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Intrafraction motion in intra-cranial multi-target stereotactic radiosurgery plans: A multi-institutional investigation on robustness

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ABSTRACT

Purpose: Even with modern immobilisation devices, some amount of intrafraction patient motion is likely to occur during stereotactic radiosurgery (SRS) delivery. The aim of this work was to investigate how robustness of plans to intrafraction motion is affected by plan geometry and complexity.
Methods: In 2018, the Trans-Tasman Radiation Oncology Group conducted a multiple-target SRS international planning challenge, the data from which was utilised in this study. Patient geometry included five intracranial targets with a prescription of 20 Gy. A previously validated in-house algorithm was used to simulate realistic intrafraction patient motion for these plans. Three scenario types were simulated: translational intrafraction motion; rotational motion; and simultaneous rotational and translational motion. Dosimetric impact was assessed using: dose covering 98 % of planning target volume, dose covering 99 % of gross tumour volume (GTV D99%), volume of normal brain receiving 12 Gy and maximum dose covering 0.03 cc brainstem.
Results: GTV D99% was reduced by up to 70 %, with the strongest correlations between planning factors and robustness to intrafraction motion found for plan complexity. Despite only moderate correlation strength at $r = 0.4$, lower complexity plans had, on average, 5 % – 9 % less intrafraction motion scenarios with failing targets compared to the highest complexity plans.
Conclusions: SRS plans with lower complexity, in particular larger mean multi-leaf collimator (MLC) gap and MLC aperture irregularity, were shown to improve plan robustness to intrafraction patient motion.

1. Introduction

Frameless patient immobilisation technology in combination with image guidance has been previously determined to be accurate for stereotactic radiosurgery (SRS) and is currently commonly used [1–3]. However, even with accurate setup and patient immobilisation devices, some amount of intrafraction patient motion is likely to occur, the magnitude of which may be difficult to predict.

The reported magnitude of intrafraction patient shifts in recent studies varies with mean values between (0.3 – 0.9) mm [4–10] for translations and (0.2—0.6)° [4,8–10] for rotations. There is contradicting evidence to support [4,10,11] or deny [2,5,7–9] a correlation between treatment duration and magnitude of intrafraction patient motion. Immobilisation device used may also affect the extent of motion as the reported magnitudes vary across devices [4,5,7–10]. Significantly, even though the range of reported means of intrafraction patient motion is < 1 mm/°, several studies observed large maximum shifts of >2 mm/° [4,5,9,10].

The significant dosimetric impact of intrafraction patient motion has been highlighted previously by Foster *et al.* [12] where planned dose

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was compared to dose recalculated when replicating intrafraction motion recorded throughout treatment delivery. In their work, the gross tumour volume (GTV) minimum dose was found to differ by a median of 16 % but up to 86 %. Therefore, treatment plans should be created with a high level of robustness to minimize the dosimetric impact should this intrafraction patient motion occur.

Previous work has confirmed a correlation between plan complexity and robustness to setup errors [13]. This study extended upon that with the aim of determining how planning characteristics relate to robustness to patient-induced intrafraction motion rather than system-related uncertainties. This study also aimed to investigate the dosimetric impact of realistic patient motion in multiple axes simultaneously based on previously reported motion tracking data.

2. Methods

Utilising multi-institutional data submitted to a 2018 Trans-Tasman Radiation Oncology Group (TROG) planning challenge [14], realistic

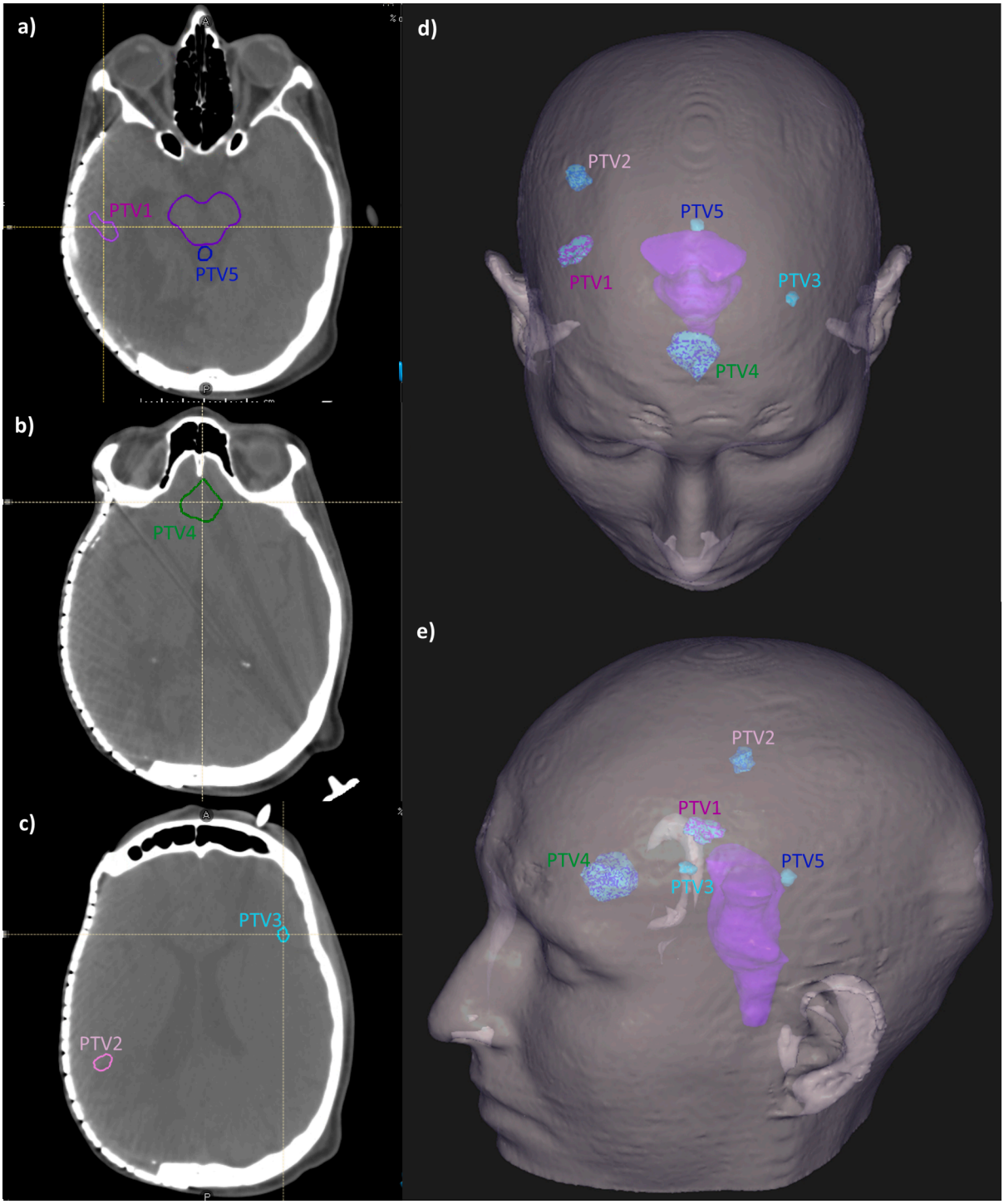

Fig. 1. PTV locations relative to patient anatomy from the patient CT scan for a) axial slice showing PTV1 and 5, b) axial slice showing PTV4 and c) axial slice showing PTV2 and 3, with d) and e) showing 3D renders of all targets in blue, with the brainstem in purple. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

intrafraction patient motion was simulated to investigate the dosimetric impact upon multi-target SRS plans.

The challenge provided a predefined protocol and scoring matrix (see supplementary material) for a single patient with five pre-contoured planning target volumes (PTVs) visualised in Fig. 1, each with a 20 Gy prescription. In this study, PTVs were isotropically contracted by 1 mm to retrospectively create GTVs with an expansion margin representative of current clinical practices [15]. The geometric properties of the targets are outlined in Table 1. Note the close proximity of PTV5 to the brainstem (Fig. 1.a).

It has previously been suggested by a review of multi-institutional stereotactic body radiotherapy planning challenges that dose volume histogram parameters and dose calculations should be performed independent of the submitting departments' treatment planning system (TPS) for consistency of plan comparisons [16]. Further, the planning challenge submissions included dose grids calculated per plan only. Therefore, in order to obtain dose grids calculated per beam, the plans were first imported and recalculated on generic beam models within the RayStation® TPS (v.10.1, RaySearch Laboratories, Stockholm, Sweden) as described in detail in May *et al.* [17]. The final dataset of 51 baseline plans used in this study is outlined in Table 2, and further detailed in May *et al.* [13].

The treatment plans, the calculated per-beam dose grids and the corresponding structure sets were exported to be utilised by an in-house plan robustness tool.

2.1. In-house patient positioning error simulation

RayStation does not include a functionality to automatically implement rotational patient positioning errors. Furthermore, although calculation of translational errors is possible through both the built-in robustness tool [18] and by moving the isocentre, the processing time for very large numbers of scenarios would make this infeasible. Given that we aimed to calculate over 10,000 error scenarios in this study, a previously developed and validated in-house plan robustness tool was used [13].

The in-house robustness tool uses static dose cloud approximation [19], whereby: treatment plans, the dose per-beam files, and the patient structures were imported; structures were rasterised to a 0.5 mm by 0.5 mm by 1.0 mm grid; and a patient motion generator was used to alter the sampling location of the structure on the dose grid without recalculating the distribution. Tri-linear interpolation was used with 2x anti-aliasing for dose sampling. Rotational patient motion was simulated about the midpoint of the C1 and C2 cervical vertebrae to replicate human anatomical motion [20].

Dose to 10 structures with randomised motion could be re-sampled and accumulated for a single plan containing 10 beams in less than 7 s, irrespective of structure size. Thus, it took approximately 12 min to calculate 100 uncertainty scenarios for a given plan.

Table 1
Target distribution and properties. Point of rotation refers to the atlantoaxial joint at the C1/C2 vertebrae where rotations were simulated about for anatomical reasons.

Target	PTV volume (cc)	GTV volume (cc)	Minimum length along x-, y- and z-axes (cm)	Distance from centre of target distribution (cm)	Distance from point of rotation (cm)
PTV1	0.5	0.2	1.0	5.5	9.8
PTV2	0.4	0.1	0.9	6.7	11.4
PTV3	< 0.1	< 0.1	0.4	5.0	13.7
PTV4	2.8	1.8	1.6	2.0	13.1
PTV5	0.1	< 0.1	0.6	5.5	7.7

Table 2
Plan properties for the dataset used.

Treatment planning system	Machine	MLC	Energy	VMAT plans	IMRT plans	Total plans
Eclipse	TrueBeam	Millennium	6FFF	5	0	5
		HD120	6FFF	24	2	26
			10FFF	4	0	4
Monaco	Versa HD	Standard	6FFF	14	0	14
Pinnacle	TrueBeam	Millennium	6FFF	0	1	1
RayStation	Versa HD	Agility	6FFF	1	0	1

2.2. Introducing intrafraction patient motion

To simulate intrafraction patient motion, random rotational and translational errors were applied per beam. The magnitudes and frequency of these errors were sampled from the intrafraction motion data reported in Barnes *et al.* [5] (replicated in Table 3) which presented patient motion data from 101 patients obtained using the Brainlab ExacTrac Frameless SRS system (Brainlab AG, Germany) with images obtained after each beam. In their study, the direction of motion was found to be uniformly distributed in each axial direction and no significant correlations were found between translational or rotational axes.

Patient-related motion is a complex issue as rotations facilitated by human physiology about the cervical vertebrae would result in a translation of isocentre position. Therefore, to simulate this distribution of translational and rotational errors, three types of scenarios were considered. A pseudo-random number generator was used to sample the distribution created by the data in Table 3 where for each beam: 1) a shift magnitude was randomly selected from the generated distribution for each translational axis and applied without rotations; 2) a random rotation magnitude was selected and applied in each axis without translations; and 3) both translations and rotations of randomly selected magnitude were applied. Each of the three scenario types were repeated 100 times in order to adequately sample the distribution for every plan of the 51 plan dataset and a total of 475 beams. The plans with intrafraction motion simulated are referred to hereafter as error plans.

2.3. Data analyses

The dose metrics used were: near-minimum (D98%) and near-maximum (D2%) for each PTV as recommended in the international commission on radiation units and measurements (ICRU) report 91 [21]; D99% for GTVs; volume of normal brain receiving 12 Gy (V12Gy) and maximum dose covering 0.03 cc (D0.03 cc) of brainstem.

Due to the differences in baseline plan dosimetry as a result of recalculation on generic beam models [17] dosimetric analyses were conducted in two ways: qualitative comparison of dose metrics as a percentage (calculated as [error plan – baseline]/baseline); and development of a modified plan-specific pass/fail threshold. The threshold was set so that recalculated plans had acceptable PTV coverage (which was true for submitted plans). Hence, the baseline PTV D98% specific to

Table 3
The percentage of fractions as a function of the largest translational and rotational error. Values obtained from Fig. 4 in Barnes et al. [5].

Maximum translation/rotation (mm/°)	Translations: percentage of fractions (%)	Rotations: percentage of fractions (%)
<0.7	57.6	75.3
0.7—1.0	25.9	15.7
1.0—1.2	9.4	5.1
1.2—1.4	3.1	2.0
1.4—1.6	3.1	1.6
1.6—1.8	0.4	0.0
>1.8	0.4	0.4

each plan was set as the dosimetric value required to preserve GTV D99%.

Plan characteristics included in analyses were the number of isocentres, number of arcs and number of couch angles, as well as MLC complexity metrics. The following predefined complexity metrics were calculated using PlanAnalyzer implemented in MATLAB (Mathworks, Massachusetts, USA) [22]: edge metric, modulation complexity score (MCS), mean MLC gap, mean MLC speed and plan modulation (PM). Spearman's correlation coefficient was used to identify correlations between dose metrics and plan characteristics. A strong correlation was defined as $|r| \geq 0.6$, moderate as $0.4 \leq |r| < 0.6$ and weak as $|r| < 0.4$.

Significant difference between number of failing target scenarios when comparing the 1st and 4th complexity quartiles was tested using a two proportions Z-test. To reduce other possible contributing factors, as the majority of the dataset were single-isocentre, only single-isocentre plans were used when comparing complexity quartiles.

Comparison of the distribution of randomly sampled intrafraction motion across directional axes was conducted with a Kruskel-Wallis test with post-hoc Dunn's pair-wise testing and Bonferroni correction.

3. Results

The mean absolute magnitude of randomly sampled translations and rotations in each axis was 0.63 mm and 0.51° respectively, with a maximum of 3.00 mm/° (Fig. 2). There were no significant differences across directions or rotational axes ($p > 0.05$ for all). With simultaneous rotational and translational intrafraction motion applied, the average total translation of the centre of target distribution including translation as a result of rotations was also 0.63 mm with a maximum value of 3.21 mm (Fig. 2.c).

3.1. Impact of intrafraction motion on target coverage

The impact on target coverage was similar for translational and rotational intrafraction motion (Fig. 3). However, rotations showed a greater impact for GTV2 (the median size and distance from POR) and GTV3 (the smallest and furthest off-axis). Median change in GTV D99% with translations for GTV2 and 3 were −5% and −7% while there was a slightly larger decrease for rotational errors of −9% and −10 %. Median values for the remaining GTVs 1, 4 and 5 agreed to within ~ 1 % between translations and rotations.

With a 1 mm GTV-PTV expansion used in this study, 545 of 25,500 total target scenarios (2 %) with only translations (Fig. 3.a) had GTV D99% reduced to below the plan-specific threshold of baseline PTV D98%. This was mostly related to GTV5 (31 % of failing target scenarios), the second smallest target which was in close proximity to the brainstem (Table 4). For only rotational motion (Fig. 3.b), 1534 target scenarios (6 %) had GTV D99% reduced below the threshold with 31 % of which being related to GTV2 and 32 % related to GTV3. A slightly greater impact was seen when both rotations and translations were simulated (Fig. 3.c) with 5510 target scenarios (22 % of total scenarios) below the threshold, 27 % of which were GTV3.

As shown in Table 5, almost all correlation coefficients between plan parameters and target coverage were low, however of these the strongest correlation was found for mean MLC gap and edge metric where a lower plan complexity (i.e. larger mean MLC gap and lower edge metric) correlated with a lesser reduction in target coverage. Higher mean MLC gap was related to lower edge metric with a strong inverse correlation between these two parameters ($r = -0.77$, $p < 0.01$).

There were less failing target scenarios found for the lower complexity plans when both translational and rotational intrafraction motion was applied (Table 6). The median[range] difference where $p < 0.05$ was 6 %[5 % – 9 %]. This is with the exception of GTV3 for which the opposite was found with 4 % more failing targets for lower complexity plans. The same trend was observed for translational only and rotational only intrafraction motion, however less significant differences were identified, likely due to the lower overall number of failing targets (Table S.1 and Table S.2, supplementary information).

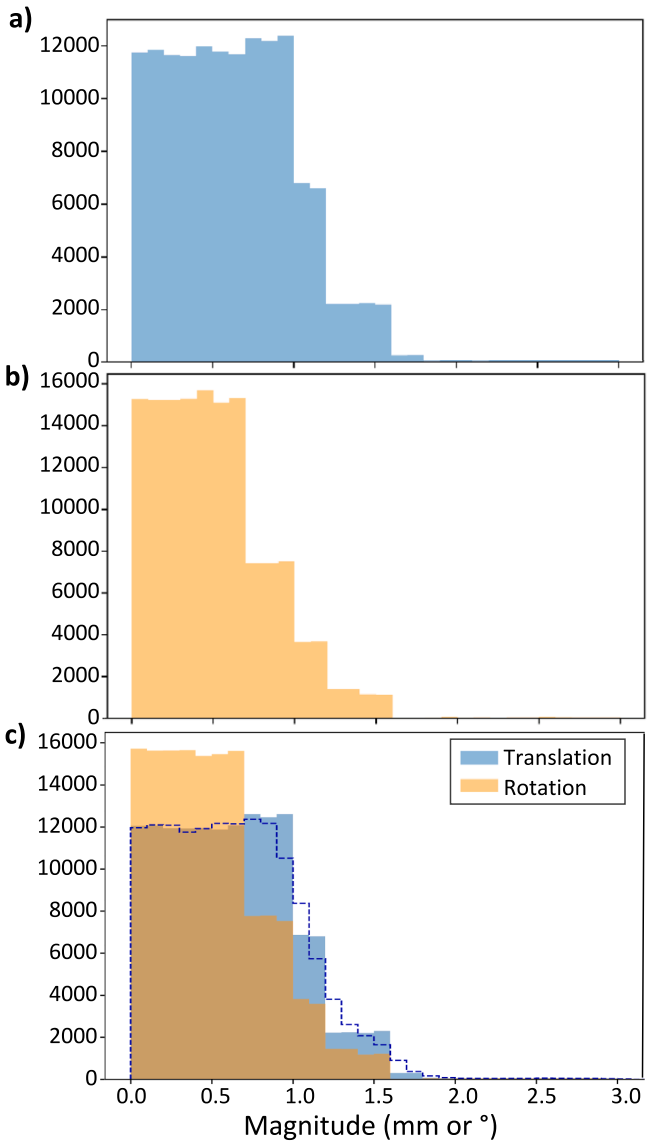

Fig. 2. Distribution of shift magnitudes for scenarios with a) translational intrafraction motion, b) rotational intrafraction motion and c) both translational and rotational intrafraction motion where the blue dashed line indicates the total translation of the centre of the target distribution including translation as a result of rotation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.2. Impact of intrafraction motion on dose to OARs

Translational and rotational intrafraction motion had very similar impact on dose to OARs, with a slightly greater impact for both motions combined (Fig. 4). The impact on normal brain V12Gy was minimal with very low median values and a maximum increase of 12.3 %. Change in brainstem D0.03 cc similarly had low median values but with a large range and a maximum of 124.6 %.

Change in dose to OARs showed few correlations with plan parameters or complexity metrics with intrafraction patient motion, especially for brainstem near-maximum all of which were insignificant ($r < 0.1$). Change in normal brain V12Gy showed some moderate correlations with edge metric, followed by mean MLC gap as the next strongest correlation (Table 7).

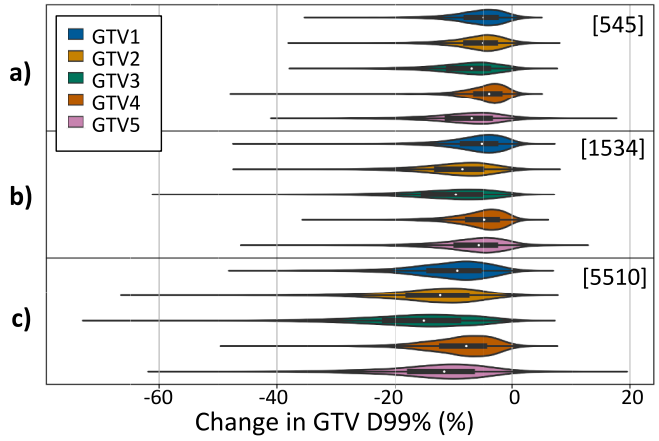

Fig. 3. Change in target coverage with intrafraction patient motion as a percentage calculated as (error plan − baseline)/baseline for GTV D99% for a) translations only, b) rotations only and c) both translations and rotations. The data is divided by target number: GTV1 = 0.2 cc, GTV2 = 0.1 cc, GTV3 < 0.1 cc, GTV4 = 1.8 cc, GTV5 < 0.1 cc. The value in square brackets is the number of target scenarios of 25,500 total with GTV D99% below the threshold of baseline PTV D98%.

Table 4
The number of target scenarios with GTV D99% reduced to below the plan specific threshold of baseline PTV D98% when intrafraction motion is applied. Shown in brackets for the final row is the percentage of the total number of target scenarios (22500).

	Translations only	Rotations only	Both translations and rotations
GTV1	55	147	863
GTV2	94	475	1124
GTV3	95	485	1477
GTV4	130	304	1085
GTV5	171	123	961
Total targets	545 (2 %)	1534 (6 %)	5510 (22 %)

Table 5
Correlation coefficients for plan parameters and complexity metrics with intrafraction motion for GTV D99%; $p < 0.05$ for all values shown, otherwise a dash is used. Abbreviations: point of rotation (POR), centre of target distribution (CTD). *moderate correlation.

Parameters and complexity metrics	Translations only	Rotations only	Translations & rotations
Volume	0.25	0.25	0.29
No. arcs	0.15	0.14	0.15
No. isocentres	−0.03	–	−0.05
No. couch angles	−0.06	−0.06	−0.07
Mean MLC gap	0.37	0.36	0.40*
Mean MLC speed	−0.12	−0.13	−0.13
MCS	0.16	0.17	0.18
PM	−0.04	−0.07	−0.06
Edge metric	−0.34	−0.32	−0.37
Distance from POR	0.03	−0.16	−0.07
Distance from CTD	−0.06	−0.11	−0.10
Mean translation	−0.23	N/A	−0.14
Max translation	−0.10	N/A	−0.03
Mean rotation	N/A	−0.27	−0.16
Max rotation	N/A	−0.11	−0.06

4. Discussion

The robustness of intra-cranial multi-target SRS plans to intrafraction motion was investigated using an in-house plan robustness tool. The in-house tool was able to generate over 10,000 scenarios in this study, a number that would have been infeasible using a TPS that re-calculates every plan. As such, realistic patient intrafraction motion was able to be replicated based on previously reported ExacTrac data [5] with the average values of the randomly sampled rotations and translations (0.63 mm and 0.51°, respectively) well within the range of values reported by other studies [4–10].

Table 6
Number of target scenarios (of 1000 total per GTV) with GTV D99% below the threshold of baseline PTV D98% with rotational and translational intrafraction motion for the 1st and 4th quartiles of mean MLC gap and edge metric. Shown in bold is $p < 0.05$ with a proportions z test between the quartiles. Note that the 1st quartiles refer to lower complexity i.e. the lowest values for edge metric and the greatest values for mean MLC gap. *trend for GTV3 is in contrast to other targets.

Complexity metric	Quartile	GTV1	GTV2	GTV3	GTV4	GTV5	Total
Edge Metric	1st	133	**136**	274	**142**	**135**	**546**
	4th	163	**223**	261	**195**	**184**	**765**
Mean MLC gap	1st	146	**156**	**311***	**151**	**168**	**621**
	4th	161	**228**	**270***	**225**	**221**	**835**

In human anatomy, head motion originates from the cervical vertebrae with the majority of motion attributed to the atlanto-occipital joint (C0-C1) for flexion and extension and the atlantoaxial junction (C1-C2) for rotation [20]. Though some studies discuss the impact of intrafraction patient motion for single-isocentre plans as a function of distance from the isocentre [9], it has also been discussed that the patient-related rotations do not occur about this point [10]. As a result, such rotations would also contribute to the measured translation of the isocentre as shown in Fig. 2.c in this study. The magnitude and direction of this translation would be dependent on the isocentre distance and direction from the POR. Therefore, without extensive analyses of tied translational and rotational measurements and isocentre positions it is impossible to determine the contribution of rotations to the measured translations in previously reported data. Hence the three scenario types of translational only, rotational only, and simultaneous translational and rotational intrafraction motion were simulated to encompass different situations.

Across the three scenario types, a 1 mm margin was sufficient to preserve GTV D99% above the plan specific threshold of baseline PTV D98% for the majority of target scenarios (98 % for translation only, 94 % for rotations only and 78 % for both translations and rotations). This margin was chosen to be representative of current clinical practices as it was the most commonly used margin in a survey study of 437 departments that deliver brain stereotactic radiotherapy, closely followed by a 2 mm margin [15]. While use of a 2 mm margin would increase the robustness of GTV coverage to delivery errors, it has previously been shown that this also may increase the risk of complications [23]. Variation in the margin used across different departments may be dependent on factors including equipment availability, immobilisation devices, whether a department uses patient motion tracking and delivery technique [24]. Margin size should be selected to create a robust plan incorporating all of these factors. However, as demonstrated in this study, an additional consideration for plan robustness should be plan complexity.

A lower plan complexity was shown to correlate with a higher robustness of target coverage to intrafraction motion. Across all three scenario types the strongest correlations were for mean MLC gap and edge metric, even more so than the magnitude of the randomly sampled motion (Table 5). Despite these correlations being only of moderate strength, lower complexity plans (with lower edge metric and larger mean MLC gap) were shown to have less target scenarios with GTV D98% reduced to below the acceptable threshold (Table 6). However, it should be noted as a limitation of use of complexity metrics with multiple targets that metrics are calculated on a per plan basis and may fail to capture potential target-specific differences in terms of complexity. This could explain why the smallest target (GTV3) shows the opposite

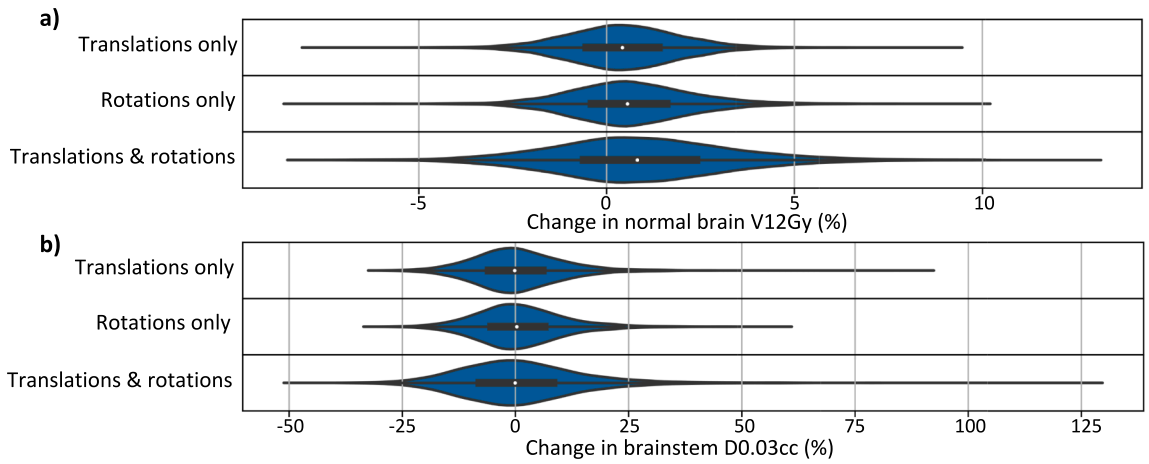

Fig. 4. Change in dose to OARs with intrafraction patient motion for a) normal brain V12Gy and b) brainstem D0.03 cc.

Table 7
Correlation coefficients for plan parameters and complexity metrics with intrafraction motion for normal brain V12Gy; $p < 0.05$ for all values shown, otherwise a dash is used. *moderate correlation.

Parameters and complexity metrics	Translations only	Rotations only	Translations & rotations
No. arcs	−0.05	−0.07	−0.11
No. isocentres	−0.05	−0.06	−0.06
No. couch angles	–	−0.03	–
Mean MLC gap	−0.29	−0.35	−0.37
Mean MLC speed	0.15	0.21	0.20
MCS	−0.20	−0.25	−0.26
PM	0.15	0.14	0.15
Edge metric	0.34	0.41*	0.43*
Mean translation	0.05	N/A	0.03
Max translation	–	N/A	–
Mean rotation	N/A	0.09	0.04
Max rotation	N/A	–	–

trend to the other targets when comparing complexity quartiles with intrafraction motion.

Correlation between higher robustness and lower complexity was also observed for normal brain V12Gy, however, not for brainstem near-maximum which showed no significant correlations (Table 7). This was likely because large increases in the brainstem near-maximum were a result of shifts that moved the high dose region of PTV5 (in close posterior proximity) into the brainstem which therefore limited overall correlations observed. However, this study is supplemented by a previous investigation of setup errors using this dataset [13] where directionally distinguished analysis showed strong correlation between complexity metrics and robustness of brainstem near-maximum.

The importance of understanding the interplay of plan complexity, quality and robustness has been previously highlighted [25]. Caution must be taken in order to maintain plan quality while reducing complexity, however it has also previously been shown that similar plan quality is achievable with lower complexity [26–28]. In this study, plan complexity was shown to be one of the most influential planning factors affecting plan robustness to intrafraction patient motion. Mean MLC gap is an indicator of aperture size while edge metric relates to aperture irregularity. These two metrics are linked with a higher mean MLC gap generally being associated with a lower edge metric as determined with a strong inverse correlation in this study. Reducing plan complexity has been previously achieved by reducing the number of monitor units [26,27] and through other TPS specific tools such as the aperture shape controller in the Varian Eclipse TPS (Varian Medical Systems, Inc., Palo Alto, CA) [26,28]. Reducing the number of monitor units delivered may also reduce treatment duration, however there is mixed findings regarding whether shorter treatment duration reduces the likelihood of intrafraction motion [2,4,5,7–11]. A previous study using this same patient dataset showed that lower plan complexity impacted the dose distribution in terms of conformity and isodose sphericity resulting in a greater robustness to setup error [13]. Furthermore, reducing plan complexity has the advantage of reducing dose calculation and delivery uncertainties [25] with patient specific quality assurance (PSQA) gamma analysis passing rates being strongly influenced by plan complexity [29–31]. Planning with lower complexity has also been previously shown to result in treatments which are more robust to uncertainties in MLC modelling and machine QA errors [17].

One of the limitations of this study arises from the replication of realistic patient intrafraction motion which restricted data from being differentiated by direction and magnitude of motion for analyses, potentially reducing the correlations observed. Another limitation is that the study was conducted using plans for a single challenge patient geometry which limited possible analyses based on target geometry. This includes a limited possibility of investigating further reductions in target margins due to the small size of the PTVs used. Planned future work involves using data from a range of patients to further investigate the role plan complexity plays in robustness of intracranial SRS plans.

5. Conclusion

This study replicated realistic patient intrafraction motion based on previous motion tracking data. This enabled a thorough investigation into the robustness to intrafraction motion of intra-cranial multi-target SRS plans obtained from a range of departments through a planning challenge. For this dataset, a 1 mm GTV-PTV margin was able to preserve target coverage above our determined threshold for the majority of plans, however margin selection should incorporate a range of considerations including available equipment, delivery technique and the use of motion tracking. Additionally, this study found plan complexity to be one of the most influential factors affecting plan robustness to intrafraction motion. Although correlations with complexity metrics were only of moderate strength, less complex plans were found to have significantly fewer scenarios with target coverage falling below the acceptable threshold. Therefore, it is recommended to plan with lower complexity, in particular larger mean MLC gap and lower edge metric to achieve a higher robustness to intrafraction patient motion.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejmp.2025.104900.

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