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Evaluation of the dosimetric impact of patient positioning errors on single-isocenter multitarget stereotactic radiosurgery

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Abstract: Treating multiple brain metastases with a single isocenter enhances efficiency, but requires higher accuracy to account for rotation-induced shifts, which increase with the distance from the target to the isocenter. Twenty patients, previously treated at the institution, with single-isocenter radiosurgery for two targets were evaluated. This retrospective analysis's objective was to assess if the setup margins sufficed to guarantee the minimum GTV coverage (V100% ≥ 95%), correlating target volumes and their respective distances to the isocenter with observed dosimetric impact. Plans with theoretical deviations were generated for translational and rotational errors of one millimeter and one degree, respectively. Coverage with prescription dose was evaluated for each of the plans, and such data was used to generate computational models. Rotational errors caused significantly larger coverage decreases, up to 60%, approximately. Any patient positioning deviation, translational or rotational, impaired coverage with statistical significance. However, only errors for pitch (LR) and roll (PA) caused significant GTV coverage decrease. It was possible to identify a negative correlation between the analyzed parameters, with target volume leading to greater dosimetric impact compared to distance to plan isocenter. In conclusion, for the evaluated sample, acceptable limits for patient setup deviations were adequate to ensure minimum GTV coverage for translational deviations up to one millimeter. Nevertheless, for one-degree rotational deviations, half of the patients presented insufficient GTV coverage. Data also indicates that smaller and farther targets might be at greater risk of compromised coverage considering patient positioning errors.

Keywords: radiosurgery, single isocenter, patient positioning errors.

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Avaliação do impacto dosimétrico de erros de posicionamento do paciente em radiocirurgia de isocentro único

Resumo: Tratar múltiplas metástases cerebrais com isocentro único melhora a eficiência, mas exige maior acurácia para compensar os deslocamentos induzidos pela rotação, que aumentam com a distância entre o alvo e o isocentro. Foram avaliados vinte pacientes previamente tratados na instituição com radiocirurgia de isocentro único para duas lesões. A fim de estudar se as margens de setup foram suficientes para garantir a cobertura mínima desejada no GTV (V100% ≥ 95%), foram gerados planos com desvios teóricos de um milímetro e um grau. De tais planos de incerteza, foram avaliados os valores de cobertura da isodose de prescrição. Por fim, para correlacionar as variações de cobertura observadas com o volume das lesões e suas respectivas distâncias ao isocentro, um modelo computacional de aprendizado de máquina foi utilizado. Os erros de rotação foram muito mais significativos se comparados aos de translação, sendo responsáveis por decréscimo máximo de cobertura de 60%, aproximadamente. Qualquer desvio, translacional ou rotacional, impactou com significância estatística a cobertura do PTV. No entanto, somente os desvios nos eixos pitch (LR) e roll (PA) acarretaram em variação significativa da cobertura do GTV. Foi possível inferir, ainda, que existe uma correlação inversa entre os parâmetros avaliados e a diferença de cobertura; sendo que o volume dos alvos apresenta maior impacto dosimétrico se comparado com a distância ao isocentro. Conclui-se que, para a amostra avaliada, os limites aceitáveis para desvio de posicionamento do paciente foram suficientes para assegurar a cobertura do GTV para desvios translacionais de até um milímetro. Contudo, ao avaliar desvios rotacionais, 50% dos pacientes apresentaram cobertura do GTV insuficiente. Os dados indicam, ainda, que alvos menores e mais distantes podem ser mais impactados por desvios do posicionamento do paciente.

Palavras-chave: radiocirurgia, isocentro único, desvios de posicionamento do paciente.

1. INTRODUCTION

In general terms, up to 50% of the patients with malignant neoplasms will develop brain metastases (BMs) [1]. At present, standard care is composed of neurosurgery, whole brain radiation therapy (WBRT) and stereotactic radiosurgery (SRS) [2]. The latter is a non-invasive technique characterized by administration of ablative radiation doses within one or few sessions and a steep gradient falloff. Similarly to WBRT, SRS can be safely used to treat multiple BMs at a time using a single isocenter approach [3]. However, the reduction of irradiated normal tissue might be related to fewer side effects, such as alopecia, fatigue, confusion, cognitive dysfunction and subsequent decreased quality of life [4].

Considering the high administered doses, the execution of SRS requires submillimeter precision. Inherently, the delivery of a radiotherapy treatment is associated with errors of various types; with patient positioning deviation being a notorious example. Such deviation refers to the disparity of patient positioning between the computed tomography simulation and treatment delivery. The addition of setup margins is the most common method used to account for such disparity [5].

Nevertheless, since SRS is oriented by maximal normal tissue preservation, the added margins must be as small as possible and assure the minimum desired coverage in the tumor simultaneously. As of single isocenter radiosurgery for multiple intracranial targets (SIRMIT), localization accuracy is even more critical, since rotational errors have greater impact when compared to the single-target radiosurgery [6]. It is also discussed in the literature that the volume of the planning target volumes (PTVs) and their respective distances to the isocenter might impact SIRMIT treatments. Current evidence supports the idea that smaller and more distant lesions are at greater risk of compromised coverage [7], [8].

Dosimetric accuracy is also of great importance. For SRS planning using a multileaf collimator (MLC), the PTV must fulfill a minimum volume that is related to the dosimetric precision of the linear accelerator in question. Institutionally, the addition of setup margins for SRS and definition of conformation method is described as follows : A one-millimeter margin is added to the gross tumor volume (GTV). If the final planning target volume (PTV) is equal to or greater than the requirement, the target is eligible for treatment with MLC. If the resulting PTV is smaller than the minimum value, a two-millimeter margin may be added. In case that, after this last procedure, the lesion is still smaller than the reference value, it shall be planned using stereotactic cones.

Institutional margins for radiosurgery were previously evaluated, considering treatments for a single target and translational patient positioning errors [9]. The objective of this research was to assess the variation of coverage for the selected cases of SIRMIT for two target volumes, accounting for both translational and rotational deviations. Furthermore, the dosimetric impact was correlated with volume of the PTVs and their respective distances from the isocenter.

2. MATERIALS AND METHODS

Twenty patients previously treated at the institution were analyzed in this retrospective study. All patients were treated with SIRMIT for two target volumes, delivered in a single fraction in a Varian CLINAC 6Ex with a robotic couch. All treatments were planned with static gantry techniques (conformal or IMRT).

The magnitude of the simulated errors was chosen based on the institutional limits for patient positioning deviation. Such values were one degree and one millimeter for rotational and translational errors, respectively, and are based on the precision of the image guided radiation therapy (IGRT) systems available. Translational errors were simulated with a builtin feature of the used treatment planning system (Eclipse v. 16.3), that recalculates the dose-volume histogram considering a patient shift relation to the plan isocenter. Rotational errors, on the other hand, were simulated by applying a one-degree shift to the structure set using 3DSlicer (v 5.6.2). The original plan was then recalculated, with fixed monitor units, considering the angulated contours. Since Eclipse does not accept tilted computed tomography (CT) scans for dose calculations, the planning CTs were not angulated.

For both studied deviations, the plans were recalculated for positive and negative displacements in the respective axes – longitudinal (Z), vertical (Y) and lateral (X) for translational errors; yaw (IS), pitch (LR) and roll (PA) for rotational errors. Aiming to analyze the impact of target volumes and their respective distance to the isocenter, categories were defined. L1 and L2 correspond to the greater and smaller lesions of the plan, respectively. Analogously, D1 is the closest target to the isocenter, and D2 is the farthest one. A point at the center of each PTV was created, and the distance from the target to the isocenter was determined by the algebraic distance between this point and the isocenter.

Thirteen plans per patient were created and evaluated: the original plan, without displacements and considering the non-angulated structure set, six rotational-error plans and six translational-error plans. Coverage with the prescription dose of PTVs and GTVs were collected for every plan. In order to correlate the variations with volumes and distances, these data were used as input for an artificial intelligence computational model.

Extreme Gradient Boosting (XGBoost) algorithm was employed to produce a model that describes the target's coverage variation considering patient positioning shifts. The computational analysis was conducted using R programming language and RStudio. Cross-validation was performed. Eighty percent of the patient data was used to train the model, and the remaining twenty percent was applied for its validation. The hyperparameters used, their respective descriptions [10], and their ranges are described in Table 1. Two different models were studied: the first considered the data discretization by L1, L2, D1, and D2;

whereas the second one consisted of a global analysis. The input parameters were volume, distance, GTV margin and coverage variation.

Table 1 : Hyperparameters used in the computational model.

Hyperparameter	Range	Description
subsample	0.2 - 0.7	Fractions of observation each step
colsample_bytree	0.2 - 0.7	Fraction of used resources
max_depth	2 -10	Maximum number of node
min_child	1	Minimum weight for node creation
eta	0.1 - 0.0001	Learning rate

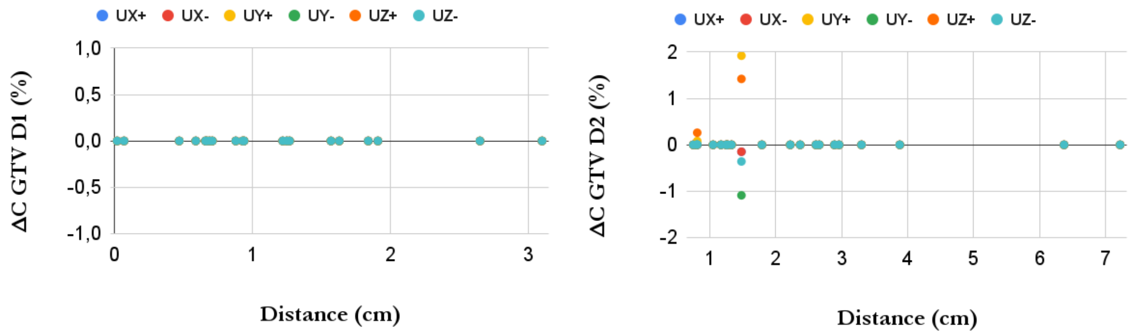
3. RESULTS AND DISCUSSIONS

Minimum desired GTV coverage is defined as at least 95% of the target volume irradiated with the prescribed dose (V100% ≥ 95%). Considering that the present work consists of a retrospective analysis, no intrinsic parameter of the plans, such as field arrangement or structure contour were altered. In this manner, the study aimed to estimate the dosimetric impact on clinical cases if patient positioning deviations were not corrected before treatment. Such impact was evaluated by target coverage variation (ΔC), that is, the difference between the calculated percent of the evaluated volume (GTV or PTV) that receives prescription dose considering both perfect patient positioning and shifted positioning. Thus, the results represent what the maximum error would be in that scenario and the data does not relate to the clinical conditions in which the patients were treated.

3.1 Translational errors

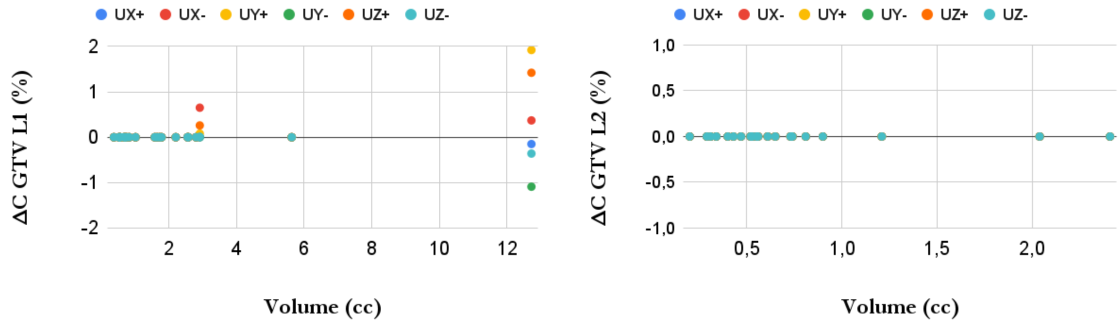
Translational errors with a magnitude of one millimeter resulted in a maximum decrease of 15% in PTV coverage. Deviations in the longitudinal axis (Z) had a greater impact on coverage compared to the other axes. However, no translational shift in any direction resulted in significant loss of GTV coverage: the lower GTV coverage value for the sample considering the errors was 97.27%.

Figure 1: GTV coverage variation (ΔC) for translational deviations in function of the distance of each target to the plan isocenter. The chart contains overlapped data.



Source: The author.

Figure 2: GTV coverage variation (ΔC) for translational deviations in function of the volume of each target. The chart contains overlapped data.



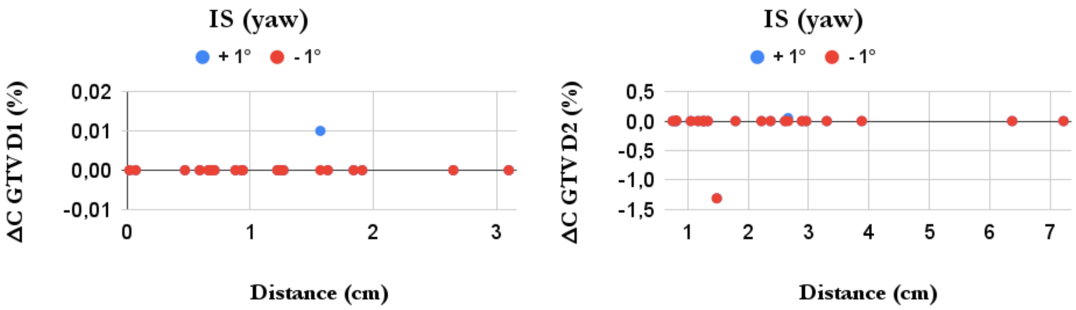
Source: The author.

Figures 1 and 2 represent GTV coverage variation as a function of the distance and volume, respectively. UX+ indicates a one-millimeter shift in the positive direction of the lateral axis, while UX- indicates a negative shift. The pattern is analogous to Y and Z axes. Definitions of the axes and target categories can be revisited in Section 2. These results imply that the acceptable limits for patient positioning deviations are sufficient to guarantee the minimum GTV desired coverage for translational deviations of one millimeter.

3.2 Rotational errors

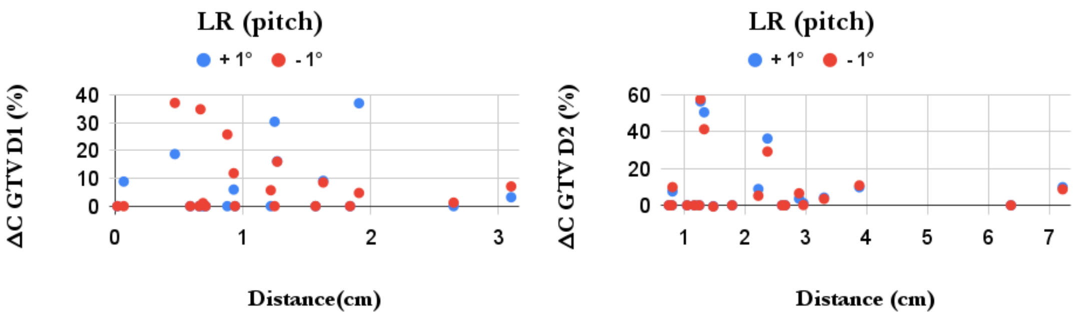
Rotational errors, on the other hand, presented a much greater impact when compared to translational ones, with a maximum decrease in PTV coverage of approximately 60%. For half of the reviewed patients, GTV coverage was compromised below the minimum desired value of 95% target coverage with prescription dose. Therefore, the limits for acceptable patient positioning errors might be inadequate

Figure 3: GTV coverage variation (ΔC) for rotational deviations in the yaw axis (IS) in function of the distance of each target to the plan isocenter. The chart contains overlapped data.



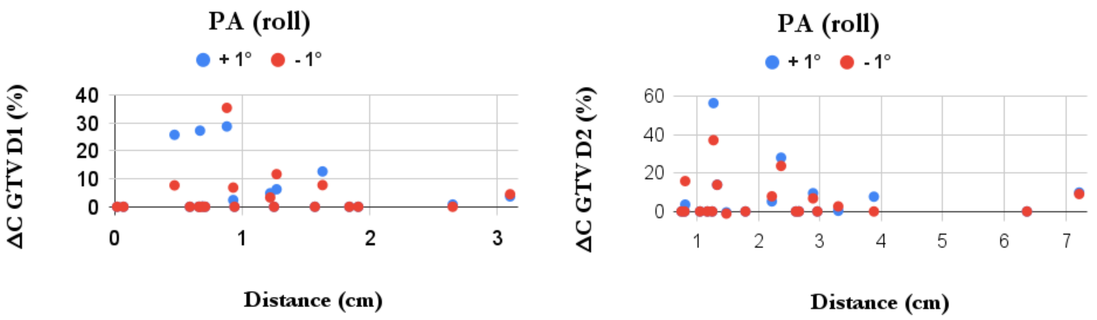
Source: The author.

Figure 4: GTV coverage variation (ΔC) for rotational deviations in the pitch axis (LR) in function of the distance of each target to the plan isocenter. The chart contains overlapped data.



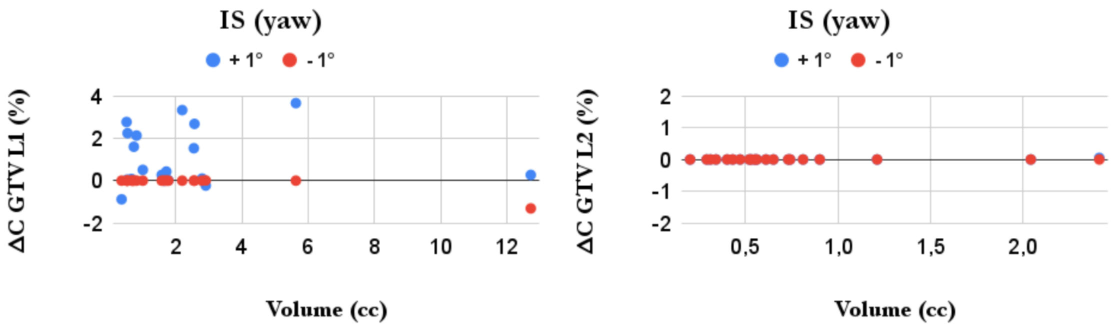
Source: The author.

Figure 5: GTV coverage variation (ΔC) for rotational deviations in the roll axis (PA) in function of the distance of each target to the plan isocenter.



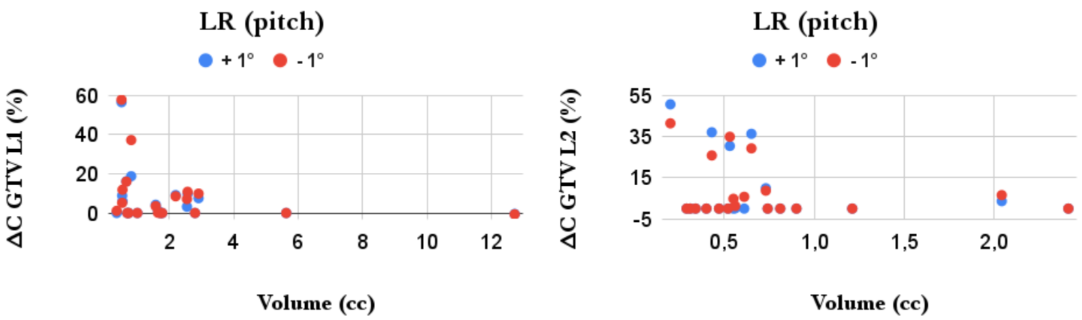
Source: The author.

Figure 6: GTV coverage variation (ΔC) for rotational deviations in the yaw axis (IS) in function of the volume of each target.



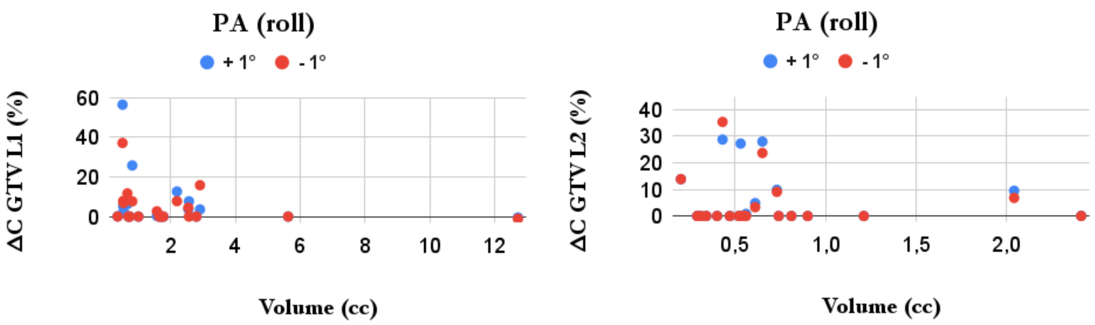
Source: The author.

Figure 7: GTV coverage variation (ΔC) for rotational deviations in the pitch axis (LR) in function of the volume of each target.



Source: The author.

Figure 8: GTV coverage variation (ΔC) for rotational deviations in the roll axis (PA) in function of the volume of each target.



Source: The author.

No significant decrease was observed for yaw (IS) axis. The disparity between coverage variation of IS axis and LR or PA ones could be explained considering that a yaw shift represents a rotation around the vertical axis of the isocenter. That is, the resulting motion is centered on in the isocenter, and would minimally affect the radial and spatial distribution of the targets in respect to the beam incidences in the case of slight deviations. Furthermore, the selected 20 cases could also have beam arrangements and localization of the lesions in a way that reduced the influence of yaw shifts. Reanalysis of the chosen cases, and also sample enlargement would benefit the understanding of this result.

As mentioned, the institutional standard for setup margins in radiosurgery is 0.1 mm for targets of volume. However, for a few patients, protocol noncompliance was identified. The risk of coverage loss decreases as the added margin increases. Consequently, data from lesions that received a greater margin than stipulated may be biased. For the 10 patients that presented insufficient GTV coverage, one had an incorrect margin. Censoring this patient, it was investigated if the smaller and farthest targets were the ones that undergo major dosimetric impact. Results are exhibited on Tables 2 and 3.

Table 2 : Percentage of patients for who the smallest target (L2) suffered greater GTV coverage decrease.

Axis	% of patients that presented L2 at greater disadvantage
PA+	50%
PA-	40%
LR+	50%
LR-	50%

Table 3 : Percentage of patients for who the farthest target (D2) suffered greater GTV coverage decrease.

Axis	% of patients that presented L2 at greater disadvantage
PA+	60%
PA-	60%
LR+	60%
LR-	50%

For the majority of the evaluated plans, in the case of maximum uncorrected setup error of one degree, at least 50% of the patients showed a greater risk of coverage loss for targets with smaller volumes and at greater distances from the isocenter, in accordance with current available literature.

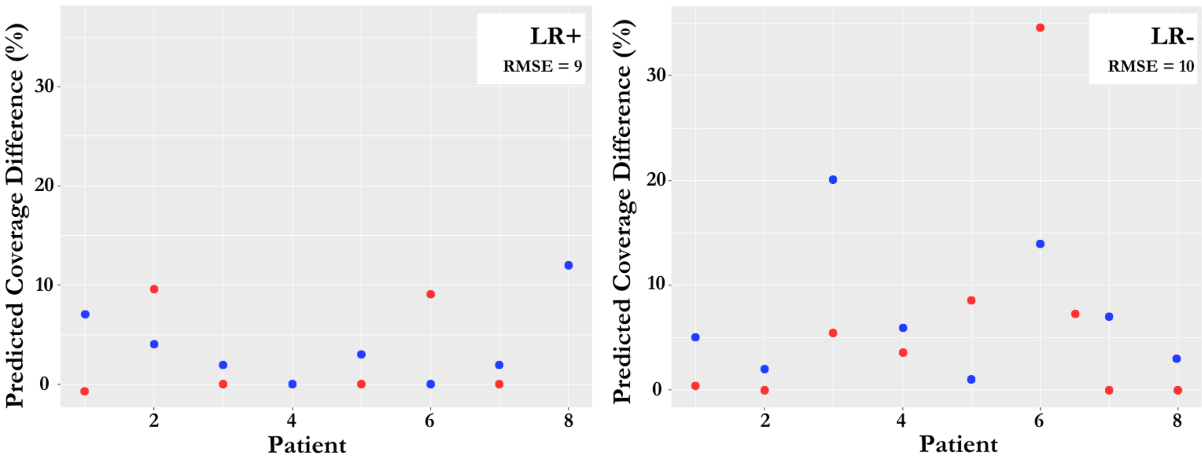
3.3 Computational analysis

Since translational models did not cause a significant dosimetric impact on GTV, computational analysis was performed for rotational deviations alone. Two models were developed. The first model considered the categories D1, D2, L1 and L2 for data discretization, correlating distance and volume with coverage to identify variation patterns for each axis. The second one consisted of a global analysis, without target classification. The latter one aimed to identify critical values for distance to isocenter and volume, in order to predict what the dosimetric impact would be considering a one-degree rotation. Eighty percent of the data was used for training the models, and the remaining twenty percent was used in the validation stage.

Global analysis model indicated a negative correlation between the deviations and the coverage difference; and the volume of the lesions had greater impact in comparison with the distance. Figures 9 and 10 represent the models for global analysis for LR and PA axes, obtained for the validation stage. Blue circles represent predicted values, and red circles correspond to experimental data. Visual representation for IS axis modeling results is omitted since, for all patients, no coverage difference between predicted values and experimental data was observed.

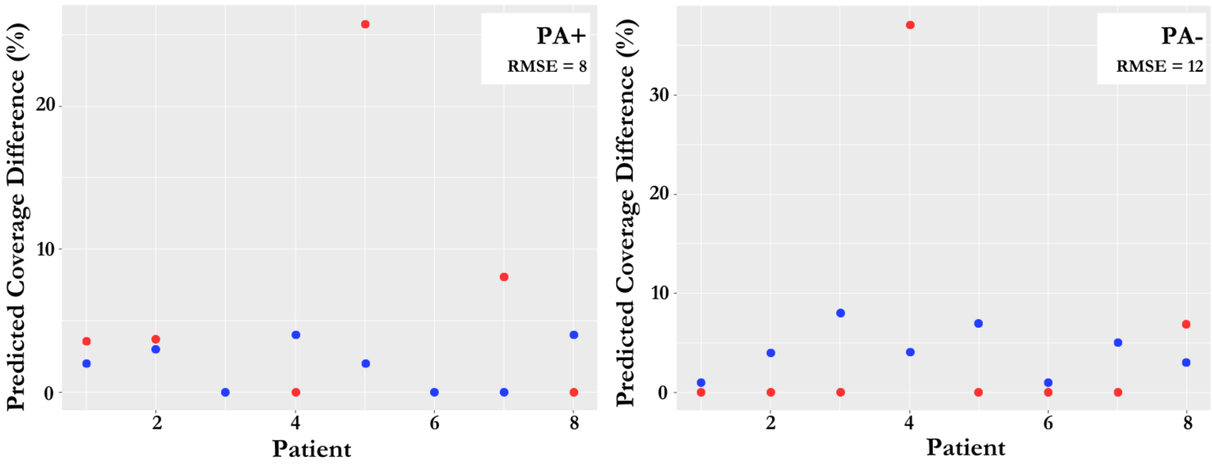
As of the discretized analysis model, using Cox test, it was possible to verify with statistical significance that all deviations, translational and rotational, impact in PTV coverage. Studying GTV discoverage, Cox test revealed significant p-values for ± 1 degree shifts in pitch (LR) and roll (PA) axes, only. T-test returned no significant values for correlation of coverage variation with volume nor distance. It is possible that such a result is due to the small sample size (n = 20).

Figure 9: Computational model using XGBoost algorithm for pitch (LR) axis.



Source : The author.

Figure 10: Computational model using XGBoost algorithm for roll (PA) axis.



Source : The author.

The root mean square error (RMSE) for each model is presented on the charts. RMSE is an important parameter to quantify the accuracy and predictive ability of the model, as it relates to the disparity between experimental data and theoretical results. Therefore, its value should be as small as possible. As no difference was observed for IS axis, RMSE value was equal to zero, and computational predictions are in perfect agreement with treatment planning system (TPS) calculations.

However, TPS calculated coverage for LR and PA axes presented complex variation with both distance to isocenter and target volumes (Figures 4, 5, 7 and 8). In this manner, computational modeling is arduous and the high RMSE values for such axes are most likely a consequence of the small sample size. Thus, in order to implement such models in clinical practice, the algorithm must be refined and more data is required in order to simulate treatment impairment in the case of uncorrected patient positioning deviations with greater accuracy.

4. CONCLUSIONS

Twenty treatment plans of single isocenter radiosurgery for two targets were studied. In order to evaluate the dosimetric impact of rotational and translational patient positioning errors, theoretical deviation plans were created. The coverage with prescription dose was assessed by the dose-volume histogram for every analyzed axis. The variations were correlated to lesion volumes and target distances to plan isocenter through a computational model.

Evaluated translational errors resulted in a maximum decrease of 15% in PTV coverage. However, no shift in any direction resulted in significant loss of GTV coverage, with the minimum value being 97.27%. Deviations in the longitudinal axis (Z) had a greater impact compared to the others. Therefore, the acceptable limits for patient positioning deviations are sufficient to guarantee the minimum GTV desired coverage for translational deviations of up to one millimeter.

Rotational deviations, however, presented substantially greater impact in dependence on both target volume and distance to isocenter. The maximum decrease in PTV coverage was of approximately 60% and half of the reviewed patients presented GTV coverage below the minimum desired value. Deviations of one degree in pitch (LR) and roll (PA) axes caused, in respective order, the greatest GTV coverage variations. Nevertheless, for all studied cases, no significant GTV decrease was observed for yaw (IS) axis. This might be explained since shifts in the IS direction represent a rotation around the vertical axis, and the resulting deviation is centered on in the isocenter, leading to minimal difference in the spatial distribution in respect to beam incidences. Further studies correlating the location of the targets, patients anatomy and beam geometry could enlighten the impact of positioning errors on each axis. Additionally, in accordance to current literature evidence, targets with the smallest volume and farthest from the isocenter had greater coverage loss for the majority of patients.

Computational models were developed using XGBoost algorithm for the purpose of predicting GTV coverage for rotational deviations. The clinical implementation of such models can be a useful tool to estimate treatment efficiency considering patient positioning errors. IS axis model RMSE value was equal to zero, and the predictions were in agreement with treatment planning system (TPS) calculations. LR and PA axes presented complex variation with both distance to isocenter and target volumes and presented high RMSE values. Consequently, for the latter models additional data is required in order to refine the predictions and achieve greater accuracy before clinical use.

Statistical tests were conducted. T-test returned no significant values for correlation of coverage variation with volume nor distance. Such a result is probably a consequence of the study's small sample size. Cox test revealed that both translational and rotational deviations exercised influence in PTV coverage. However, as of GTV coverage, p-values were significant only for rotational shifts in pitch (LR) and roll (PA) axes. A negative correlation was observed for the latter two axes, with target volume being more relevant to coverage variation.

It is suggested that a subsequent study is conducted in order to evaluate if the margins are adequate for the institution's population, considering the deviations on delivery moment and that 95% of the patients shall receive at least 95% GTV volume coverage with the prescribed dose. In addition, corrections indicated by the imaging and localization system should be applied whenever possible in order to minimize the risk of dosimetric prejudice. Reducing the deviation tolerance for angular shifts for SIRMIT cases is also recommended, as it would reduce the chance of compromised coverage.

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CONFLICT OF 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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