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Scientific Article

Improving the Efficiency of Single-Isocenter Multiple Metastases Stereotactic Radiosurgery Treatment

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Purpose: Multiple brain metastases can be treated efficiently with stereotactic radiosurgery (SRS) using a single-isocenter dynamic conformal arc (SIDCA) technique. Currently, plans are manually optimized, which may lead to unnecessary table angles and arcs being used. This study aimed to evaluate an automatic 4π optimization SIDCA algorithm for treatment efficiency and plan quality.

Methods and Materials: Automatic 4π-optimized SIDCA plans were created and compared with the manually optimized clinical plans for 54 patients who underwent single-fraction SRS for 2 to 10 metastases. The number of table angles and number of arcs were compared with a paired t test using a Bonferroni-corrected significance level of $P < .05/4 = .0125$. The reduction in treatment time was estimated from the difference in the number of table angles and arcs. Plan quality was assessed through the volume-averaged inverse Paddick Conformity Index (CI) and Gradient Index (GI) and the volume of normal brain surrounding each metastasis receiving 12 Gy (local V12 Gy). For a 5-patient subset, the automatic plans were manually adjusted further. CI and GI were assessed for noninferiority using a 1-sided t test with the noninferiority limit equal to the 95% interobserver reproducibility limit from a separate planning study (corrected significance level $P < .05/[4 - 1] = .017$).

Results: The automatic plans significantly improved treatment efficiency with a mean reduction in the number of table angles and arcs of -0.5 ± 0.1 and -1.3 ± 0.2, respectively ($\pm$SE; both $P < .001$). Estimated treatment time saving was -2.7 ± 0.5 minutes, 14% of the total treatment time. The volume-averaged CI and GI were noninferior to the clinical plans (both $P < .001$), although there was a small systematic shift in CI of 0.07 ± 0.01. The resulting difference in local V12 Gy, 0.25 ± 0.04 cm^3, was not clinically significant. Minor manual adjustment of the automatic plans removed these slight differences while preserving the improved treatment efficiency.

Conclusions: Automatic 4π optimization can generate SIDCA SRS plans with improved treatment efficiency and noninferior plan quality.

Introduction

Approximately 10% to 20% of patients with cancer will develop brain metastases,[1] with the proportion increasing as improvements in primary treatments lead to improved overall survival.[2] In recent years, there has been a shift in treatment strategy for these patients from whole-brain radiation therapy to stereotactic radiosurgery (SRS) due

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to equivalent overall survival with substantially reduced neurocognitive toxicity.[2] This is now the established treatment for patients with up to 4 metastases, with increasing evidence of its efficacy for patients with up to 10 or even more metastases.[3]

The increasing number of metastases being treated motivated the development of the single-isocenter dynamic conformal arc (SIDCA) technique.[4] This uses a single isocenter to treat all targets, rather than a separate isocenter for each one, significantly improving the treatment efficiency while maintaining similar plan quality.[5] The SIDCA technique uses multiple noncoplanar arcs, with each arc treating multiple targets. It is available in commercial treatment planning systems designed for SRS.[6] However, currently, selecting the optimum number of table angles and arcs is a manual process. This may result in a larger number of table angles and arcs being used than necessary. This reduces treatment efficiency in addition to being time-consuming to plan. With the increasing numbers of patients being treated and the increasing number of metastases per patient, methods of further improving the efficiency of delivering SIDCA SRS treatments would be beneficial.

An improved version of SIDCA that incorporates 4π table angle optimization is now commercially available. This replaces the manual process of selecting table angles and number of arcs. It is postulated that this will improve treatment efficiency without impacting plan quality. The aim of this study was to compare the treatment efficiency and plan quality of SIDCA SRS treatments with and without 4π table angle optimization in the SRS treatment of multiple brain metastases.

Methods

Patient details

Fifty-four patients with 171 cranial metastases (between 2 and 10 metastases per patient) treated at a single center between December 2017 and May 2021 were included in this study. There were 23 men and 31 women patients, with a median age of 68.5 years (range, 32-83 years). Patients were prescribed 21 Gy (52 patients) or 18 Gy (2 patients) in 1 fraction. All patients received frameless SRS treatment using a SIDCA technique, delivered on a TrueBeam STx linear accelerator with high definition multileaf collimator (version 2.7 MR3, Varian Medical Systems) using cone-beam computed tomography (CBCT) and ExacTrac (Brainlab) for image guidance. Patients were treated with either 6 MV flattened or 10 MV flattening filter-free beams. Planning target volume margins of 1 mm were used for all metastases except those >7 cm from the isocenter or <0.1 cm^3 in volume, in which case 2-mm margins were applied.

Automatic treatment planning

All treatment plans were created in Elements Multiple Brain Mets SRS (MBM, Brainlab). There were 3 treatment plans created for each patient: 1 clinical plan using manual optimization of table angles and arcs in MBM version 2.0.0.749 and 2 automatic plans using 4π optimization in MBM version 3.0.0.454. The 4π optimization requires a set of table angles as a starting point for the optimization. One of the automatic plans used the table angles from the clinical plan as the starting point (clinical starting tables) and the other used a generic 7-table protocol (generic starting tables). This was to test whether there was any difference in plan quality between starting with a "best guess" set of table angles and using the same generic set for all patients. The automatic plans were generated with no manual involvement at any point.

Finally, for a subset of 5 patients, the generic starting tables plan was further manually adjusted by an experienced planner. These 5 patients were selected as the 5 patients with the largest differences in plan quality metric (conformity index) between the automatic plans and the manual clinical plan.

Plan comparisons: treatment efficiency

Treatment efficiency was quantified using the difference in the number of table angles and gantry arcs between each automatic plan and the clinical plan (automatic − clinical). The statistical significance of these differences was determined with a paired t test using a Bonferroni-corrected significance level of $P = .05/4 = .0125$.

The impact on treatment time from changing the number of table angles and arcs was calculated by deriving an empirical equation to estimate the treatment time from the number of table angles and arcs. Treatment time was calculated as the time from the start of the first arc to the end of the last arc, including beam-on times, gantry rotation times between arcs, rotation times between table angles, and patient verification imaging at each table angle using ExacTrac. The treatment time did not include setting the patient up and initial patient verification using CBCT imaging because that would not be changed by using 4π-optimized plans. This empirical equation was:

$$t_{total} = (n_T - 1)\Delta t_T + (n_A - n_T + 1)\Delta t_A, \quad (1)$$

where n_T was the number of table angles and n_A was the number of arcs. Δt_T was defined as the time from the start of one arc to the start of the following arc when the table was moved (ie, 1 × beam-on time, time for gantry rotation to next arc, time for table rotation to next position, and time for treatment verification using ExacTrac). Δt_A was defined as the time from the start of one arc to the start of the following arc when the table was not moved

between arcs (ie, 1 × beam-on time and time for gantry rotation to next arc). The mean Δt_T and Δt_A were calculated for each patient's clinical plan using time stamps from the oncology information system (Aria v16.1, Varian Medical Systems). These values were applied in equation (1) to estimate the treatment time for the automatic plans and the clinical plan. For patients with only 1 arc for each table angle (2/51 patients), Δt_A was calculated as the mean of the beam-on times for all the arcs. The time saving from the automatic plans was calculated as the difference in estimated treatment times between the automatic and clinical plans.

As a quality control measure, the estimated treatment time for the clinical plans was compared with the actual treatment time measured using the time stamps from the start of the first arc to the end of the last arc. Three of 54 patients had an additional CBCT acquired midway through treatment due to ExacTrac images indicating patient movement greater than tolerance. These 3 patients were excluded from the time-saving estimate.

Plan comparisons: plan quality

Plan quality was determined by calculating the inverse Paddick Conformity Index (CI) and Gradient Index (GI) for each metastasis and then determining the volume-averaged CI and GI for each plan. If a GI for a particular metastasis could not be calculated because the 50% isodose overlapped with that of another metastasis, the volume-averaged GI was calculated excluding those metastases. The volume of normal brain local to each metastasis receiving 12 Gy (local V12 Gy) and the maximum dose to the brainstem planning organ at risk volume (PRV, created using a 1-mm margin) was also determined. Differences between each automatic plan and the clinical plan were calculated for each metric (automatic plan − clinical plan). Doses to the optic apparatus were not evaluated because both clinical and automatic plans used an automatic avoidance of arcs passing through the eyes and therefore doses would be very low for both plans.

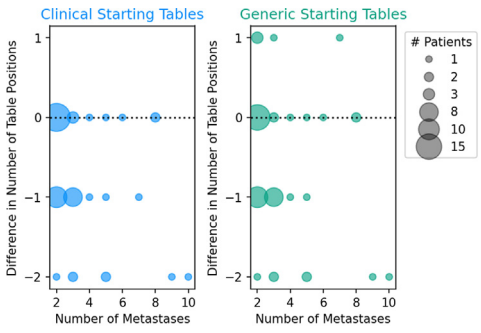
The differences in volume-averaged CI and GI were compared with the interobserver variability calculated from a planning study.[7] This reported CI and GI results from 24 centers using Elements MBM to plan a 5-metastases patient. The interobserver variability was calculated by estimating the volume-averaged GI and CI for each center's plan, calculating the differences from the mean of plans from all centers, and then determining the standard deviation of those differences. This number was multiplied by $1.96 \times \sqrt{2}$ to generate the International Organization for Standardization 95% reproducibility limit.[8]

The automatic plans were tested for noninferiority to the clinical plans using a 1-sided t test for paired data.[9] The noninferiority limit was taken as 0 plus the 95% reproducibility limit calculated from the interobserver variability from the planning study. This effectively considers whether the differences between the clinical and automatic plans would have been similar to those between 2 manual plans from different planners. A significance level of $P < .05$ was used, corrected for multiple testing by $P < .05/(4 - 1) = .017$.[10]

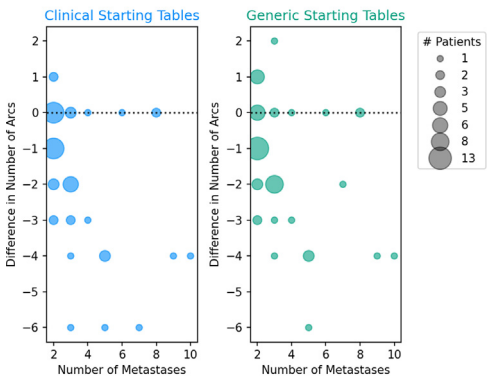
The differences in number of table angles, number of arcs, volume-averaged CI, volume-averaged GI, local V12 Gy, and the brainstem PRV maximum dose between the manually adjusted 4π-optimized plans and the clinical plans were calculated. These differences were compared with the equivalent differences for the automatic 4π-optimized plans.

Results

The automatic 4π-optimized plans resulted in a reduction in the number of table angles, with differences to the clinical plan of −0.6 ± 0.1 (mean ± SE, clinical starting tables) and −0.5 ± 0.1 (generic starting tables, see Fig. 1A). An example of the reduction in table angles is

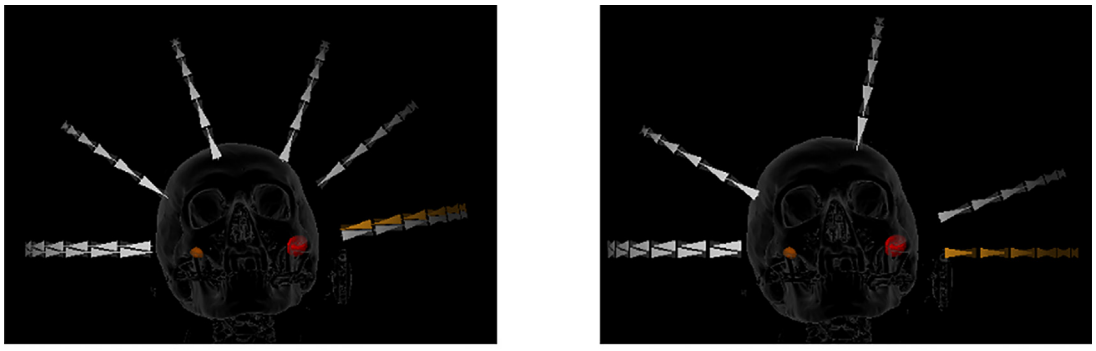


(a) Differences in number of table angles



(b) Differences in number of arcs

Figure 1 A bubble plot of differences in the number of (A) table angles and (B) arcs from the clinical plan for the clinical starting tables automatic plan (blue markers, left) and the generic starting tables automatic plan (green markers, right). The differences are shown as a function of the number of metastases being treated. The area of the bubble indicates the number of patients.



(a) Clinical Plan (b) Automatic Plan

Figure 2 Example patient with 2 metastases (volumes colored red and orange) showing the table angles and arcs for the (A) clinical and (B) automatic plans (generic starting tables). The automatic plan had 1 fewer table angle and 2 fewer arcs.

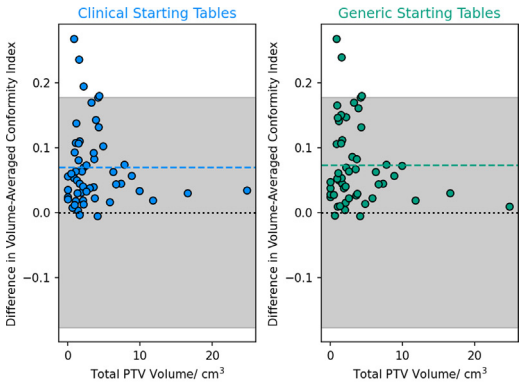
shown in Fig. 2. These differences were statistically significant ($P < .001$ for both plans).

Similarly, there was a reduction in the number of arcs with both automatic 4π-optimized plans. The clinical starting tables plans had a mean arc difference of -1.6 ± 0.2 to the clinical plans, and the generic starting tables of -1.3 ± 0.2. Both differences were statistically significant ($P < .001$ for both). There was a slight trend for plans treating larger number of metastases to have larger reductions in the number of arcs (Fig. 1B).

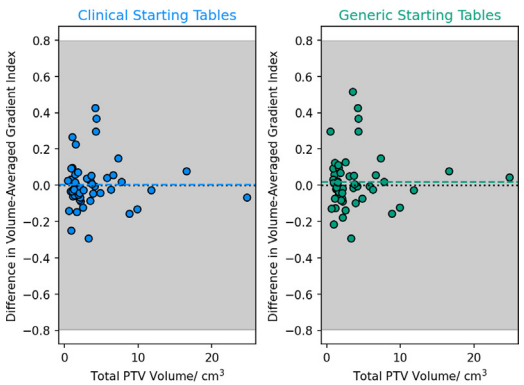
These reductions in number of table angles and arcs resulted in the reduction of estimated treatment times of -3.1 ± 0.5 minutes (clinical starting tables) and -2.7 ± 0.5 minutes (generic starting tables). The overall estimated treatment times (including intra-fraction imaging) were 19.6 ± 0.9 minutes, 16.4 ± 0.8 minutes, and 16.8 ± 0.8 minutes for the clinical plans, automatic plans with clinical starting tables and automatic plans with generic starting tables, respectively. Therefore, the 4π-optimized plans reduced the total treatment time by 16% and 14% for the clinical and generic starting tables, respectively.

The estimated treatment time algorithm—equation (1)—appeared accurate, with the mean difference between estimated and actual treatment times for the clinical plans being 0.1 ± 0.1 minutes.

There was a small but systematic increase in volume-averaged CI from the automatic plans compared with the clinical plan of 0.07 ± 0.01 (-0.01, 0.27), (mean $\pm$ SE [minimum, maximum]) for both the clinical and generic starting tables plans. There was a clear dependence on total planning target volume, with larger volumes having smaller differences (Fig. 3A). The differences in volume-averaged GI values to the clinical plans were smaller for both automatic plans, 0.01 ± 0.02 (-0.29, 0.43) and 0.02 ± 0.02 (-0.29, 0.52) for the clinical and generic starting tables, respectively (Fig. 3B). There was also a small systematic increase in local V12 Gy volume for both automatic plans compared with the clinical plan: 0.31 ± 0.07 cm^3 (-1.28 cm^3, 8.96 cm^3, clinical starting tables) and 0.25 ± 0.04 cm^3 (-1.28 cm^3, 4.38 cm^3, generic starting tables; Fig. 4). There was a very small difference in maximum dose to the brainstem PRV of 0.3 ± 0.1 Gy (clinical starting tables) and 0.1 ± 0.1 Gy (generic starting tables).



(a) Volume-averaged CI



(b) Volume-averaged GI

Figure 3 Plot of the difference in volume-averaged (A) Paddick Conformity Index (CI) and (B) Gradient Index (GI) between the clinical plan and the clinical starting tables automatic plan (blue markers, left) and the generic starting tables automatic plan (green markers, right). Differences are given as a function of total planning target volume, with the dashed line indicating the mean difference. The solid gray area indicates 0 difference $\pm$ the 95% reproducibility limits in volume-averaged CI or GI from a multicenter planning study.[7]

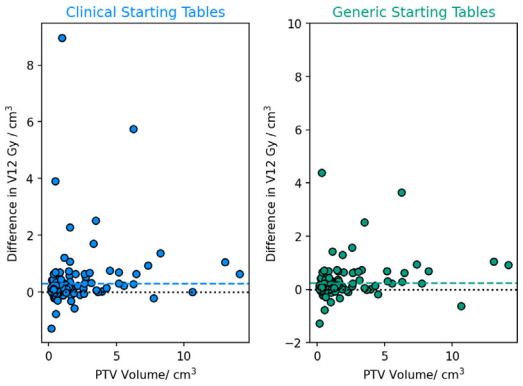


Figure 4 Plot of the differences in the volume of normal brain local to each metastasis receiving 12 Gy (local V12 Gy) for each planning target volume (PTV) between the clinical plan and the automatic plans with clinical starting tables (blue markers, left) and generic starting tables (green markers, right). Differences are shown as a function of PTV volume. The dashed line indicates the mean difference.

The interobserver 95% reproducibility limit from the multicenter planning study was 0.18 for volume-averaged CI and 0.80 for volume-averaged GI, which were used as noninferiority limits (see Fig. 3A, B, respectively). Both sets of automatic plans were noninferior to the clinical plans within these limits for both volume-averaged CI and GI ($P < .001$ for all).

The 4π-optimized plans followed by manual optimization reduced the differences to the clinical plans except for the brainstem PRV maximum dose which was similar (Table 1) for the 5-patient subcohort. The manual adjustment preserved the reduction in the number of table angles and arcs.

Discussion

This study has evaluated the treatment efficiency and plan quality of an automatic 4π-optimization algorithm for SIDCA treatments of multiple brain metastases. There was a significant improvement in treatment efficiency, with a reduction in the number of table angles of -0.5 ± 0.1 and number of arcs of -1.3 ± 0.2 (both $P < .001$), leading to a reduction in treatment time of -2.7 ± 0.5 minutes (14% of the total treatment time). For plan quality, there was a small increase in volume-averaged CI of 0.07 ± 0.01 compared with the manually optimized clinical plans, although the differences were less than the 95% interobserver planning variability range for 91% of patients and the automatic plan was statistically noninferior to the clinical plan within this variability range ($P < .001$). The difference in volume-averaged GI was 0.02 ± 0.02 and was also statistically noninferior ($P < .001$). Manual adjustment of the automatic 4π-optimized plan improved the plan quality while preserving the improved treatment efficiency.

The 4π-optimized plans demonstrated significant reductions in the number of table angles and number of arcs. This was true even for the plans that started with the generic set of table angles, which had reductions that were close to those of the automatic plans starting with the clinical table angles. There was no difference in plan quality between the automatic plans with the clinical starting tables or the generic starting tables. This suggests that it would be appropriate to use automatic 4π-optimized plans with generic starting table angles for all patients, without requiring manual identification of the best starting table angles for each patient.

There appeared to be a trend with greater reductions in numbers of arcs for patients with more metastases (Fig. 1). This is important in light of the increasing evidence of the safety and efficacy of treating large numbers of metastases with SRS.[11]

The improvements in treatment efficiency translated into estimated reductions in treatment time from beam-on of the first arc to beam-off for the final arc of -2.7 ± 0.5 minutes for the generic starting tables plans. This was 14% of the total estimated treatment time of 19.6 ± 0.9 minutes. Improved treatment efficiency enables a higher

Table 1 Difference from clinical plan for the 2 automatic 4π-optimized plans (clinical and generic starting tables) and the 4π-optimized plan followed by manual optimization

	Differences to clinical plan		
Parameter	**Clinical starting tables**	**Generic starting tables**	**Generic starting tables + manual adjustment**
Number of tables	-1.2 ± 0.4	-0.8 ± 0.6	-1.0 ± 0.4
Number of arcs	-3.8 ± 0.7	-3.0 ± 0.4	-3.2 ± 0.5
CI	0.21 ± 0.02	0.21 ± 0.02	0.03 ± 0.02
GI	0.15 ± 0.13	0.13 ± 0.13	-0.07 ± 0.10
Local V12 Gy (cm3)	0.30 ± 0.12	0.32 ± 0.12	0.02 ± 0.05
Brainstem max (Gy)	0.3 ± 0.4	0.3 ± 0.5	0.5 ± 0.2

Abbreviations: CI = Paddick Conformity Index; GI = Gradient Index; Local V12 Gy = volume of normal brain local to metastasis receiving 12 Gy; max = maximum.
Differences are calculated for the 5-patient subset. CI and GI results are volume-averaged. Differences are given as mean $\pm$ SE.

throughput of patients in a department, as well as improved patient experience and reduced risk of patient motion during treatment.

The improvement in treatment efficiency did appear to come with a small systematic increase in volume-averaged CI of 0.07 ± 0.01. This was within the interobserver planning variability of ±0.18 and the automatic plans were statistically noninferior to the clinical plans within this limit. This suggests that the automatic plans show the same level of agreement as multiple manual planners would. However, it is noticeable that this was a systematic shift, with only 2 patients having an improvement in volume-averaged CI compared with the manual plan (Fig. 3A). This did produce a small increase in the normal brain local V12 Gy of 0.25 ± 0.04 cm^3. However, this difference is <2.5% of the normal brain V12 Gy constraint of 10 to 15 Gy,[12] suggesting it is not a clinically significant difference. Similarly, although there was an increase in brainstem PRV maximum dose of 0.1 ± 0.1 Gy, this is <1% of the 15 Gy constraint[12] and the brainstem dose was not an optimization target in the automatic plans. This implies the automatic plans are noninferior to the manually optimized plans.

In addition, it was possible to remove the difference in volume-averaged CI and local V12 Gy using the automatic plan followed by a small amount of manual adjustment. In the subcohort of 5 patients with the biggest volume-averaged CI differences, the manual adjustment reduced the CI difference from 0.21 ± 0.02 to 0.03 ± 0.02 and local V12 Gy difference from 0.32 ± 0.12 cm^3 to 0.02 ± 0.05 cm^3. Crucially, this still preserved the same reduction in the number of table angles and arcs. The brainstem PRV maximum dose was not changed, but for 4 of 5 patients, this dose was <3 Gy, well below constraints. For the remaining patient, the automatic plan followed by manual adjustment maintained the brainstem PRV maximum dose within 0.05 Gy of the clinical plan. This implies that improved treatment efficiency and equivalent plan quality can be generated through the use of automatic 4π-optimization of plans with generic starting tables, followed by manual adjustment if required.

The use of automatic plan generation would also potentially improve planning efficiency. This could not be assessed in this study because the planning time for the clinical plans had not been recorded. Using automatic planning followed by manual optimization would increase the amount of planning time compared with using automatic planning by itself. A future study could evaluate the improvement in planning efficiency from using automated planning or automated followed by manual optimization, as compared with manual optimization.

An evaluation of this commercial 4π-optimization algorithm for multiple brain metastases has not been carried out previously, to the best of the authors' knowledge. There have been 2 small studies that have evaluated a similar 4π-optimization algorithm for single cranial targets. Loughery et al[13] replanned treatment for 9 patients with a single brain metastasis using 4π optimization and reported clinically acceptable plans with CI <1.3 and GI <4.5, with all organs at risk within dose constraints and good deliverability. Robar[14] evaluated 4π-optimized plans for 10 vestibular schwannoma and 10 pituitary adenoma patient cases compared with coplanar volumetric modulated arc therapy plan and found significant reductions in doses to the optic organs. These results are consistent with those found in this study in regard to acceptable plan quality using 4π-optimization.

Conclusions

Automatic 4π-optimization of SIDCA plans using a generic set of table angles potentially resulted in improved treatment efficiency due to the statistically significant reduction in the number of table angles and arcs of −0.5 ± 0.1 and −1.3 ± 0.2, respectively (both $P < .001$). This produced treatment time savings of −2.7 ± 0.5 minutes, a reduction of 14% of the total treatment time. The plan quality was noninferior to manually optimized clinical plans ($P < .001$ for both volume-averaged CI and GI), although there was a small systematic shift in volume-averaged CI of 0.07 ± 0.01 and local V12 Gy of 0.25 ± 0.04 cm^3. These differences were not clinically significant (<2.5% of the V12 Gy dose constraint). Minor manual adjustment after automatic 4π optimization removed the difference in volume-averaged CI and local V12 Gy for a subset of patients while preserving the treatment efficiency gains. In conclusion, automatic 4π optimization can generate SIDCA SRS plans with improved treatment efficiency and noninferior plan quality.

Disclosures

This study was funded by Brainlab (the manufacturer of the treatment planning system evaluated in this study). Brainlab also provided an automated script to extract data from the treatment planning system. This has not influenced the study design or analysis. Jonathan J. Wyatt reports payment from GE Healthcare for speaking at a global oncology webinar in 2021 and payment from Newcastle University for a research project investigating magnetic resonance −only radiation therapy planning for pelvic tumors in 2023. Judith H. Mott reports financial support and administrative support from Brainlab AG and reports that article publishing charges were provided by Brainlab AG.

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