

Original Article

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# Quantitative CT characterization of normal lung anatomy: In relation to locations and gender and study of various lung volume estimation

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## Abstract

**Background:** Mean lung parenchymal attenuation (MLA) may show gender differences and vary in different locations. Lung volume estimations play an important role in lung transplantation workout. In the current study, we focus on quantitative measurement of lung volume using different estimations obtained through calculated formulae from CT images and Chest Radiograph. This study could help to generate data for future references, particularly for Malaysia or Southeast Asia.

**Objective:** To study the MLA in relation to the location, patient's position and gender differences, in order to find the correlation of various lung volume estimation methods.

**Materials and Methods:** This was a retrospective cross-sectional study. A total of 62 patients' CT images were selected and measurements of MLA were analyzed at lung apex, main carinal level (MCL), and base level (BL). At MCL and BL, the MLA was measured in three regions which were anterior, middle and posterior regions. A total lung volume of 26 from the 62 study subjects was also estimated using the predictive equation (method i), estimation from the frontal chest radiograph (method ii), ellipsoid formula using measurement from CT images (method iii) and semi auto-segmentation and volumetric calculation (method iv).

**Results:** MLA of the right lungs range from  $-860 \pm 9.52$  to  $-787.66 \pm 14.8$  HU. MLA of the left lungs range from  $-845.60 \pm 10.0$  to  $-789.66 \pm 14.0$  HU. MLA at middle MCL is lower than apex and middle BL bilaterally ( $p < 0.05$ ). Male subjects have lower lung attenuation with several areas showing a statistically significant difference ( $p < 0.05$ ). The four lung volume estimations show moderate to strong linear correlation ( $r = 0.565 - 0.899$ ).

**Conclusion:** Variation of MLA among MCL, apex and BL could be related to better chest expansion at MCL. The posterior part of the lungs shows a higher value of MLA and this is related to the supine position during scanning that results in a lesser degree of chest expansion at the posterior part and gravity influence. Lung volume estimation is possible using demographic data, a chest radiograph or the ellipsoid formula.

**Keywords:** Mean lung attenuation, Lung volume estimation, Ellipsoid formula.

## Introduction

Computed Tomography (CT) scan is an important imaging modality that provides cross-sectional images with three-dimensional reconstruction [1,2]. Images are presented as a range of grayscale and can be calculated in Hounsfield Units (HU), using density number of water as the main reference “0” [1]. In other words, structures with density higher than water will be presented as a positive HU; whereas structures with lower density will be presented as a negative HU, such as lung parenchyma and adipose tissue [1].

In 2016, Stein et al. conducted an analysis on 42 CT images of a paediatrics age group and it was found that lung attenuation was in a rapid reducing trend among growing children younger than 2 years old, as the lung volume was growing larger [3]. Lung attenuation was also higher in the dependent part of the lung, related to gravity [3]. The attenuation value of a normal lung may show variation due to gender and age factors according to previous studies; however, in a cohort study by Zach et al., there was no persistent association demonstrable between lung attenuation and the age group or the gender factor on his multivariate analysis [4]. In another study by Smit HJM et. al, no significant difference in lung attenuation measurement between male and female was revealed [5]. Lung attenuation was found to be lower at the main carina level compared to the top, but the value increased upon expiration [5]. According to another study on 155 adults patients by Kauczor et. al, the mean lung density (MLD) measured -813 HU during full inspiration and it increased to -736 HU during expiration [6]. Therefore, the inspiratory effort of subjects during CT acquisition may be one of the factors affecting the mean attenuation value of the lung parenchyma.

Besides, the lung volume could be measured from CT images, using manual contour delineation or automatic lung segmentation [2]. However, CT lung volumetry was still not the gold standard in total lung volume estimations and it also exposed patients with radiation [2]. From 1930's, there were a few studies focusing on the estimation of the lung volume or lung capacity based on chest radiographs, namely the study conducted by Hurtado and Fray in 1933 [7-8],

Barnhard et al. [7 - 8], Gamsu et al. [7], Reger et al. [8] and others. These studies published data and estimations of the total lung volume from chest radiographs, correlating with plethysmography [7-8]. One of the methods published in some of these studies utilized ellipsoid formulas [7-8].

Another method published by Canal et al., assessed the estimations from the measurement based on a frontal chest radiograph of small mammals [9]. The estimation equation is  $V_L^* = 0.496 \cdot V_{RX}$ ; whereby  $V_{RX}$  is the measurement of the volume containing lungs and mediastinum and

$$V_{RX} = W \cdot \frac{(H_1 + H_2)}{2} \cdot \frac{(w_1 + w_2)}{2}$$
.  $W$  is the straight line width between two costophrenic recesses;  $H_1$  is the height from  $W$  to the top of the left lung;  $H_2$  is the height from  $W$  to the top of the right lung;  $w_1$  is the left lung width at the midpoint of the diaphragm dome;  $w_2$  is the right lung width at the midpoint of the diaphragm dome (Figure 1). This formula shows a possible similarity or correlation to the previously published calculations, where it could be correlated with ellipsoid formula: Volume,  $V = 0.523 \cdot a \cdot b \cdot c$ ; whereby  $a$ ,  $b$  and  $c$  are the diameters of the ellipsoid [9].

Furthermore, there are also equations for the predicted lung volume suggested by Konheim et al.: Predicted TLV (pTLV) =  $[-630.819 + (967.100 \cdot \text{Gender}) + (25.197 \cdot \text{Height}) - (713.838 \cdot \text{Race}) + (15.103 \cdot \text{Age})]/1000$ ; Gender: Male (1), Female (0); Race: African American (1), others (0); Height in cm, Age in years. This formula was created by correlating with 4 different variables and CT volumetry calculation of 400 patients using lasso regression, which was further tested with one of the gold standard – body plethysmography and lung function test. This predictive equation also shows a strong positive correlation between the predicted total lung volume and the total lung capacity ( $r = 0.82$ ;  $p < 0.0001$ ; 95% CI, 0.59 – 0.93) [10].

The total lung volume estimation plays an important role in the clinical procedure as well as in research fields [7]. It is important particularly in lung transplantation workout and size-matching of the lung volume for donors and

recipients [7 & 10]. This study utilized 4 different methods of quantitative measurement to estimate the total lung volume of Malaysian adults; i.e. based on the predictive equation published by Konheim (method i), based on estimation from the frontal radiograph published by Canals M (method ii), the Ellipsoid formula (method iii) and semi auto-segmentation and volumetric calculation using DICOM compatible program, Osirix Lite (method iv). Furthermore, the correlations between these four methods were looked into.

CT scan examination imposed more radiation to the patient compared to a chest radiograph. For lung transplantation patients, they may not need to undergo CT scan examination in order to estimate their lung volume, if method i and ii showed a positive correlation with the other described methods. Method i requires the patient's demographic data [10], whereas method ii needs calculation from a frontal chest radiograph [9], which is easily available [1]. Method i is considered as good as the gold standard as it shows the correlation with body plethysmography and the lung function test.

This study aims to generate local data for a mean lung volume and lung parenchymal attenuation (MLA) for Malaysian adults, which could become the reference for future studies and in clinical settings in Malaysia and perhaps in Southeast Asia. In clinical practices, the area of low lung attenuation (LAA%) is used to assess the extent of emphysema, whereas the high attenuation area (HAA%) assesses the extent of lung infections, interstitial lung diseases and ARDS [11]. The inspiratory effort, gravity and gender differences may alter the area of the low attenuation area (LAA%) as well as the high attenuation area (HAA%). Therefore, these factors should be considered during the interpretation in normal patients as well as patients with lung diseases.

## Materials and methods

This was a retrospective cross-sectional study conducted in the Radiology Department of Universiti Kebangsaan Malaysia Medical Center (UKMMC), analysing CT images and plain chest radiographs done for patients in the age group of 13 – 85 years old from 1<sup>st</sup> January 2015 to 20<sup>th</sup> June 2015. The universal sampling method was used and there were a total of 462 CT Thorax imaging cases performed in this period. Among the 462 sets of CT images, 184 CT were reported as lung fibrosis and infections, 86 CT were reported as lung malignancy or lung metastasis, 69 CT were associated with granuloma or atelectatic changes and 58 CT were associated with breathing artefacts. It was found that 65 sets of CT images were reported to be normal while 3 sets of images were performed on non-Malaysian citizens and therefore were excluded. In conclusion, a total of 62 sets of CT images (n=62) were included in this study.

### Imaging techniques of CT scans and chest radiographs

CT Thorax was conducted using a CT scanner, Siemens CT Somatom Sensation 64 (64 slices) of the helical mode in the craniocaudal direction. The patient was in a supine position during the scanning and a standard instruction in respective dialects was given to the patient: taking a deep breath and holding the breath. Images were acquired during inspiration. An approximately 1.0 - 1.5 ml/kg contrast material was injected via an intravenous assess at the upper limb with the flow rate of 2.5 - 5 mls/s. An image was acquired with 120 kVp, 200 mAs, one millimeter reconstruction (1 mm slice thickness), B30 and B70 reconstruction kernel using software Syngo CT 2006A.

A chest radiograph was carried out using Xray machine computed radiography unit, Digital Diagnost Philips Medical Systems with 100 - 110 kVp, 4 – 8 mAs exposure with the presence of grid and filter. The patient was in a standing position with his chest facing the detector. An AP view of the radiograph was acquired given the patient was unable to stand erect during the examination.

All CT and Plain radiograph images were interpreted using DICOM viewer OsiriX Lite.

### **Lung attenuation measurement from CT scans**

Mean lung parenchymal attenuation (MLA) of these 62 sets of images was analysed to measure lung attenuation at the lung apex (Figure 2a), the main carinal level (MCL) at anterior, middle and posterior regions bilaterally (Figure 2b) and the lung base level (BL) at anterior, middle and posterior regions (Figure 2c and 2d) bilaterally. The sampling location for MLA at MCL (middle) and BL (middle) was at the mid clavicular line, with additional imaginary lines to divide the lungs into anterior 1/3, middle 1/3 and posterior 1/3. The region of interest (ROI) for the measurement is round in shape and is fixed constant with an area of  $1.0 \text{ cm}^2 \pm 0.2 \text{ cm}^2$ . The ROI was placed at the lung parenchymal by avoiding large vessels.

### **Lung volume estimation calculation**

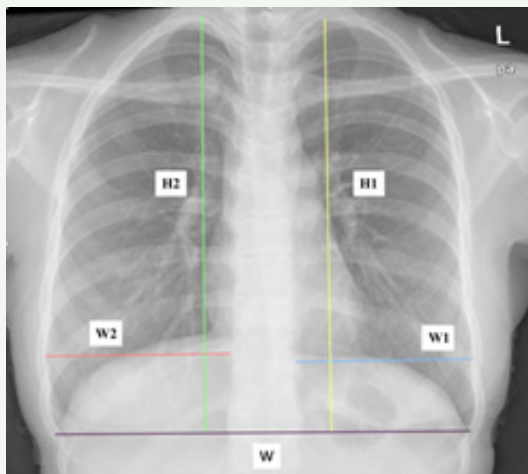
There were a total of 26 patients from the 62 study subjects who had a chest radiograph within six months from the date of CT acquisition. These was a quantitative measurement of the total lung volume methods used in the calculations:

- i. Predictive equation published by Konheim:  
Predicted TLV (pTLV) =  $[-630.819 + (967.100 \cdot \text{Gender}) + (25.197 \cdot \text{Height}) - (713.838 \cdot \text{Race}) + (15.103 \cdot \text{Age})]/1000$ ; Gender: Male (1), Female (0); Race: African American (1), others (0); Height in cm, Age in years.
- ii. Estimation from frontal radiograph, as published by Canals M (Figure 1).
- iii. Ellipsoid formula (a summation of right and left lung volumes of  $0.52 \times \text{AP} \times \text{W} \times \text{CC}$ ) based on the measurement from CT images. The AP and width diameter of both lungs was measured at lung bases, whereas for the craniocaudal measurement, it was measured by drawing a line from the apex to the posterior medial most of the costophrenic angles shown in (Figure 3a, 3b, 3c & 3d). This is a modified method after considering previous publications suggested by other authors. Some authors use the ellipsoid formula in their complex calculations. According to Canals M's formula:  $V^*_L = 0.496 \cdot V_{RX}$ , shows a possible similarity or a correlation to the previously published calculations, where it could be correlated with ellipsoid formula: Volume,  $V = 0.523 \cdot a \cdot b \cdot c$ ; whereby a, b and c are the diameters of the ellipsoid.

- iv. Semi auto-segmentation and volumetric calculation using DICOM compatible program, OsiriX Lite. The lungs were differentiated into right and left lungs with the dead space (air in the trachea and bronchus) and major blood vessels excluded in the calculation (Figure 4a, 4b, 4c, 4d, 4e & 4f). Correlations between these four methods were made.

### Statistical analysis

T test was used to determine a statistical difference of MLA of both lungs. Subsequently, the independent T test was used to determine the statistical significance of MLA among female and male data. Pearson-correlation was used to analyse the correlation of the four methods of the total lung volume estimations i.e. based on predicted calculations (method i), the frontal chest radiograph (method ii), the ellipsoid formula with measurement from CT images (method iii) and volumetry calculation using DICOM compatible program, OsiriX (method iv). A statistical analysis was done using IBM SPSS Statistics 20.



**Figure 1.** Frontal radiograph displays the reference line for calculation of  $V_{RX}$ . (reproduced referring to Canal et. al [9]).

*W:* straight line width between two costophrenic recesses

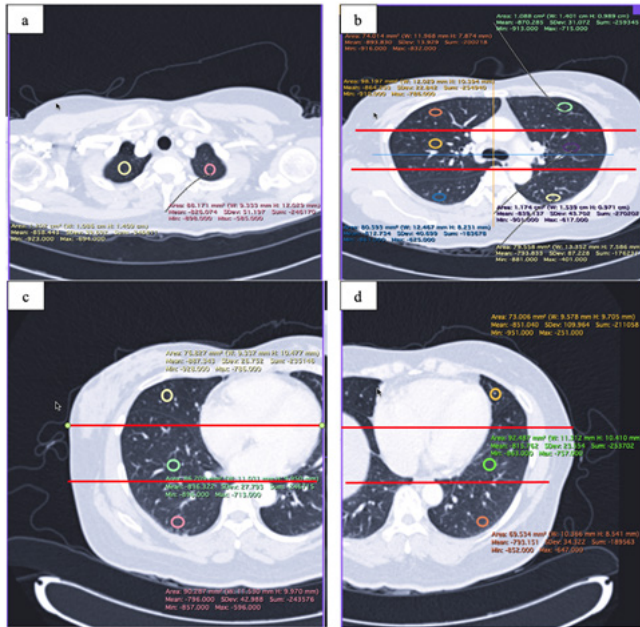
*H1:* height from *W* to the top of left lung

*H2:* height from *W* to the top of right lung

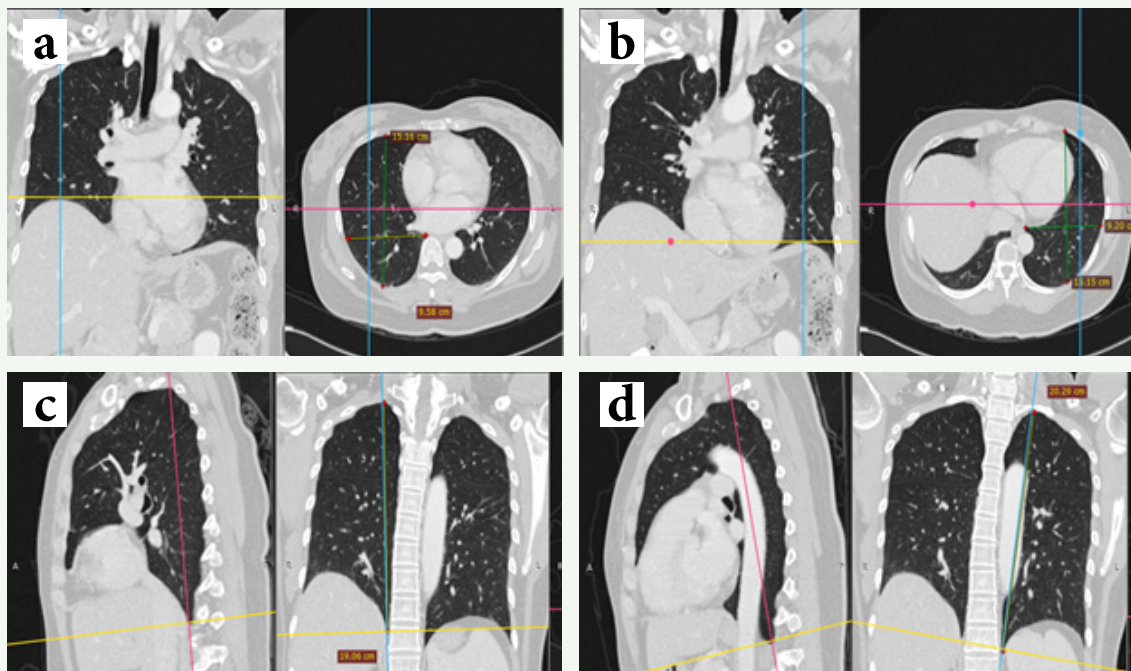
*W1:* left lung width at the midpoint of the diaphragm dome

*W2:* right lung width at the midpoint of the diaphragm dome

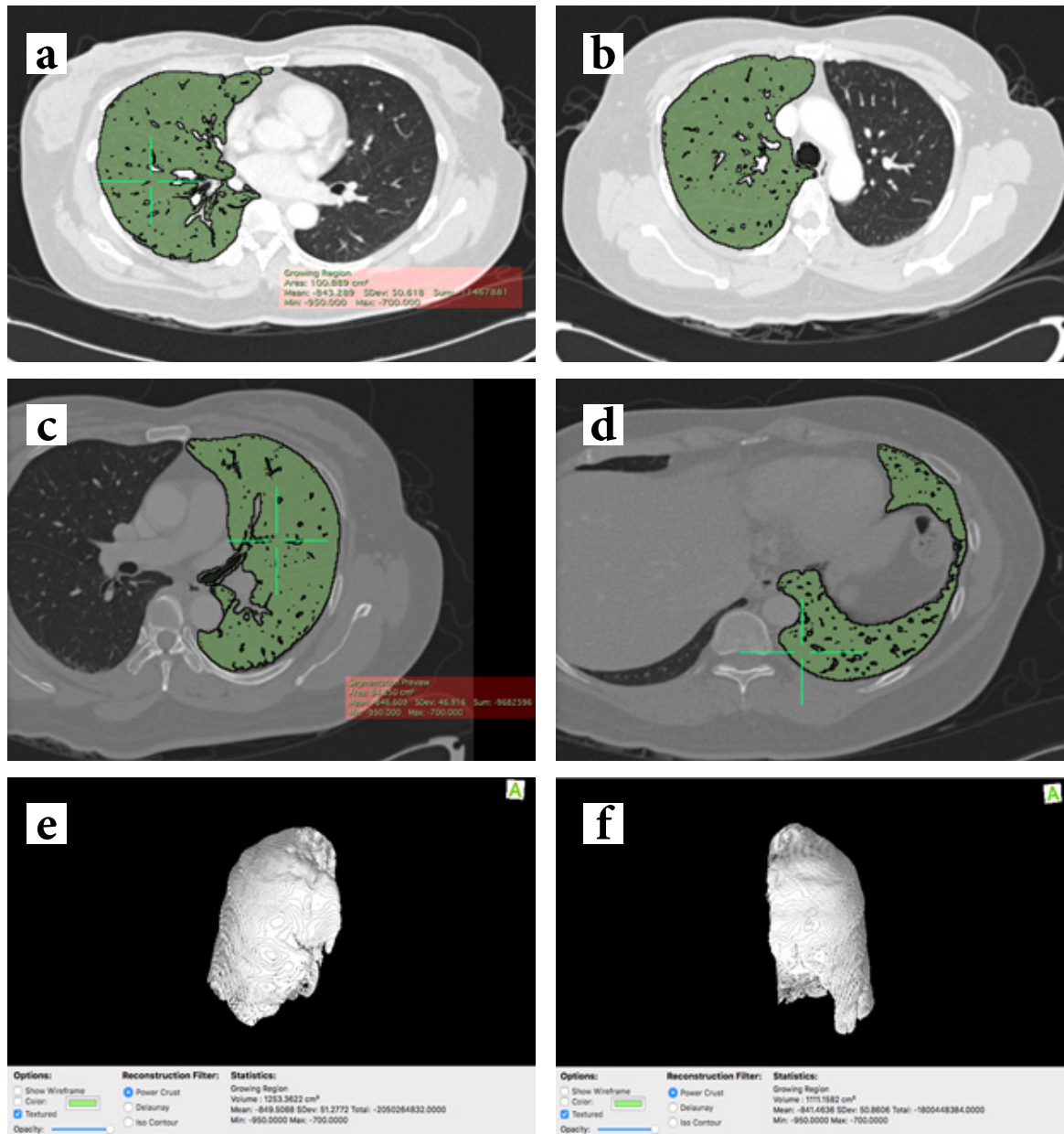




**Figure 2.** Multiplanar reformat shows lung attenuation of apical regions (a), main carinal level (anterior, mid and posterior) (b) and at base level (anterior, mid and posterior) of right (c) and left lungs (d).



**Figure 3.** Multiplanar reformat shows measurement of AP diameter and width of right (a) and left (b) lungs and craniocaudal measurement of right (c) and left (d) lungs.



**Figure 4.** Images show semi auto-segmentation of right (a, b) and left (c, d) lungs with the right (e) and left (f) lung volume calculations using DICOM compatible program, OsiriX Lite.

## Results

There are 62 sets of CT images included in this study. Majority of the CT images were done for Malay patients (n = 38, 61%), followed by Chinese (n = 18, 29%), Indian (n = 4, 6%), Orang Asli and Kadazan (n = 1, 2%) respectively, as shown in Figure 5.

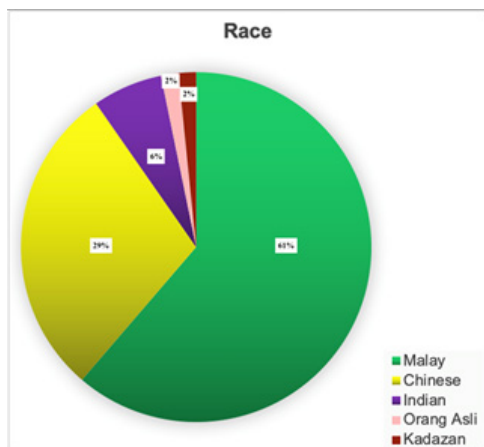


Figure 5. Demographic data based on different race.

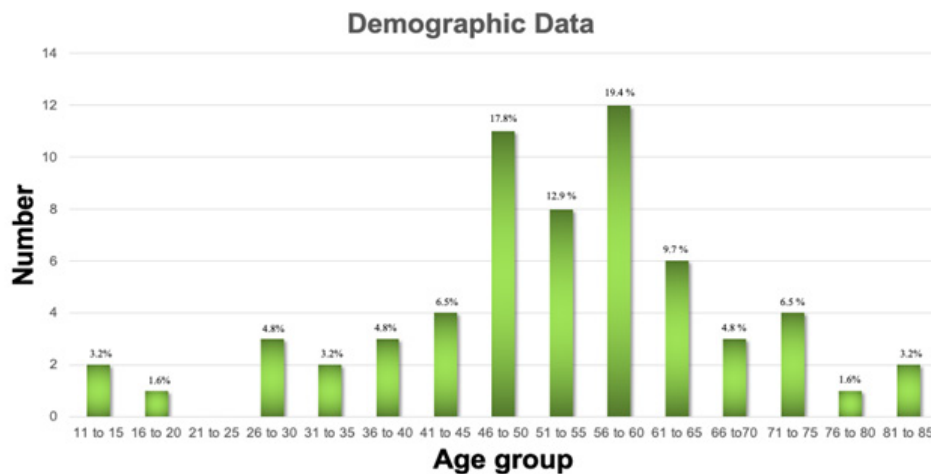


Figure 6. Demographic data based on age groups.

### Lung parenchymal attenuation

There were a total of 62 sets of CT images (n = 62) analysed for lung attenuation, with 34 female patients and 28 male patients. Demographic data was classified based on race and age group of the study subjects (Figure 5 and 6).

The mean of lung parenchymal attenuation (MLA) of both lungs at apical, main carinal levels (anterior, middle and posterior) and at a base level (anterior, middle and posterior) is shown in Table 1.

**Table 1.** Mean lung attenuation of 62 subjects with T test result.

Lung locations	Lung attenuation (HU), mean ± SD	Comparing with	P
R Apex (-HU)	821.77 ± 8.67	R Middle MCL (-HU)	< 0.05
R Anterior MCL (-HU)	849.23 ± 9.41	R Middle MCL (-HU)	< 0.05
R Middle MCL (-HU)	838.85 ± 9.67	R Middle BL (-HU)	< 0.05
R Posterior MCL (-HU)	802.39 ± 12.9	R Middle MCL (-HU)	< 0.05
R Anterior BL (-HU)	860.26 ± 9.52	R Middle BL (-HU)	< 0.05
R Middle BL (-HU)	823.53 ± 11.4	R Middle MCL (-HU)	< 0.05
R Posterior BL (-HU)	787.66 ± 14.8	R Middle BL (-HU)	< 0.05
L Apex (-HU)	819.76 ± 8.62	L Middle MCL (-HU)	< 0.05
L Anterior MCL (-HU)	845.6 ± 10	L Middle MCL (-HU)	< 0.05
L Middle MCL (-HU)	834.16 ± 10.6	L Middle BL (-HU)	< 0.05
L Posterior MCL (-HU)	806.42 ± 11.2	L Middle MCL (-HU)	< 0.05
L Anterior BL (-HU)	842.65 ± 11.2	L Middle BL (-HU)	< 0.05
L Middle BL (-HU)	816.44 ± 11.8	L Middle MCL (-HU)	< 0.05
L Posterior BL (-HU)	789.66 ± 14	L Middle BL (-HU)	< 0.05

\*R = right, L = left, MCL = main carina level, BL = base level

For the right and the left lungs, the differences in MLA at the middle MCL vs the apex and the middle MCL vs middle BL were statistically significant ( $p < 0.05$ ). At the main carina level, the MLA values at the anterior vs the middle and the posterior vs the middle parts revealed a statistically significant difference ( $p < 0.05$ ). At the base level, the differences in the MLA value at the anterior vs the middle and the posterior vs the middle parts also showed statistical significance ( $p < 0.05$ ). Additionally, MLA of both lungs for male and female at the apical, main carinal level (anterior, middle and posterior) and at the base level (anterior, middle and posterior) was tabulated in Table 2.

**Table 2.** Mean lung attenuation of male and female with independent T test result.

Lung locations	Lung attenuation (HU), mean $\pm$ SD		P
	Male (n = 28)	Female (n = 34)	
R Apex (-HU)	828.68 $\pm$ 12.7	816.09 $\pm$ 11.7	0.158
R Anterior MCL (-HU)	862.54 $\pm$ 11.1	838.26 $\pm$ 13.6	< 0.05
R Middle MCL (-HU)	854.14 $\pm$ 11.5	826.26 $\pm$ 13.6	< 0.05
R Posterior MCL (-HU)	819.43 $\pm$ 15	788.35 $\pm$ 19	< 0.05
R Anterior BL (-HU)	873.89 $\pm$ 13.1	849.03 $\pm$ 12.5	< 0.05
R Middle BL (-HU)	835.39 $\pm$ 16	813.76 $\pm$ 15.6	0.065
R Posterior BL (-HU)	799.07 $\pm$ 17.2	778.26 $\pm$ 22.7	0.172
L Apex (-HU)	826.32 $\pm$ 13.9	814.35 $\pm$ 10.6	0.178
L Anterior MCL (-HU)	864.36 $\pm$ 11.1	830.15 $\pm$ 13.9	< 0.05
L Middle MCL (-HU)	851.25 $\pm$ 14	820.09 $\pm$ 14	< 0.05
L Posterior MCL (-HU)	818.89 $\pm$ 15.6	796.15 $\pm$ 15.3	< 0.05
L Anterior BL (-HU)	854.71 $\pm$ 14.2	832.71 $\pm$ 16.1	0.054
L Middle BL (-HU)	833.5 $\pm$ 16	802.38 $\pm$ 15.7	< 0.05
L Posterior BL (-HU)	803.21 $\pm$ 15.4	778.5 $\pm$ 21.7	0.086

\*R = right, L = left, MCL = main carina level, BL = base level

### Lung Volume Estimation

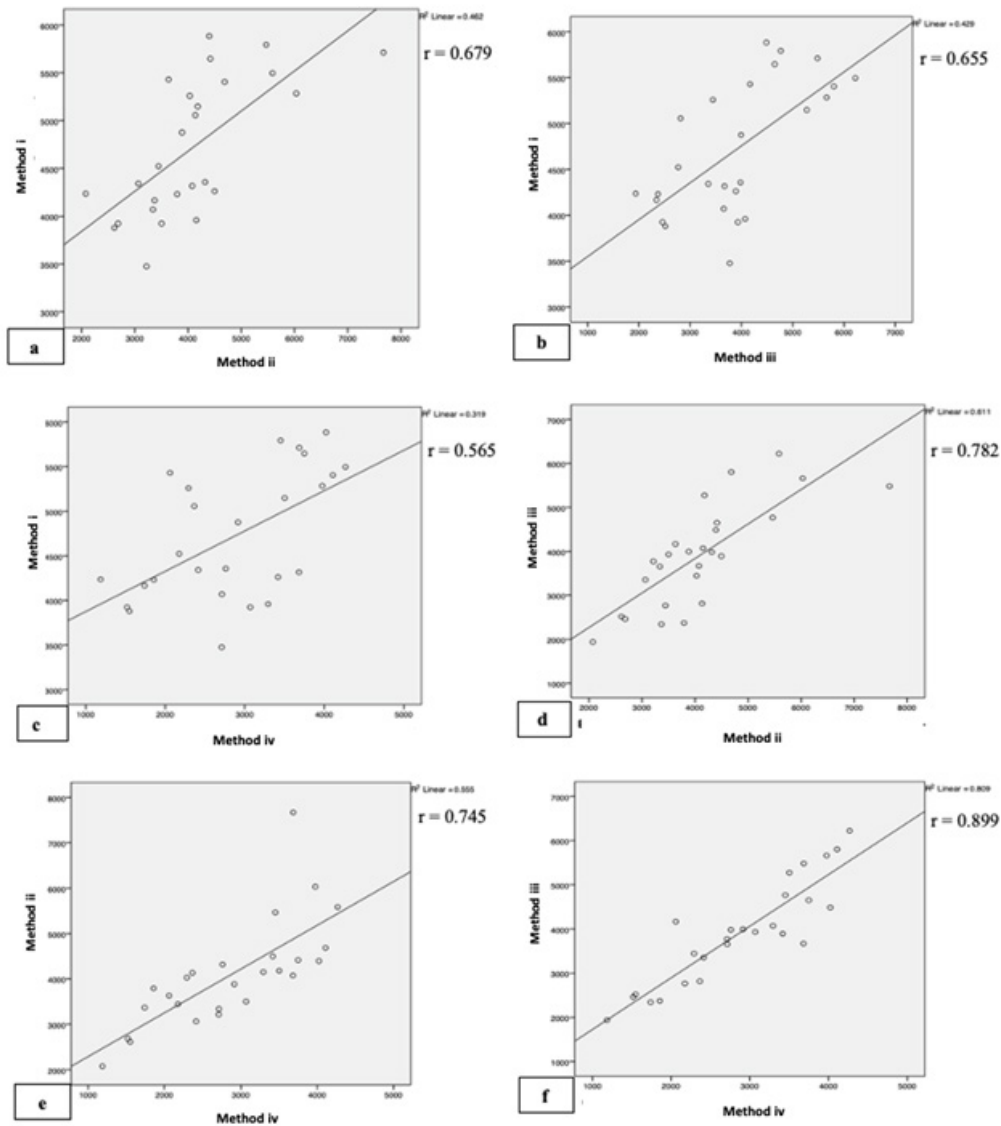
The mean of the estimated total lung volume using method i was  $4717.58 \pm 276$  ml (95% CI 4440 – 4990), method ii was  $4086.96 \pm 446$  ml (95% CI 3640 – 4530), method iii was  $3903.27 \pm 448$  ml (95% CI 3460 – 4350), whereas method iv was  $2864.54 \pm 345$  ml (95% CI 2520 – 3210). Based on method i, the range of the lung volume for the study population ranged between 3476 until 5884 ml. (Table 3)

Quantitative estimations of the total lung volume using four methods are summarized in a scatter plot and it showed positive linear relations (Figure 7a - f).

A moderate to strong correlation was observed between the estimation of the total lung volume using these 4 methods: method i versus ii ( $r = 0.679$ ;  $p < 0.005$ , 95% CI, 0.396 - 0.844), method i versus iii ( $r = 0.655$ ;  $p < 0.005$ , 95 % CI, 0.359 - 0.831), method i versus iv ( $r = 0.565$ ;  $p < 0.005$ , 95% CI, 0.228 – 0.781), method ii versus iii ( $r = 0.782$ ,  $p < 0.005$ , 95% CI, 0.567 - 0.897), method ii versus iv ( $r = 0.745$ ;  $p < 0.005$ , 95% CI, 0.503 - 0.878) and method iii versus iv ( $r = 0.899$   $p < 0.005$ , 95% CI, 0.786 – 0.954) (Table 4).

**Table 3.** Estimations of total lung volume (in unit mls) with 4 different methods.

Estimation methods	Total lung volume (ml)			
	Min	Max	Mean	95 % CI
Calculating total volume using formula by Konheim et al.	3476	5884	$4717.58 \pm 276$	4440 – 4990
Estimating lung volume using formula by Canals et al. (Chest X-Ray)	2076	7669	$4086.96 \pm 446$	3640 – 4530
Estimating total lung volume using Ellipsoid formula (0.52xAPxWxCC)	1938	6222	$3903.27 \pm 448$	3460 – 4350
Calculating lung volume using semi automatic segmentation with CT images	1187	4267	$2864.54 \pm 345$	2520 – 3210



**Figure 7.** (a) Positive correlation between calculated total lung volume using method i and ii, (b) using method i and iii, (c) using method i and iv, (d) using method ii and iii, (e) using method ii and iv, and (f) using method iii and iv.

\*Method i: Calculated total volume using formula by Konheim et al, Method ii: Estimated lung volume using formula by Canals et al (Chest X-Ray), Method iii: Estimated total lung volume using Ellipsoid formula ( $0.52 \times AP \times W \times CC$ ), Method iv: Calculated lung volume using semi auto segmentation with CT images.

**Table 4.** *Pearson Correlations between estimations of total lung volume with 4 different methods.*

Estimation methods*	Pearson correlation**				p-value***			
	Method i	Method ii	Method iii	Method iv	Method i	Method ii	Method iii	Method iv
Method i	1	.679	.655	.565		.000	.000	.003
Method ii	.679**	1	.782**	.745**	.000		.000	.000
Method iii	.655	.782	1	.899	.000	.000		.000
Method iv	.565	.745	.899	1	.003	.000	.000	

\*Method i: Calculating total volume using formula by Konheim et al., Method ii: Estimating lung volume using formula by Canals et al. (chest X-ray), Method iii: Estimating total lung volume using Ellipsoid formula, Method iv: Calculating lung volume using semi automatic segmentation with CT images.

\*\*Correlation is significant at the 0.01 level (2-tailed).

\*\*\*Sig. (2-tailed)

## Discussion

The quantitative measurement of mean lung parenchymal attenuation (MLA) among Malaysian citizens with normal chest CT and methods of total lung volume estimations are described in this study.

### Lung attenuation

Differences in MLA during inspiration in relation to the location of the lung, were described in previous studies [5,11]. In this study, MLA at the middle main carinal level (MCL-M) was lower than the value at the apex and the middle base level (BL-M). At MCL, MLA at anterior MCL (MCL-A) was the lowest followed by MCL-M and posterior MCL (MCL-P); whereas at the base level, MLA at the anterior base level (BL-A) was also the lowest followed by BL-M and the posterior base level (BL-P).



MLA at MCL was lower compared to the apex and could be related to more chest expansion at the carinal level compared to a relatively fixed apex [5]. MLA was higher in BL compared to MCL probably also related to better chest expansion at MCL. The variation seen across MCL and BL (anterior, middle and posterior) could be related to the supine position during image acquisition as the chest expansion at the posterior part of the chest is reduced compared to the anterior part of the chest. Chest expansion or lung volume measurement in the sitting position (using the single breath gas dilution method) was found greater than in the supine position, as in during the CT scan [11]. Therefore, in the supine position, lung expansion is reduced with the most affected part located posteriorly, as seen in this study, whereby, MLA of the posterior part of the lung (MCL-P and BL-P) was higher than the middle (MCL-M and BL-M) and the anterior part (MCL-A and BL-A) at the same corresponding levels. This finding was also observed in the previous study and the MLA regional differences could be related to the lung volume, chest expansion or inflation and gravity influence on the blood flow [3, 12].

According to a study conducted by Smit et al., there was no statistical difference in MLA due to gender differences [5]. However, the low attenuation area in male was found larger compared to females in a study conducted among Chinese population [11]. According to Kim et al., quantitative variation due to gender differences was significant in his study [13]. In this study, it was observed that the MLA of males was lower than females' in both lungs, at the apex, MCL and BL bilaterally. It was a statistically significant variation of MLA due to gender differences ( $p < 0.05$ ) at MCL (anterior, middle and posterior) bilaterally, right BL-A and left BL-M. The possible explanation for lower MLA in males could be related to a larger lung volume [11] and more chest expansion compared to females [14] as males were found to have a larger thoracic rib cage [15]. Even though the ratio of the alveoli amount over a standard unit area or volume was similar in both sexes, males were found to have a higher amount of alveoli than females in general [15]. This is however, the variation due to gender differences at both apical regions and BL-P showed no statistical significance ( $p > 0.05$ ), which could be related to a poor degree of expansion at these regions in both females and males.

## Lung Volume Estimation

Lung volume was generally higher among males, taller and thinner individuals [11]. There are prediction formulas for the total lung volume estimations published and some of these equations take into consideration of an individual's height [10 & 11], gender [10 & 11], age [10], race [10] and weight [11].

The lung volume for the study population ranged from 3476 to 5884 mls with the mean of 4717.58 mls (95% CI 4440 – 4990) using method i; Predicted TLV (pTLV) =  $[-630.819 + (967.100 \times \text{Gender}) + (25.197 \times \text{Height}) - (713.838 \times \text{Race}) + (15.103 \times \text{Age})]/1000$ ; Gender: Male (1), Female (0); Race: African American (1), others (0); Height in cm, Age in years. The mean of the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> methods was lower compared to the 1<sup>st</sup> method, but the 2<sup>nd</sup> and 3<sup>rd</sup> methods showed a 95% confidence interval of 3640 – 4530 mls and 3460 – 4350 mls, respectively, whereby the upper limit values were relatively closer to the lower limit value of the 1<sup>st</sup> method. The mean of the estimated lung volume using method ii, iii and iv was found to be lower and this could be attributable to positioning and inspiratory effort during image acquisition. For method iv, the airway and blood vessels' volume were not included and this is another additional explanation leading to a lower estimated lung volume mean.

A moderate to strong correlation (r value range from 0.565 until 0.899) was seen between all the four different estimation methods described [16]. Method i has a simple method to estimate the lung volume by filling in demographic data of the patient such as gender, height, race and age, without the need of any invasive intervention.

Method ii required information from a frontal chest radiograph. A plain chest radiograph was a routine pre-operative workout prior to anaesthesia administration in some centres [16,17]. The total lung volume could be estimated without any additional unnecessary radiation to the patients, as all patients will have a baseline chest radiograph done prior to their operation. However, some authors do not recommend a chest radiograph as a routine preoperative workout without a clear clinical indication [17 & 18].

Ellipsoid formula and measurement from CT images (Anterior-posterior distance, width and cranio-caudal length) were used in method iii. This method yielded a positive linear correlation with other methods of total lung estimations (with method i, ii and iv). Even without a sophisticated software for auto-segmentation and calculation of the lung volume, estimation of the total lung volume from CT images was possible by using ellipsoid formula.

Comparing all the 4 methods for lung volume estimation, method iv showed the lowest mean value, as the chest expansion of an individual was reduced on the supine position, during CT scan examination. This may not be as accurate compared to method i and ii. Method i only required demographic data from the patient, whereas method ii needed data from a frontal chest radiograph, which was a routine pre-operative examination done in most centres. By considering the risk from radiation exposure, method ii was as good as method i due to no additional radiation given to the patient.

In the occasion when a CT scan examination was already done for the patient with the absence of a sophisticated software to do auto-segmentation and lung volume auto-calculation, method iii (ellipsoid formula) could be used to estimate the lung volume easily.

Several limitations were encountered in this study. Smoking history was not considered during data collection and this could also be one of the factors in causing variation in mean lung attenuation [11] although a study by Smit et al., showed no correlation of smoking or number of pack years with lung attenuation [5].

In this study, four different methods of total lung volume estimation were derived and the correlations between these four methods were demonstrated. The estimations of the lung volume using calculation for the chest radiograph and CT images could be lower compared to the spirometry or body plethysmography due to variation in chest expansion in sitting versus the supine position [11]. During CT image acquisition, there were challenges to ensure all patients were in their maximum effort of full inspiration [10].

To further strengthen the next related projects, it is suggested to correlate the study of mean lung parenchymal attenuation (MLA) with smoking history and differences in lung attenuation changes during respiration such as during full inspiration and forceful expiration. The correlation of lung volume estimation methods can be made with findings in spirometry, body plethysmography or gas dilution technique, in a prospective trial in the future.

## Conclusion

MLA at MCL was lower than the apex and the base level bilaterally. It was also lower at the anterior part compared to the middle and the posterior part at MCL and BL. This could be related to better chest expansion and inspired air distribution at the MCL. The posterior part of the lungs showed higher lung attenuation which was likely related to the position during scanning, a lesser degree of chest expansion at the posterior part of the lung and gravity influences. Generally, MLA of the male subjects was lower than females, except at both apices and part of the lung bases. Lung volume estimations using methods i, ii, iii and iv showed a linear positive moderate to strong correlation among all the four methods. Therefore, it was possible to estimate the total lung volume using demographic data, a plain chest radiograph or ellipsoid formula.

The area of low attenuation (LAA%) and high attenuation area (HAA%) could be affected by inspiratory effort, gravity and gender differences. Therefore, these factors should be considered during the interpretation of LAA% and HAA% in normal patients as well as patients with lung diseases.

This study could help to generate data for future references for lung parenchymal attenuation and the lung volume particularly for Malaysia or Southeast Asia.

## Ethics

This study was approved by the Universiti Kebangsaan Malaysia Research and Ethics Committee, numbered FF-2018-327.

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