Original Article

Comparison of Phase-Gated and Amplitude-Gated Dose Delivery to a Moving Target using Gafchromic EBT3 Film

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Abstract

Introduction: This study compared phase-gated and amplitude-gated dose deliveries to the moving gross tumor volume (GTV) in lung stereotactic body radiation therapy (SBRT) using Gafchromic External Beam Therapy (EBT3) dosimetry film. **Materials and Methods:** Eighty treatment plans using two techniques (40 phase gated and 40 amplitude gated) were delivered using dynamic conformal arc therapy (DCAT). The GTV motion, breathing amplitude, and period were taken from 40 lung SBRT patients who performed regular breathing. These parameters were re-simulated using a modified Varian breathing mini phantom. The dosimetric accuracy of the phase- and amplitude-gated treatment plans was analyzed using Gafchromic EBT3 dosimetry film. The treatment delivery efficacy was analyzed for gantry rotation, number of monitor unit (MU), and target position per triggering window. The time required to deliver the phase- and amplitude-gated treatment techniques was also evaluated. **Results:** The mean dose (range) per fraction was 16.11 ± 0.91 Gy (13.04–17.50 Gy) versus 16.26 ± 0.83 Gy (13.82–17.99 Gy) ($P < 0.0001$) for phase- and amplitude-gated delivery. The greater difference in the gamma passing rate was 1.2% ±0.4% in the amplitude-gated compared to the phase gated. The gantry rotation per triggering time (tt) was 2° ±1° (1.2°–3°) versus 5° ±1° (3°–6°) ($P < 0.0001$) and MU per tt was 10 ± 3 MU (6–13 MU) versus 24 ± 7 MU (12–32 MU) ($P < 0.0001$), for phase- versus amplitude-gated techniques. A 90 beam interruption in the phase-gated technique impacted the treatment delivery efficacy, increasing the treatment delivery time in the phase gated for 1664 ± 202 s 1353–1942 s) compared to 36 interruptions in the amplitude gated 823 ± 79 s (712–926 s) ($P < 0.0001$). **Conclusion:** Amplitude-gated DCAT allows for better dosimetric accuracy over phase-gated treatment patients with regular breathing patterns.

Keywords: Amplitude, moving target, phase, respiratory gating radiation therapy, stereotactic body radiation therapy

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Introduction

Lung stereotactic body radiation therapy (SBRT) is used for the treatment of early-stage nonsmall cell lung cancer and metastatic lung tumors.[1,2] SBRT treatments are delivered in a hypofractionation mode, with high doses in a few fractions (from 3 to 8 fractions), depending on tumor localization (central or peripheral tumors).[3] The treatment of lung cancer with high doses can be impacted by tumor motion and proximity to the organ at risk.[4-7] Various techniques were developed to take into consideration tumor motion during treatment delivery to accurately target the moving tumor and to spare healthy tissues.[8-10] The abdominal compression technique is used to reduce the breathing amplitude, reducing the amplitude of the tumor motion throughout the respiratory cycle.[8] Radiation during a certain phase of the respiratory cycle can be performed using respiratory gating radiation therapy (RGRT).[9] Real-time tumor tracking allows for tumor irradiation throughout the respiratory cycle.[10]

RGRT does not require controlled breathing or breath hold during simulation and dose delivery. There are three types of gating: phase gating, amplitude gating, and breath-hold gating techniques. With phase gating, the treatment is delivered during a certain phase of the respiratory cycle. With amplitude gating, the treatment is delivered when a chosen threshold of the breathing amplitude is reached, which is generally during the

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end exhalation of the respiratory cycle.[4,11-13] With breath-hold gating, treatment is delivered during breath-hold time with a well-defined threshold and used only to stop the respiratory motion.[14]

Four-dimensional-computed tomography (4D-CT) can be used to evaluate the waveform of the patient's respiration and to determine the overall tumor motion.[15] Image acquisition using the amplitude gating technique manages respiratory motion artifacts on the reconstructed images better than the phase-gated technique.[16] Furthermore, worse dosimetric results were obtained using the phase-gated mode for irregular breathing patterns, rather than with the amplitude-gated mode.[17]

The amplitude-gated technique allowed for a shorter treatment time than the phase gated, which is highly recommended if we want to ensure the accuracy of the treatment's dose delivery.[18-20] A shorter treatment time can reduce the impact of the patient's movement and intrafraction tumor variation.[21,22]

In this study, dose delivery to the moving target between the phase-gated and amplitude-gated techniques with a regular breathing amplitude was evaluated. In comparison to other studies, the target volumes (gross tumor volume [GTV] and lung tissues) were developed in-house, using materials with the same density as density found in the patient cohort (40 patients who underwent lung SBRT treatments). In addition, the breathing mini phantom (Varian Medical Systems, Palo Alto, CA, USA) was modified to perform the amplitude of tumor motion, the breathing amplitude, and period from the same patient cohort. The dynamic conformal arc therapy (DCAT) was used to deliver the dose to the moving target using phase-and amplitude-gated techniques. Furthermore, the efficacy of the RGRT treatment delivery was evaluated for a different gating window and target position, using cine mode.

Materials and Methods

The breathing amplitude depends on the patient's respiration, which can be regular or irregular.[23] In this study, only patients' respiratory waveforms with regular breathing patterns were used [Figure 1a].

Modification of the breathing mini phantom

The real-time position management (RPM) breathing mini phantom, combined with the external marker block, was used to simulate the respiratory motion. The motion of the breathing mini phantom can be performed in only one direction, the anteroposterior (AP) or z-direction, indicated with a yellow arrow [Figure 2a]. To simulate the breathing amplitude and tumor motion, two synchronized systems were needed. To obtain the synchronized motion, the breathing mini phantom was modified.

First, one potentiometer variable and one adapter variable were added, allowing variations in the amplitude of target motion, breathing amplitude, and period [Figure 2b]. Thereafter, another circle (white) was affixed to the initial circle (black) and carried by its motion. The added circle was shifted in phase from the initial circle, with attention to moving another platform (white) affixed on the other side of the breathing mini phantom (rotated by 90°) compared to the initial platform (black) [Figure 2c]. These two systems were synchronized to simulate the breathing amplitude in the AP or z-direction (yellow arrow) and target motion in the craniocaudal (CC) or y-direction (orange arrow) [Figure 2d].

The parameters of the amplitude of target motion, breathing amplitude, and period were taken from 40 lung SBRT patients who performed regular breathing patterns. These parameters were evaluated using the 4D-CT acquisition. The amplitude of target motion was 14 ± 6 mm (5–20 mm). The breathing amplitude (the difference between minimal and maximal displacements of the external marker block, located near the caudal end of the xiphoid processes during patient respiration) was 18 ± 3 mm (15–22 mm) and the breathing period was 4.3 ± 3.2 s (2.6–8.2 s).

Data acquisition

Image acquisition was performed using the GE LightSpeed CT (General Electric Medical Systems, Waukesha, WI,

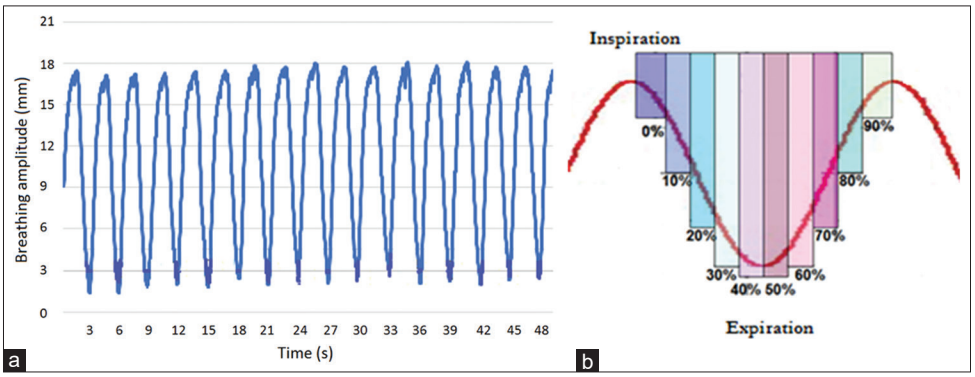

Figure 1: Shows a breathing curve of one patient sample with regular breathing patterns. (a) performed during the acquisition of a four-dimensional-computed tomography and taken from a Real-time Position Management System version 1.7 (RPM, Varian Medical Systems, Palo Alto, CA, USA). The patient's respiration is presented in a waveform with a respiratory cycle divided into ten equidistant phases, from 0% to 90% and with a step of 10% between phases. (b) The maximum breathing amplitude corresponds to 0% phase (end of inspiration), while the minimum breathing amplitude corresponds to 50% phase (end of the expiration)

USA) equipped with the RPM System (RPM, Varian Medical Systems, Palo Alto, CA, USA). The acquisition of regular breathing patterns was performed using an infrared charged coupled device camera mounted on the treatment couch, which captured the motion of a block marker placed on the platform of the modified breathing mini phantom. The helical CT and the 4D-CT were acquired using the following parameters for all of the patients: 120 kV, mA ranged from 10 to 440 mA, automatic exposure control turned on, 0.7 s/rotation period, 20-mm beam collimation width (16 slice detector and slice thickness of 1.25 mm), and field of view of 55 cm. The same protocol was used for a lung SBRT treatment with a small tumor size (≤5 cm), as well as for the breathing mini phantom.

After the helical CT acquisition, the 4D-CT acquisition was performed and the gating window was determined, depending on the phase or amplitude. The image reconstruction was performed retrospectively, sorting axial images into a series of 3D-CT images based on their breathing phases [Figure 1b] and slice positions.[24]

Treatment volume

First, the Pinnacle 9.10 treatment planning system (TPS) (Koninklijke Philips N. V., Amsterdam, The Netherlands) was used to evaluate the median values of the GTV and lung densities, as median values of the GTV diameter, taken from 40 lung SBRT patients.

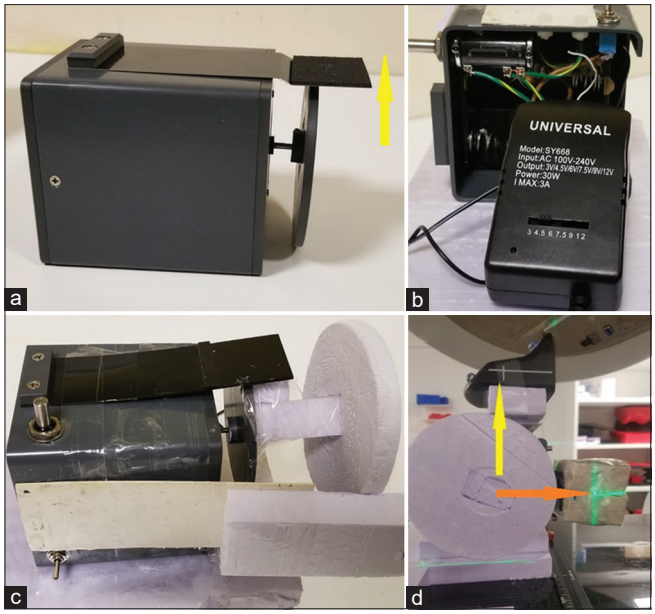

Figure 2: The steps of the breathing mini phantom modifications. The breathing mini phantom performed motion in the anteroposterior or z-direction, indicated with a yellow arrow (a). One potentiometer variable and one adapter variable were added, allowing variations in the amplitude of target motion, breathing amplitude, and period (b). Another platform and another circle were added to create two synchronized systems (c), simulating a breathing amplitude in the anteroposterior or z-direction (yellow arrow) with regular patterns and tumor motion in the craniocaudal direction (orange arrow) (d)

Successively, the treatment volumes (GTV and lung tissues) were developed in-house, using materials with a corresponding density. The target was fabricated as two hemispheres (yellow) with a diameter of 26 mm using Palavit (copolymer methacrylate of methyl) and resin for permanent models, with a density of 1.32 g/cm^3.

The target was inserted into a cube (mineral fiber) with a medium density of 0.34 g/cm^3, which corresponded to lung density.

A GTV-sized EBT3 dosimetry film (26 mm diameter) was placed in the target (black circle – irradiated film with planned dose per fraction) to measure the delivered dose to the GTV [Figure 3]. Together, they were attached to the platform of the breathing mini phantom [Figure 2d], to perform motion in a CC direction.

Delineation

In this study, the stability in the GTV motion was found during the end-expiration, between 30% and 60% phase. The 50% phase was chosen as a reference scan to perform the GTV delineation.

To consider tumor deformation and/or tumor instability between stable phases, the internal GTV (IGTV) was created within the stable phases (30%–60%), near the end exhalation of the respiratory cycle. The planning target volume (PTV) was created from the IGTV, adding isotropic margins of 3 mm.

Treatment planning

The treatment was planned within the 50% phase, used as a reference scan, and in the Pinnacle 9.10 TPS, with two partial dynamic conformal arcs, from 0° to 179.9°, where the multileaf collimator (MLC) was fitted to target each 5°. The treatment field size was 5 cm × 5 cm, created with an MLC (HD 120, with leaves of 2.5 mm in the center and 5 mm in the periphery) of the TrueBeam Novalis STx (Varian Medical Systems, Palo Alto, CA, USA). After that, the target was surrounded by secondary collimating jaws to reduce interleaf leakage.

The dose was calculated using the collapsed cone convolution algorithm, with a grid size of 2 mm, 6 MV beams, and a dose

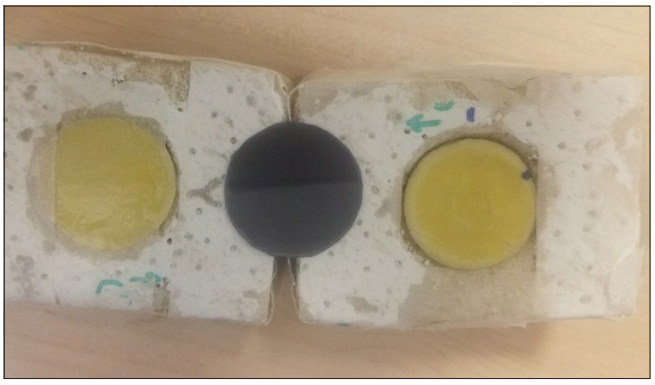

Figure 3: Treatment volume represented by the tumor (two yellow semicircles, left and right), inserted into a cube with mineral fiber and a black circle (in the middle) presenting an irradiated EBT3 dosimetry film

rate of 600 monitor unit (MU)/min. For all patients, the dose regimen of 60 Gy in 4#s over 1 week was prescribed. The prescription was normalized to 80% isodose lines. The planned dose to the moving GTV was 16.21 ± 0.46 Gy per fraction, delivered at 890 ± 10 MU.

Treatment delivery

The mechanical and electronic modifications allow the breathing mini phantom to simulate different amplitudes of the tumor motion, breathing amplitude, and period. The same parameters were used for both techniques, phase and amplitude gated (in total 80 deliveries), to compare the dose delivered to the moving GTV with regular breathing patterns. For the phase gated, four phases were used between 30% and 60% (found in 85% of the patient cohort). In the amplitude gated, treatments were delivered using a gating window based on a third of the breathing amplitude of 7 ± 1 mm (6–8 mm) observed in the patients' cohort and at the end-expiration. The breathing period varied from 2 to 8 s, as observed in the cohort.

To evaluate GTV stability and position in the predetermined gating window, cine mode was used during the treatment delivery. The GTV position within the gating window was evaluated as the distance from the center of the target and center of the beam.

Furthermore, the gantry rotation and number of MUs were evaluated for the entire triggering time.

Film analysis

The dose delivered to the Gafchromic ETB3 dosimetry film was analyzed after 24 h post irradiation. The films were scanned using the Epson color scanner 11000XL (Seiko Epson Corporation, Nagano, Japan) and analyzed in the Film QA Pro software (Ashland Advanced Materials, Bridgewater, NJ, USA). The minimum, median, and maximum doses delivered to the moving target were evaluated. Furthermore, the global gamma analysis was performed with 3% dose difference and 3 mm distance to the agreement of the (DTA) gamma criteria.

Data analysis

A paired sample *t*-test (significance level: $P < 0.05$) was used to evaluate the significance of the dose delivered to the moving GTV, the duty cycle, the treatment time, the gantry rotation (per triggering window), and the number of MU (per triggering window), using the Origin Pro 8.6 software (Northampton, MA, USA).

Results

The mean dose delivered to the moving target was greater using amplitude gated 16.26 ± 0.83 Gy (13.82–17.99 Gy), rather than phase gated 16.11 ± 0.91 Gy (13.04–17.50 Gy) ($P < 0.0001$). The gamma passing rate was 99.1% ± 0.6% (98.4%–99.4%) in the phase gated, compared to 99.4% ± 0.4% (98.8%–99.8%) in the amplitude gated ($P < 0.001$). The greater difference in the gamma passing rate was 1.2% ±0.4% in the amplitude gated compared to phase gated.

Table 1 compares the results of the duty cycle, the gantry rotation (per triggering window), the number of MUs (per triggering window), and the *P* value between phase- and amplitude-gated techniques.

The value of the duty cycle impacts on treatment delivery time. A larger duty cycle (59%) decreases treatment delivery time in the amplitude-gated technique 823 ± 79 s (712–926 s), compared to a lower duty cycle (30%) which increases treatment delivery time in the phase gating technique 1664 ± 202 s (1353–1942 s) ($P < 0.0001$). These results are provided by a larger number of beam interruptions of 90 in the phase gated, compared to 36 beam interruption in the amplitude-gated technique.

The treatment delivery was evaluated by comparing the duty cycle between the phase- and amplitude-gated techniques, which is presented with a gating window [Figure 4].

Choosing a breathing amplitude with a threshold of 6 mm, a larger duty cycle was obtained using the amplitude gated (53.3%), rather than the phase gated, using a threshold of 30%–60% phases for a duty cycle of 29.8%, during the same breathing amplitude (12.5 mm) and period (2.7 s) [Figure 4].

To evaluate the dose delivery's efficacy with the linear accelerator TrueBeam STx (Varian), using the RGRT technique and observing the tumor's presence in the predetermined gating window (30%–60%), the same breathing period (3.7 s) was used, and the tumor position and phase in the gating window were changed [Figure 5].

Within the planned parameters, the GTV stayed in the middle of the gating window during treatment delivery, receiving the planned dose of 16.21 Gy [Figure 5a]. In this case, the GTV distance from the center of the beam was <1 mm.

In Figure 5b and c, the GTV was moved within the gating window (shifted ≤3 mm from the center of the beam), staying within the treatment volume and receiving the planned dose (16.21 Gy).

The parameters such as the gating window of 40%–70% and a displacement from the isocenter of 3 mm, clinically inadequate, allowed the GTV to move outside of the gating window. The distance from the center of the beam was 5 ± 2 mm (4–7 mm), and the moving GTV received only 9.72 Gy of the planned dose (16.21 Gy) [Figure 5d].

Table 1: Duty cycle, gantry rotation, and monitor units were compared between phase-and amplitude-gated techniques, per triggering window

Parameters	Phase	Amplitude	*P*
Duty cycle (%)	30±4 (26-32)	59±12 (43-78)	<0.0001
Gantry rotation (°)	2±1 (1.2-3)	5±1 (3-6)	<0.0001
MU	10±3 (6-13)	24±7 (12-32)	<0.0001

MU: Monitor units

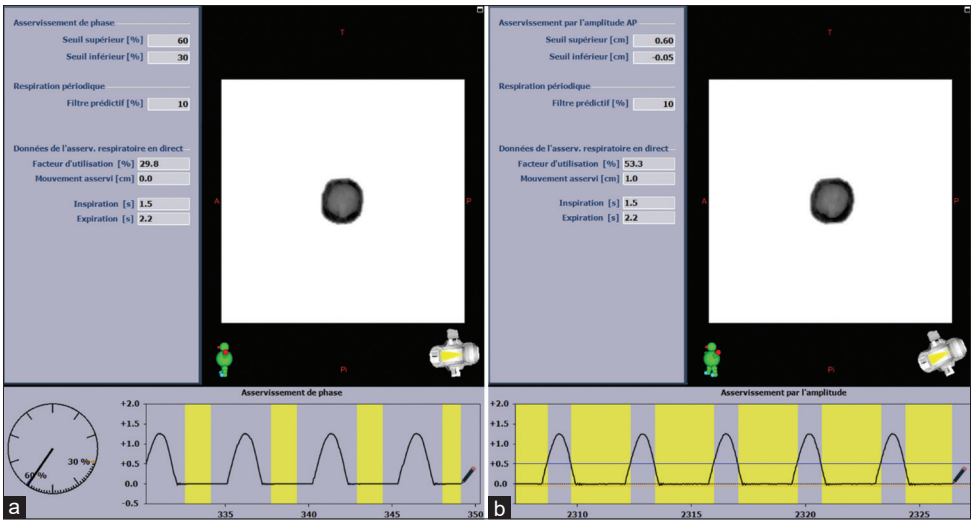

Figure 4: Comparison of the duty cycle between the phase (a) and amplitude (b) gating techniques

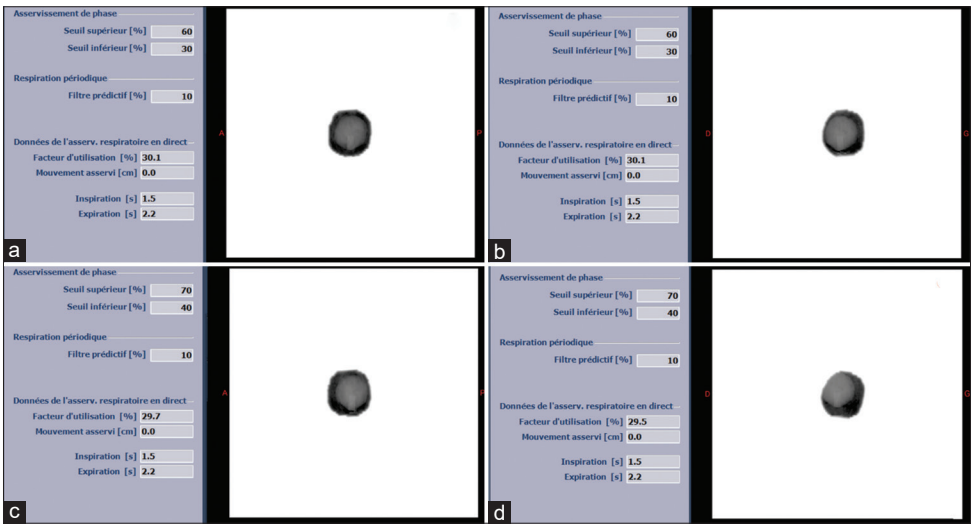

Figure 5: The tumor was stable during treatment delivery and with chosen adequate parameters (gating window [30%–60% phases], breathing cycle [3.7 s], and position in the isocenter) (a). The gross tumor volume motion within the gating window was observed when the tumor shifted (3 mm) from the isocenter (b). The gross tumor volume motion within the gating window was observed for a different gating window (40%–70%) (c), and tumor motion outside the gating window was observed within inadequate parameters (when the tumor shifts from the isocenter [3 mm] and by changing the gating window [40%–70%]) (d)

Discussion

In this study, the dose delivered to the moving GTV was evaluated with a DCAT, for the phase- and amplitude-gated techniques, using in-house treatment volume.

In phase gated, the dose delivered to the moving target is underestimated by 0.6% (0.10 Gy), while amplitude gated overestimated the dose delivered to the moving target by 0.3% (0.05 Gy) compared to the planned dose (16.21 Gy). For the different respiratory cycles, the gantry rotation varies by 1.8°, MU by 7, the duty cycle of 6%, and with a variation in the treatment delivery time of 589 s in the phase gated, while a larger variation was observed in the gantry rotation by 3°, MU by 20, a duty cycle of 25%, and treatment delivery time of 214 s in amplitude gated.

Comparing the phase- versus amplitude-gated techniques, the results show that a higher dose was delivered to the moving GTV using amplitude gated. The maximum gamma passing rate of the amplitude gating was 1.2 ± 0.4% greater than the phase gated. The amplitude gated allows for a shorter treatment delivery time (49%) due to a larger duty cycle (44%) and a larger gantry rotation (50%) ($P < 0.05$). Due to a larger duty cycle, the number of beam interruptions decreases by 60%, delivering more MU (61%) than phase gated ($P < 0.05$).

The treatment delivery time and dosimetric impact were compared between the phase- and amplitude-gated volumetric modulated arc therapies for lung SBRT using a 3D printed lung phantom.[18] Using phase gating, the treatment delivery time was 366 s due to frequent beam interruptions compared

to amplitude gating by 183 s. The lesser difference in dose, presented with an average gamma passing rate, was in the favor of the amplitude gated (98.7%) compared to the phase gated (98.3%). Compared to the results from this current study, the same difference in treatment delivery time was observed in this study (49%) and the study of Lee *et al*. (50%). Better results in the average gamma passing rate (3%/3 mm) were observed for both techniques, 0.5% in the phase gated and 0.7% in this current study. Similar results were obtained using a different treatment technique Volumetric modulated arc therapy (VMAT) and different treatment volumes developed in-house. Riley *et al*. reported that amplitude gating is better in terms of dosimetric impact where the gamma passing rate (3%/3 mm) was <1.4%, which confirms the results which we obtained in this current study (1.2%).[17]

The efficacy of the RGRT treatments was evaluated using the cine mode where tumor stability and the presence within the gating window were verified during treatment delivery. In the case where the adequate parameters were chosen for the RGRT treatment, such as gating window (30%–60% phases), breathing cycle (3.7 s), and precise positioning (<1 mm), the tumor will be stable within the gating window during treatment delivery [Figure 5a].

In the case where the target shifts from the isocenter (3 mm in this case), the target becomes unstable and will move within the gating window [Figure 5b] but still remain covered by the predefined margin of the PTV (3 mm). This result tends to validate the choice of a 3 mm margin to the IGTV.

In some cases, the gating window was changed (40%–70% phases), and tumor instability and residual motion were found within the gating windows [Figure 5c]. This result does not have an impact on the delivered dose, which means that the present IGTV to PTV margin remains sufficient.

If the tumor was shifted from the isocenter (3 mm) and inadequate phases were selected (40%–70% phases), the GTV would move outside the gating window, receiving only 60% of the planned dose (16.21 Gy) [Figure 5d]. The predefined margin of 3 mm was not enough to cover the target motion, which resulted in underdosing to the moving GTV.

Using phase gated with a dose rate of 600 MU/min and a low breathing period (<3 s), the limitation of the treatment delivery was reached by the accelerator TrueBeam Novalis STx. Due to a low breathing period, the machine does not have enough time to reach its previous control point before starting a new irradiation.[18] Due to a short pulse duration time, the machine starts to rock and goes into security mode, displaying the beam generated mode error.[25] When the pulse duration time is extended, the treatment is delivered every other breathing cycle, increasing the treatment time duration.

Irradiation in gating technique is very time consuming, with limiting the treatment's duration and reducing the risks of patient motion. It appears necessary to use a dose rate superior to 600 MU/min to deliver the dose, regardless of the period of the respiratory cycle. If the dose is delivered over 4 phases (40% of the respiratory cycle), it is necessary to keep an irradiation time at least comparable to a treatment delivery time without gating. In this case, it is necessary to increase the dose rate by a factor of 2.5, or 1500 MU/min. This factor could be 5 for 2 phases, etc., [Eq. 1].

$$Periode * \dot{D}_{FFF} * DC \gg Periode * \dot{D}_{FF} \quad (1)$$

Where D_{FFF} – dose rate for flattened filter free beams (FFF) and – dose rate of flattened filter (FF), DC – duty cycle.

The use of FFF beams with a dose rate ≥1400 MU/min seems to provide an adequate solution to deliver the dose in RGRT, decreasing treatment delivery time.

The notion of treatment delivery time is very important in radiotherapy, in particular the time between the first beam and the last treatment beam. If the duration of treatment becomes longer than 15 min, the effectiveness of the treatment may be compromised and lead to the loss of its biological effect, which may affect the survival of the cells.[26,27]

This study was limited to regular breathing patterns. With simplified treatment, only Truebeam efficacy to deliver dose in phase-a nd amplitude-gated modes was evaluated for lung SBRT treatment.

Conclusion

The results of this study showed that the amplitude-gated DCAT proved to be more effective in delivering treatment with a larger duty cycle, which increases the gantry rotation and the number of MUs per triggering window, as well as decreasing the number of beam interruptions and treatment delivery time.

To deliver the planned dose to the moving target and to reduce treatment delivery time, this study shows that it is recommended to ensure precise patient positioning, to choose an adequate threshold for the gating window, and to use amplitude-gated DCAT techniques with FFF beams with a greater dose rate (≥1 400 MU/min).

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Nil.

Conflicts of interest

There are no conflicts of interest.

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