Journal of Associated Medical Sciences 2018; 51(1): 51-56

JAMS
Journal of Associated Medical Sciences

Thai-Journal Citation Index Centre (TCI) & ASEAN Citation Index (ACI)

Journal of Associated Medical Sciences

Journal homepage: https://www.tci-thaijo.org/index.php/bulletinAMS/index

Volumetric and dosimetric comparison of helical tomotherapy treatment planning using different strategies of four dimensional computed tomography images for target volume definition in non-small cell lung cancer patients

Kanyawee Payungkulanan[*1] **Pitchayaponne Klunklin** **Somsak Wanwilairat**

Division of Therapeutic Radiology and Oncology, Department of Radiology, Faculty of Medicine, Chiang Mai University, Chiang Mai Province, Thailand

ARTICLE INFO

Article history:
Received 16 November 2017
Accepted as revised 28 January 2018
Available online 30 January 2018

Keywords:
Four-dimensional computed tomography, non-small cell lung cancer, helical tomotherapy, maximum intensity projection, internal target volume

ABSTRACT

Background: Four-dimensional computed tomography (4DCT) images were used to generate internal target volume (ITV) in lung cancer. However, the drawback is time consumed to delineate all sets of CT scans. Maximum intensity projection (MIP) and select phases of 4DCT datasets were used to reduce time consumed to delineate the ITV.

Objectives: To compare the volume of ITV and dosimetric parameters of planning target volume (PTV) based on three different 4DCT datasets in non-small cell lung cancer (NSCLC) patients of helical tomotherapy treatment planning.

Materials and methods: The 4DCT image datasets of 7 patients diagnosed with stage I-III NSCLC were used. All gross target volumes (GTVs) were delineated by the same radiation oncologist in 3 different 4DCT datasets (10 phases, 3 phases, and MIP image) using Oncentra Master Plan v.4.3 contouring software. $PTV_{10phases}$, $PTV_{3phases}$ and PTV_{MIP} were generated and treatment planning were performed. From PTVs contour, volume and ratio of ITV as well as matching index (MI) were compared. Helical tomotherapy planning was done for each PTV then dosimetric parameters for PTVs and organs at risk (OARs) were evaluated. Statistical analysis was performed using Pair t- test and a $p<0.05$ was considered to be statistically significant.

Results: Mean volume of ITVs were 64.09±63.05 cc, 60.40±60.99 cc, 59.85±60.23 cc for $ITV_{10phases}$, $ITV_{3phases}$ and ITV_{MIP}, respectively. The $ITV_{3phases}$ and ITV_{MIP} were significantly smaller than the $ITV_{10phases}$ ($p<0.05$). The mean ratios between $ITV_{3phases}$ and $ITV_{10phases}$ and between ITV_{MIP} and $ITV_{10phases}$ were 0.93 and 0.92, respectively. The mean MI between $ITV_{3phases}$ and $ITV_{10phases}$ and between ITV_{MIP} and $ITV_{10phases}$ were 0.90 and 0.87, respectively. For the mean MI and the mean ratios of ITVs, there was no significant difference between $ITV_{3phases}$ versus $ITV_{10phases}$ and ITV_{MIP} versus $ITV_{10phases}$. For dosimetric parameters of PTVs, the average V95 of $PTV_{10phases}$, $PTV_{3phases}$ and PTV_{MIP} were 99.51%, 99.65% and 99.68%, respectively. The average V107 of $PTV_{10phase}$, $PTV_{3phases}$ and PTV_{MIP} were 0.24%, 0.22% and 0.23%, respectively. About OARs dose, only statistically significant difference was found in the Ipsilateral lung dose (V20 and V30) of $PTV_{10phases}$ and PTV_{MIP}.

Conclusion: MIP images are reliable for creating ITVs in early stage patients. The 3 phases images data sets are reliable for generating ITVs for all stages of NSCLC

* **Corresponding author.**
Author's Address: Division of Therapeutic Radiology and Oncology, Department of Radiology, Faculty of Medicine, Chiang Mai University, Chiang Mai Province, Thailand
** **E-mail address:** kanyaweepoon@gmail.com
doi: 10.14456/jams.2018.9
E-ISSN: 2539-6056

in which tumor moves straightforward superoinferior (SI) direction and that tumor deformation during breathing are minimal. Dosimetric parameters of all 3 PTVs generated by using 3 different ITV definitions are similar.

Introduction

Respiration is the major cause of intrafraction motion in radiotherapy treatment delivery especially in Non small cell lung cancer (NSCLC)[1]. In radiotherapy treatment planning, to ensure the target volume was covered by prescription dose, the margin needs to be added to clinical target volume (CTV) for forming Internal target volume (ITV) to account intrafraction motion. Four-dimensional computed tomography (4DCT) is an advance technique to create many data sets images tag with respiration movement. This technique is suitable for tumor that move due to respiration especially lung cancer. The 4DCT images can be used to create Internal target volume (ITV) of tumor. Various methods for generating an ITV from 4DCT dataset have been reported. Ideally, the method to create an ITV is contouring all individual CT dataset but the drawback for this method is the time required to delineate all sets of CT scans. To reduce the workload and time consuming, the Maximum intensity projection (MIP) and selected phases images were used to generate ITV. Briefly, the MIP is the post processing tool that reflects the maximum CT number value in each voxel and displays in full intensity with brightest object on projection image[2]. In this study, the MIP image was created from 10 phases of 4DCT datasets. There were several researches[2-8] studied about these methods (MIP and selected phases) compared to all 10 phases images method in terms of the accuracy and efficiency to generate ITV. Therefore, this study studied about MIP and 3 phases methods compared to all 10 phases images method in term of the accuracy and efficiency to generate ITV. This study purpose to compare volume of ITV and dosimetric parameters of different target volume that were created by MIP images and selected phases (3 phases) images with 10 phases images (standard method) in Non small cell lung cancer (NSCLC).

Materials and methods

1. Patient characteristics

Prospective analysis performed on 4DCT datasets from 7 patients who were diagnosed stage I-III with Non-small cell lung cancer (NSCLC) who received external radiotherapy in Radiotherapy Department of Maharaj Nakhon Chiangmai hospital from March - May 2017. The patient characteristics are summarized in Table 1.

Table 1 Patients characteristics

No.	Sex	Age (years)	TNM Staging	Stage grouping	Tumor site
1	Male	61	T3N3M0	Stage IIIB	LUL
2	Male	70	T2aN2M0	Stage IIIA	RML
3	Female	62	T3N2M0	Stage IIIA	LUL
4	Female	56	T4N3M0	Stage IIIB	RUL
5	Male	54	T4N2M0	Stage IIIB	RUL,RLL
6	Male	60	T4N3M0	Stage IIIB	RUL,RML
7	Male	79	T1bN0M0	Stage IA	LLL

TNM = Tumor, Node, Metastasis; RUL = Right Upper Lobe; RML=Right Middle Lobe; RLL= Right Lower Lobe; LUL= Left Upper Lobe; LLL = Left Lower Lobe

2. CT simulation and image acquisition

All patients were immobilized with wing board in supine position with arms above the head during simulation. The 4DCT scanning was performed during free breathing on 64-slice CT scanner (Sensation Open AS, Siemens, Erlangen, Germany). The respiratory signal for the 4DCT was generated by the respiratory gating system AZ-733VI (AZ-733V, Anzai Medical Co. Tokyo, Japan). The 3DCT with intravenous contrast was performed with scanning parameters as shown in Table 2.

After that, 4DCT imaging acquired with scanning parameters are shown in Table 3. Then, the 4DCT datasets were sorted according to phases in 10 CT volumes (CT0%, CT 10%,...,CT90%). The 0% is full maximum inspiration and 50% correspond to full maximum expiration. Moreover, post processing tool, MIP image dataset was created by the software using raw data of all 10 scan phases. All CT datasets were transferred to Oncentra master plan (v 4.3) for contouring target volumes and organs at risk (OARs)

Table 2 Scanning parameters of 3DCT acquisition.

Acquisition Parameters	3D CT
Voltage (kV)	120 kV
Effective current (mAs)	CARE DOSE
Slice thickness (mm)	5 mm
Gantry rotation time (s)	0.5 s (default)
Pitch	0.83

Table 3 Scanning parameters of 4DCT acquisition.

Acquisition Parameters	4D CT
Voltage (kV)	120 kV
Effective current (mAs)	CARE DOSE
Slice thickness (mm)	5 mm
Gantry rotation time (s)	0.5 s (default)
Pitch	0.09

3. Target volume generation

All 4DCT image datasets and MIP image dataset were transferred to the Oncentra Master Plan v.4.3 contouring software. For each patient, the Gross tumor volumes (GTVs) were delineated on each of the 10 phases of 4DCT datasets ($GTV_{10phases}$), $GTV_{3phases}$ was delineated on 3 phases image (full-maximum inspiration, mid-expiration, full-maximum expiration) of 4DCT datasets and GTV_{MIP} was delineated on MIP image dataset by the same radiation oncologist using lung window setting (WW1600, WL-600). The 5 mm expansion was added around $GTV_{10phases}$, $GTV_{3phases}$ and GTV_{MIP} to account the microscopic disease extent and defined as $CTV_{10phases}$, $CTV_{3phases}$ and CTV_{MIP}, respectively. Then three different Internal target volumes (ITVs) and Planning target volumes (PTVs) were generated as follow,

i) $ITV_{10phases}$ derived from combining all CTVs (CTV0% - CTV90%) in the 10 respiratory phases. PTV was created by adding 5 mm isotropic margin around $ITV_{10phases}$ for set up error and determined as $PTV_{10phases}$.

ii) $ITV_{3phases}$ derived from combining 3 CTVs that encompassed CTV0% (full-maximum inspiration), CTV20% (mid-expiration) and CTV50% (full-maximum expiration). The PTV was created by adding 5 mm isotropic margin around $ITV_{3phases}$ for set up error and determined as $PTV_{3phases}$.

iii) ITV_{MIP} was equivalent to CTV_{MIP}. The reason why ITV_{MIP} was equivalent to CTV_{MIP} because the disease outlined on MIP image includes all movement of tumor. For the PTV was created by adding 5 mm isotropic margin around ITV_{MIP} for set up error and determined as PTV_{MIP}.

iv)

4. Analysis of internal target volume (ITV)

Three different ITV definitions were measured and compared using ratio of ITVs and matching index(MI). In this study, $ITV_{10phases}$ was set as a reference volume.

4.1 Ratio of ITVs

The ratio of ITV is defined as the ratio volume of $ITV_{10phases}$ to ITVtest ($ITV_{3phases}$ and ITV_{MIP}). The formula is as follow,

$$\frac{ITV_{test}}{ITV_{10phases}}$$

The ideal value of the ratio of ITV is 1 if two volumes are identical.

4.2 Matching index (MI)

Matching index (MI) is defined as the ratio of the intersection of ITV A ($ITV_{10phases}$) with ITV B ($ITV_{3phases}$ or ITV_{MIP}) to the union of ITV A and ITV B. The formula is as follow,

$$MI(A,B) = \frac{ITV\,A \cap ITV\,B}{ITV\,A \cup ITV\,B}$$

The maximum value of MI is 1 if two volumes are identical and the minimum value is 0 if values are completely non-overlapping.

5. Helical tomotherapy treatment planning

For each patient, treatment plans of $PTV_{10phases}$, $PTV_{3phases}$ and PTV_{MIP} were designed on 3DCT data set. All plans were optimized using the Tomotherapy Hi-Art TPS, version 5.1.0.4 using the same optimization parameters with 2.5 cm field width (FW), 0.287 pitch factor (PF) and 3.5 modulation factor (MF). Dose distribution for each beamlet was calculated using a convolution/superposition algorithm. Dose prescription was 60 Gy for 2 Gy per fraction delivered to the PTVs.

6. Dosimetric parameters evaluation

Planning target volumes (PTVs) obtained using three different ITV definitions were evaluated and compared. For this study, $PTV_{10phases}$ was set as a reference volume. D50 was normalized to 60 Gy in all cases and all types of PTV following ICRU 83[9]. For each plan, dosimetric parameters of PTV were evaluated including V95 and V107, while organs at risk (OARs) were evaluated in according to radiation therapy oncology group (RTOG) 0617[10] report that include the following parameters: percentage volume of Ipsilateral lung receiving 20 Gy and 30 Gy (V20, V30); percentage volume of contralateral lung receiving 20 Gy (V20); Dmax of Spinal cord; Dmean of Esophagus and D33 of Heart.

7. Statistical analysis

Statistical analysis was performed using the SPSS 19.0 for window. Volume of ITV, ratios of ITV, matching index (MI) and dosimetric parameters were compared using pair t- test and $p<0.05$ was considered to be statistically significant difference.

Results

Volume of Internal target volume (ITV)

Volume of ITVs of each patient is shown in Table 4. Mean volume of ITVs were 64.09±63.05 cc, 60.40±60.09 cc and 59.85±60.23 cc for $ITV_{10phases}$, $ITV_{3phases}$ and ITV_{MIP}, respectively. The $ITV_{10phases}$ was the largest volume for all patients. $ITV_{3phases}$ and ITV_{MIP} were significantly smaller than $ITV_{10phases}$ ($p<0.05$). Extreme large absolute volume differences were observed for case number 3, 4 and 5 with the difference in range of 5.46 to 8.34 cc. For case 7 with early stage patient, the volume of $ITV_{3phases}$ and ITV_{MIP} are very closed to $ITV_{10phases}$ with the volume differences of 0.07 and 0.11 cc for $ITV_{3phases}$ and ITV_{MIP}, respectively.

Table 4 Volume of internal target volume (ITV) for $ITV_{10phases}$, $ITV_{3phases}$ and ITV_{MIP}.

Patient No.	Volume of ITVs (cc.)		
	$ITV_{10phases}$	$ITV_{3phases}$	ITV_{MIP}
1	32.66	31.89	31.11
2	16.00	13.18	13.34
3	186.67	181.03	178.33
4	88.60	80.78	82.41
5	86.37	79.98	78.54
6	33.18	30.86	30.16
7	5.15	5.08	5.04
Mean±SD	64.09±63.05	60.40±60.99	59.85±60.23

Ratio of Internal target volume (ITV)

Table 5 shows the ratios of internal target volume (ITV) for $ITV_{3phases}$ and ITV_{MIP} relative to the reference $ITV_{10phases}$. If consider in the percent volume change, case number 2 was the maximum difference with the changed around 20% volume. All of the ratio values were less than 1 that represented to the smaller of $ITV_{3phases}$ and ITV_{MIP} compared with $ITV_{10phases}$. Mean ratios between $ITV_{3phases}$ and $ITV_{10phases}$ and between ITV_{MIP} and $ITV_{10phases}$ are 0.93±0.06 and 0.92±0.05, respectively. There was no statistic significant differences supported by *p* value between mean ratios of $ITV_{3phases}$ to $ITV_{10phases}$ and between ITV_{MIP} to $ITV_{10phases}$ (*p*=0.182)

Table 5 Ratio of internal target volumes (ITVs) for $ITV_{3phases}$ and ITVMIP relative to the reference $ITV_{10phases}$.

Patient No.	Ratio of ITVs	
	$ITV_{3\ phases}$ / $ITV_{10phases}$	ITV_{MIP}/ $ITV_{10phases}$
1	0.98	0.95
2	0.82	0.83
3	0.97	0.96
4	0.91	0.92
5	0.92	0.91
6	0.92	0.90
7	0.99	0.98
Mean±SD	0.93±0.06	0.92±0.05
	p=0.182	

Matching index (MI)

Table 6 shows Matching index (MI) for $ITV_{3phases}$ and ITV_{MIP} relative to the reference $ITV_{10phases}$. MI index presented good agreement with ratio of ITV results that case number 2 was the worst case for matching and vice versa in case number 7. From the data as shown in Table 6, the mean MI of $ITV_{3phases}$ and ITV_{MIP} compared with $ITV_{10phases}$ were 0.90±0.05 and 0.87±0.07, respectively. There were no significant differences of the mean MI between $ITV_{3phases}$ and ITV_{MIP} related to $ITV_{10phases}$ (*p*=0.38).

Table 6 Matching index (MI) for $ITV_{3phases}$ and ITV_{MIP} relative to the reference $ITV_{10phases}$.

Patient No.	Matching Index (MI)	
	$ITV_{3phases}$ vs. $ITV_{10phases}$	ITV_{MIP} vs. $ITV_{10phases}$
1	0.87	0.85
2	0.80	0.74
3	0.94	0.90
4	0.91	0.92
5	0.92	0.87
6	0.90	0.82
7	0.95	0.96
Mean±SD	0.90±0.05	0.87±0.07
	p=0.38	

Dosimetric parameters of PTV and OARs

Dosimetric parameters are presented in Table 7. PTV coverage was very closed for three ITV definitions. Average D50 of $PTV_{10phases}$, $PTV_{3phases}$ and PTV_{MIP} were 60 Gy. The average V95 of $PTV_{10phases}$, $PTV_{3phases}$ and PTV_{MIP} were 99.51%, 99.65% and 99.68%, respectively. Average V107 of $PTV_{10phases}$, $PTV_{3phases}$ and PTV_{MIP} were 0.24%, 0.22% and 0.23%, respectively. For dosimetric parameters of OARs, only statistically significant difference was found in the Ipsilateral lung dose (V20 and V30) of PTV_{MIP} compared to $PTV_{10phases}$ as shown in Table 8.

Table 7 Dosimetric parameters result of PTVs.

Dosimetric parameter	$PTV_{10phases}$ (mean±SD)	$PTV_{3phases}$ (mean±SD)	PTV_{MIP} (mean±SD)
V95 (%)	99.51±0.75	99.65±0.65	99.68±0.62
V107 (%)	0.24±0.40	0.22±0.40	0.23±0.39

Table 8 Dosimetric parameters result of OARs.

OARs	Parameters	$PTV_{3phases}$ (±SD)	$PTV_{10phases}$ (±SD)	*p* value	PTV_{MIP} (±SD)	$PTV_{10phases}$ (±SD)	*p* value
Ipsilateral lung	V_{20} (%)	37.46±8.55	38.07±8.75	0.055	37.47±8.68	38.07±8.75	0.032
	V_{30} (%)	27.81±8.10	28.24±8.17	0.053	27.53±8.05	28.24±8.17	0.008
Contralateral lung	V_{20} (%)	8.88±9.44	8.98±9.47	0.087	8.83±9.21	8.98±9.47	0.569
Heart	D_{33} (Gy)	4.88±6.50	4.93±6.42	0.280	4.59±5.98	4.93±6.42	0.121
Esophagus	D_{mean} (Gy)	3.97±3.76	4.85±4.10	0.174	3.85±3.86	4.85±4.10	0.206
Spinal cord	D_{max} (Gy)	26.76±10.50	26.80±10.72	0.923	26.36±10.65	26.80±10.72	0.418

Discussion

In lung cancer, respiration is the major cause of tumor motion during treatment. Four-dimensional computed tomography (4DCT) images were used to generate Internal target volume (ITV), but the drawback is the time required to delineate all sets of CT scans, the post processing tool of Maximum intensity projection (MIP) and selected phases of 4DCT datasets were used to delineate the ITV to solve the drawback of time consuming. This study purpose to compare volume of ITV and dosimetric parameters of different target volume that were created by MIP images and selected phases (3 phases) images compared with 10 phases images (standard method) in Non small cell lung cancer (NSCLC).

This study found, that the ratios of ITV and MI value from $ITV_{3phases}$ and ITVMIP are similar to the value from $ITV_{10phases}$. The best case of smallest difference in volume change that presented the ITV ratio and MI values near ideal value was patient no.7. It was because of early stage NSCLC with tumor locate at peripheral lung that relatived to the study of Underberg RWM[2] and Muirhead R.[6] The explanation about these ratios depend on position of the tumor, if tumor locates in peripheral lung, it is liable to distinguish the tumor from nearby organ. For locally advance stage NSCLC (Case 1-6), ratios of ITV and MI values from ITV_{MIP} are not similar to the value from $ITV_{10phases}$ because tumor locate adjacent to tissue of equal density that resemble of CT number value such as mediastinum and chest wall. Thus, on MIP image, boundaries between tumor and nearby organ may not be clearly seen by observer. This study can conclude that MIP method may not suitable for creating an ITV in locally advance stage NSCLC patients compared to the study of Ezhil et al.[8] Ezhil reported the value of MI decrease in patients who have locally advance stage NSCLC that tumor involve to nearby organ such as chest wall, diaphragm or mediastinum. About 3 phases method, volume of ITV, ratios of ITV and matching (MI) value are similar to the value of $ITV_{10phases}$ in both early stage and locally advance stage NSCLC. Results represent that movement of tumor in all patients in this study are moving in straightforward superoinferior (SI) direction and tumor deformation during breathing are minimal.

For PTV coverage, no significant differences were observed for PTVs that generating from three different ITV definitions because of using the same dose constraints.

Limitation of this study was small sample size due to short timing of study and small number of early stage NSCLC patient. Future study should increase the sample size to confirm the accuracy of study.

Conclusion

MIP images are reliable and fast tool for creating ITVs from 4DCT images of early stage NSCLC patients. However, it should be considered in case of tumor near mediastinum or chest wall. The 3 phases images are reliable for generating ITVs for all stage of NSCLC which tumor moves straightforward superoinferior (SI) direction and that tumor deformation during breathing are minimal. For dosimetric parameters, there is no significant differences observed for 3 PTVs that generating from three different ITV definitions.

Acknowledgements

I would like to thank the Division of Therapeutic Radiology and Oncology, Department of Radiology, Faculty of Medicine, Chiang Mai University. Many thanks for Lecturer Pitchayaponne Klunklin, M.D and Asst.Prof. Somsak Wanwilairat for suggestions and supports in this research work.

References

[1] Keall PJ, Mageras GS, Balter JM, Emery RS, Forster KM, Juang SB, et al. The management of respiratory motion in radiation oncology report of AAPM Task Group76. Med Phys 2006; 33: 3874-900.

[2] Underberg RWM, Lagerwaard FJ, Slotman BJ, Cuijpers JP, Senan S. Use of maximum intensity projections (MIP) for target volume generation in 4DCT scans for lung cancer. Int Radiat Oncol Biol Phys2005;63:253-60.

[3] Khan F, Bell G, Antony J, Palmer M, Balter P, Bucci K, et al. The use of 4dct to reduce lung dose: a dosimetric analysis. Med Dosim 2009; 34: 273-8.

[4] Bai T, Zhu J, Yin Y, Lu J, Shu H, Wang L, et al. How does four-dimensional computed tomography spare normal tissue in non-small cell lung cancer radiotherapy by defining internal target volume. Thoracic Cancer2014; 5: 537-42.

[5] Wang L, Hayes S, Paskalev K, Jin L, Buyyounouski MK, Ma CM, et al. Dosimetric comparison of stereotactic body radiotherapy using 4D CT and multiphase CT images for treatment planning of lung cancer: evaluation of the impact on daily dose coverage. Radiother Oncol 2009; 91: 314-24.

[6] Muirhead R, Stuart G, Featherstone C, Moore K, Muscat S. Use of maximum intensity projections (MIPs) for target outlining in 4DCT radiotherapy planning. Journal of Thorac Oncol 2008; 3: 1433–8.

[7] Rietzel E, Liu AK, Doppke KP, Wolfgang JA, Chen AB, Chen GT, et al. Design of 4D treatment planning target volumes. Int Radiat Oncol Biol Phys2006; 66: 287-95.

[8] Ezhil M, Vedam S, Balter P, Choi B, Mirkovic D, Starkschall G, et al. Determination of patient-specific internal gross tumor volumes for lung cancer using four-dimensional computed tomography. Radiat Oncol 2009; 4: 1-4.

[9] Menzel HG, Wambersie A, Jones DTL, et al. The ICRU report 83, Prescribing, Recording, and Reporting Photon-Beam Intensity-Modulated Radiation Therapy (IMRT). Journal of the ICRU 2010 april;10.

[10] Bradley J, Schild S, Bogart J, Dobelbower M, Choy H, Adjei A, et al. A randomized phase III comparison of standard- dose (60 Gy) versus high- dose (74 Gy) conformal radiotherapy with concurrent and consolidation carboplatin/paclitaxel +/- cetuximab (ind #103444) in patients with stage IIIA/IIIB non-small cell lung cancer [Internet]. 2016 [cited 2017 Jul 20]. Available from: https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0617

[11] Zhou YQ, Xie CY, Yi JL,Han C, Zheng XM, Jin XC. Volumetric and Dosimetric Influences of Internal Target Delineation Based on 4D CT Measured Tumor Motion in the Treatment of Lung Cancer with Stereotactic Body Radiotherapy. Austin J Radiat Oncol & Cancer 2015; 1(1): 1005