiosurgery system in comparison to those of the gold standard frame-based radiosurgery systems [18,20]. Keeling et al. reported that mask uncertainty is the greatest among the various

patient setup uncertainties in the frameless 6D ExacTrac system [21].

In this study, it was observed that the systematic and random uncertainties could be significantly reduced with a dedicated stereotactic mask, compared to those by a conventional cranial immobilization mask. The frequency distribution of the 3D vector showed that the cumulative frequencies of the 3D vector less than 2 mm were 53% and 15% in stereotactic immobilization and 3-clamp immobilization, respectively. Furthermore, cumulative frequencies less than 4 mm were 98% and 55% in stereotactic immobilization and 3-clamp immobilization, respectively.

Figure 6 depicts the comparison of the systemic errors between the two immobilization systems, and Figure 7 illustrated the comparison of the random errors between the two immobilization systems. In the lateral and vertical directions, the systematic uncertainties were significantly higher (137% and 145%, respectively) in the 3-clamp immobilization. In addition, in the longitudinal and rotational dimensions, the systematic uncertainties were marginally higher (28% and 51-67%, respectively) in the 3-clamp immobilization.

Both systematic and random setup deviations can be reduced to negligible values if daily on-line imaging corrections are applied, thereby reducing the immobilization uncertainties. Intra-fraction motion depends on patient health condition and cooperation. Intra-fraction motion can decrease by frequent X-ray verification based on the accuracy requirements of the case and duration of treatment. Random assessments showed that the amount of intra-fraction variations were minimal with both masks. With daily image-guided positioning and correction, it might be concluded that both the immobilization systems produced similar end results; however, this could be different with the limitations of uncorrected rotational deviations.

The PTV margin estimates for rotational deviations with the Van Herk and Stroom margin recipes for the setup errors associated with the immobilization showed that the PTV margins were within the range of 2.1°-2.9° and 3.1°-4.4° in stereotactic immobilization and 3-clamp immobilization, respectively. This margin estimates would be helpful in assessing the dosimetric effects of uncorrected rotational errors in immobilization if sophisticated 6D corrections were not performed.

In the ExacTrac 6D Couch, the system correctable limit is 3.0° in the longitudinal rotation (i.e., pitch) and 2.5° in the lateral rotation (i.e., roll). The frequency distribution of maximum rotational deviations demonstrated that the rotational deviations could be restricted to less than 2.5° in 90% of setups in stereotactic immobilization, compared to 65% in the 3-clamp immobilization. These limitations lead to a higher residual error in conventional cranial immobilization mask treatments.

Translational variations yield isotropic margins; however, rotational variations will yield anisotropic margins indicating that the size of the margin will vary depending on the position with respect to the axis of

rotation. The results of studies have revealed that the correction of rotational error increased the plan quality and organ at risk sparing [11-14]. These studies have specified that for nonisocentric treatments, the acceptance threshold for the rotational setup error may be as low as $\pm 0.5^\circ$ for the tumors far from isocenter. The findings of the present study suggested that a dedicated stereotactic mask is preferred to keep the rotational variations within these threshold values or system correctable limits. The obtained data on rotational deviations would be helpful in future studies in estimating rotational margins in the treatment planning system and addressing the impact of uncorrected rotational deviation.

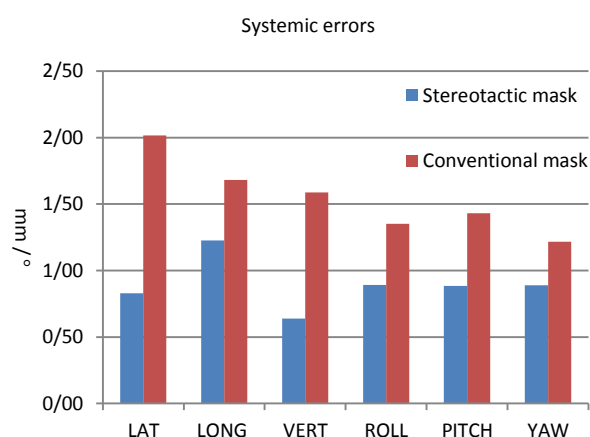


Figure 6. Comparison of systemic errors between the two immobilization systems

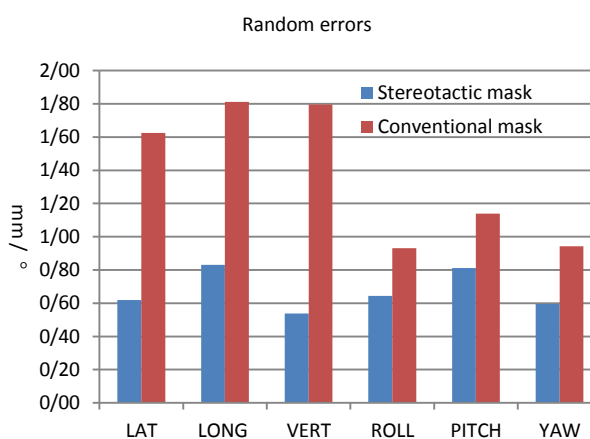


Figure 7. Comparison of random errors between the two immobilization systems

Conclusion

The present study evaluated the translational and rotational setup deviations observed during the treatment positioning with two different immobilization systems. Furthermore, the PTV margin requirements for rotational deviations could be estimated. The obtained results revealed that there was a significant reduction in the target positioning errors with a dedicated stereotactic mask, compared to that reported with a conventional

cranial mask. With daily ExacTrac image guidance, similar outcomes might be expected for both the immobilization systems; however, due to residual errors and system limitations, a dedicated stereotactic mask provides better target localization accuracy.

Acknowledgment

The authors would like to acknowledge the Department of Oncology, Apollo Cancer Hospital, Hyderabad, India for the facilities offered in this study and the authors would really like to thank the oncology staff for their valuable support and contributions.

References

1. Stroom JC, de Boer HC, Huizenga, Visser AG. Inclusion of geometrical uncertainties in radiotherapy treatment planning by means of coverage probability. *Int J. Radiat. Oncol. Biol. Phys.* 1999;43: 905-19.
2. Van Herk M, Remijer P, Rasch C, Lebesque JV. The probability of correct target dosage: dose-population histogram for deriving treatment margins in radiotherapy. *Int J. Radiat. Oncol. Biol. Phys.* 2000; 47: 1121-35.
3. Lightstone AW, Benedict SH, Bova FJ, Solberg TD, Stern RL. Intracranial stereotactic positioning systems: Report of the American Association of Physicists in Medicine radiation therapy committee Task Group No. 68. 2005.
4. Meeks SL, Bova FJ, Friedman WA, Buatti JM, Moore RD. IrLED-based patient localization for linac radiosurgery. *Int J. Radiat. Oncol. Biol. Phys.* 1998; 41:433-9.
5. Burton KE, Thomas SJ, Whitney D, Routsis DS, Benson RJ, Burnet NG. Accuracy of a relocatable stereotactic radiotherapy head frame evaluated by use of a depth helmet. *Clin Oncol.* 2002; 14:31-9.
6. Masi L, Casamassima F, Polli C, Menichelli C, Bonucci I, Cavedon C. Cone beam CT image guidance for intracranial stereotactic treatments: Comparison with a frame guided setup. *Int J. Radiat. Oncol. Biol. Phys.* 2008; 71:926-33.
7. Tryggstad E, Christian M, Ford E, Kut C, Le V, Sanguineti G, et al. Inter-and intrafraction patient positioning uncertainty for intracranial radiotherapy: A study of four frameless thermoplastic mask based immobilization strategies using daily cone-beam CT. *Int J. Radiat. Oncol. Biol. Phys.* 2011; 80:281-90.
8. Infusino E, Trodella L, Ramella S, D'Angelillo RM, Greco C, Lurato A, et al. Estimation of patient setup uncertainty using BrainLAB ExacTrac X-ray 6D system in image-guided radiotherapy. *J Appl Clin Med Phys.* 2015; 16:99-107.
9. Se An Oh, Ji Woon Yea, Min Kyu Kang, Jae Won Park, Sung Kyu Kim. Analysis of setup uncertainty and margin of the daily ExacTrac 6D image guide system for patients with brain tumors. *PLoS ONE.* 2016; 11.
10. Dhakaan A, Schreibmann E, Siddiqi A, Elder E, Fox T, Ogunleye T, et al. Six degrees of freedom CBCT-based positioning for intracranial targets treated with frameless stereotactic radiosurgery. *J Appl Clin Med Phys.* 2012; 13:215-25.
11. Guckenberger M, Meyer J, Vordermark D, Baier K, Wilbert J, Flentje M. Magnitude and clinical relevance of translational and rotational patient setup errors: A cone-beam CT study. *Int J. Radiat. Oncol. Biol. Phys.* 2006; 65:934-42.
12. Winey B, Bussiere M. Geometric and dosimetric uncertainties in intracranial stereotactic treatments for multiple non-isocentric lesions. *J Appl Clin Med Phys.* 2014; 15: 122-32.
13. Roper J, Chanyavanich V, Betzel G, Switchenko J, Dhakaan A. Single-isocenter multiple target SRS: Risk of compromised coverage. *Int J. Radiat. Oncol. Biol. Phys.* 2015; 93:540-6.
14. Briscoe M, Voraney JP, Ploquin N. Establishing a threshold for rotational patient setup errors in linear accelerator based stereotactic radiosurgery. *Biomed Phys Eng Exp.* 2016; 2:045018.
15. Van Herk M. Errors and margins in radiotherapy. *Seminars in radioation oncology.* 2004; 14: 52-64.
16. Stanhope C, Chang Z, Wang Z, Yin FF, Kim G, Salama JK, et al. Physics considerations for single-isocenter volumetric modulated arc radiosurgery for treatment of multiple intracranial targets. *Practical Radiation Oncology.* 2016; 6:207-13.
17. Lutz W, Winston KR, Maleki N. A system for stereotactic radiosurgery with a linear accelerator. *Int J. Radiat. Oncol. Biol. Phys.* 1988; 14: 373-81.
18. Gevaert T, Verellen D, Tournel K, Linthout N, Bral S, Engels B, et al. Setup accuracy of the Novalis ExacTrac 6DOF system for frameless radiosurgery. *Int J. Radiat. Oncol. Biol. Phys.* 2012; 82: 1627-35.
19. Schell Mc, Bova FJ, Larson DA, Leavitt DD, Lutz WR, Podgarsak EB, et al. AAPM Report No.54:Stereotactic radiosurgery. Report of Task Group 42 Radiation Therapy Committee. American Institute of Physics. 1995.
20. Takakura T, Mizowaki T, Nakata M, Yano S, Fujimoto T, Miyabe Y, et al. The geometric accuracy of frameless stereotactic radiosurgery using a 6D robotic couch system. *Phys Med Biol.* 2010; 55:1-10.
21. Keeling V, Hossain S, Jin H, Algan O, Ahmad S, Ali I. Quantitative evaluation of patient setup uncertainty of stereotactic radiotherapy with the frameless 6D ExacTrac system using statistical modeling. *J Appl Clin Med Phys.* 2016; 17:111-27.