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Evaluation of spirometry-gated computed tomography to measure lung volumes in emphysema patients

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CT-derived lung volumes in severe emphysema patients are strongly correlated to lung volumes measured by body plethysmography and spirometry gating in CT helps to improve agreement with body plethysmography results <https://bit.ly/3DFvqmf>

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Abstract

Introduction In emphysema patient being evaluated for bronchoscopic lung volume reduction (BLVR), accurate measurement of lung volumes is important. Total lung capacity (TLC) and residual volume (RV) are commonly measured by body plethysmography but can also be derived from chest computed tomography (CT). Spirometry-gated CT scanning potentially improves the agreement of CT and body plethysmography. The aim of this study was to compare lung volumes derived from spirometry-gated CT and “breath-hold-coached” CT to the reference standard: body plethysmography.

Methods In this single-centre retrospective cohort study, emphysema patients being evaluated for BLVR underwent body plethysmography, inspiration (TLC) and expiration (RV) CT scan with spirometer guidance (“gated group”) or with breath-hold-coaching (“non-gated group”). Quantitative analysis was used to calculate lung volumes from the CT.

Results 200 patients were included in the study (mean±SD age 62±8 years, forced expiratory flow in 1 s 29.2±8.7%, TLC 7.50±1.46 L, RV 4.54±1.07 L). The mean±SD CT-derived TLC was 280±340 mL lower compared to body plethysmography in the gated group (n=100), and 590±430 mL lower for the non-gated group (n=100) (both p<0.001). The mean±SD CT-derived RV was 300±470 mL higher in the gated group and 700±720 mL higher in the non-gated group (both p<0.001). Pearson correlation factors were 0.947 for TLC gated, 0.917 for TLC non-gated, 0.823 for RV gated, 0.693 for RV non-gated, 0.539 for %RV/TLC gated and 0.204 for %RV/TLC non-gated. The differences between the gated and non-gated CT results for TLC and RV were significant for all measurements (p<0.001).

Conclusion In severe COPD patients with emphysema, CT-derived lung volumes are strongly correlated to body plethysmography lung volumes, and especially for RV, more accurate when using spirometry gating.

Introduction

COPD is the third leading cause of death worldwide [1]. The disease is primarily caused by smoking, inducing airway inflammation and the degradation of lung tissue causing airway obstruction and collapse, thereby decreasing the capacity for expiration, leading to airtrapping, which in turn results in hyperinflation causing dyspnoea as a symptom. The airtrapping, leading to hyperinflation, is reflected by an increase in both residual volume (RV) and total lung capacity (TLC). The ratio of RV to TLC is increased as well, making this an important marker for hyperinflation [2]. RV/TLC is a predictor for mortality too, indicating the importance of the marker [3, 4]. Furthermore, both RV and RV/TLC are the key pulmonary function inclusion criteria for lung volume reduction treatment options [5].

RV and TLC are generally measured by either body plethysmography or helium dilution. However, dilution methods are not suitable for patients with severe COPD, since areas with air trapping do not



participate in the dilution process and therefore lead to underestimation of lung volumes. Therefore, the preferred method in this population is body plethysmography. However, body plethysmography involves a challenging manoeuvre, especially for patients with severe COPD.

In severe COPD patients with emphysema, eligibility screening for bronchoscopic lung volume reduction (BLVR) treatment includes body plethysmography and chest computed tomography (CT) scanning. The CT scans are used for a descriptive evaluation mostly in terms of emphysema phenotyping, as well as a quantitative evaluation, and consist of a scan acquisition in inspiration and expiration. Quantitative analysis refers to the amount of emphysema, lobe volumes and fissure integrity scoring [5, 6]. The volume of the lungs in inspiration and expiration scans is analogous to the TLC and RV, respectively, normally derived by body plethysmography. The CT scans are commonly performed with use of a voice recording instructing the patient. However, spirometry gating is expected to improve the CT volume measurements, since it allows for more precise synchronisation of acquiring the CT scan at complete inspiration or expiration [7].

In this study, we compared lung volume measurements derived from spirometry-gated CT and breath-coached CT to body plethysmography, which served as the reference standard. This type of study has not been done on a population this severely affected by COPD.

Methods

Study design and oversight

This was a retrospective single centre study performed at the University Medical Center Groningen, The Netherlands. We included all patients who visited our outpatient clinics between January 2019 and June 2020 for lung volume reduction evaluation. Patients were included if they underwent a flow-volume and body plethysmography and an evaluable inspiratory and expiratory high-resolution CT scan with or without spirometry guidance on the same day. Bronchodilator was administered before all measurements. Spirometry guidance was introduced in a clinical setting on September 1, 2019. This analysis was part of a study which was approved by our local medical ethics committee. All patients provided written informed consent.

Pulmonary function test protocol

Patients' pulmonary function was assessed according to the guidelines of the European Respiratory Society (ERS)/American Thoracic Society (ATS) [8].

The flow-volume measurement was performed, using a pneumotachograph (MasterScreen-PFT PRO/ Body; Vyair Medical, Chicago, IL, USA). A slow vital capacity manoeuvre was performed, consisting of maximum expiration followed by maximum inspiration. At least three technically well-performed measurements were made, with a maximum of eight measurements, of which two had to be within at least 10% or 150 mL of each other, whichever was smaller [9]. The highest value was taken for calculation of the RV.

The intrathoracic gas volume (ITGV) was established using body plethysmography (Masterscreen-PFT Pro/ Body, Vyair Medical); an inspiratory capacity measurement was performed directly after the shutter manoeuvre. Measurements were repeated at least three times, of which two had to be within at least 5% of each other [10]. The mean of the measurements served as the ITGV. The mean inspiratory capacity (IC) was added to the ITGV to amount to the TLC. Subsequently, the TLC was subtracted by the vital capacity to amount to the RV. This constitutes the unlinked method, meaning that the added and subtracted volumes are measured separately from the body plethysmography established ITGV.

CT protocol

CT scans were all performed using a second-generation dual source CT scanner (CT Somatom Definition Flash; Siemens, Erlangen, Germany). Scan pitch was 2.5. Scanning time was 1.5 s for a 40-cm thorax. Tube voltage was adjusted to the weight of the patient. Tube voltage was 100 kV_p in patients <80 kg, 120 kV_p in patients 80–110 kg and 140 kV_p in patients >110 kg. CareDose was used with reference dose 80 mAs. Collimation was 64×0.6 mm. Reconstruction was performed using a hard kernel (B60f), with a recon increment of 0.7 mm and a slice thickness of 1 mm, for a descriptive evaluation, and a smooth kernel (B31f), with a recon increment of 1.5 mm and slice thickness of 1 mm, for the quantitative evaluation (Siemens).

Breath-hold-coached and spirometry-gated CT scanning

In the non-gated group, patients were breath-hold-coached by a standard voice recording. For the gated group, a pneumotachograph (MasterScreen-pneumo, Vyair Medical) was used to monitor the inspiration and expiration during the CT scan [11]. The patients in both groups were instructed to breathe normally followed by maximum expiration, which was to be maintained for 2–3 s at RV level. During this time an expiration CT scan was made. Subsequently, the patient could breathe normally again and was then

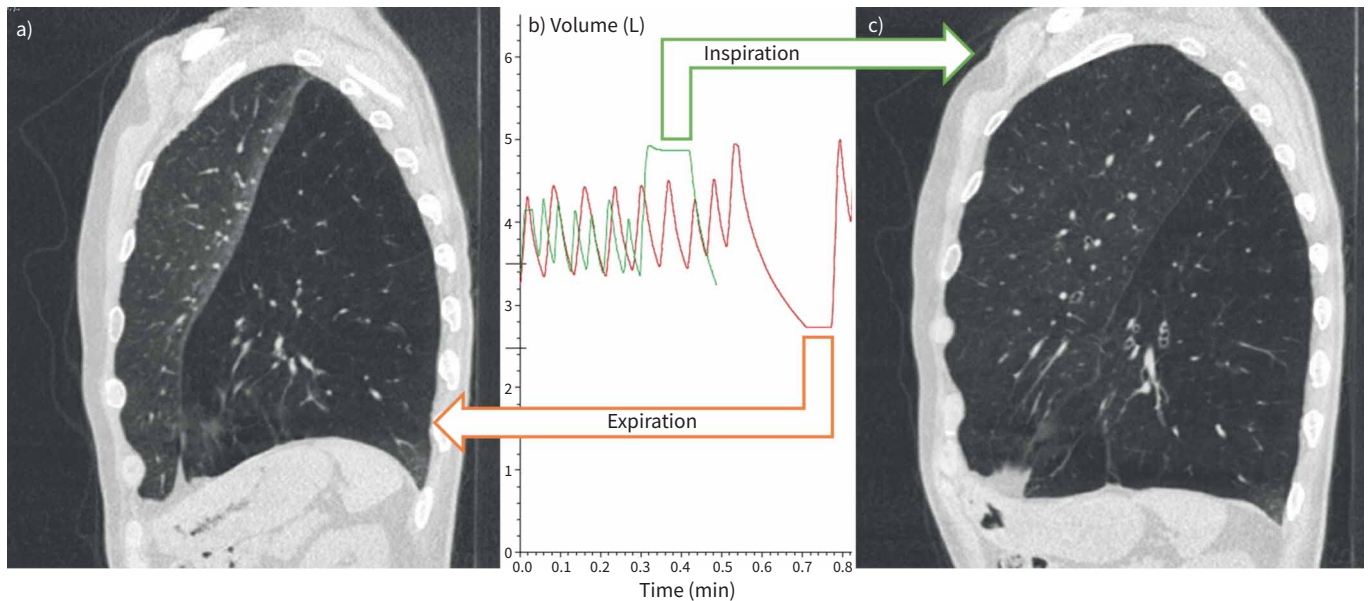


FIGURE 1 a) Sagittal slice of lungs during complete expiration. b) Graph plotting volume against time. The red plot is an example of what the pneumotachograph measured during the expiration manoeuvre, first tidal breathing for approximately 30 s followed by a maximum expiration (residual volume level) with a breath hold (plateau in the curve) for a few seconds. During the breath hold, the expiration scan was acquired. The green plot is an example of what the pneumotachograph measures during the inspiration manoeuvre, first tidal breathing for approximately 30 s followed by a maximum inspiration (total lung capacity level) with a breath hold for a few seconds. During the breath hold, the inspiration scan was acquired. c) Sagittal slice of the lungs during complete inspiration.

instructed to fully inhale, which was to be maintained for 2–3 s at TLC level. During this time, the inspiration CT scan was made (figure 1). This process was guided by a trained technician. For the gated group, this technician decided on the basis of the pneumotachograph data when the patient should breath-hold and when the scan was acquired.

Quantitative CT analysis

CT scans were quantitatively analysed (LungQ; Thirona, Nijmegen, The Netherlands). This software automatically segments the lungs; the segmentations were checked visually. Volume of the lung segmentations were calculated by the software, which sums the voxels within the lung segmentation. Lung volume of the inspiration scan represented CT-derived TLC, while lung volume of the expiration scan represented CT-derived RV. CT-derived TLC and CT-derived RV were used to calculate the % predicted values using European Coal and Steel Community formulas [12], which were used for the plethysmography-derived % predicted values as well. Emphysema score was calculated using the percentage of voxels below -950 Hounsfield units (HU).

Statistical analysis

All data were visually checked for normality by assessing histograms. Demographic data between groups were tested using an independent t-test. To assess the association of the lung volumes as measured by CT and the lung volumes derived from body plethysmography, Pearson correlations between analogous measurements were calculated. t-tests were performed to analyse the difference in lung volumes between CT scan and body plethysmography. Differences between the two groups (gated and non-gated CT) were assessed by an independent t-test and a Fisher's exact test for the categorical parameters. We further assessed differences between corresponding measurements by Bland–Altman plots [13]. The absolute differences used in the Bland–Altman plots are further utilised to assess if other parameters have an influence on these differences by association. p-values below 0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 23.

Results

Demographic data

200 patients (100 in each group) with advanced COPD (mean \pm SD forced expiratory flow in 1 s (FEV₁) 29.2 \pm 8.7%, RV 4.54 \pm 1.07 L) were included in the study. All patient demographics for both the gated and

the non-gated group were comparable, except for a significant difference ($p < 0.05$) in all CT-derived parameters, except for RV (table 1).

TLC and RV: comparing CT with body plethysmography

Within groups, the mean \pm SD difference in TLC between CT and body plethysmography was 280 \pm 340 mL in the gated group and 590 \pm 430 mL in the non-gated group ($p < 0.001$) (figure 2). CT yielded on average lower TLC values than body plethysmography. For RV, the mean difference between CT and body plethysmography amounted to 300 \pm 470 mL for the gated group and 700 \pm 720 mL for the non-gated group ($p < 0.001$). CT yielded on average higher RV values than body plethysmography.

Between groups, the difference in the mean disparity between body plethysmography and CT was always smaller in the gated group in comparison to the non-gated group. The mean differences of gated versus non-gated CT were 310 mL for TLC, 400 mL for RV and 9.23% for %RV/TLC.

The Bland–Altman plots comparing CT and body plethysmography all show systemic bias. For the non-gated RV, RV % predicted, TLC % predicted and gated TLC % predicted there was a proportional bias, meaning that there was an ascending or descending trend noticeable in the plot (figures 3 and 4). The difference between the limits of agreement (Δ LoA) serves as a quantitative indicator of the variability. The Δ LoA for gated TLC was 1.32 L compared to 1.69 L for non-gated TLC. The Δ LoA for TLC % predicted was 23% in the gated group compared to 31% for the non-gated group. For gated RV it was 1.85 L, while it was 2.81 L for the non-gated RV. The Δ LoA for RV % predicted was 86% for the gated group, while it was 130% in the non-gated group.

The difference between plethysmography-derived TLC and CT-derived TLC is associated with body mass index (gated: $r = -0.23$, $p = 0.021$; non-gated: $r = -0.198$, $p = 0.049$). Furthermore, a difference in TLCs is associated with a big difference in RVs (gated: $r = 0.39$, $p < 0.001$; non-gated: $r = 0.277$, $p = 0.005$).

TABLE 1 Baseline characteristics

Characteristics	Gated	Non-gated	p-value
Subjects n	100	100	
Female/male %	68/32	73/27	0.535 [#]
Age years	62 \pm 7	62 \pm 8	0.918
BMI kg·m ⁻²	23.6 \pm 4.1	24.7 \pm 4.2	0.124
GOLD 2/3/4	3/37/60	3/43/54	0.723 [#]
Spirometry			
FEV ₁ L	0.81 \pm 0.27	0.79 \pm 0.24	0.464
FEV ₁ % predicted	29 \pm 9	29 \pm 9	0.923
FVC L	2.73 \pm 0.77	2.53 \pm 0.78	0.074
FVC % predicted	76 \pm 15	72 \pm 18	0.107
FEV ₁ /FVC %	30 \pm 6	32 \pm 6	0.067
VC L	2.98 \pm 0.73	2.90 \pm 0.81	0.416
Body plethysmography			
TLC L	7.64 \pm 1.45	7.36 \pm 1.47	0.169
TLC % predicted	134 \pm 13	132 \pm 13	0.352
RV L	4.64 \pm 1.09	4.45 \pm 1.04	0.206
RV % predicted	217 \pm 39	212 \pm 40	0.408
RV/TLC %	60.6 \pm 7.3	60.4 \pm 7.5	0.884
Computed tomography			
Emphysema score –950 HU %	34.3 \pm 9.1	31.7 \pm 9.7	0.044
TLC L	7.37 \pm 1.45	6.78 \pm 1.48	0.005
TLC % predicted	129 \pm 12	122 \pm 14	<0.001
RV L	4.94 \pm 1.10	5.14 \pm 1.29	0.227
RV % predicted	231 \pm 39	245 \pm 48	0.024
RV/TLC %	67.2 \pm 8.4	76.2 \pm 11.7	<0.001

Table contains information, mean \pm SD and a p-value based on an independent t-test, for the studied population. The population is divided into two groups, gated (n=100) and non-gated (n=100). All CT-derived values are significantly different between groups, except for RV. Bold denotes a significant p-value ($p < 0.05$). BMI: body mass index; GOLD: Global Initiative for Chronic Obstructive Lung Disease; FEV₁: forced expiratory flow in 1 s; FVC: forced vital capacity; VC: vital capacity; TLC: total lung capacity; RV: residual volume. #: the test applied was the Fisher's exact test.

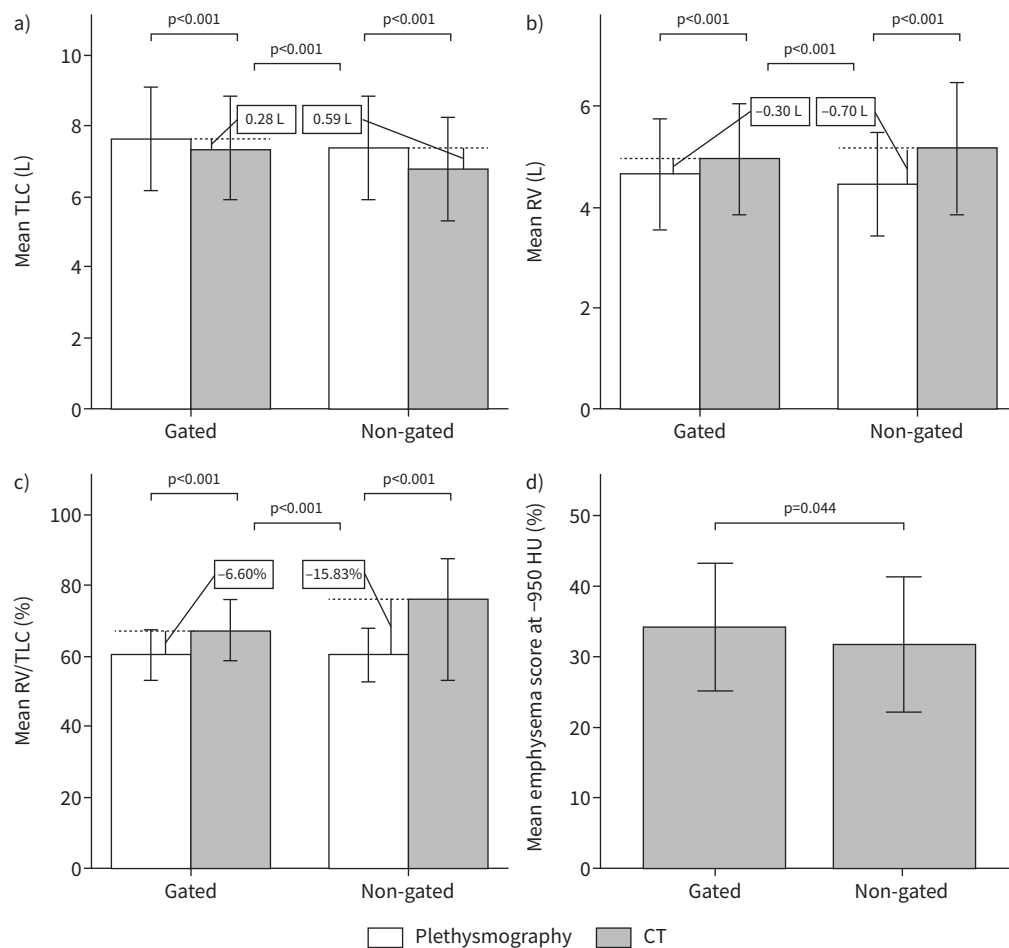


FIGURE 2 Comparison of the means of computed tomography (CT) to body plethysmography measurements. Grey bars represent CT-derived measurements, while white bars represent body plethysmography-derived measurements. **a)** Comparison of total lung capacity (TLC), **b)** comparison of residual volume (RV), **c)** comparison of % RV/TLC and **d)** comparison of emphysema scores at -950 HU. All comparisons are significant. Error bars represent 1 SD.

Associations between CT and body plethysmography-derived volumes

The Pearson's correlation factors for the associations between CT and body plethysmography-derived volumes were 0.947 for TLC in the gated group and 0.917 in the non-gated group. For RV the factors were 0.823 in the gated group and 0.693 in the non-gated group (all $p < 0.001$) (figure 5).

Associations between body plethysmography % predicted volumes and CT-derived % predicted volumes resulted in linear regression formulas that could be used to correct for the systemic bias between the two modules. The following formulas were found for the gated group: % predicted TLC = $8.32 + 0.97 * \% \text{ predicted CT-derived TLC}$ ($r = 0.89$, $p < 0.001$); % predicted RV = $23.42 + 0.84 * \% \text{ predicted CT-derived RV}$ ($r = 0.84$, $p < 0.001$).

Discussion

In this study we compared CT-based lung volume measurements with body plethysmography and investigated the effects of spirometry gating on CT-derived RV and TLC in a cohort of patients with severe COPD.

We found that CT volumes were comparable to body plethysmography volumes. The mean CT-derived TLC was lower compared to the mean plethysmography-derived TLC, while the situation was reversed for RV. Spirometry gating lowered the differences found between the two modalities.

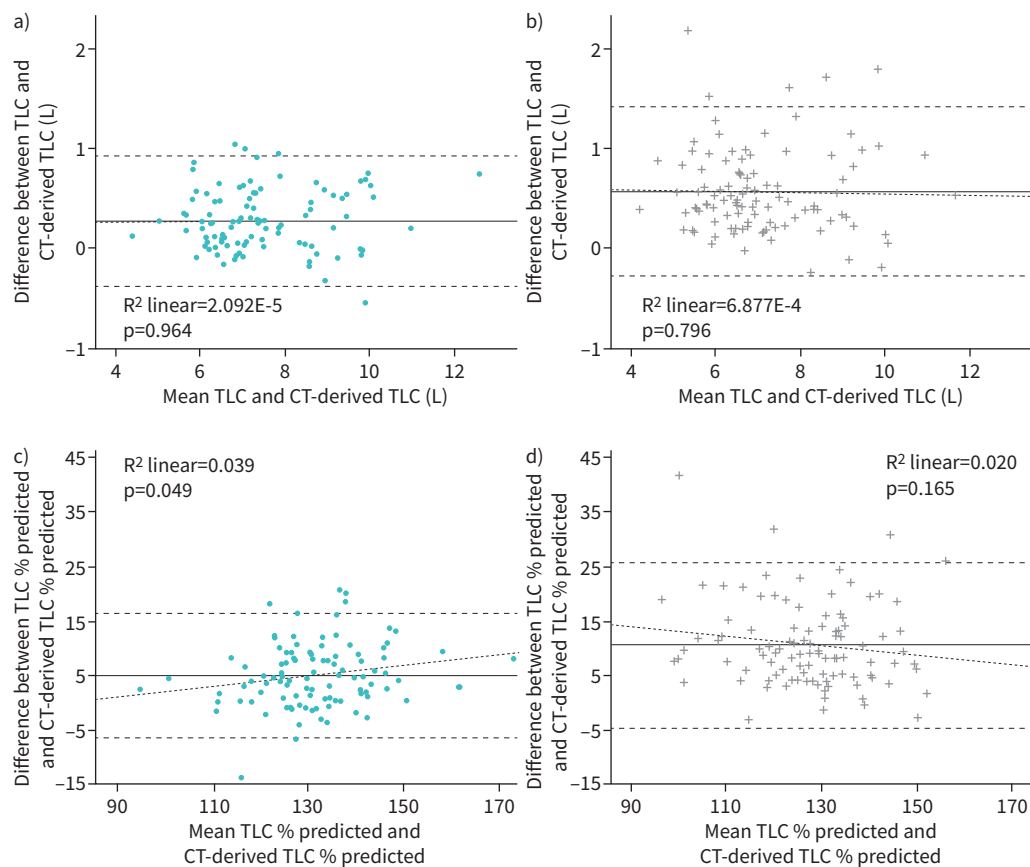


FIGURE 3 Bland-Altman plots comparing computed tomography (CT) and body plethysmography-derived analogous measurements. **a)** Total lung capacity (TLC) gated, **b)** TLC non-gated, **c)** TLC % predicted gated and **d)** TLC % predicted non-gated. The continuous lines indicate the mean difference between CT and body plethysmography, the outer dashed lines indicate the 95% confidence intervals in the differences between CT and body plethysmography, and the difference between these is the difference in limits of agreement (Δ LoA). The finer dashed lines in the middle of the figures indicate the linear regression signifying the proportional bias.

Effects of spirometry gating as observed by other studies

Multiple studies have evaluated the similarity of CT-derived and body plethysmography-derived lung volumes [14–29]. Notably, some of these studies included COPD patients, although the populations were not as severely affected by COPD as in our study. The difference found between CT-derived and body plethysmography-derived TLC ranged between 0.5 and 1 L, with a higher TLC for body plethysmography. This was comparable to our finding of a mean difference of 0.59 L. For RV, the difference found between CT and body plethysmography ranged between 0.3 and 1 L, with a lower RV for body plethysmography. This was comparable to our finding of a mean difference of 0.70 L. However, to our knowledge, none of these studies investigated the effects of spirometry gating on these measurements, with the exception of TANTUCCI *et al.* [15], who studied this in a much milder COPD population (mean FEV₁ 49% predicted). TANTUCCI *et al.* corrected for patient positioning, which was supine in CT *versus* seated in plethysmography. Therefore, their study results cannot be compared to our study results.

Effects of spirometry gating on CT-derived TLC

Support for an effect of spirometry gating is the mean difference between the disparity of the CT-derived TLC and body plethysmography-derived TLC in the gated group compared to the non-gated group, which was significantly smaller in the gated group. Both groups had a significantly lower mean \pm SD value for CT-derived TLC compared to the body plethysmography-derived TLC, namely 280 \pm 340 mL in the gated group and 590 \pm 430 mL in the non-gated group. Therefore, spirometry gating clearly helps to improve the accuracy of CT-derived TLC when compared to body plethysmography-derived TLC. Furthermore, the precision increases as well due to spirometry gating, since the Δ LoA improves from 1.69 L to 1.32 L.

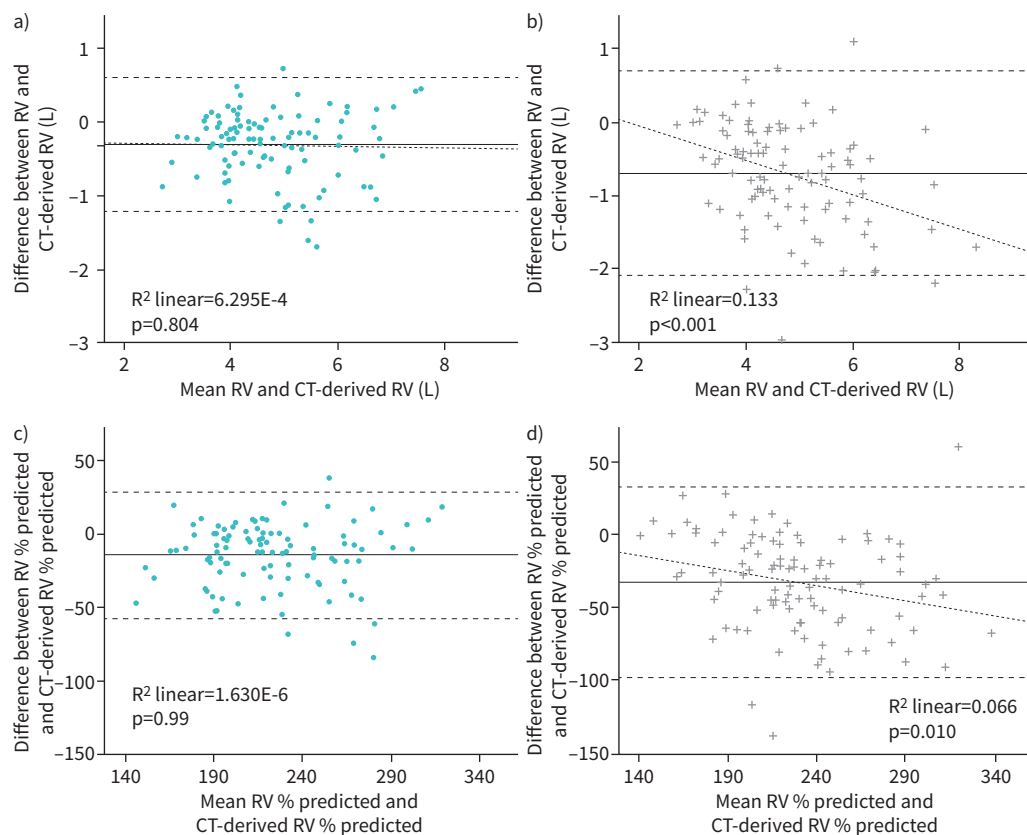


FIGURE 4 Bland–Altman plots comparing Computed tomography (CT) and body plethysmography-derived analogous measurements. **a)** Residual volume (RV) gated, **b)** RV non-gated, **c)** RV % predicted gated and **d)** RV % predicted non-gated. The continuous lines indicate the mean difference between CT and body plethysmography, the outer dashed lines indicate the 95% confidence intervals in the differences between CT and body plethysmography, and the difference between these is the difference in limits of agreement (Δ LoA). The finer dashed lines in the middle of the figures indicate the linear regression signifying the proportional bias.

The disparity between CT-derived and body plethysmography-derived TLC might be due to the fact that body plethysmography included air outside the lungs (mainly central airways), as well as the difference in body position (seated vs supine). The difference in measuring position has been verified to result in higher volumes in a seated position [15, 23, 30–32].

The TLC % predicted values demonstrated a significant proportional bias in the opposite direction for both groups. These biases are difficult to explain and may be the result of an artefact, due to the derived nature of the predicted values.

Effects of spirometry gating on CT-derived RV

To our knowledge, the effects of spirometry gating on RV as measured by CT have not been studied. However, considering that COPD patients mainly experience difficulty with expiration, it is expected that spirometry gating will have the greatest effect on CT-based RV measurements.

We have found that the difference between CT-derived RV and body plethysmography-derived RV was significantly lower in the gated group compared to the non-gated group. Furthermore, in contrast to TLC, RV as measured by CT was significantly higher compared to RV as measured by body plethysmography in both the gated and non-gated group, 300 ± 470 mL lower in the gated group and 700 ± 720 mL lower in the non-gated group. Furthermore, precision increased as shown by the Δ LoA, which improved from 2.81 L to 1.85 L. This difference is at least of a similar order as the known minimal important difference for RV (310–430 mL) [33]. This means that adjustments to the interpretation of the lung volumes as found by CT compared to body plethysmography are probably needed. The direction of change of the RV shown

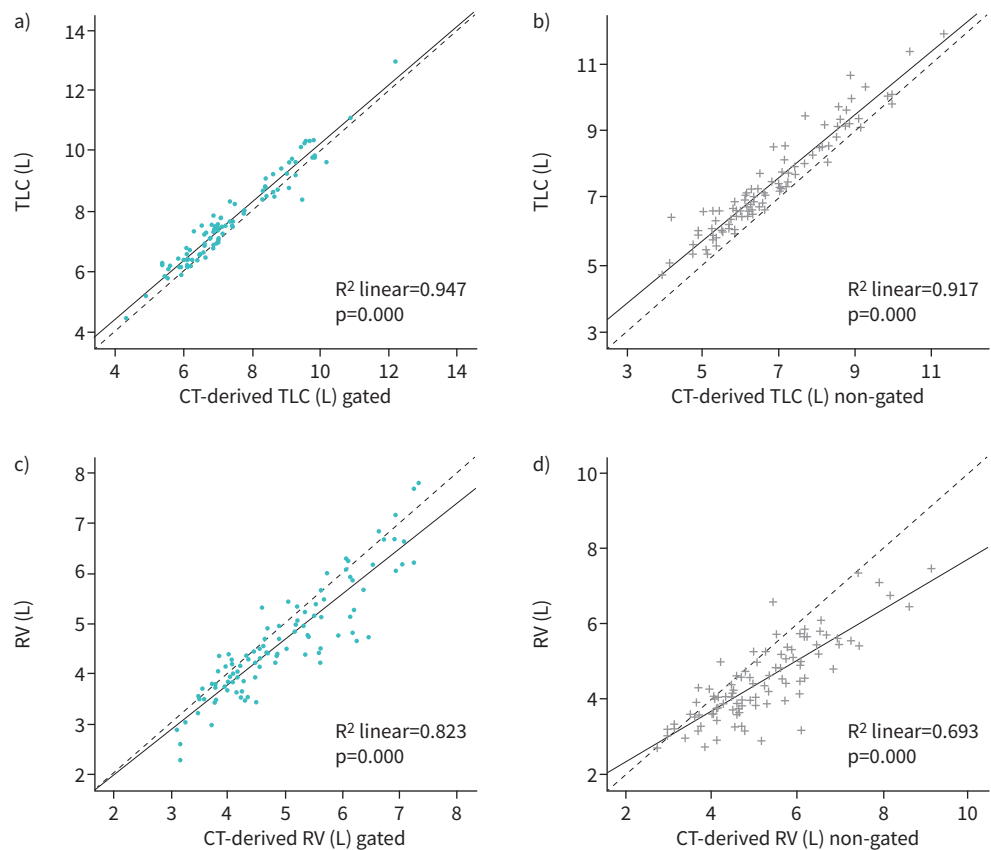


FIGURE 5 Figures show association of computed tomography (CT) with body plethysmography-derived analogous measurements. **a)** Total lung capacity (TLC) gated, **b)** TLC non-gated, **c)** residual volume (RV) gated and **d)** RV non-gated. All correlations are significant ($p < 0.001$). The dashed lines indicate the line for identity and the continuous lines show the functions derived by linear regression.

in this study is opposite to the finding of others that seated RV volumes were higher compared to supine volumes [23, 30–32]. This change is likely mostly explained by the way the expiratory scan is made. The CT scan is often made before a real flow plateau is reached, and timing is instead based on the spirometry-based forced expiratory time, measured before the CT acquisition. This is done, because patients with severe COPD need a considerable effort in reaching and holding complete expiration. Another hypothetical explanation for the difference between the higher RV measured by CT might be the inclusion of solid lung tissue volume in the CT lung volume segmentation, whereas body plethysmography measures air volume exclusively. This effect is larger in RV, since the ratio air to tissue is relatively lower compared to the TLC measurement.

In the non-gated group, RV showed a proportional bias; the higher the mean RV, the higher the difference between both RV values. This is shown by a weak, but significant correlation in figure 4. This effect is completely mitigated by gating. An explanation may be that patients with a high RV struggle more with complete unmonitored expiration, which results in a stronger negative difference between both RVs. RV % predicted followed the patterns of absolute RV in this regard.

Effects of spirometry gating on CT-derived RV/TLC

The TLC is on average lower in CT-derived measurements compared to body plethysmography measurements, and for RV the situation is reversed. Both changes contribute to a higher mean CT-derived %RV/TLC in both gated and non-gated groups. The mean difference between body plethysmography and CT for both RV and TLC is less in the gated group than the non-gated group. This trend is, unsurprisingly, followed in a parameter that is composed of the ratio between RV and TLC, therefore indicating that spirometry gating contributes to a closer alignment in the measurement of %RV/TLC through CT and body plethysmography.

Effects of spirometry gating on associations between CT-derived and body plethysmography-derived volumes

When associating CT-derived parameters and corresponding body plethysmography-derived measurements, higher Pearson's correlation factors were found in the gated group compared to the non-gated group. This indicates that the variability decreased by spirometry gating. Similarly, Bland–Altman plots demonstrated smaller limits of agreement in the gated group compared to the non-gated group, without proportional bias for both groups. Decreased variability is one of the main advantages of spirometry gating, due to the inability to correct for it, unlike a systemic difference between the measurements. The higher Pearson's correlation factors and lower variability in the Bland–Altman plots in the gated group compared to the non-gated group further suggest that spirometry gating reduces the disparity between body plethysmography-derived measurements and CT-derived measurements.

Effect of spirometry gating on emphysema scoring

The effect of spirometry gating is demonstrated in our results by the significant difference in emphysema scoring between both groups, which showed a difference of 2.6% at -950 HU ($p=0.044$), with higher emphysema scores for the gated group. Effects of spirometry gating have traditionally been focused on the effects on densitometry measurements [7, 34–36], mainly because this has been the primary CT quantification of emphysema in use to date. The change in densitometry might be caused by additional air in the lungs as compared to breath-coached methods. However, the emphysema score differences found between groups might reflect real differences in emphysema between groups. In that case, one would expect to find differences as well in other baseline pulmonary function test parameters, which were not present. The direction of change between mean emphysema scores is in line with the expected change. A similar change in densitometry parameters was found by other studies [7, 35, 36]. This may imply that spirometry gating leads to more accurate emphysema scoring, which is beneficial for a more precise BLVR evaluation.

On the possibility of body plethysmography replacement by spirometry-gated CT

Spirometry gating has the disadvantage that it is more time-consuming. However, the closer alignment to body plethysmography may justify its use. Dedicated quantitative CT scan evaluation of lobar emphysema scores and fissure evaluation in COPD patients, who are being evaluated for lung volume reduction options, are nowadays becoming mainstream, and the addition of measuring lung volumes is an easy next step. The replacement of body plethysmography by CT would increase cost-efficiency and decrease patient effort [37], since these patients already undergo CT evaluation [38].

Replacing body plethysmography with CT-derived volumes may be supported, especially in the gated group, by high correlation factors and, at least in the gated group, no proportional bias in Bland–Altman plots. The Bland–Altman plots did, however, show systemic differences, which can be corrected for and are therefore not evidence against the possibility of replacement.

Acceptable levels of variability are still key in obtaining reliable volume measurements, since variability cannot be corrected for. In body plethysmography, the final measurement (ITGV) consists of three measurements, of which two are within 5% of each other [39]. TLC and RV are subsequently derived by addition and subtraction of the IC and ERV, respectively. Volume measurements using CT, on the other hand, are directly calculated from the size of the segmentation and show good repeatability compared to body plethysmography even in COPD patients according to CHONG *et al.* [21]. Additionally, BROWN *et al.* [17] found better reproducibility in lung volume measurements as measured by CT than body plethysmography. This indicates that CT volumes may be more accurate than body plethysmography volumes.

However, the capability of CT to replace body plethysmography in the measurement of the discussed volumes should ultimately be based on the implications for the patients, meaning that the inclusion of patients for lung volume reduction should not change or even improve. Improvement in this context means that extra responders are included, or non-responders are excluded, where they would have been included otherwise. Further studies are therefore needed before lung volumes are to be fully evaluated on the basis of CT.

Lung volume measurement by CT might offer additional information to existing lung volumes in terms of lobar volumes, for which reference equations are already established [40]. Improvement of the lung volumes by spirometry gating implies improvement of these lobar volumes as well. Apart from this, CT allows evaluation of the type, severity and distribution of emphysema, information that cannot be derived from body plethysmography. The lobar lung volumes and emphysema distribution would be used to evaluate which lobe can be treated by the BLVR. Ideally, the target lobe has a lot of emphysema and

therefore contributes scarcely to the gas exchange, while trapping air [41]. This can only be determined by use of quantitative CT.

Study limitations

This study consists of a comparison of techniques that are used on two unrelated groups of patients. A more conclusive study would compare the same patient with spirometry gating and breath-coaching. However, we are limited by the medical ethical considerations regarding radiation exposure for such evaluations.

Furthermore, this study was performed retrospectively; therefore, we cannot evaluate the effect of using spirometry-gated CT lung volumes instead of body plethysmography-derived lung volumes on patient/lobe selection.

We have compared two measurements that were taken in different positions. The positioning of a patient affects their lung volume, thereby limiting the validity of the comparison.

Generalizability to other hospitals may suffer because we used a high-pitch scan. This is not available in many hospitals. High pitch causes the overall scan time to be very short (about 1 s). Low scan time may be a requirement, since patients with severe COPD are not able to hold their breath well in maximum inspiration or expiration, in particular for the latter.

Conclusion

CT-derived lung volumes are strongly associated with body plethysmography results in severe emphysema patients. A significant systemic difference remains for TLC (lower for CT) and RV (higher for CT), with presumably limited clinical relevance. Spirometry gating brings CT-derived volumes into a closer alignment to body plethysmography-derived volumes and as well decreases variability, especially for RV, thereby significantly improving the quality of the CT-derived lung volumes. This in turn potentially implies improved densitometry measurements and improved lobar volumes. Utilising CT-derived volumes may reduce patient effort and costs associated with plethysmography. Future prospective studies using CT-derived pulmonary function outcomes will need to show its real validity in clinical practice.

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References

- 1 World Health Organization. The top 10 causes of death. www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death Date last accessed: 26 October 2020.
- 2 Fessler HE, Scharf SM, Ingenito EP, et al. Physiologic basis for improved pulmonary function after lung volume reduction. *Proc Am Thorac Soc* 2008; 5: 416–420.
- 3 Shin TR, Oh YM, Park JH, et al. The prognostic value of residual volume/total lung capacity in patients with chronic obstructive pulmonary disease. *J Korean Med Sci* 2015; 30: 1459–1465.
- 4 Budweiser S, Harlacher M, Pfeifer M, et al. Co-morbidities and hyperinflation are independent risk factors of all-cause mortality in very severe COPD. *COPD J Chronic Obstr Pulm Dis* 2014; 11: 388–400.
- 5 Klooster K, Slebos DJ. Endobronchial valves for the treatment of advanced emphysema. *Chest* 2021; 159: 1833–1842.
- 6 Herth FJF, Slebos D-J, Criner GJ, et al. Endoscopic lung volume reduction: an expert panel recommendation – update 2019. *Respiration* 2019; 97: 548–557.
- 7 Kalendar WA, Rienmuller R, Seissler W, et al. Measurement of pulmonary parenchymal attenuation: use of spirometric gating with quantitative CT. *Radiology* 1990; 175: 265–268.
- 8 Miller MR, Crapo R, Hankinson J, et al. General considerations for lung function testing. *Eur Respir J* 2005; 26: 153–161.
- 9 Graham BL, Steenbruggen I, Barjaktarevic IZ, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am J Respir Crit Care Med* 2019; 200: E70–E88.
- 10 Wanger J, Clausen JL, Coates A, et al. Standardisation of the measurement of lung volumes. *Eur Respir J* 2005; 26: 511–522.

- 11 Salamon E, Lever S, Kuo W, *et al.* Spirometer guided chest imaging in children: it is worth the effort! *Pediatr Pulmonol* 2017; 52: 48–56.
- 12 Quanjer PH, Tammeling GJ, Cotes JE, *et al.* Lung volumes and forced ventilatory flows. *Eur Respir J* 1993; 6: Suppl 16, 5–40.
- 13 Martin Bland J, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 327: 307–310.
- 14 Shen M, Tenda ED, McNulty W, *et al.* Quantitative evaluation of lobar pulmonary function of emphysema patients with endobronchial coils. *Respiration* 2019; 98: 70–81.
- 15 Tantucci C, Bottone D, Borghesi A, *et al.* Methods for measuring lung volumes: is there a better one? *Respiration* 2016; 91: 273–280.
- 16 Matsumoto AJ, Bartholmai BJ, Wylam ME. Comparison of total lung capacity determined by plethysmography with computed tomographic segmentation using CALIPER. *J Thorac Imaging* 2017; 32: 101–106.
- 17 Brown MS, Kim HJ, Abtin F, *et al.* Reproducibility of lung and lobar volume measurements using computed tomography. *Acad Radiol* 2010; 17: 316–322.
- 18 Kauczor HU, Heussel CP, Fischer B, *et al.* Assessment of lung volumes using helical CT at inspiration and expiration: comparison with pulmonary function tests. *Am J Roentgenol* 1998; 171: 1091–1095.
- 19 Chen F, Kubo T, Shoji T, *et al.* Comparison of pulmonary function test and computed tomography volumetry in living lung donors. *J Heart Lung Transplant* 2011; 30: 572–575.
- 20 Zaporozhan J, Ley S, Eberhardt R, *et al.* Paired inspiratory/expiratory volumetric thin-slice CT scan for emphysema analysis: comparison of different quantitative evaluations and pulmonary function test. *Chest* 2005; 128: 3212–3220.
- 21 Chong D, Brown MS, Kim HJ, *et al.* Reproducibility of volume and densitometric measures of emphysema on repeat computed tomography with an interval of 1 week. *Eur Radiol* 2012; 22: 287–294.
- 22 Iwano S, Okada T, Satake H, *et al.* 3DCT volumetry of the lung using multidetector row CT: comparison with pulmonary function tests. *Acad Radiol* 2009; 16: 250–256.
- 23 Yamada Y, Yamada M, Chubachi S, *et al.* Comparison of inspiratory and expiratory lung and lobe volumes among supine, standing, and sitting positions using conventional and upright CT. *Sci Rep* 2020; 10: 1–12.
- 24 Brown MS, McNitt-Gray MF, Goldin JG, *et al.* Automated measurement of single and total lung volume from CT. *J Comput Assist Tomogr* 1999; 23: 632–640.
- 25 Song L, Leppig JA, Hubner RH, *et al.* Quantitative CT analysis in patients with pulmonary emphysema: do calculated differences between full inspiration and expiration correlate with lung function? *Int J COPD* 2020; 15: 1877–1886.
- 26 Jung WS, Haam S, Shin JM, *et al.* The feasibility of CT lung volume as a surrogate marker of donor-recipient size matching in lung transplantation. *Medicine (Baltimore)* 2016; 95: 1–7.
- 27 Garfield JL, Marchetti N, Gaughan JP, *et al.* Total lung capacity by Plethysmography and high-resolution computed tomography in COPD. *Int J COPD* 2012; 7: 119–126.
- 28 Becker MD, Berkmen YM, Austin JHM, *et al.* Lung volumes before and after lung volume reduction surgery: quantitative CT analysis. *Am J Respir Crit Care Med* 1998; 157: 1593–1599.
- 29 Coxson HO, Nasute Fauerbach PV, Storness-Bliss C, *et al.* Computed tomography assessment of lung volume changes after bronchial valve treatment. *Eur Respir J* 2008; 32: 1443–1450.
- 30 Blair E, Hickam JB. The effect of change in body position on lung volume and intrapulmonary gas mixing in normal subjects. *J Clin Invest* 1955; 34: 383–389.
- 31 Allen SM, Hunt B, Green M. Fall in vital capacity with posture. *Br J Dis Chest* 1985; 79: 267–271.
- 32 Fromageot C, Lofaso F, Annane D, *et al.* Supine fall in lung volumes in the assessment of diaphragmatic weakness in neuromuscular disorders. *Arch Phys Med Rehabil* 2001; 82: 123–128.
- 33 Hartman JE, Ten Hacken NHT, Klooster K, *et al.* The minimal important difference for residual volume in patients with severe emphysema. *Eur Respir J* 2012; 40: 1137–1141.
- 34 Gierada DS, Yusen RD, Pilgram TK, *et al.* Repeatability of quantitative CT indexes of emphysema in patients evaluated for lung volume reduction surgery. *Radiology* 2001; 220: 448–454.
- 35 Moroni C, Mascalchi M, Camiciottoli G, *et al.* Comparison of spirometric-gated and -ungated HRCT in COPD. *J Comput Assist Tomogr* 2003; 27: 375–379.
- 36 Otjen JP, Swanson JO, Oron A, *et al.* Spirometry-assisted high resolution chest computed tomography in children: is it worth the effort? *Curr Probl Diagn Radiol* 2018; 47: 14–18.
- 37 Shore SA, Huk O, Mannix S, *et al.* Effect of panting frequency on the plethysmographic determination of thoracic gas volume in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1983; 128: 54–59.
- 38 Bakker JT, Klooster K, Vliegenthart R, *et al.* Measuring pulmonary function in COPD using quantitative chest computed tomography analysis. *Eur Respir Rev* 2021; 30: 210031.
- 39 Criée CP, Sorichter S, Smith HJ, *et al.* Body plethysmography – Its principles and clinical use. *Respir Med* 2011; 105: 959–971.

- 40 Come CE, Diaz AA, Curran-Everett D, *et al.* Characterizing functional lung heterogeneity in COPD using reference equations for CT scan-measured lobar volumes. *Chest* 2013; 143: 1607–1617.
- 41 Slebos DJ, Shah PL, Herth FJF, *et al.* Endobronchial valves for endoscopic lung volume reduction: best practice recommendations from expert panel on endoscopic lung volume reduction. *Respiration* 2017; 93: 138–150.