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Original Research Article

Geometric accuracy in patient positioning for stereotactic radiotherapy of intracranial tumors

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ABSTRACT

Background/Purpose: This study determines and compares the geometric setup errors between stereoscopic x-ray and kilo-voltage cone beam CT (CBCT) in phantom tests on a linear accelerator (linac) for image-guided (IG) stereotactic radiotherapy of intracranial tumors. Additionally, dose-volume metrics in the target volumes of the setup errors of CBCT were evaluated.

Materials/Methods: A Winston-Lutz- and an anthropomorphic phantom were used. The mean deviation and root mean square error (RMSE) of CBCT and stereoscopic x-ray were compared. Dose-volume metrics of the planning target volume (PTV) and gross target volume (GTV) for CBCT were calculated.

Results: The RMSEs in the tests with the Winston-Lutz-Phantom were 0.3 mm, 1.1 mm and 0.3 mm for CBCT and 0.1 mm, 0,1 mm and <0.1 mm for stereoscopic x-ray in the translational dimensions (right-left, anterior-posterior and superior-inferior). The RMSEs in the tests with the anthropomorphic phantom were 0.3 mm, 0.2 mm and 0.1 mm for CBCT and 0.1 mm, 0,1 mm and <0.1 mm for stereoscopic x-ray. The effects on dose-volume metrics of the setup errors of CBCT on the GTV were within 1 % for all considered dose values. The effects on the PTV were within 5 % for all considered dose values.

Conclusion: Both IG systems provide high accuracy patient positioning within a submillimeter range. The phantom tests exposed a slightly higher accuracy of stereoscopic x-ray than CBCT. The comparison with other studies with a similar purpose emphasizes the importance of individual IG installation quality assurance.

1. Introduction

Stereotactic radiotherapy (SRT) is a common treatment option to irradiate brain lesions. In the past, SRT was mainly used for the treatment of oligometastases. Nowadays, SRT can be used for the treatment of multiple brain metastases because of technical improvements [1–7]. SRT can be performed by fully robotic radiotherapy devices specialized for SRT or conventional linear accelerators (linac) modified to perform SRT. Due to high doses and steep dose gradients in single fraction radiosurgery (SRS) and fractionated SRT (FSRT), it is necessary to achieve high repeatable geometric accuracy in those linac systems to prevent side effects like radionecrosis. Technical improvements in linac-based treatments enable to use small safety margins (0–2 mm) in treatment planning depending on treatment system and individual settings [8–10]. Therefore, it is important to ensure high accuracy in patient positioning for intracranial stereotactic radiotherapy. There are different image guidance (IG) systems like cone-beam computed tomography (CBCT) and stereoscopic x-ray that provide accuracy in a submillimeter range.

Technical requirements for SRT in frequent end-to-end (E2E) phantom tests vary by publication and investigated device. They are usually set to a geometric accuracy of around one millimeter [11–13]. Yet, it is difficult to assess which IG system is more accurate. Several studies report comparable accuracy of both positioning methods, albeit with different tendencies [14–18]. This emphasizes the importance of installation-related quality assurances of IG systems. The effects on dose-volume metrics are not considered in those studies. Due to above mentioned demand on accuracy and variation between different devices, it is necessary to obtain more individual data on accuracy of different system installations. Determining the effects of the actual geometric uncertainties on dose-volume metric is also an important issue to explore.

The objective of this study was to determine and compare the geometric accuracy of kV-CBCT and stereoscopic x-ray in phantom

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measurements, specifically focusing on the pure three degrees of freedom (3-DoF). Additionally, the study aimed to assess the impact of setup errors for CBCT on the dose-volume metrics in the target volume.

2. Materials and methods

2.1. Phantom measurements

All measurements and treatments were performed at a TrueBeamSTx (Varian Medical Systems Inc., Palo Alto, USA) incorporated with the Novalis radiosurgery program (BrainLAB AG, Feldkirchen, Germany). The used linac was equipped with kV-CBCT (Varian Medical System Inc.) and a stereoscopic x-ray, an ExacTrac v6.0 (ETX, BrainLAB AG), for image-guided radiotherapy (IGRT). The CBCT scans were acquired at 0.8 mm slice thickness. The patients and phantoms were positioned on the PerfectPitch 6-DoF couch (Varian Medical System Inc.). It provided patient shifts in right-left (RL), anterior-posterior (AP) and superior-inferior (SI) axes and in three rotational axes (yaw, pitch and roll). The gantry of the TrueBeam STx was equipped with an HD 120 Multi-Leaf-Collimator (MLC). The oncology information system ARIA v.16 (Varian Medical Systems Inc.) was used for treatment planning and dose-volume metric calculations.

A Winston-Lutz-Phantom (frameless SRS QA target pointer, BrainLAB AG) with a 3.5 mm diameter and an anthropomorphic phantom (Alderson phantom) were used for measurements. The Alderson phantom was immobilized with a closed customized thermoplastic mask (BrainLAB AG) with three metallic markers (Beekley spots) for prepositioning.

First, the phantoms were isocentrically aligned to define a reference point. Before conducting the measurements with CBCT, a pre-positioning with room-lasers was performed. A correction and verification scan by CBCT was performed. For isocentrical alignment with ETX, the pre-positioning was performed with a frameless-radiosurgery-positioning-array with integrated infrared-markers. The correction and verification scans were performed with ETX. The detected coordinates were used as reference and defined as isocenter. A schematic overview is given in Section 1 of the supplementary material.

After isocentric positioning the phantoms were shifted by 2 mm from the defined isocenter in RL axis and the position was determined by CBCT or ETX. The shifts were executed by moving the PerfectPitch 6-DoF couch for the defined distance. The difference between the predefined position and the measured position was calculated and presented the uncertainty. The phantoms were repositioned in the isocenter, and the position of the phantom was determined again by CBCT or ETX. The difference between the defined isocenter coordinates and the determined position of the phantom illustrates the uncertainty. This process was repeated with shifts in all three translational axes at once (RL: 2 mm; AP: 1 mm; SI: 2 mm). The differences from the target positions were notated. Overall, 40 scans per phantom were performed by each, CBCT and ETX.

2.2. Uncertainties in image registration

To determine uncertainties in image registrations a retrospective analysis of patient treatment plans was performed. In total 75 rigid image registrations (IR) between planning CT and CBCT scans of patients, treated at the TrueBeam STx at University Hospital of Schleswig-Holstein, Kiel, were reviewed by a medical specialist regarding matching of bony structures in the oncology information system ARIA v.16. Duplicates of all CBCT scans were generated. These scans were re-registered in 6-DoF using ARIA offline review with mutual information algorithm. We visually verified the auto-registration results and repeated the image fusion if necessary. The original online IRs were compared with the optimized offline IRs. The RMSE of the differences in each axis was calculated.

More information about the treatment population can be found in Section 2 of the supplementary material. The patients in this study gave informed consent for data processing for scientific purposes for our clinic.

2.3. Dose-volume metrics

The effect on the dose-volume metrics of the previously found uncertainties in CBCT imaging combined with the uncertainties in 3D/3D-IR were determined. A $RMSE_{total}$ combining RSME from the measurements with the Alderson phantom and the RMSE from the 3D/3D-IR uncertainties considering all three translational axes (RL, AP and SI) was determined. The $RMSE_{total}$ was calculated similarly to Stroom and Heijmen (2002) [19].

$$RMSE_{total} = \sqrt{RMSE^2_{phantom} + RMSE^2_{IR-Registration}}$$

The dose distribution of the original treatment plans of the patient base and the treatment plans including the $RMSE_{total}$ in all three translational dimensions were calculated. The dose distribution in the original plan serves as a reference. The uncertainties were integrated into the plan as $RMSE_{total}$ (RL, AP and SI) producing a virtual shift. In total dose distributions for 45 PTVs and 48 GTVs were calculated. The calculated uncertainties ($RMSE_{total}$) were used to move the treatment plan in the treatment planning system Eclipse to simulate the uncertainties. After that, the plans were calculated again to get the differences in dose-volume metrics between the treatment and the simulated plan.

D_{98} , D_{95} , D_{50} , D_5 , D_2 values and homogeneity index (HI) were used for comparison. In this study, HI is defined as $HI=D_{95}/D_5$. The Eclipse Anisotropic Analytical Algorithm v.13.7.14 (AAA) algorithm was used for dose calculation with a grid size of 1.25 mm.

The setup errors were analyzed as means, standard deviations, and RMSE. Uncertainties and differences between CBCT and ETX were analyzed through two-tailed t-tests with Microsoft Excel v.16.42. A p-value < 0.05 was considered statistically significant.

3. Results

The RMSEs of the setup errors using the Winston-Lutz-Phantom were 0.3 mm, 1.1 mm and 0.3 mm with CBCT and 0.1 mm, 0,1 mm and <0.1 mm with ETX in the translational dimensions (RL, AP and SI).

The RMSEs of the setup errors using the Alderson phantom were 0.3 mm, 0.2 mm, and 0.1 mm with CBCT and 0.1 mm, 0,1 mm, and <0.1 mm with ETX in RL, AP and SI.

An overview of the means and standard deviations of the setup errors with the Winston-Lutz- and Alderson phantom with CBCT and ETX is given in Table 1.

The difference of the total RMSE regarding the measurements with Winston-Lutz-Phantom was 0.6 mm and was statistically significant with a p-value < 0.01 The differences in each translational axis were also statistically significant. A graphic overview of the deviation of the Winston-Lutz-Phantom from the expected position is given in Fig. 1a.

The setup errors measured with CBCT and ETX in Alderson phantom tests were in a range of 0.1 to 0.2 mm (Fig. 1b). The difference for total

Table 1
Means and standard deviations of setup errors in measurements with CBCT and ETX with the Winston-Lutz-Phantom and Alderson phantom in millimeters.

	Mean ± SD [mm]	Winston-Lutz-Phantom	Mean ± SD [mm]	Alderson phantom
	CBCT	ETX	CBCT	ETX
total	−0.1 ± 0.7	0.0±0.1	0.0±0.2	0.0±0.1
RL	0.0±0.3	0.0±0.1	0.0±0.3	0.0±0.1
AP	−0.2 ± 1.1	0.0±0.1	0.0±0.2	0.0±0.1
SI	0.0±0.3	−0.1 ± 0.1	0.0±0.1	0.0±0.1

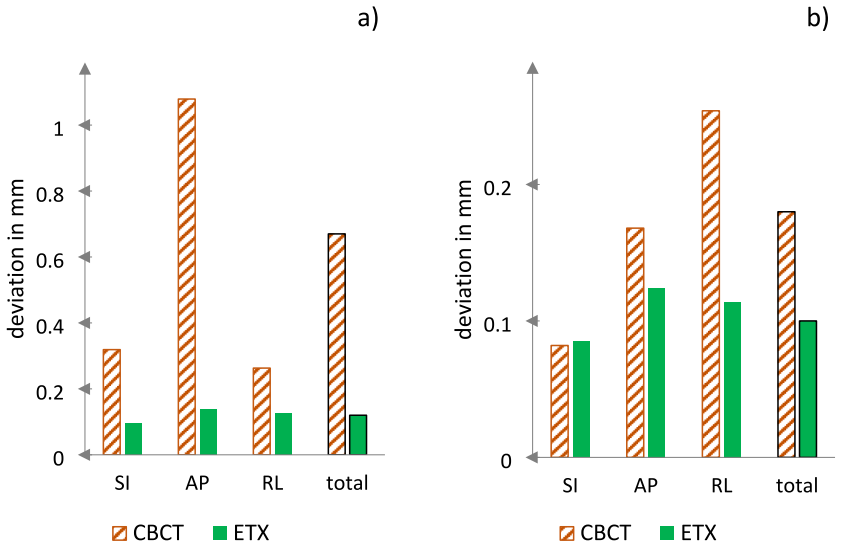

Fig. 1. RMSE of IG with CBCT and ETX. a) Winston-Lutz-Phantom b) Alderson phantom.

RMSE was statistically significant with <0.1 mm deviation and a p-value < 0.01. A statistically significant difference of 0.2 mm was found in the RL axis (p-value < 0.01). No statistically significant difference was observed in AP and SI axis. Rotational setup errors without performing a rotation were within 0.1°.

The means ± SD of the differences between the original and the optimized 3D/3D- IR were −0.5 ± 0.6 mm, 0.0±0.5 mm and 0.0±0.5 mm for each translational axis (RL, AP and SI). The RMSE of the differences were 0.8 mm, 0.5 mm, and 0.5 mm. Rotational setup errors were within 0.5°.

The determined $RMSE_{total}$ which were used for calculating the dose-volume metrics were 0.8 mm, 0.6 mm and 0.5 mm (RL, AP and SI).

Mean dose changes in the GTV were under one percent in all analyzed dose indices (Table 2). A statistically significant dose loss was found in the D_{98} value, D_{95} value and homogeneity index. Overall, 46 of 48 analyzed GTVs showed a dose loss of under five percent for the D_{98} value with a maximum dose loss of eight percent in one case. The dose changes for the D_{50} values were all within a range of two percent from the original dose calculation. The mean dose change for the D_{50} value in $GTV_{RMSE_{total}}$ was an increase of 0.2±0.7 %. These marginal changes in dose distribution in the GTV illustrate the high accuracy of the CBCT patient positioning.

Table 2
Percentage of the mean dose of $GTV_{RMSE_{total}}$ from $GTV_{Original}$ for different dose indices.

	Mean Dose of $GTV_{RMSE_{total}}$ from $GTV_{Original}$	95 %-confidence interval
D_{98} [Gy]	99.1±2.1 % **(p = 0.002)**	[98.5 %; 99.7 %]
D_{95} [Gy]	99.3±1.8 % **(p = 0.009)**	[98.8 %; 99.8 %]
D_{50} [Gy]	100.2±0.7 % (p = 0.06)	[100.0 %; 100.4 %]
D_5 [Gy]	100.2±1.3 % (p = 0.38)	[99.8 %; 100.5 %]
D_2 [Gy]	100.2±1.2 %(p = 0.31)	[99.8 %; 100.5 %]
HI	100.9±1.5 % **(p < 0.001)**	[100.5 %; 101.4 %]

The effects on dose-volume metrics in the PTV were slightly higher than in the GTV. For the D_{98} value, there was a statistically significant mean dose loss of four percent. The D_{50} value had a statistically significant mean dose increase of 0.2 %. Table 3 illustrates an overview of the dose changes for the dose indices in the PTV.

Table 3
Percentage of the mean dose of $PTV_{RMSE_{total}}$ from $PTV_{Original}$ for different dose indices.

	Mean Dose of $PTV_{RMSE_{total}}$ from $PTV_{Original}$	95 %-confidence interval
D_{98} [Gy]	96.0±3.8 % **(p < 0.001)**	[95.0 %; 97.1 %]
D_{95} [Gy]	97.4±3 % **(p < 0.001)**	[96.5 %; 98.2 %]
D_{50} [Gy]	100.2±0.7 % **(p = 0.03)**	[100.0 %; 100.4 %]
D_5 [Gy]	100.4±0.6 % **(p < 0.001)**	[100.2 %; 100.5 %]
D_2 [Gy]	100.1±2.1 % (p = 0.88)	[99.4 %; 100.7 %]
HI	103.2±3.2 % **(p < 0.001)**	[102.3 %; 104.2 %]

4. Discussion

Based on phantom measurements with the Alderson phantom, both imaging systems (CBCT and ETX) provide an IG patient positioning accurate to a millimeter. The results in Tables 1 and 2 show a slightly higher SD for CBCT than for ETX, whereas the mean deviation is in close agreement. This leads to the assumption that the ETX has a slightly higher precision than the CBCT with similar accuracy.

The RMSE of the ETX is 0.1 mm less for the Alderson phantom, and 0.5 mm for the Winston-Lutz Phantom, respectively. These setup errors are within the range of 1.25 mm for fractionated stereotactic RT and of 1.0 mm for radiosurgery required from the DGMP and DEGRO [13].

In comparison to other publications, the accuracy and precision of both IG positioning techniques in this study are quite high [14,16–18]. The setup errors of ETX and CBCT reported by Ma et al. [14] and Chang et al. [20] were accurate to a millimeter and slightly smaller for ETX. Oh et al. [15] analyzed residual setup errors in patient positioning with CBCT and ETX within a cohort of 107 patients. They found minor discrepancies between CBCT and ETX. This was confirmed by our results. Graulieres et al. [16] performed phantom tests on two identical constructed linacs. They report comparable, sub-millimetric results for both, CBCT and ETX. They pointed out differences between the two linacs. The fact, that one of the two identical constructed linacs provides a higher accuracy, illustrates the importance of individual accuracy tests for patient positioning and treatment installations in stereotactic RT. An overview of their results and ours is illustrated in the supplementary material in Section 3.

Another noticeable finding is, that all means and SD measured at Winston-Lutz-Phantom and Alderson phantom were consistent in a range of at most 0.5 mm except in one test series. In the series with CBCT

and the Winston-Lutz-Pointer performing shifts in three axes, there is a noticeably larger SD in the AP axis than in any test series. A possible explanation for this could be a non-sufficient system calibration. Another possible reason is the uncertainty of the 6-DoF couch in AP-direction. The findings of Zollner et al. [21] show that the limiting factor in patient positioning, excluding patient motion, is the accuracy of the patient shifts. We recommend looking and evaluating this part carefully. In our opinion measurements with the Alderson phantom are more meaningful anyway because they present a scenario closer to a real human head.

The evaluation of the dose-volume metrics in the target volumes is limited to the uncertainties found in patient positioning with CBCT due to technical restrictions. It must be considered that we report the pure geometric uncertainties of the image positioning system (CBCT). Neither patient-related uncertainties, such as motion or deformations, nor mechanical properties of the delivery device were included in our analysis.

The effects on dose-volume metrics of rotational setup errors were analyzed in various papers, whereas studies for effects of translational setup errors are rare [22–24]. To discuss the effects on dose-volume metrics of rotational errors it is important to differentiate between single and multiple targets in the treatment plan. For multiple target volumes, it is also important to distinguish between plans with single and multiple isocenters because of different effects of rotational setup errors on dose distribution [22]. Roper et al. [23] investigated rotational setup errors in treatment plans with multiple targets and a single isocenter. The D_{95} values of the PTV were $\geq$95 % in all cases with a rotational error of 0.5°. Sagawa et al. [22] determined dosimetric effects on PTV for mean rotational errors of around 0.3° for pitch, yaw, and roll. The dosimetric effects were <2% for single target cases. Those studies illustrate the importance of rotational setup accuracy in multiple target treatments and the small dosimetric effects in single target treatments.

One finding of Wang et al. [24] was that the translational errors had bigger dosimetric effects on the target volume than the rotational setup errors. They report of only one V_{95}-loss of more than 5 % for the GTV for a rotational setup error of 2°. Thus, we conclude that the dosimetric effects of our determined rotational setup errors of under 0.5° are quite small.

The ICRU Report No. 91 exposes the D_{50} value as a good option to evaluate a radiation treatment plan even for volumes with heterogeneous dose distribution. In our results, the deviations of the D_{50} values in the GTV and PTV from the original plan are <1 %. This underlines the high accuracy of the CBCT.

One limitation is that we did not include the rotational setup errors in our study. This was not possible due to technical restrictions. To counter this problem, different other studies were used to discuss the dosimetric effects of rotational errors.

The second limitation is a heterogeneous patient cohort. Due to the small number of patients treated with stereotactic RT, patients with single and multiple target volumes were included. As reported this differentiation is important to evaluate the dosimetric effects of rotational setup errors. In our study, only the effects of translational setup errors were assessed. Therefore, we assume that our results are reliable.

Another limitation is the lack of a direct comparison of the dose-volume metric between CBCT and ETX. Due to technical restrictions, it was not possible to get the data of the 2D/3D-IR from the patients. In turn, we could not calculate the $RMSE_{total}$ for ETX. Li et al. [25] investigated the difference in accuracy between 2D/3D- and 3D/3D-image registration. The difference between both methods was 0.0° ± 0.5 mm in translational and 0.1° ± 0.4° in rotational axes. In another study, the mean difference was determined at 0.3 mm in translational and 0.3° in rotational axes [26]. Thus, we proceeded on the assumption of a similar accuracy of both, 2D/3D- and 3D/3D-IR. For further investigations to evaluate patient positioning a test series with shifts and rotations in all 6-DoF combined would be useful.

Summarized both IGRT systems, CBCT and ETX provide a high accuracy and precision in patient positioning in a submillimeter range. In our phantom setup, the ETX was slightly more precise than the CBCT. The effects on the dose-volume metrics on GTV and PTV of the setup error of patient positioning with CBCT were quite small with <1 % deviation in the D_{50} value from the original plan. Therefore, the ETX system is the preferred image guidance for our stereotactic installation relating to geometric accuracy. However, in inconclusive cases, we suggest the use of both patient positioning systems.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2023.100461.

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