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GTV volume estimation using different mode of computer tomography for lung tumors in stereotactic body radiation therapy

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Abstract

Aim: To estimate the Gross Tumor Volume (GTV) using different modes (axial, helical, slow, KV-CBCT & 4D-CT) of computed tomography (CT) in pulmonary tumors.

Materials & Methods: We have retrospectively included ten previously treated case of carcinoma of primary lung or metastatic lung using Stereotactic Body Radiation Therapy (SBRT) in this study. All the patients underwent 4 modes of CT scan Axial, Helical, Slow & 4D-CT using GE discovery 16 Slice PET-CT scanner and daily KV-CBCT for the daily treatment verification. For standardization, all the patients underwent different modes of scan using 2.5 mm slice thickness, 16 detectors rows and field of view of 400mm. Slow CT was performed using axial mode scan by increasing the CT tube rotation time (typically 3 – 4 sec.) as per the breathing period of the patients. 4D-CT scans were performed and the entire respiratory cycle was divided into ten phases. Maximum Intensity Projections (MIP), Minimum Intensity Projections (MinIP) and Average Intensity Projections (AvIP) were derived from the 10 phases. GTV volumes were delineated for all the patients in all the scanning modes (GTV_{AX} - Axial, GTV_{HL} - Helical, GTV_{SL} – Slow, GTV_{MIP} - 4DCT and GTV_{CB} – KV-CBCT) in the Eclipse treatment planning system version 11.0 (M/S Varian Medical System, USA). GTV volumes were measured, documented and compared with the different modes of CT scans.

Results: The mean ± standard deviation (range) for MIP, slow, axial, helical & CBCT were 36.5 ± 40.5 (2.29 – 87.0), 35.38 ± 39.52 (2.1 – 82), 31.95 ± 37.29 (1.32 – 66.9), 28.98 ± 33.36 (1.01 – 65.9) & 37.16 ± 42.23 (2.29 – 92). Overall underestimation of helical scan and axial scan compared to MIP is 21% and 12.5%. CBCT and slow CT volume has a good correlation with the MIP volume.

Conclusion: For SBRT in lung tumors better to avoid axial and helical scan for target delineation. MIP is a still a golden standard for the ITV delineation, but in the absence of 4DCT scanner, Slow CT and KV-CBCT data may be considered for ITV delineation with caution.

Key words: GTV; SBRT; CT; delineation.

Introduction

Radiotherapy has evolved into high precision with the introduction of highly conformal radiotherapy treatment techniques like Intensity Modulation Radiation Therapy (IMRT), Volumetric Modulated Arc Therapy (VMAT) and conformal arc radiotherapy. Organ motion in radiotherapy is always a concern, especially in ablative radiotherapy. Underestimation / overestimation of moving target in pulmonary tumors leads to geographical miss of the target or ends up in treating the large volume of normal tissue to a very high radiation dose. Hence precise estimation of target motion using the current imaging technology mandates for performing the highly conformal ablative treatments in the moving tumors.

Precise target volume definitions is a mandate for the use of IMRT, VMAT, SRS, SBRT and other high precision radiotherapy techniques, as the treatment planning and delivery is purely based on the defined target volumes [1]. The target volume definition for the thoracic and abdominal tumors with the high-speed 3D scans always underestimates the target motion, it is recommended to add an additional margin to create Internal Target Volume (ITV) to compensate for the tumor motion as per the ICRU 62 recommendations [2]. Conventional 3 dimensional (3D) CT images are routinely used in the radiotherapy for the target delineation, but using the conventional 3D CT with axial or helical mode will always underestimate the tumor motion in thoracic and abdomen. After the introduction of the four-dimensional (4D) CT which can determine the tumor motion with respect to the breathing pattern of the patient, it became the golden standard for treating moving target volumes. Organ motion is a major angst in medical imaging and radiotherapy, which resulted in motion artifacts and poor target definition.

Several authors have studied and quantified the volume variation of the target volume with different modes of the CT. Shang *et al*. have quantified the Gross Tumor Volume (GTV) with different CT modes for the solitary pulmonary lesion [3]. Most of the authors compared the GTV volume difference using 3D CT and 4D CT for specific sites, Fenngxing Li *et al*. [4] analyzed the geometrical difference for non-small-cell lung cancer, whereas Wang *et al*. [5] compared the patient-specific GTV volume variation on esophageal cancer in 3D and 4D-CT. In this research work, we would like to estimate the GTV volume variation in lung tumors and validate our results with a phantom study.

Materials and methods

Patients

We have retrospectively included ten previously treated case of carcinoma of primary lung or metastatic lung using Stereotactic Body Radiotherapy in this study. The patient's demographic data were listed below in **Table 1**.

Table 1. Patient's demographic data.

S No.	Stage	Age	Sex	Location	Co-Morbidities
1	T2bN0MO	52	F	Rt. Upper	-
2	T2aN0MO	65	M	Rt. Middle	COPD
3	T2aN0MO	45	F	Lt. Upper	Heart Disease
4	T2bN0MO	32	M	Lt. Lower	COPD
5	T1cN0MO	72	M	Rt. Upper	Hypertension
6	T2bN0MO	61	M	Rt. Lower	COPD
7	T1cN0MO	48	F	Lt. Upper	Heart Disease
8	T2aN0MO	53	M	Rt. Middle	-
9	T2aN0MO	52	F	Rt. Lower	Heart Disease
10	T2bN0MO	65	F	Rt. Upper	-

Ten patients with a mean age of 54.5 years (range, 32 to 72 years) were retrospectively included in this study from our previously treated SBRT patients record. Among the ten patients five were male (four out of five were smokers) and five were female. The selected lung patients were mostly peripheral localized lung tumor, mostly had co-morbidities (i.e., COPD, Hypertension, etc.,) and not fit for surgery. The gender, age, stage and the location of the primary tumor along with the co-morbidities were listed in the **Table 1**.

CT simulation

All the patients were immobilized with custom-made vaclok (M/S Civco, USA) fixed with 'T' shaped wing board indexed to the couch. A computed tomography (CT) with a slice thickness of 2.5 mm was obtained for all the patients using GE Discovery 600 16 slice PET-CT scanner. Varian real-time position management (RPM) equipped with an infra-red camera and 6 dot reflective markers, which are integrated with the GE CT was used for all the patients to obtain the DIBH scans and 4D-CT scans. All the patients underwent four modes of CT scan; Axial, Helical, Slow and 4D-CT using GE discovery 16 Slice PET-CT scanner and daily KV-CBCT for the daily treatment verification. For standardization, all the patients underwent different modes of scan using 2.5 mm slice thickness, 16 detectors rows and field of view of 400 mm. Slow CT was performed using axial mode scan by increasing the CT tube rotation time (typically 3 – 4 sec.) as per the breathing period of the individual patient. 4D-CT scans were performed and and the respiratory cycle was divided into 10 phases. Maximum Intensity Projection (MIP), Minimum Intensity Projection (MinIP) and Average Intensity Projection (AveIP) were derived from the 10 Phases. GTV volumes were delineated for all the patients in all the scan modes (GTV_{AX} - Axial, GTV_{HL} - Helical, GTV_{SL} – Slow, GTV_{MIP} - 4DCT and GTV_{CB} – KV-CBCT) in the Eclipse treatment planning system version 11.0 (M/S Varian Medical System, USA). The GTV volumes were measured, documented and compared with the different modes of CT scan.

The 4DCT scans were acquired using a cine mode acquisition, with 2.5 mm slice thickness, 8-row detectors, 400 mm field of view, cine acquisition duration (breathing period of the individual patient + 0.5 sec), cine acquisition gap 0.45 sec and without any inter-slice gap. Once the cine acquisition was completed the breathing pattern with CT data acquisition information file was automatically transferred from the RPM system to the CT console. Using this file the cine acquisition data were divided into ten bins of respiratory phases (CT-0, CT-10, CT-20, CT-30, CT-40, CT-50, CT-60, CT-70, CT-80, and CT-90). From the ten respiratory bins, the maximum intensity projection (MIP) and the average intensity projection (AveIP) were also derived for all the patients.

Target Delineation

Once the patients CT data were acquired, the CT images were exported to the Eclipse treatment planning system, Ver. 11.0 (M/S Varian Medical Systems, Palo Alto, CA, USA). The body structure was segmented automatically by the treatment planning system. For all the ten patients DICOM images were imported and labeled appropriately as per the CT scan modes. To avoid the inter-observer variability, the same oncologist countered the GTV volumes slice by slice in different modes of CT scans for all the patients using a lung window level. The GTV delineated in the axial, helical, slow, MIP and KV-CBCT were stored in the structures GTV_{AX}, GTV_{HL}, GTV_{SL}, GTV_{MIP} and GTV_{CB} respectively. The illustration of the GTV comparisons of different modes for a patient is presented in the **Figure 1**.

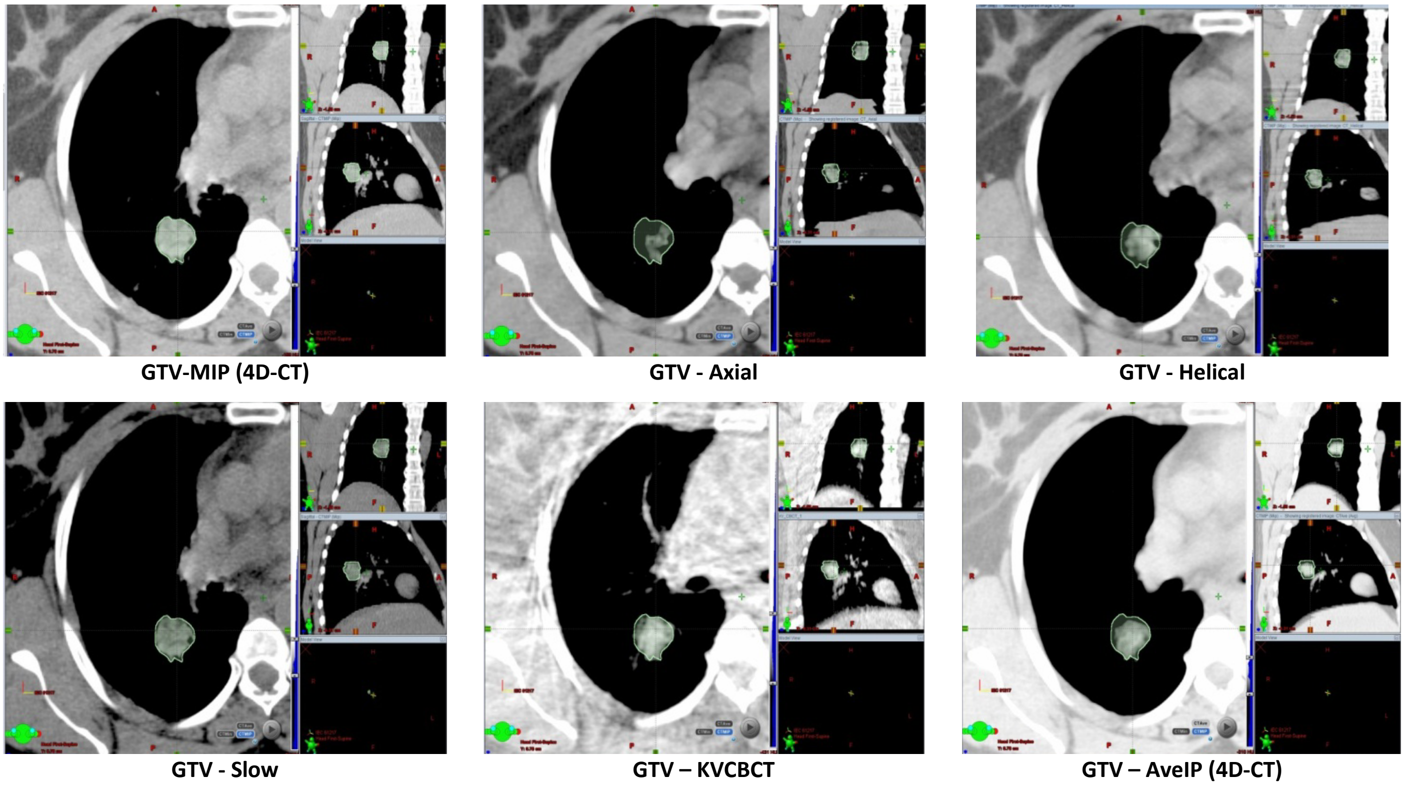

Figure 1. Comparison of GTV volumes in different modes of CT Scans.

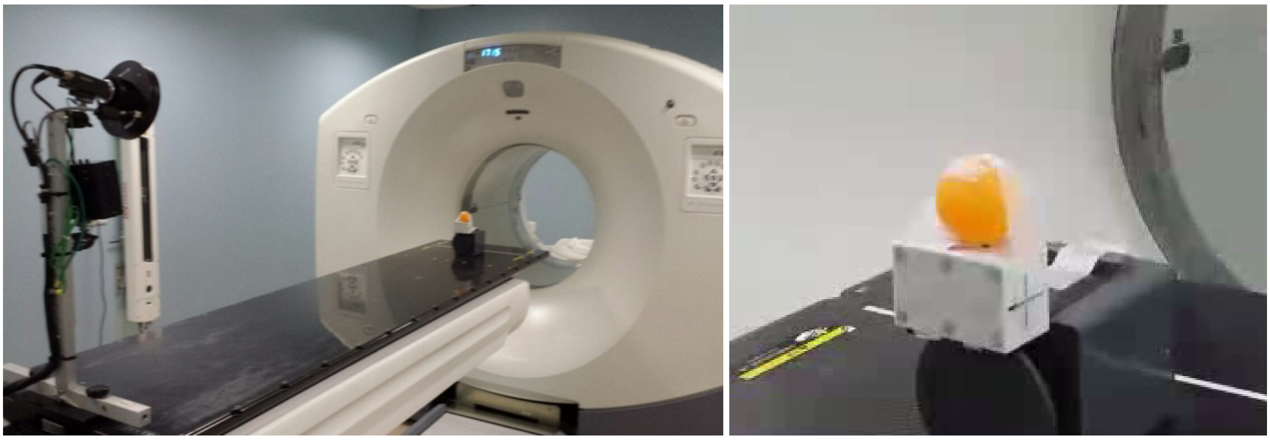

Figure 2. Moving Phantom Study with adjustable breathing cycles.

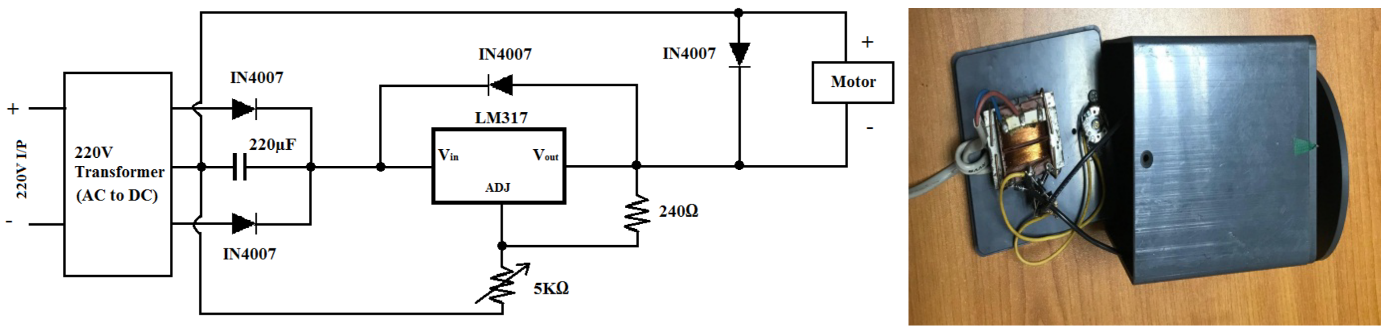

Figure 3. Modified Varian breathing phantom with an adjustable respiratory cycle.

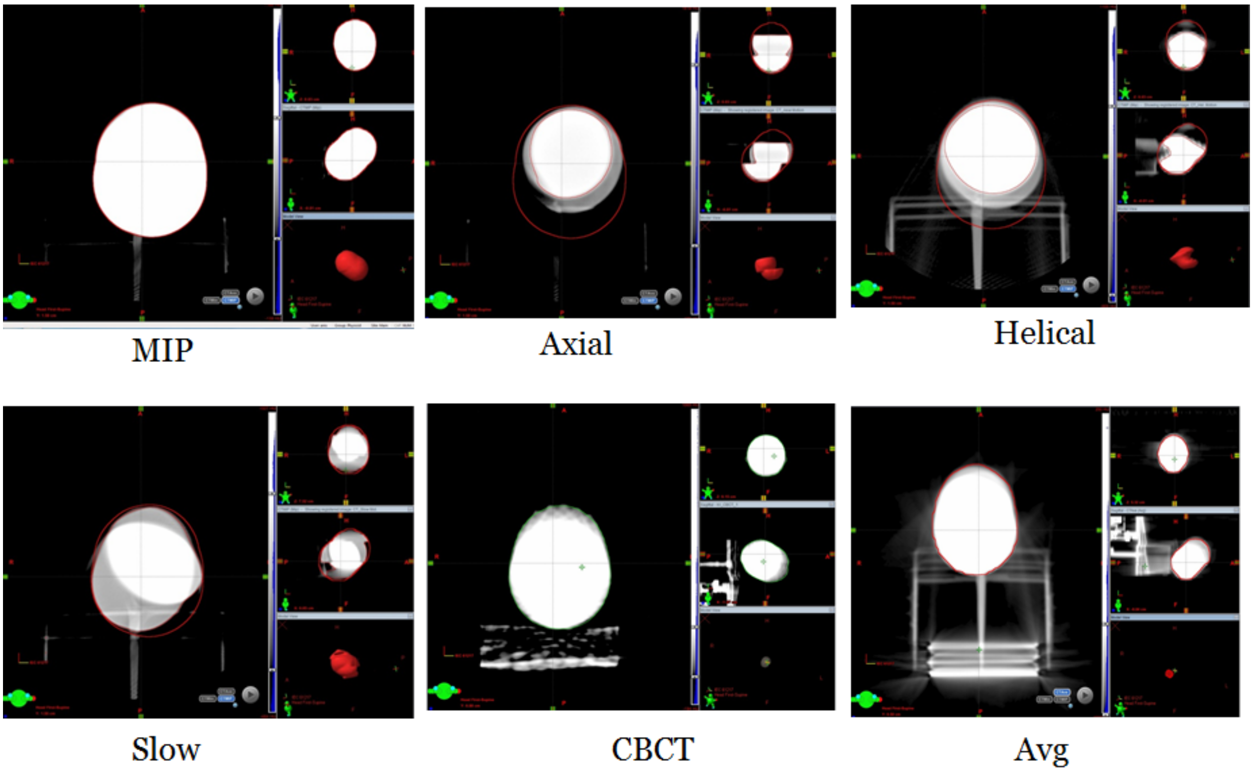

Figure 4. Comparison of moving spherical ball volumes in different modes of CT Scans.

Phantom Study

The Varian medical system provides a simple breathing phantom, which simulates the respiratory motion, has a quite limited range of motion with a constant speed. The phantom can simulate a waveform with the maximum amplitude not more than 4 cm (from crest to trough). The breathing phantom is a quite simple and economical mechanical design, where an elliptical rotating disc moves a hinged platform. The Varian breathing phantom energy supplied by a DC battery, which rotates the elliptical disc, the hinged platform simulates a sinusoidal waveform pattern. With the breathing phantom, we would like to investigate the effect of the variation of the moving volumes with different CT scan modes. A spherical plastic ball, with 3.5 cm diameter filled with iodine intravenous contrast solution, was kept above the six dots reflective marker and combined together by a micro-pore tape, then placed on the hinged platform of the breathing phantom (**Figure 2**).

CT data were acquired with an axial, helical, slow and 4DCT mode using modified Varian breathing phantom with a similar amplitude but varying the breathing cycle (2.0 Sec, 2.5 Sec, 3.0 Sec, 3.5 Sec & 4.0 Sec). The DICOM data of the moving phantom were transferred to the planning system and the volume of the contrast-filled ball was delineated in all the CT scan modes with a lung window level. The respiratory cycle (time required for one complete inspiration and expiration) will be dissimilar for different patients; hence we would like to investigate the effect of the volume variation of the moving target in various respiratory cycles. As we understand the breathing phantom provided by the Varian will move with a constant velocity and the velocity changes involuntarily as per the power of the battery. To simulate a different respiratory cycle, we altered the Varian breathing cycle electrical circuit as shown in **Figure 3**. With this simple modification, we can alter the breathing cycle from two to five seconds with a resolution of 0.2 seconds. The CT scan using different modes were acquired with various breathing cycles (**Figure 4**) and the volume was delineated and documented for analysis.

The CBCT were also acquired for the moving phantom with variable breathing cycles in the TrueBeam (Varian Medical Systems, Palo Alto, USA) linear accelerator using full fan mode, and the volume of the contrast-filled ball was delineated and documented for analysis

Statistical Data Analysis

All the statistical data presented in this work as a mean of all the data followed by the standard deviation ($\bar{X} \pm \sigma_{\bar{X}}$). The paired samples 't' test were performed using the Microsoft Word/Excel version 2010 with $p < 0.05$ considered as significant.

Results

MIP derived for all the phases of the 4D-CT is the golden standard for estimating the target motion and clear visualization of the target without motion artifacts during the free breathing. MIP data are the golden standard for the internal target volume delineation in the SBRT of thoracic and abdomen sites. The mean of all the ten patients followed by standard deviation for GTV_{MIP} 36.50 ± 40.47cc (range 2.29 -

87.0 cc), GTV_{SL} 35.38 ± 39.52cc (range 2.1 - 82.0 cc), GTV_{AX} 31.95 ± 37.29 cc (range 1.32 - 77.87 cc), GTV_{HL} 28.98 ± 33.36 cc (range 1.01 - 65.9cc) and GTV_{CB} 37.16 ± 42.23 cc (range 2.29 - 92.0 cc) respectively. GTV_{MIP} was significantly larger than GTV_{AX} and GTV_{HL}, the mean ratio ± standard deviation of the GTV_{AX} and GTV_{HL} to GTV_{MIP} were 0.87 ± 0.14 and 0.79 ± 0.12. The target volumes measured using axial and helical scans underestimated the organ motion by 13% and 21% with comparison to the GTV_{MIP}. The mean of all the ten patients followed by standard deviation, range and the ratio of the volumes to the GTV_{MIP} were listed in **Table 2**.

Slow CT volumes have a very good correlation with the MIP volumes, the mean ratio ± standard deviation of the slow CT to the MIP was 0.97 ± 0.12, which clearly illustrates the slow CT underestimates on average by only 3%. CBCT volume has also a good correlation with the MIP volume and the ratio is 1.02, due to its longer scan time and image-distorting effect due to organ motion.

CT data were acquired for a moving ball attached to the modified Varian breathing phantom for various breathing cycles with similar amplitude. The volumes of the moving ball for the different CT modes with varying breathing cycle were listed in **Table 3**. We found that there is an increase in the volume as the breathing cycle increases; this effect is predominant in the helical CT. The helical CT volume for 2 sec (31.96 cc), 2.5 sec (34.02 cc), 3.0 Sec (38.52 cc), 3.5 sec (41.86 cc) and 4.0 sec (43.21 cc) respectively. The ratio to the golden standard MIP for the helical CT for 2 sec is 0.60 and it increases with the breathing cycle. The helical scans underestimate by 40% in the 2 sec breathing cycle and 24% for 4 Sec breathing cycle compared to the golden standard MIP data derived from the 4DCT, the axial scans also follow the same pattern as helical scans. The Slow CT volume has a very close match with the MIP data volumes for varying breathing cycles.

Table 2. Volume comparison of different CT modes on Lung patients.

CT Mode	GTV volume (cc) ($\bar{X} \pm \sigma_{\bar{X}}$)	GTV volume Range (cc)	Ratio to MIP	p- value (respect to MIP)
4DCT (MIP)	36.50 ± 40.47	2.29 - 87.0	1.00	-
Slow	35.38 ± 39.52	2.1 - 82.0	0.97	0.672
Axial	31.95 ± 37.29	1.32 - 77.87	0.87	0.005
Helical	28.98 ± 33.36	1.01 - 65.9	0.79	0.004
CBCT	37.16 ± 42.23	2.29 - 92.0	1.02	0.689

Table 3. Volume comparison moving the ball in the modified Varian breathing phantom for various CT modes.

Breathing Cycle (Seconds)	4DCT (MIP)	Slow CT		Axial CT		Helical CT		CBCT	
	(cc)	(cc)	Ratio to MIP	(cc)	Ratio to MIP	(cc)	Ratio to MIP	(cc)	Ratio to MIP
2.0	53.33	51.8	0.97	32.07	0.60	31.96	0.60	51.85	0.97
2.5	55.23	53.57	0.97	37.25	0.67	34.02	0.62	53.87	0.98
3.0	55.51	54.31	0.98	41.73	0.75	38.52	0.69	54.13	0.98
3.5	56.26	55.61	0.99	45.69	0.81	41.86	0.74	55.65	0.99
4.0	56.62	55.98	0.99	46.01	0.81	43.21	0.76	56.12	0.99

Discussion

Precise localization and target delineation are the basic mandates for successful and effective SBRT treatment. SBRT delivers a precise conformal ablative radiation dose to the target in a hypo-fractionated schedule. SBRT with a biological equivalent dose greater than 100 Gy achieves a tumor control of 85% irrespective of tumor size in the primary or metastatic lung tumors [6]. Organ motion during precise conformal radiotherapy is a major concern, overestimation of the target motion will increase the acute toxicity and underestimation may lead to the treatment failure. In the recent years, organ motion management has evolved and MIP derived from 4DCT became a golden standard for ITV delineation in moving target SBRT.

Several authors investigated the volume variation of the moving targets using different CT modes for various clinical sites. Shang *et al.* [3] compared the GTV volumes in 3DCT modes for the solitary pulmonary lesion to the 4DCT-MIP and also investigated the impact of the centroid position of the GTV by the axial and helical scans. Shang *et al*. found that the 4DCT-MIP data were significantly larger than GTV_{AX} and GTV_{HL} and they were statistically significant. In our study, we also found similar results, where the GTV_{AX} ($p = 0.005$) and GTV_{HL} ($p = 0.004$) underestimate the MIP volume by 13% and 21% respectively and they were statistically significant.

Li *et al*. [4] investigated the geometrical differences in the GTV between the 3DCT and 4DCT for non-small-cell lung cancer patients and found that the internal GTV resulting from the 4DCT does not completely comprise the GTV from the 3DCT, and extra margin may be required to define the ITV based 4DCT.

In our study, we found that the mean ± standard deviation of the MIP volume of all the ten patients is 36.50 ± 40.47, whereas the slow CT and CBCT volumes were 35.38 ± 39.52 and 37.16 ± 42.23 respectively. We found a good correlation between the MIP volume to slow and CBCT volumes. In case of absence of the 4DCT in the clinic, the slow or CBCT scans may be considered for determining ITV volumes with a small additional isotropic margin for safer SBRT treatment.

Peng *et al*. [7] studied the accuracy of ITV derived from the 4DCT to predict the real target dose in the lung SBRT and found that ITV does not predict accurate target motion in large moving targets. Restricting the tumor motion the target dose heterogeneity could be reduced in lung SBRT.

The axial and helical scans performed using varying breathing cycle (2 Sec to 4 Sec) with the modified moving phantom resulted in 24% to 40% volume underestimations compared to the golden standard MIP volumes. This clearly illustrates that axial and helical scan modes should be avoided for moving tumors in SBRT. On the other hand, the slow CT and the CBCT volumes of the moving phantom were very close to the MIP Volume, hence in the absence of the 4DCT in the clinic, we may try to substitute slow or CBCT data for ITV delineation with caution. The phantom study and the patient study reveal a similar result, which credentials the accuracy of our study.

Conclusion

During CT simulation for SBRT in lung tumors better to avoid axial and helical scan mode for target delineation, these may underestimate the target motion by 15 to 20%. MIP is still a golden standard for the ITV delineation. In the absence of 4DCT scanner, Slow CT or KV-CBCT data may be used for ITV delineation. Our moving phantom data and the patient's data has a good correlation with our patient data, which is an evidence of our data credentials.

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