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Set up errors in Brain tumours – A retrospective study to review the current practice of PTV margins in the institution

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Background: Radiotherapy in brain tumors needs accuracy and reproducibility of the patient's position. There may be set-up errors that are taken care of by adding planning target volume (PTV) margin. Lesser PTV margins may lead to tumour mass or greater margins may lead to unnecessary radiation of normal brain tissue. The present study is done to evaluate whether the current practice of PTV margins in our institute is optimum or not. **Materials and methods:** Eleven patients with brain tumours who received adjuvant radiotherapy were retrospectively selected for determining the setup errors. These patients were immobilised in the supine position and contrast-enhanced CT of the head was taken for radiotherapy planning. Delineation of gross tumor volume and clinical target volume was done with a 5 mm PTV margin. The treatment was delivered by 3-Dimensional Conformal Radiotherapy or Intensity Modulated Radiotherapy Technique. The setup errors in three dimensions were determined retrospectively for all images. PTV margins were calculated using International Commission on Radiation Units and Measurements Report 62, Stroom's and Van Herk formulae. **Results:** The overall population set-up error was 0.034, -0.048, 0.028 in X, Y, Z directions respectively. The population systematic error was calculated to be 0.107, 0.069, 0.092 and population random error was 0.221, 0.202, 0.217 in X, Y, Z directions respectively. The calculated setup margin as per the three formulas was less than 5 mm in all directions. **Conclusion:** The present study showed that the institutional protocol of 5 mm is optimum to counter the setup errors.

Keywords: Set up errors, Brain tumours, PTV margins, 3DCRT

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Background

Radiation therapy in brain tumor needs precision which is achieved by accuracy and reproducibility of the patient's position daily. Despite all precision and accuracies, some aspects of radiotherapy are always subjected to uncertainty which may lead to delivery errors and treatment failures.[1].

These uncertainties are taken care of by adding a margin to the tumour volumes (gross and microscopic) being planned termed as Planning Target Volume (PTV) margin. This PTV margin varies according to the site of the tumor, immobilization device and imaging technique used [2].

The brain tumours have minimal internal organ motion which is limited due to the skull boundary. Brain tumours may be surrounded by various critical structures that pose a complex situation of preventing high doses to these organs at risk (OAR). Hence, the determination of optimal margin is important to prevent overlapping of these PTV with OARs.

A lesser margin can lead to the marginal miss of the tumour and a higher setup margin can lead to unnecessarily high doses to normal brain tissue or nearby OARs. As per our institutional protocol presently, the PTV margin for brain tumours is 5 mm. The study was designed to evaluate whether this PTV margin is adequate or not.

Materials and Methods

Eleven patients with brain tumours who received adjuvant radiotherapy from November 2019 to April 2021 were retrospectively selected for determining the setup errors and PTV margin.

Immobilisation and simulation: These patients underwent immobilisation in a supine position with a three-pin thermoplastic cast indexed to the treatment couch. The contrast-enhanced CT of the head (CT-RTP) with 3 mm slice thickness were taken. These images were then imported to the treatment planning system (TPS) via the Digital Imaging and Communication in Medicine (DIACOM). These CT slices were reconstructed.

Delineation: The delineation of Gross Tumour Volume (GTV) and clinical target volume (CTV) was done according to RTOG guidelines. [3, 4]. A *PTV* expansion of 5mm was taken from the CTV.

Radiotherapy planning:

A total dose of 54 Gy in 30 fractions for low-grade gliomas and 59.4 Gy in 33 fractions for high-grade gliomas was planned. The dose constraints to OARs were given as per ESTRO recommendations [5]. The treatment was done by 3-Dimensional Conformal Radiotherapy technique or Intensity Modulated Radiotherapy Technique. The planning objective was to deliver 95% to 107% of the prescribed dose to the PTV.

Collection of data for setup error: The patient's position on the first day of treatment was done as per the planning. An orthogonal pair of X-Ray based Mega Voltage (MV) imaging (anterior-posterior and right lateral) with double exposure were acquired using an Electronic Portal Imaging Device (EPID). These images were matched with the Digitally Reconstructed Radiograph (DRR). The setup errors in three dimensions were corrected and applied for the subsequent sessions of treatment.

Daily EPI was taken with MV X rays in two directions (anterior and right lateral). The superposition of EPI and DRR was performed by matching the region of the outer table of the skull. The daily set-up errors were measured.

Positive X value indicates a lateral movement to the right and negative X value movement to left, positive Y value indicates a posterior movement and negative Y anterior movement and positive Z value indicates cranial movement and negative Z caudal movement.

Calculation of Systematic and Random Errors: Individual and population-based systematic and random errors were calculated along the X (left to right), Y (anterior to posterior) and Z (superior to inferior) direction. This was calculated according to the report by the Royal College of Radiologists [6].

It provides information about the individual mean set-up error Individual as the mean set-up error for an individual patient. The overall population mean set-up error Mpop was defined as the overall mean for the analysed patient group. The population systematic error was defined as the standard deviation of the individual mean set-up error about the overall mean Mpop. The individual random (daily) set-up was defined as the standard deviation of the set-up error around the corresponding mean individual value. The population random error was defined as the mean of all the individual random errors.

Calculation of CTV – PTV margin: Once the systematic and random errors were calculated population-based CTV – PTV margins were found out for all patients using International Commission on Radiation Units And Measurements (ICRU) Report 62,[7] Stroom's [8] and Van Herk formulae [9].

Results

The maximum and minimum displacement in the three-axis are described in the given table 1. The displacement varied from minimum -0.6 and maximum 0.72 setup error in X, Y, and Z-axis.

Table 1: Table showing systematic individual setup errors M individual in the X, Y, Z-axis.

M INDIVIDUAL	X (mm) LR	Y (mm) AP	Z (mm) SI
1	0.065	-0.002	0.07
2	-0.040	-0.120	0.07
3	0.161	-0.06	0.05
4	0.14	-0.120	0.08
5	0.195	-0.084	-0.04
6	-0.018	-0.049	0.01
7	-0.032	0.069	0.13
8	0.016	-0.004	-0.12
9	-0.126	-0.105	-0.13
10	-0.090	-0.115	0.06
11	0.109	0.058	0.12

Table 2: Table showing individual Random Error in the X, Y, and Z axis.

Individual Random Error	X (mm)	Y	Z
1	0.342	0.135	0.210
2	0.216	0.266	0.224
3	0.352	0.280	0.159
4	0.220	0.267	0.183
5	0.165	0.258	0.304
6	0.208	0.137	0.100
7	0.229	0.148	0.264
8	0.141	0.101	0.191
9	0.328	0.170	0.253
10	0.130	0.295	0.284
11	0.106	0.170	0.219

Mean individual set up errors for 11 patients and mean individual random error for 11 patients is demonstrated. (Table 2).

The overall population set-up error (M_{pop})was calculated to be 0.034,-0.048, 0.028 in X, Y, Z directions respectively. The population Systematic error was calculated to be 0.107, 0.069, 0.092 in X, Y, Z directions respectively. The population random error was calculated to be 0.221, 0.202, 0.217 in X, Y, Z directions respectively.

Table 3: Table showing the calculated CTV to PTV margin (cm).

AXIS	VAN HERK	STROOM	ICRU62
X	0.42	0.37	0.25
Y	0.32	0.28	0.21
Z	0.38	0.34	0.24

The calculated setup margin as per the three formulas was less than 5 mm in all directions. The highest setup error was observed on X-axis and minimum on the Y-axis. The PTV margins were less than 3mm in all directions as per the ICRU 62 formula.7

Discussion

Every institution defines its own PTV margins for brain tumors which are affected by the type of immobilisation used, type of radiotherapy technique in planning and verification imaging available. This PTV margin depends upon the setup errors occurring in three dimensions.

In a study by Park et al,10 of 49 patients with brain tumours, the mean patient setup errors at the lateral (X-axis), longitudinal (Y-axis), and vertical (Z-axis) directions were 0.1±1.4mm, 0.0±1.1mm, and -0.4±1.2 mm respectively. But in our study the setup errors were relatively higher being 0.24 +/- 0.42 mm, 0.21+/- 0.32 mm, and 0.24 +/- 0.38 mm in the lateral (X-axis), longitudinal (Y-axis), and vertical (Z-axis) directions respectively. The difference in the results can be attributed to the different imaging modalities used. Park et al 10 utilised CBCT for the first-day setup and setup error detection. The Hexa POD model was used to correct the set-up errors in three directions of translation and three directions of rotation. On the contrary, in our study, Kilo Voltage (KV) X-ray imaging was utilised and the rotational errors were not evaluated due to the non-availability of the facility.

Se An Oh et al [11] analysed PTV margins in 28 patients with brain tumors taking 844 image verifications. The criterion for image registration between CT simulation image and Exact Trac image was the bony anatomy matching. After

The planning and during the patient's set up verification images were obtained with the Brain LAB ExacTrac system. The set-up errors were automatically obtained by the BrainLAB 6D Fusion algorithms. In the study, according to Van Herk et al [9] and Stroom et al,[8] the recommended lateral PTV margins were 0.97 and 1.66 mm, the longitudinal margins 1.26 and 3.47mm and the vertical margins 0.21 and 2.31mm, respectively. In our study, PTV margins are more in comparison to this study. The PTV margins in lateral direction were 4.2 and 3.7 mm, longitudinal direction 3.2 and 2.3 mm and in vertical direction 3.9 and 3.4 mm for Van Herk and Stroom et al [9,8] formulas respectively. The reason for increased set-up errors is first that in our study the measurements of displacements were done manually in comparison to automatic readings by the BrainLAB 6D Fusion algorithms. Secondly, in our study, only translational setup errors were considered and additional rotational setup errors were not done. These limitations were present in our study due to the lack of advanced technology in our department.

Vos et al [12] studied the optimal margin for intracranial tumors in their centre on 20 patients. The CTV to PTV margin was taken as 1cm. the set up errors seen in mediolateral (ML), superior-inferior (SI) and anterior-posterior (AP) directions were less than 3 mm in 87.7%, 76.2% and 91.6% respectively. The errors were largest in the SI direction, followed by the ML direction and smallest in the AP direction. There were no errors larger than 5 mm in the ML and AP direction and 6.1% of errors were larger than 5 mm in the SI direction. The margins calculated by Stroom's recipe were 3.42, 4.58 and 2.67 mm in ML, SI and AP directions respectively. The study changes their practice of PTV margins from 1cm to 5mm. In the present study, margins calculated by Stroom's recipe is almost similar in ML (3.7 mm) and AP (2.8 mm) directions but comparatively lesser in SI (2.8 mm) direction. In contrast to Vos et al,12 none of the patients had more than 5mm set up errors in any direction which can be due to the better immobilisation system utilised. The role of anisotropic margins is suggested for future studies which we would like to support since it will reduce the dose to the normal brain and may be useful where critical OARs are very near to the PTV.

Similarly, the anisotropic margins referred to as custom PTV is also suggested by Shields L B E et al, [13] where PTV may be closer to OARs in some cases. In their study of 29 patients with brain tumours, custom PTVs were made in three patients and analysed that dose to the OARs like brainstem, hippocampus and temporal lobes was reduced. This approach may help to spare the hippocampus and therefore the neurocognitive functions in patients where the brain tumour lies in the central location or near the hippocampus.

The PTV margins can further be decreased by practising daily imaging. This may lead to more machine time and therefore the institution needs to decide these protocols depending upon the patient load and human resources available. Further, while determining the institutional protocol for setting up errors, besides imaging protocols and type of immobilization system used, other factors like delineation errors, the expertise of treatment team members and quality assurance should also be considered.

Conclusion

The calculated CTV to PTV margin for brain tumours was less than 5 mm in all three directions. The present study showed that the institutional protocol of 5 mm is optimum to counter the setup errors. Anisotropic margins may be the scope for further studies in set up errors of brain tumours.

What does this study add to our existing knowledge?

The present study proved the adequacy of setup margins that are currently being practiced in brain malignancies. Also it highlights the scope for further reduction in setup margins that needs to be validated in future research.

Author's Contribution: Dr. Diksha Chaturvedi: Data collection, Statistical analysis, Drafting and editing the manuscript. **Dr. Ankita Mehta:** Statistical analysis, Verification of data, Drafting and editing the manuscript. **Dr. Piyush Kumar:** Study designing, Manuscript editing, Finalising and intellectual content.

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