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Dose-Volume Comparison for Optimal Beam Findings for Stereotactic Body Radiation Therapy in Lung Carcinoma

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Abstract

Aim: To study the dosimetric differences of using different energy in the case of lung SBRT VMAT treatment planning.

Materials & methods: A total of 12 patients with stage I non-small cell lung cancer (36 plans) with PTV of 63.3cc to 115.4cc were selected for this study retrospectively. Three different treatment plans were generated using 6XFF, 6XFFF, and 10XFFF energies with same optimization constraints to deliver 60Gy in 8 fractions with two partial arcs on Eclipse TPS. A progressive resolution optimizer and Acuros algorithm were employed for optimization and dose calculation, respectively. Planning evaluation was carried out qualitatively and quantitatively for PTV and OARs doses, as per RTOG guidelines (0813/0915). Delivery quality assurance for each plan was performed using the PTW Octavious-4D phantom. In addition, the point dose was verified using a thimble ion chamber.

Results: The Coverage Index (CI) ($p<0.05$) was the same 96%±0.008 for 6XFF and 6XFFF, while 94% ± 0.012 for 10XFFF. The mean Conformity Index (COIN) ($p>0.05$) for 6XFF, 6XFFF and 10XFFF was 0.956 ± 0.036, 0.957 ± 0.037, and 0.936 ± 0.043, respectively. Mean treatment time ($p<0.05$) for 6XFF, 6XFFF and 10XFFF was 3.7 ± 0.41, 1.55 ± 0.21 and 1.13 ± 0.13 minutes, respectively. Mean gamma (3%, 3mm) was 96.5 ± 1.12, 96.3 ± 1.03 and 97.4 ± 1.3 for 6XFF, 6XFFF and 10XFFF, respectively. Mean point dose difference in % between TPS and measurement was 2.2 ± 0.4, 2.4 ± 0.9 and 2.68 ± 0.9 for 6XFF, 6XFFF and 10XFFF respectively.

Conclusion: We found 6XFFF to be the optimal choice based on OAR sparing with no compromise for coverage and conformity index.

Keywords: Lung SBRT • Flattening Filter Free (FFF) beam • Non-Small Cell Lung Cancer (NSCLC) • Lung dosimetry • Lung carcinoma

Introduction

Stereotactic Body Radiotherapy (SBRT), Stereotactic Ablative Radiotherapy (SABR) and Stereotactic Radiosurgery (SRS) are advanced treatment techniques and effective modalities for cancer treatment at sites such as the lung, liver, kidney, brain, spine, and pancreas. In SBRT, a high dose of radiation is delivered over a short period, therefore, the accuracy of treatment delivery is of paramount importance to ensure adequate target coverage and sparing of the normal tissues.

SBRT is considered a viable treatment option for early stage-I Non-Small Cell Lung Cancer (NSCLC), in both operable and inoperable settings [1]. There are several complexities and challenges in generation of lung SBRT plans for heterogeneous targets. Moreover, planning algorithms are based on electron densities, which add uncertainties to dose calculations [2,3]. Other challenges include the proximity of organs at risk, such as the spinal cord, normal lung, esophagus, heart, Proximal Bronchus Tree (PBT), and chest wall, and if the target location is peripherally located, skin sparing seems to be a concern.

In the entire course of treatment, respiratory motion of the target is unpredictable. While delineating the target as well as normal structures, it is necessary to keep in mind inter and intrafraction motion strategies. Hence, several methods have been developed to account for respiratory motion during simulation and treatment to reduce the uncertainty in target delineation and treatment delivery, such as respiratory gating and breath-hold techniques [4]. All these techniques reduce variability throughout the treatment. However, such methods increase the treatment time on the couch, resulting in patient discomfort and treatment delivery uncertainty.

At present, linear accelerators can deliver treatment using both Flattening Filter (FF) beams and Flattening Filter-Free (FFF) beams [5]. There are numerous technical benefits of FFF beam over the FF beam for Volumetric Modulated Arc Therapy (VMAT) planning. First, the major benefit of the FFF beam is its high dose rate, which results in a shorter treatment time. The primary beam has a non-uniform profile and offers less energy variation in the lateral direction when the flattening filter is removed [6,7]. This characteristic of a linear accelerator supports limiting head scattering, less peripheral dose, high conformity, limiting the body integral dose, Multileaf Collimator (MLC) transmission, and leakage [8]. Because of the numerous variability in FFF and FF beams, the dosimetric outcomes have been variable.

Therefore, we compared the dosimetric differences among 6XFF, 6XFFF, and 10XFFF beam for previously treated cases of lung SBRT. Plan Delivery Quality Assurance (DQA) for absolute dose and gamma analysis was performed for each plan.

Materials and Methods

Study design, target delineation and treatment unit

For this study, a total of 12 previously treated lung patients with stage-I non-small lung cell carcinoma were enrolled from the institutional database. This was a retrospective study to evaluate the dosimetry impact of changing beam energy for plan evaluation. The patients were simulated using a four-dimensional computed tomography (4DCT) GE CT scanner (Light Speed 16,

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Version, Waukesha, WI, USA) and were immobilized with vaclok. The image slice width of 1 mm was acquired for the target and OAR delineation. These images were transferred for contouring and planning purposes to the Eclipse treatment planning system (Varian Medical System, Palo Alto, USA), version 13.5. Target delineation was carried out according to the guidelines for lung SBRT [9].

First, Gross Tumor Volume (GTV) and Clinical Target Volume (CTV) were segmented. Furthermore, the phase-based Internal Target Volume (ITV) was segmented in each phase so that the target was drawn throughout the respiratory cycle. Therefore, the Planning Target Volume (PTV) was delineated by considering all phases of the ITVs, with a appropriate additional margin of 5 mm for setup accuracy. Subsequently, the organs at risk (spinal cord, esophagus, normal lung, heart, and skin) were drawn.

The plans were generated for True Beam linear accelerator (Varian Associates, Palo Alto, CA, USA), version 2.5. It has five photon energies with Photon energy 6XFF, 10XFF, 15XFF having a maximum dose rate of 600MU/min. The maximum dose rates for the photon energies 6XFFF and 10XFFF is 1400 MU/min and 2400 MU/min respectively. The linear accelerator was tuned for 1cGY per MU at a 100 cm Target to Surface Distance (TSD) at a depth of 10cm from the surface for 10 × 10cm^2 field size. True Beam linear accelerator comprises of a total of 60 pairs of tertiary Millennium MLC with a maximum field size of 40 × 40 cm^2 at 100 cm TSD. Further, the central 40 MLC pairs width at isocentre (20 cm treatment length) is 5mm, and the remaining peripheral MLC width is of 10mm at isocentre. Hence all the plans were generated only using 5mm width central mlc.

Treatment planning

First, the VMAT plans were generated using a 6XFF beam with the highest available dose rate. All VMAT plans were generated using Eclipse TPS, and optimization was performed using the Progressive Resolution Optimizer (PRO) algorithm. The final dose calculation was carried out with the Acuros XB algorithm, which takes into accounts all the inhomogeneity corrections during dose calculation (calculation dose to medium), depending on Linear Boltzmann Transport Equation (LBTE). The grid size for planning was kept at 1.25mm. All the dynamic VMAT plans were generated with two co-planar partial arcs (contralateral lung saved while choosing a partial arc) and the collimation angle for each patient plan was set at 45°. For sharp dose gradient fall-off, the Normal Tissue Objective (NTO) value was kept at 30% fall-off at 0.5 cm a distance of PTV. The plans were generated using jaw tracking, and the total dose was prescribed 60Gy in 8 fractions means 7.5Gy per fraction. The best possible plan using a 6XFF beam was generated with one optimization without changing any dose constraints during the optimization for each patient and was assumed as a base plan [9].

Further, for each patient, two new plans were generated with FFF beams, 6XFFF and 10XFFF, with their maximum available dose rates for the same treatment unit. For the true planning comparison, the arc angles, collimator angles, and optimization parameters were kept the same for each patient plan. Data collection was performed after the completion of the plans in the same manner, without allowing further improvements to any constraints. A total of 36 plans were generated for 12 patients included in the study.

Plan evaluation

Plan acceptance was set using the Radiation Therapy Oncology Group (RTOG) guidelines 0813 and 0915. All 6XFFF and 10XFFF plans were compared with respect to their 6XFF plans using a cumulative dose-volume histogram (DVH). For dosimetry comparison of OARs of each plan w.r.t. 6XFF plan, the ratios of the 6XFFF and 10XFFF plans were analyzed as 6XFF/6XFFF and 6XFF/10XFFF.

The following PTV parameters were used to evaluate the plan quality Coverage Index (CI) (institutional acceptance criteria: 95% of the prescription dose to 95% of PTV volume), Conformity Index (COIN), Homogeneity Index (HI), dose to healthy tissue (DHT = body – PTV), D2 cm (maximum dose point in cGy at any 2 cm diameter farther away from PTV in any direction), R50% (ratio of volume of 50% prescription isodose volume to the volume, Body Integral Dose (body mean dose), Monitor Units (MU), treatment time, and average dose rate. The remaining organs at risk doses to the spinal cord, esophagus, brachial plexus, and heart were recorded (Figure 1).

Plan delivery quality assurance

Delivery Quality Assurance (DQA) is required prior to accepting the plan because of the significant level of uncertainty in such a heterogeneous lung target. Each of the 36 plans in this study had its validity confirmed twice. Data from the TPS and measurements were compared in terms of absolute dosage. For fluency verification, a gamma evaluation was carried out. Here, fluence verification was performed on the Truebeam through an Octavius phantom (Seven29, PTW, Freiburg, Germany). Gamma Evaluation Scores (GES) were determined for a Dose Difference (DD), a Distance to Agreement (DTA) of 3%, 3 mm, and 2%, 2 mm, with a 10% threshold. Absolute dose measurements were also performed using a solid water phantom (PTW, RW3 phantom) and a thimble chamber (volume 0.13cc). In addition, the acceptance criterion for the absolute dose variation between the actual and delivered plans was approved within 3%.

Statistical analysis

In order to determine the statistical significance of all parameters that were studied, a one-way repeated ANOVA test was applied using SPSS software (version 26.0, IBM Corp., South Asia Pvt. Ltd., India). For Statistical significance was set at $p < 0.05$. It was decided to assess the coverage index using a box-and-whisker graphic.

Results

Patient's characteristics

The GTV and PTV volume range from minimum to maximum was from 7.4cc to 62.1cc and 63.3cc to 115.4cc, respectively. The mean (±SD) and median GTV were 31.6 (±38.9) cc and 29.7cc. Similarly, the mean (± SD) and median PTV were 86.3 (±17.6) cc -and 85.7cc respectively.

Planning target volume assessment

The mean coverage indices of the PTV for the 6XFF and 6XFFF plans were 96%±0.008 and 94%±0.012 for 10XFFF plan respectively. The cumulative DVH of the three-beam plans 6XFF, 6XFFF, and 10XFFF are showed in figure 2. The mean coverage index for PTV ($p < 0.01$) of 6XFFF was 1.002 times more than that of 6XFF, while opposite for 10XFFF, it was 0.989 times less than that of 6XFF. The mean Conformity Index (COIN) of the PTV was 0.956±0.036, 0.957±0.037, and 0.936±0.043 for the 6XFF, 6XFFF and 10XFFF plans respectively. The results showed that 6XFFF plans were more conformal than 6XFF and 10XFFF plans. The mean homogeneity index ($p < 0.007$) for 6XFF, 6XFFF, and 10XFFF was 1.109 ± 0.01, 1.108 ± 0.01, and 1.128 ± 0.02, respectively. R50% was obtained 3.59 ± 0.58, 3.55 ± 0.56 and, 3.55 ± 0.59 for 6XFF, 6XFFF and 10XFFF plans, respectively. Similarly, D2 cm was 47.97 ± 4.2Gy, 48.38 ± 4.27Gy and, 48.3 ± 4.07Gy for 6XFF, 6XFFF, and 10XFFF plans, respectively.

The Monitor Units (MU) obtained from the plans were subjected to depth,

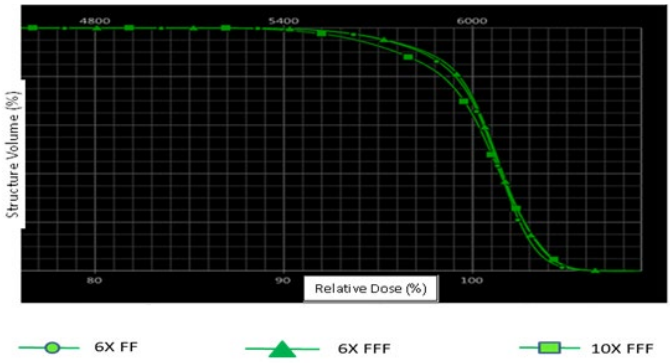

Figure 1. Coverage Index for 6XFF, 6XFFF and 10XFFF.

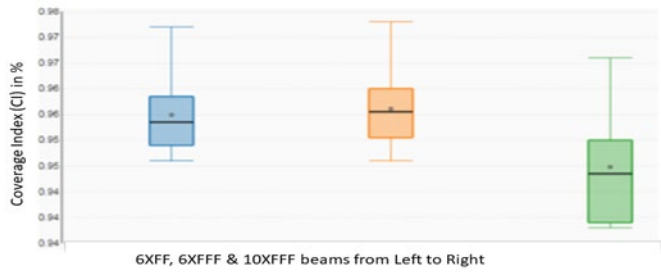

Figure 2. Box and whisker plot for coverage index for 6xff, 6xfff, and 10xfff from left to right.

plan complexity, and dose constraint modulation. The average monitor units for 6XFF, 6XFFF, and 10XFFF plans were 2029.5±253.3, 2161.5 ± 305.1, and 2103.9 ± 323.7 respectively, which were 1.07 and 1.04 times more for 6XFFF and 10XFFF as compared to 6XFF. A statistically significant difference was found in treatment time ($p < 0.001$). The estimated average treatment time for the 6XFF base plan was 3.37 ± 0.41 min, while it was reduced 0.46 times for plan 6XFFF and 0.33 times for 10XFFF than the 6XFF plan. The average dose rate was 2350 MU/min for the 10XFFF plan. The 6XFF and 6XFFF plans were delivered with constant maximum dose rates. The average integral dose of the body for 6XFF, 6XFFF, and 10XFFF was 352.6 ± 96.3cGy, 348.1 ± 96.9cGy, and 351.3 ± 97.1cGy, respectively. The 6XFFF beam produced the lowest integral dosage.

In summary, 6XFFF plan was the optimum plan in terms of coverage index and conformity index compared to the base plan. 10XFFF was the best option in terms of therapy delivery time.

Evaluation of organ at risks

Table 1 provides a summary of the OARs results for the 6XFF base plan. OAR doses with 6XFFF and 10XFFF plans were normalized in relation to 6XFF summarized in Table 2. The predominant OAR was the normal lung during planning. With decreases of 0.979, 0.971 and 0.978 times for V5, V20, and mean lung dosage, respectively, the result demonstrates a statistically significant difference ($p < 0.01$) in the normal lung dose for the 6XFFF plans compared to the 6XFF plan, making it extremely useful for plan evaluation. Now, V5 for the heart was reduced by 0.953 times for the 6XFFF plan, while it was 1.037 times more for 10XFFF as compared to 6XFF plan. The spinal cord dose was higher in the 6XFFF plan as compared to base plan, but the difference was not statistically significant.

The skin dose (10cc dose), proximal bronchial tree maximum dose, and chest wall dose volume (V30 and V60) were higher for 6XFFF than for 6XFF, but the difference was not statistically significant. However, the Skin dose for 10cc and chest wall dose-volume V30 was less compared to 6XFF.

Delivery quality assurance

Table 3 lists the DQA outcomes for gamma evaluation and absolute dose variation. The results show, for 10XFFF plans, the average gamma passing rate was 97.4% for 3%, 3 mm ($p = 0.07$). This was 1.01% more than the base plan, while the opposite was reduced 0.99 times for the 6XFFF plans compare to the base plan. One set of plans had gamma passing rates of 94.7%, 94%, and 94.1% for the 6XFF, 6XFFF, and 10XFFF plans respectively, which were not acceptable. In short, the gamma fluence for the 6XFFF plan was less than that for the 6XFF and 10XFFF plans, but acceptable except for one plan.

The absolute dose variation ($p = 0.41$) was better in the 6XFF plan than that in both beam plans. In one patient plan, the absolute dose discrepancy was found to be 3.08% in the case of the 6XFF base plan. In the case of the 6XFFF plan, two plans did not satisfy the acceptance criteria (4.08% and 4.15%), and for 10XFFF, four plans were out of acceptance criteria (3.06%, 3.38%, 3.99%, and 4.23%).

Discussion

The focus of this study was to estimate the optimal beam consistency for non-homogeneous cases in terms of PTV evaluation, OARs comparison, and treatment delivery time among all beam plans. The low dosage rate and lengthy treatment delivery time of the 6XFF beam are two of its key potential drawbacks. 6XFF is one of the most commonly used beams for conventional fractionation, but is not appropriate for hypo-fractions. In the case of hypo-dose fractions, many of the publications concluded that a shorter treatment delivery time is the only advantage of the FFF beam over the FF beam.

The benefits of radiosurgery with unflattened 6MV photon beam over flattened 6MV photon beam for small fields (but not clinical). Furthermore, tomotherapy is the only treatment unit that results in an unflattened 6XFFF single beam. Reported the first dosimetry advantages of the FFF beam over the FF beam (6XFFF *vs*. 6XFF) for lung SBRT on Clinac 21-EX, however, the calculation algorithm was a pencil-beam calculation (PBC) algorithm with Batho power law inhomogeneity correction.

In this paper, the authors report both dosimetric comparison and reduction in the treatment time. Evaluating the target coverage is the first step in figuring out whether planning is clinically acceptable. In this study, the authors considered various conditions of the target, such as different sizes, electron

Table 1. The mean doses of the Organs At Risk (OARs) for 6XFF plans along with ranges (min-max).

Oar Name	Evaluated Parameters	Observed Dose	Range(min-max)
Normal Lung	V5	32.17% ± 11.8	12.4%-47.1%
	V20	9.55% ± 5.2	4.7%-12.2%
	Mean Lung Dose (Gy)	5.98 Gy ± 2.0	2.44 Gy-8.52 Gy
Ipsilateral Lung	V25 (cc)	471.9 cc ± 200	84.6 cc-805.6cc
Heart	V5	25.87% ± 24.7	8.0 %-82.5%
	Mean Heart Dose (Gy)	1.96 Gy ± 0.8	1.04 Gy-3.72 Gy
Esophagus	D(5cc) (Gy)	12.1 Gy ± 7.3	0.5 Gy-17.03 Gy
Spinal Cord	D(0.5 cc) (Gy)	10.05 Gy ± 2.3	4.3 Gy-12.9 Gy
Skin	V10 (cc)	16.97 Gy ± 4.12	9.8 Gy-20.4Gy
Proximal Bronchial Tree (PBT)	Max Dose (cGy)	52.2 cGy ± 14.6	25.3 cGy-64.9 cGy
Chest Wall	V 30 (cc)	93.7 cc ± 50.6	19.6 cc-113.1 cc
	V 60 (cc)	5.5 cc ± 6.8 cc	0.7 cc-19.7 cc

Table 2. The organs at risk doses for 6XFF, 6XFFF and 10XFFF plans, normalized w.r.to 6XFF plans along with p-value, for dosimetry comparison.

Oar Name	Evaluated Parameters	6XFF/6XFF	6XFFF/6XFF	10XFFF/6XFF	p-value
Normal Lung	V5	1	0.979	1.062	< 0.01
	V20	1	0.971	1.011	0.01
	Mean Lung Dose (GY)	1	0.978	1.021	< 0.01
Heart	V5	1	0.953	1.037	0.015
	Mean Heart Dose (Gy)	1	0.984	0.984	0.18
Spinal Cord	V5 (cc)	1	0.986	1.001	0.95
Body Integral Dose	Mean Dose	1	0.984	0.995	0.09
Ipsilateral Lung	V25	1	0.98	1.005	0.98
Skin	V10 (cc)	1	1.06	0.89	0.25
Proximal Bronchial Tree (PBT)	Max Dose (cGy)	1	1.01	1.007	0.99
Chest Wall	V 30 (cc)	1	1.002	0.97	0.98
	V 60 (cc)	1	1.08	1.06	0.98

Table 3. Summarizing the dqa for 3%, 3 mm fluence, 2%, 2 mm fluence and absolute dose variation between tps and measurements with range.

		Gamma Value	Range in % (min-max)	Gamma Value	Range in % (min-max)	Difference between TPS and Measurements	Range in % (min-max)
Energy		3%, 3mm	3%, 3mm	2%, 2 mm	2%, 2 mm	%	%
	6XFF	96.5 ± 1.12	(94.7-98.7)	86.1 ± 3.28	(80.8-90.3)	2.22 ± 0.38	1.16-3.08
	6XFFF	96.± 1.04	(94-97.5)	84.7 ± 3.08	(78.5-89.1)	2.40 ± 0.97	1.06-4.15
	10XFFF	97.4 ± 1.31	(94.1-99.1)	88.4 ± 3.41	(81.4-93.6)	2.68 ± 0.96	0.75-4.23

densities, and modalities. The authors came to the conclusion that under-dosing is unquestionably shown for small targets and lower lung density based on these criteria. In some cases, the target coverage may be reduced by up to 10% of the prescribed dose. However, the authors finalized the report with a conclusion; the modest coverage can be increased by replacing the FF beam by the FFF beam.

The middle line shows the median (which is less than the mean, except for 10XFFF), while the lower and upper boundaries of the boxes represent the 25th and 75th percentiles. The plot shows the largest range in 10XFFF. The minimum and maximum ranges for 6XFF and 6XFFF ranged from 95.4% to 97.7% and 95.6% to 97.8% (which is acceptable), respectively, while for 10XFFF it ranged from 93.9% to 97.1% (not acceptable for a few plans). Following a very thorough dosimetry study of 6XFF, 6XFFF, and 10XFFF beams. However, 10XFFF cuts down on the lengthy beam-on time. However, this study used the AAA algorithm for the final dose calculation. The dose calculation in the present study was carried out by Acuros XB algorithm, considering heterogeneity.

Our study clearly shows a reduction in the body integral dose and greater conformity in the case of the 6XFFF beam. For 6XFFF and 10XFFF, the mean body integral dose was recorded 98% and 99% times as compared to 6XFF beam. Due to beam hardening, the transmission through the MLC and jaw will be greater, hence the body integral dose in the 6XFF beam may need to be raised. For OARs doses, the 6XFFF beam is statistically superior to spare healthy OARs, except for the skin dose. Using a 10XFFF beam, skin-sparing is more effective, but at the cost of other predominant OARs. The authors recommended the 6XFFF beam to be more efficient for OARs sparing and lower NTCP for SBRT stage I lung cancer, whereas 10XFFF was better for treatment efficacy. Hence, the authors concluded in favor of 6XFFF for more than one fraction. Our results are in agreement with this conclusion.

Apart from *in vitro* studies, it is important to know the outcome of patients treated with FFF beams. The patient outcome treated with the FFF beam, for toxicity and treatment efficacy was found to be within the same range as with the FF beam. Therefore, the authors recommended patient treatment with the FFF beam, because of the short treatment time and OARs dose benefits. The increase in the skin dose is only a potential limitation when using the 6XFFF beam compared to the 10XFFF beam, additional more treatment time. Our results revealed agreement when comparing the range of the gamma passing rate for all energies. Specifically, 6XFFF is the optimal beam choice for target coverage, conformity, and organs at risk perspective.

Study Limitations

The sample size was smaller for dosimetry comparison. However, this seems quite appropriate, as many authors have reported a dosimetry comparison with this sample size.

Conclusion

Our study demonstrates that 6XXFFF and 10XFFF both beams are beneficial for reducing the treatment delivery time compared to the 6XFF beam plan. Optimal lung SBRT plan can be obtained using the 6XFFF beam with an average delivery dose rate of 1400 MU/min without compromising the coverage index, conformity index, integral dose of the body, and OAR doses. 6XFFF delivers slightly less OARs doses but the reduction in few OARs were not statistical significance. The 10XFFF beam plan provides a lower skin dose and treatment time but at the cost of less coverage and conformity. Long-term clinical outcomes are required in future studies.

Acknowledgement

None.

Conflict of Interest

No conflict of interest.

Statement of Ethics Data

This is retrospective dosimetry study by virtual treatment planning using patient images (who were already treated), therefore, ethical approval is not required.

Availability Statement

Data are available in the manuscript to editors, reviewers and readers without unnecessary restriction wherever possible.

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