Original Article

Quantitative evaluation of accumulated and planned dose deviations in patients undergoing gated and non-gated lung stereotactic body radiation therapy patients: a retrospective analysis

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Background: Stereotactic body radiation therapy (SBRT) is crucial for treating early-stage inoperable non-small cell lung cancer (NSCLC) due to its precision and high-dose delivery. This study aimed to investigate the dosimetric deviations in gated (GR) versus non-gated radiotherapy (NGR), analyzing the impact of tumor location, target volume, and tumor motion range on dose distribution accuracy.

Methods: Sixty patients treated with either gated (n=30) or non-gated (n=30) SBRT for early-stage NSCLC were retrospectively analyzed. The planned dose distributions were determined using four-dimensional computed tomography simulations to account for breathing motion, while the actual dose delivered was determined by accumulating each fractional dose with synthetic computed tomography (sCT) methods. The deviations between the planned and actual accumulated doses were statistically analyzed for both groups. The effects of tumor location and volume on dose distribution were also assessed.

Results: Gated SBRT showed significantly higher dosimetric precision with median relative changes in the minimum dose within the ITV (ITV_D_{min}), mean dose received by the ITV (ITV_D_{mean}), and maximum dose within the ITV (ITV_D_{max}) of –0.44%, –0.33%, and –0.49%, respectively. Non-gated SBRT presented with larger median relative changes in these parameters (P<0.001 for the ITV_D_{min}). In gated SBRT, the PTV_D_{min} (minimum dose within the PTV) and PTV_D_{mean} (mean dose received over the entire PTV) differences were significantly lower favoring gated SBRT (P=0.01 and P=0.007, respectively), and for the prescribed dose volumes, the volume of PTV receiving 90% prescription dose ($PTV\_V_{90\%PD}$) and the volume of PTV receiving 100% prescription dose ($PTV\_V_{100\%PD}$) were more accurately delivered, also favoring gated SBRT (P=0.006 and P=0.03, respectively). The tumor location and volume analyses demonstrated that the dosimetric benefits of gated SBRT were particularly significant in the smaller internal target volumes (ITVs) and in the left lower central lung region (P<0.001 for the ITV_D_{min} in small volumes).

Conclusions: Gated SBRT affords dosimetric accuracy compared to non-gated SBRT, and thus could improve the therapeutic outcomes of NSCLC patients. These results should advocate for the preferential use of gated SBRT in cases requiring precise dose delivery due to large respiratory motion or small target volumes.

Keywords: Stereotactic body radiation therapy (SBRT); non-small cell lung cancer (NSCLC); gated radiotherapy (GR); synthetic computed tomography (sCT)

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Introduction

Background

Stereotactic body radiation therapy (SBRT) has established itself as a key treatment for early-stage inoperable lung cancer. It is notable for its precise targeting, delivery of high 'ablative' radiation doses, and steep dose gradients that minimize exposure of normal tissues to high doses (1,2). These attributes result in excellent local control and low rates of toxicity after SBRT for early-stage non-small cell lung cancer (NSCLC) (3). The success of SBRT depends critically on the accurate delivery of radiation doses to the tumor, a challenge compounded by physiological movements such as breathing (4). These movements can cause significant discrepancies between the planned dosimetry and the actual radiation doses delivered (5,6), particularly in tumors located in the lower lung regions (7). Accounting for motion is crucial, as it can decrease the risk of toxicity to normal tissues and improve local control rates (8,9).

Highlight box

Key findings

- Gated stereotactic body radiation therapy (SBRT) has significantly higher dosimetric precision than non-gated SBRT with smaller deviations in dose parameters. It also has lower variation in planning target volume (PTV) doses and enables the more accurate delivery of prescribed dose volumes. The benefits were particularly noticeable in smaller tumors and also tumors in the left lower central region of lung. These results support the use of gated SBRT to improve dose accuracy and therapeutic outcomes in non-small cell lung cancer (NSCLC) patients.

What is known, and what is new?

- SBRT is effective in treating early-stage NSCLC, but its success depends on the accurate delivery of the radiation dose, which can be affected by respiratory movements, particularly in tumors located in the lower lung regions.
- This study showed that gated SBRT has significantly higher dosimetric accuracy than non-gated SBRT that particularly benefits smaller tumors and also tumors in the lower lung regions. These findings support its preferential use in clinical practice.

What is the implication, and what should change now?

- The retrospective design and limited sample size of the study highlight the need for caution in generalizing these results. To strengthen the evidence base, future research should focus on prospective studies with larger and more diverse patient populations. This approach will help confirm the benefits of gated SBRT and guide its broader implementation in clinical practice, potentially improving treatment precision and outcomes for a wider range of NSCLC patients.

Literature review

According to the recommendations by the American Association of Physicists in Medicine in Task Group Report 76, motion management strategies are crucial when intended displacement during radiotherapy exceeds a threshold of 5 mm (10). In this context, respiratory-gated radiotherapy (respiratory-GR) presents a viable solution, as it incorporates tumor mobility during breathing into the treatment regimen (11-13). The integration of respiratory-gated radiotherapy (GR) into treatment protocol for thoracic malignancies has been facilitated by developments in radiation therapy technologies (14-16). However, the relative effectiveness of GR compared to non-gated radiotherapy (NGR) in clinical practice remains unclear (12,17,18). While gating techniques have shown potential in reducing dose deviations, particularly for patients at higher risks for toxicities or with highly mobile tumors (19-21), comprehensive evaluations of actual dose delivery in lung SBRT are still lacking (6).

Previous studies have used theoretical and simulated methods to analyze the effect of respiratory motion on thoracic tumors (22-25); however, real-world quantitative analyses comparing dose deviations between the planned dose and the actual accumulated dose for GR and NGR in lung SBRT are few (6). This gap is especially notable in lung SBRT, where respiratory-induced tumor motion poses significant challenges (17,26,27). Lung SBRT should have its own set of methodologies for assessing dose accumulation and deviations. We hypothesized that GR would result in significantly lower dose deviations than NGR in lung SBRT patients, particularly in tumors located in the lower lung regions and those with higher mobility.

Study objective

The current study aimed to address the gap in understanding the practical impact of respiratory GR versus NGR on dose deviations in SBRT for NSCLC. We hypothesize the GR will significantly reduce dose deviations compared to NGR, particularly in cases involving tumors with high mobility or those located in the lower lung regions. By analyzing a cohort of 60 NSCLC patients treated between January 1, 2021, and December

Table 1 Clinical characteristics of the enrolled patients

Variables	Techniques	
	Gated (N=30)	Non-gated (N=30)
Sex		
Male	21 (70.0)	20 (66.7)
Female	9 (30.0)	10 (33.3)
Age (years)	72 [51–89]	68 [34–86]
Tumor location		
LLCR	6 (20.0)	6 (20.0)
LLPR	10 (33.3)	10 (33.3)
RLCR	2 (6.7)	1 (3.3)
RLPR	10 (33.3)	8 (26.7)
Other	2 (6.7)	5 (16.7)
Tumor volume (ITV) (cc)	7.2 [1.4–58.8]	7.1 [0.7–48.7]

Data are presented as n (%) or median [range]. Other, refers to regions of the lung that are outside those previously mentioned. LLCR, left lower central region of lung; LLPR, left lower peripheral region of lung; RLCR, right lower central region of lung; RLPR, right lower peripheral region of lung; ITV, internal target volume.

31, 2023, we seek to provide a detailed comparison of the actual versus planned dose deviations for both treatment approaches. Our goal is to enhance the understanding of how respiratory gating influences treatment accuracy and to inform the optimization of SBRT protocols, ultimately improving patient outcomes. We present this article in accordance with the STROBE reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-992/rc).

Methods

Patient selection

A total of 60 patients with NSCLC who underwent SBRT (with prescription doses ranging from 40 to 50 Gy, delivered in 5 to 10 fractions) using the TrueBeam (Varian Medical System, Palo Alto, CA, USA) at Tongji University Affiliated Shanghai Pulmonary Hospital from January 1, 2021 to December 31, 2023 were enrolled in this retrospective study. All of the patients completed their SBRT treatment courses. Patients were divided into two groups based on clinical and technical criteria: 30 patients received GR, while 30 patients received NGR. The assignment to these groups was not random but based on specific criteria derived from respiratory motion assessment. Patients were categorized into the GR group if their tumors exhibited significant respiratory motion on four-dimensional computed tomography (4D-CT) scans, especially in the lower lung regions, with a motion range exceeding 5 mm. Conversely, those with minimal respiratory motion, defined as a motion range of less than 5 mm, were assigned to the NGR group. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics board of Tongji University Affiliated Shanghai Pulmonary Hospital (No. K21-312Y), and informed consent was taken from all the patients. The clinical characteristics of the participating patients, including gender distribution, age range, tumor locations, and tumor volumes, are summarized in *Table 1*.

4D-CT acquisition

Each patient was immobilized using vacuum cushion to minimize movement during treatment, and positioned with their arms above their head, in the supine position. The DiscoveryRT scanner (GE Healthcare, Waukesha, WI, USA) with a real-time position management system (Varian Medical System, Palo Alto, CA, USA) was used to scan each patient. A set of 4D-CT images was obtained using phase-based binning, with a resolution of 0.977 mm × 0.977 mm × 2.5 mm, using 120 kVp and 300 mA, and covering the area from 2 cm above the jaw to the second lumbar vertebra. Each patient was scanned under free-breathing conditions. The waveform generated by the breathing track system was used during scanning to visually confirm that the breathing pattern was maintained uniformly and reproducibly. For patients requiring respiratory-GR, it was necessary to outline the position of the reflective block marker (with 2 reflecting dots) placed between the xiphoid and umbilicus to ensure that the respiratory signals collected during treatment closely matched those obtained during simulation. These procedures were applied to all the patients involved in this study.

Target and organ at risk (OAR) delineation

After the 4D-CT scan was completed, the data were transmitted via the Digital Imaging and Communications in Medicine (DICOM) protocol to the treatment planning

system (TPS) Eclipse for delineation of the target volume and organs at risk (OARs). For patients who required gated treatment, the physician delineated the gross tumor volume (GTV) at selected respiratory phases in the lung window [between –600 and 1,600 Hounsfield units (HU)], and accumulated the GTVs from these phases to the maximum intensity projection (MIP). The MIP was generated based on images acquired at the chosen respiratory phases (commonly between 30% and 60% phases), ensuring that the residual tumor motion was kept within 5 mm. The internal target volume (ITV) was created after ensuring that no tumor was missed under 4D play, and subsequently, the ITV was copied (via rigid registration) to the average intensity projection (AIP), which was also generated from the selected respiratory phases. An additional 0.5-cm isocentric margin was added to the ITV to create the planning target volume (PTV). For non-gated patients, the only difference was that the physician delineated the GTV throughout all the respiratory phases, and both the MIP and AIP were generated from all respiratory phases. The following OARs were outlined: the heart, esophagus, spinal cord, great vessels, chest wall, bronchus, and lungs.

Treatment planning

In this study, all the treatment plans were created using the Eclipse (version 15.6, Varian Medical Systems, Palo Alto, CA, USA) TPS. Dose calculation was performed on three-dimensional (3D) images that did not include respiratory phases, such as the average image. Whether the lung SBRT plan was gated or non-gated, typically 10 to 12 coplanar static photon beams were employed without rotating the collimator angles. To shorten treatment time and minimize the effect of respiratory motion on dose delivery, a 6-MV flattening filter-free energy mode was used. To address tissue inhomogeneity, the Acuros XB algorithm was employed for dose optimization. The dose calculation grid size was set to 1.25 mm. The prescription dose ranged from 40 to 50 Gy in 5 to 10 fractions, prescribed to an isodose line ≥80%. All plans were required to meet the prescription dose covering 95% of the PTV volume, and 90% of the prescription dose needed to encompass 99% of the PTV volume, with the prescription dose line also encircling 99% of the ITV volume. The dose fall-off outside the target and the dose limits for critical organs met the requirements specified by the Radiation Therapy Oncology Group (RTOG) 0813 guidelines (28).

Cone-beam computed tomography (CBCT) imaging

The on-board imaging system of the Varian TrueBeam (Varian Medical Systems, Palo Alto, CA, USA) was used to perform 3D CBCT and 4D CBCT imaging. Prior to image acquisition, each patient was immobilized in the same position as that used for the 4D-CT simulation to ensure consistency in patient setup. For patients undergoing gated SBRT, a reflective block was strategically placed to mirror the position in the 4D-CT scan, allowing for precise tracking of respiratory signals. Position verification for non-gated patients was achieved by registering the 3D-CBCT images with the planning computed tomography (CT). For the gated patients, average density projections were derived from the gated phases; these projections were then registered with the planning CT to verify patient positioning. Radiotherapy could proceed only after translational discrepancies were confirmed to be within 3 mm, and rotational discrepancies within 1°. Additionally, the tumor and anatomical structures were validated prior to each treatment by the radiation oncologist to ensure precise treatment delivery. 3D-CBCT or 4D-CBCT images were obtained at every fraction.

sCT and accumulated dose calculation

The planning CT was designated as the reference image in VelocityAI (version 3.2.0, Velocity Medical Solutions, Atlanta, Georgia, USA), while subsequent CBCT images or 4D-CBCT subset images were used as secondary images. Prior to proceeding, two sets of images were aligned manually by referring to the bony structures. Following this, a rigorous registration process was initiated between the planning CT and the daily CBCT or 4D CBCT images. Next, a CBCT correction procedure was executed to enhance low-signal regions of the CBCT and apply a fade correction before the subsequent registration. Deformable image registration (DIR) was performed using modified B-spline deformable registration with mutual information-based matching. To ensure the quality of the DIR, a manual evaluation was conducted on the deformable vector field (DVF). Anatomical landmarks, such as the bifurcation of major vessels and airways, were used to assess the accuracy of the DIR. After the operator verified that the deformation was satisfactory, a set of sCT images were produced by deforming of the planning CT according to the DVF. For dose calculations, the sCT was then exported to the Eclipse TPS.

In the Eclipse TPS, the CT couch was replaced, and the original plan was copied to the sCT for dose recalculation, ensuring that all beam settings were consistent with the original treatment plan. Subsequently, using the previously obtained DVF, the dose recalculated on the sCT was deformed back to the planning CT through Velocity. The above operations were repeated for all fractions of the CBCT or 4D-CBCT subsets. Next, after each fraction dose that had been deformed back to the planning CT was scaled, the doses of all fractions were accumulated to obtain the actual dose under the treatment position. The dose distribution calculated from the planning CT was referred to as the original (or planned) dose distribution. The dose distribution obtained from the sCT was referred to as the accumulated dose distribution. The following dosimetric parameters were obtained in the original and accumulated plans: ITV: minimum dose (ITV_D_{min}), mean dose (ITV_D_{mean}), maximum dose (ITV_D_{max}), and volume receiving prescription dose (ITV_$V_{100\%PD}$); PTV: minimum dose (PTV_D_{min}), mean dose (PTV_D_{mean}), maximum dose (PTV_D_{max}), volume receiving prescription dose (PTV_$V_{100\%PD}$), and volume receiving 90% prescription dose (PTV_$V_{90\%PD}$); and the maximum dose for the great vessels, esophagus, heart, spinal cord, and chest wall, respectively.

Statistical analyses

In this study, the dosimetric parameters for both gated and non-gated lung SBRT were reported as the mean with the standard deviation (mean ± SD). To assess the relative dosimetric difference between the original and accumulated plan for both gated and non-gated SBRT, the following formula was employed: [(accumulated plan – original plan)/original plan] ×100%. The outcomes are expressed as median values accompanied by their respective ranges in percentage terms. Missing data were addressed using imputation techniques and sensitivity analyses to ensure the robustness and reliability of the results. The Mann-Whitney *U* test was used to evaluate the statistical significance of the discrepancies observed between the original and accumulated plans. The Kruskal-Wallis test was also used to assess the effects of various factors, such as tumor location, tumor size, and tumor motion range, on the dosimetric outcomes. Given the exploratory nature of this research, no correction for multiple testing was applied. All the statistical analyses were conducted using SPSS software (Version 27.0, SPSS Inc., Chicago, Illinois, USA). A P value of less than 0.05 was considered statistically significant.

Results

Dosimetric variations between gated and non-gated SBRT

As *Table 2* shows, we observed significant variances in multiple dosimetric parameters between the original and accumulated plans for both gated and non-gated SBRT techniques. For the ITV, the gated SBRT technique exhibited median relative changes of –0.44% for the minimum dose (D_{min}), –0.33% for the mean dose (D_{mean}), and –0.49% for the maximum dose (D_{max}), indicating higher precision in dose adherence and deposition compared to the non-gated SBRT. The non-gated SBRT technique showed larger median relative reductions of –6.62% for D_{min}, –3.54% for D_{mean}, and –0.07% for D_{max}, with D_{min} showing a statistically significant differences (P<0.001 for the D_{min}, P=0.60 for the D_{mean}, and P=0.29 for the D_{max}). Additionally, the change in $V_{100\%PD}$ was statistically significant, with no change (0%) in gated SBRT and a –0.04% reduction in non-gated SBRT, with a statistically significant difference (P=0.03). Regarding the PTV, non-gated SBRT showed a significant median relative decrease in D_{min} (–20.29%, P=0.01), D_{mean} (–2.6%, P=0.007), $V_{90\%PD}$ (–5.37%, P=0.006), and $V_{100\%PD}$ (–15.39%, P=0.03) compared to gated SBRT. Conversely, gated SBRT had smaller median relative changes of –12.28% in D_{min}, –1.04% in D_{mean}, –1.69% in $V_{90\%PD}$, and –10.5% in $V_{100\%PD}$, indicating that dose delivery was more consistent with the gated technique.

When assessing the effects on surrounding critical structures, such as the great vessels, esophagus, heart, spinal cord, and chest wall, both techniques showed negligible median relative changes in D_{max}, with no significant differences in most of these comparisons. As shown in *Figure 1*, gated SBRT presented a smaller dose discrepancy compared to non-gate SBRT. The dosimetric parameters, including D_{min}, D_{mean}, D_{max}, $V_{90\%PD}$, and $V_{100\%PD}$, exhibited a higher degree of consistency with the treatment plan using the gated SBRT method.

The effect of technique, tumor location, and volume on dosimetric variations

We conducted a comprehensive analysis to investigate the dosimetric deviations between the gated and non-gated SBRT techniques (see *Table 3*). The results demonstrated a significant improvement in the dosimetric precision of gated SBRT compared to non-gated cases. Specifically, the minimum dose to the ITV (ITV_D_{min}) and PTV (PTV_D_{min}), as well as the mean dose to the PTV (PTV_D_{mean}),

Table 2 Comparison of dosimetric changes between gated SBRT and non-gated SBRT

Variables	Gated SBRT			Non-gated SBRT			Relative change (median)		
	Original plan	Accumulated plan	P value	Original plan	Accumulated plan	P value	Gated SBRT	Non-gated SBRT	P value
ITV									
D_{min} (Gy)	48.91±5.52	47.76±6.08	0.13	50.49±6.21	46.13±8.35	<0.001	–0.44%	–6.62%	<0.001
D_{mean} (Gy)	53.73±4.37	53.39±4.33	0.02	53.48±6.07	52.97±5.94	<0.001	–0.33%	–3.54%	0.60
D_{max} (Gy)	55.92±4.52	55.70±4.51	0.06	55.05±6.12	54.95±6.25	0.61	–0.49%	–0.07%	0.29
$V_{100\%PD}$ (%)	98.47±4.74	97.43±6.51	0.21	99.93±0.22	98.36±2.94	<0.001	0.00%	–0.04%	0.03
PTV									
D_{min} (Gy)	44.22±3.86	37.86±5.97	<0.001	43.94±4.53	32.63±7.58	<0.001	–12.28%	–20.29%	0.01
D_{mean} (Gy)	52.06 ±3.73	51.20±3.68	<0.001	51.67±5.42	50.08±5.19	<0.001	–1.04%	–2.6%	0.007
D_{max} (Gy)	55.94±4.53	55.70±4.52	0.03	55.16±6.09	55.01±6.19	0.61	–0.53%	–0.73%	0.31
$V_{90\%PD}$ (%)	99.99±0.03	96.47±4.99	<0.001	99.98±0.05	92.69±6.53	<0.001	–1.69%	–5.37%	0.006
$V_{100\%PD}$ (%)	93.66±3.90	83.87±9.28	<0.001	94.37±1.54	78.16±11.77	<0.001	–10.5%	–15.39%	0.03
D_{max} (Gy)									
Great vessels	17.18±12.75	17.45±13.49	0.80	17.19±15.63	17.29±16.08	0.92	–0.22%	–0.69%	0.98
Esophagus	9.80±4.4	9.53±4.46	0.004	9.81±3.49	9.54±3.55	0.07	–2.12%	-4.45%	0.46
Heart	14.62±8.83	14.62±9.67	0.11	18.31±10.33	17.46±9.57	0.002	–1.34%	–1.53%	0.43
Spinal cord	9.51±3.36	9.30±3.37	0.01	8.87±3.47	9.03±4.01	0.50	–1.76%	–0.60%	0.23
PBT	13.86±14.66	14.86±15.28	<0.001	12.85±15.13	12.59±14.58	0.90	4.48%	0	0.28
Chest wall	40.10±10.96	40.34±11.32	0.86	40.59±11.06	40.89±11.33	0.81	–0.24%	–6.70%	0.63

Data are presented as mean ± SD. SBRT, stereotactic body radiation therapy; ITV, internal target volume; PTV, planning target volume; D_{min}, minimum dose; D_{mean}, mean dose; D_{max}, maximum dose; $V_{90\%PD}$, volume receiving 90% prescription dose; $V_{100\%PD}$, volume receiving 100% prescription dose; PBT, proximal bronchial tree; SD, standard deviation.

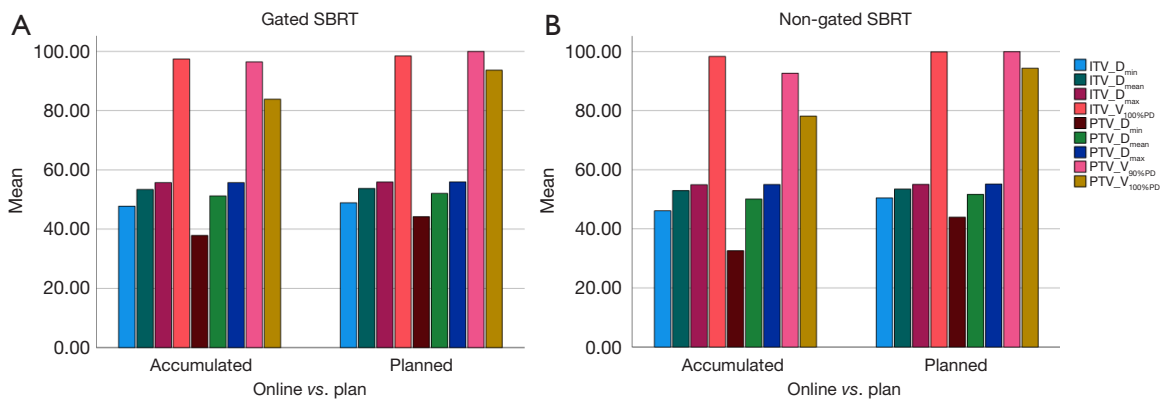

Figure 1 Comparison of the mean dosimetric parameters between accumulated and planned dose distributions in gated SBRT (A) and non-gated SBRT (B). SBRT, stereotactic body radiation therapy; ITV, internal target volume; PTV, planning target volume; D_{min}, minimum dose (Gy); D_{mean}, mean dose (Gy); D_{max}, maximum dose (Gy); $V_{100\%PD}$, volume receiving 100% prescription dose; $V_{90\%PD}$, volume receiving 90% prescription dose.

Table 3 Statistical analysis of dosimetric deviations in gated *vs.* non-gated SBRT and their relationship with location and ITV volume

Dosimetric variables	P value					
	Technique	Location* technique			ITV_volume* technique	
		LLCR (n=12)	LLPR (n=21)	RLPR (n=18)	Small (n=50)	Median (n=7)
ITV_D_{min}	<0.001	0.03	0.43	0.10	<0.001	1.00
ITV_D_{mean}	0.60	1.00	1.00	0.57	0.60	1.00
ITV_D_{max}	0.29	0.03	1.00	1.00	0.10	0.23
ITV_$V_{100\%PD}$	0.03	0.49	0.28	0.70	0.03	0.63
PTV_D_{min}	0.01	0.04	0.43	0.32	0.045	0.40
PTV_D_{mean}	0.007	0.39	0.39	0.15	0.008	1.00
PTV_D_{max}	0.31	0.03	0.81	0.76	0.07	0.11
PTV_$V_{90\%PD}$	0.006	0.09	0.39	0.07	0.02	0.63
PTV_$V_{100\%PD}$	0.03	0.49	1.00	0.15	0.03	1.00

*, interrelationship. SBRT, stereotactic body radiation therapy; ITV, internal target volume; PTV, planning target volume; D_{min}, minimum dose; D_{mean}, mean dose; D_{max}, maximum dose; $V_{90\%PD}$, volume receiving 90% prescription dose; $V_{100\%PD}$, volume receiving 100% prescription dose; LLCR, left lower central region of lung; LLPR, left lower peripheral region of lung; RLPR, right lower peripheral region of lung; Small, refers to ITV volume smaller than 20 cc; Medium, refers to ITV volume between 20 and 40 cc.

showed statistically significant differences favoring the gated technique, with P values of <0.001, 0.01, and 0.007, respectively. Additionally, the volumes receiving 90% and 100% of the prescribed dose in the PTV (PTV_$V_{90\%PD}$ and PTV_$V_{100\%PD}$) were significantly better with gated SBRT, with P values of 0.006 and 0.03, respectively.

Further, the interaction between tumor location and the chosen technique revealed that the benefits of the gating technique were particularly pronounced in the left lower central lung region (LLCR) for ITV_D_{min} and PTV_D_{max}, with P values of 0.03 in both cases. Similarly, for small ITVs (smaller than 20 cc), gated SBRT demonstrated a significant difference with P values of <0.001 for the ITV_D_{min} and 0.03 for PTV_$V_{100\%PD}$.

The boxplots in *Figure 2A-2G* illustrate the dosimetric variations between gated and non-gated SBRT. These plots show tighter interquartile ranges and medians closer to zero for gated SBRT across most dosimetric variables, indicating reduced variation and enhanced dose delivery accuracy. The dosimetric variations by location (LLCR) and ITVs (small) support the findings from the P value analysis, further demonstrating that gated SBRT provides improved precision, particularly in treatments involving small and challenging target volumes in specific anatomical locations.

Our non-parametric correlation analysis revealed a significant negative correlation between motion range and ITV size (Spearman's rho =–0.362, P=0.049), indicating that smaller ITVs tended to exhibit relatively larger motion ranges. This result was consistent with findings from an independent-samples Kruskal-Wallis test (see *Figure 3*). The distribution for small motion ranges showed a broad spread of ITVs, which may be partly due to the smaller sample size for larger ITVs (one case for gated SBRT) in this motion range.

Discussion

Dosimetric variations between non-gated and gated SBRT

The use of respiratory-gated radiation therapy for lung SBRT has increased in recent years (29), necessitating careful analyses and quantitative evaluation of cumulative and original dose variations which may occur during SBRT using these motion-management techniques. This evaluation is crucial to guarantee the accuracy and effectiveness of the treatment. Several studies have investigated these deviations and the factors that influence them. Yue *et al.* (30) developed a method to quantify the dose delivered to the residual tumor in lung SBRT patients, validating their technique with clinical data and observing a 10% deviation from the prescription dose during the inhale phase for patients with large tumor motion. Zhao *et al.* (31) found that up to half of their patients experienced significant

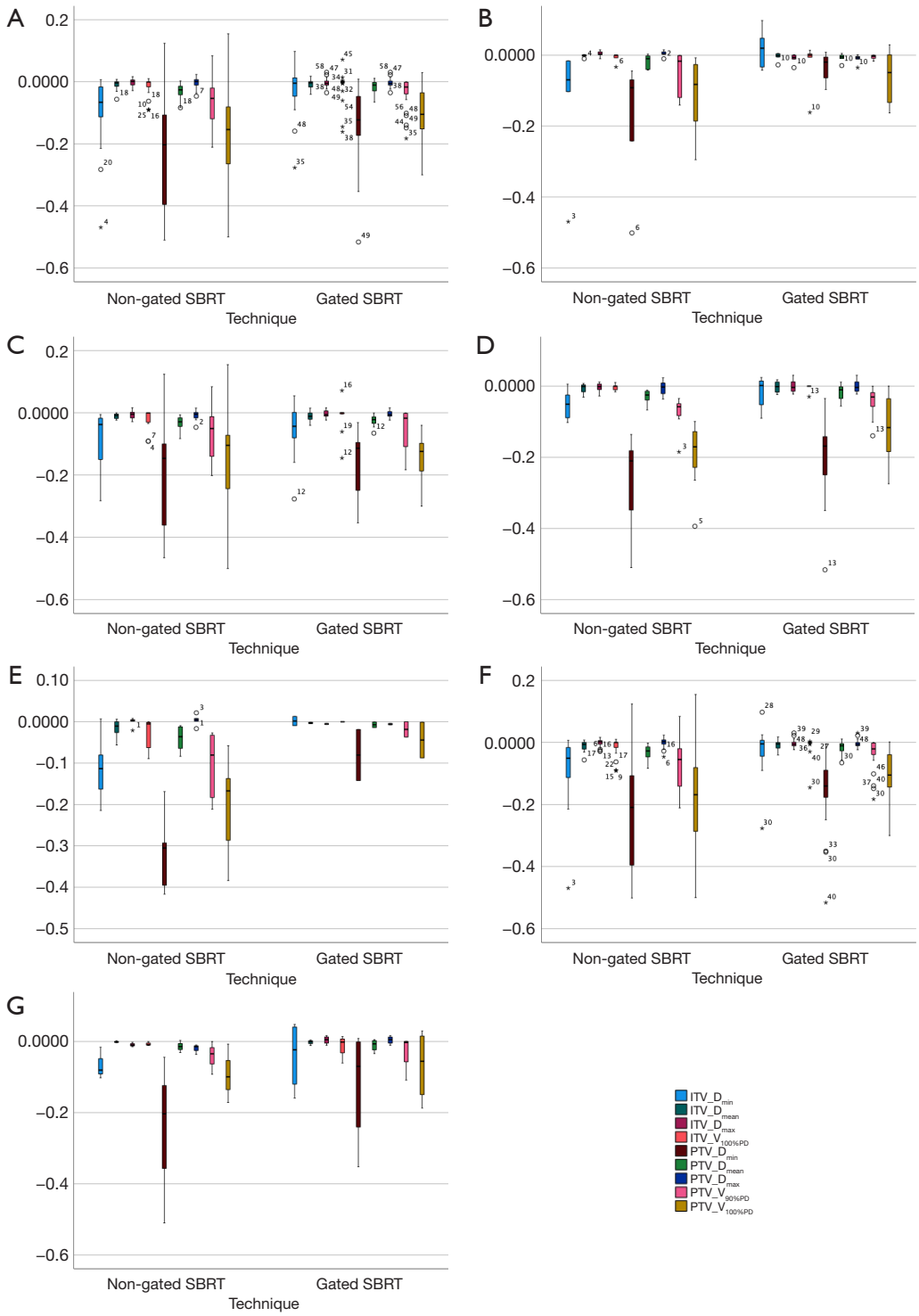

Figure 2 Comparative analysis of relative dosimetric variations (%) in SBRT: (A) overall technique differences; (B) effects of tumor location (LLCR); (C) effects of tumor location (LLPR); (D) effects of tumor location (RLPR); (E) effects of tumor location (other); (F) small ITV, and (G) medium ITV. The Y-axis represents the relative percentage difference in dosimetric parameters between non-gated and gated SBRT techniques. *, outlier, and the numbers in these figures represent individual cases corresponding to the relative dosimetric variations analyzed in this study. Other, refers to regions of the lung that are outside those previously mentioned. SBRT, stereotactic body radiation therapy;

ITV, internal target volume; PTV, planning target volume; D_{min}, minimum dose; D_{mean}, mean dose; D_{max}, maximum dose; $V_{100\%PD}$, volume receiving 100% prescription dose; $V_{90\%PD}$, volume receiving 90% prescription dose; LLCR, left lower central region of lung; LLPR, left lower peripheral region of lung; RLPR, right lower peripheral region of lung.

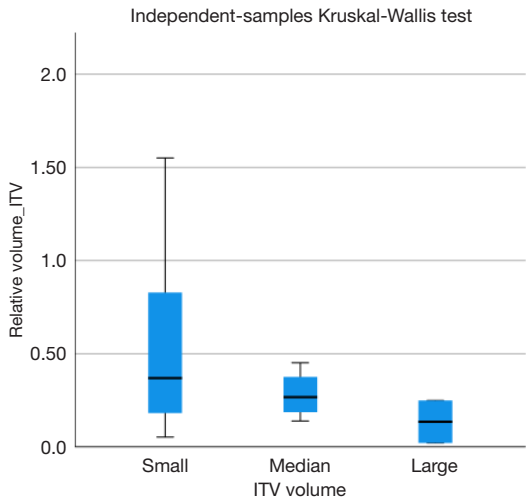

Figure 3 The relative volume change (%) of gated SBRT between gated phases and whole phases across different ITV sizes. Small, refers to ITV volume smaller than 20 cc; Medium, refers to ITV volume between 20 and 40 cc; Large, refers to ITV volume larger than 40 cc. ITV, internal target volume; SBRT, stereotactic body radiation therapy.

deviations in the prescribed dose during gated lung SBRT delivery, with deviations of up to 26% intrafractionally and 14% overall. Understanding the actual versus planned dose deviation is critical in refining the individual institutional treatment protocols (32) and optimizing patient outcomes (31,33,34). It is particularly essential to compare gated and non-gated SBRT to identify best practices that minimize dose discrepancies, thereby enhancing the precision and efficacy of lung SBRT treatments. Such comparisons could provide key insights into the optimization of treatment delivery for patients with varying respiratory patterns, tumor sizes and motions.

In the present study, the key findings indicated a more uniform dose distribution in gated SBRT, as evidenced by significant improvements in the D_{mean} for the ITV and PTV, and a notable reduction in dose deviations. Conversely, non-gated SBRT exhibited greater reductions in the D_{min}, pointing to potential underdosing. Moreover, the variability in dosimetric changes was found to be more significant in the non-gated cohort. These results emphasize the importance of gating techniques in managing tumor motion due to breathing, enhancing dose conformity, and ensuring precision. The smaller median relative changes in the D_{min}, D_{mean}, and D_{max} for the ITV in gated SBRT (–0.44%, –0.33%, and –0.49%, respectively) demonstrate a higher precision in dose adherence. This finding aligns with recent studies suggesting that motion management techniques can significantly reduce dose deviations caused by physiological movements (35,36). The larger median relative reductions in the D_{min} (–6.62%), D_{mean} (–3.54%), and D_{max} (–0.07%) for non-gated SBRT highlight the challenges in maintaining dose accuracy without motion management techniques. This observation is consistent with previous research indicating that non-gated SBRT may lead to substantial dose deviations (4), potentially causing treatment failure (37) and severe side effects (38), particularly in cases of high intra-fraction motion (39). The tighter interquartile ranges for gated SBRT, especially for the PTV parameters, showed less variability compared to non-gated SBRT cases. However, the presence of outliers in both methods indicates that some patient characteristics, such as the location and size of the tumor, may still significantly affect dose distribution independently (6,40,41), which can be a subject for further investigations.

The effects of technique, tumor location, and volume on dosimetric deviations

The impact of respiratory motion control technique (gated SBRT *vs*. non-gated SBRT), tumor size, and tumor location on potential dosimetric differences are an important consideration in lung SBRT treatment planning (42). Understanding how these factors interact could help optimize the treatment approach and minimize dose deviations. Sarudis *et al*. (43) conducted a study to evaluate the motion distribution of lung tumors in 126 patients treated with SBRT and found that tumor motion was primarily in the inferior-superior direction, with larger motion amplitudes for tumors located in the middle and lower parts of the lung. However, tumor size was not correlated with motion amplitude in any direction. Aridgides *et al*. (44) reported that SBRT with advanced respiratory management showed similar efficacy to the

all-phase treatment approach for stage I NSCLC cases. They noted that tumor location in the lower lung regions (which move more longitudinally) was more common in those treated with advanced respiratory management compared to all-phase treatment, highlighting the potential importance of respiratory motion management based on tumor location. These studies emphasize the importance of examining the interplay among factors such as tumor size, location, and the technique chosen in determining the ultimate dosimetric outcomes of lung SBRT.

In the present study, we found that the benefits of respiratory motion control provided by gating methods were particularly significant for tumors located in the LLCR, where the minimum dose to the ITV and the maximum dose to the PTV were both significantly improved. This suggests that gating techniques are not only generally useful but also crucial for tumors situated in challenging locations where diaphragmatic movements can create significant dosimetric variations that could compromise treatment effectiveness (19,20,43). Moreover, our findings suggest a possible correlation between ITV and motion range, with smaller ITVs displaying larger motion ranges. This observation aligns with some studies (42,45), though other research has reported no such correlation (43,46). This is a critical consideration, as it highlights the increased needs for gating in small-volume tumors that may be subject to greater motion-related dosimetric uncertainty, and/or localization issues.

The findings of this study contribute to the growing body of evidence that personalized radiotherapy, which tailors treatment modalities to individual patients and tumor characteristics, has the potential to optimize dosimetric and possibly clinical outcomes. The stratified analysis based on the tumor location and ITV demonstrates that a one-size-fits-all approach may not be appropriate in radiotherapy for NSCLC. This has profound implications for clinical practice, where treatment decisions may need to be more dynamic and adapted to each patient's unique clinical presentation.

An important, novel aspect of this study includes the successful integration of 4D-CT simulations with sCT methods to accurately quantify and reflect potential dose deviations. This integration represents a step forward in the application of computational imaging in radiotherapy, as supported by the work of Czajkowski *et al.* (47). The study's contribution to understanding the dosimetric effect of gating techniques in SBRT adds to the growing body of evidence supporting the refinement of motion management protocols (32).

However, the limitations of this study should also be considered. The retrospective design inherently includes potential selection biases and confounding factors that were not controlled for during the analysis. Additionally, the study focused primarily on tumors located in the lower lobes, where motion is typically greater, which could influence the generalizability of the results. The sample size, while adequate for detecting statistical differences, might not fully represent the diversity of NSCLC case presentations. Prospective studies with larger sample sizes, different tumor locations and more diverse populations are warranted to validate these findings.

Conclusions

Our comprehensive analysis confirms the potential dosimetric benefits of gated SBRT over non-gated SBRT. Specifically, gated SBRT offers enhanced precision and adherence to planned doses. These improvements are more pronounced in certain cases, such as in the LLCR and with smaller ITVs, where precision is especially critical. The dosimetric consistency of gated SBRT suggests a potential for improved treatment outcomes; however, clinical studies are needed to further validate these results. The findings advocate for the broader implementation of gated SBRT, particularly in scenarios in which high precision is indispensable. This study highlights the advances and evolution in radiation therapy techniques and underscores the ongoing commitment to refining treatment modalities. Future research should focus on quantifying the clinical outcomes associated with the dosimetric advantages provided by gated SBRT to solidify its role in standard radiation therapy practice.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-992/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics board of Tongji University Affiliated Shanghai Pulmonary Hospital (No. K21-312Y), and informed consent was taken from all the patients.

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