Published in final edited form as:
Eur Radiol. 2013 June ; 23(6): 1564–1572. doi:10.1007/s00330-012-2746-1.

Assessment of Lung Volume Collapsibility in Chronic Obstructive Lung Disease Patients Using CT

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Abstract

Objective—To investigate the collapsibility of the lung and individual lobes in patients with COPD during inspiration/expiration and assess the association of whole lung and lobar volume changes with pulmonary function tests (PFTs) and disease severity.

Methods—PFT measures used were RV/TLC%, FEV1% predicted, FVC, FEV1/FVC%, DLco% predicted and GOLD category. A total of 360 paired inspiratory and expiratory CT examinations acquired in 180 subjects were analysed. Automated computerised algorithms were used to compute individual lobe and total lung volumes. Lung volume collapsibility was assessed quantitatively using the simple difference between CT computed inspiration (I) and expiration (E) volumes (I-E), and a relative measure of volume changes, (I-E)/I.

Results—Mean absolute collapsibility (I-E) decreased in all lung lobes with increasing disease severity defined by GOLD classification. Relative collapsibility (I-E)/I showed a similar trend. Upper lobes had lower volume collapsibility across all GOLD categories and lower lobes collectively had the largest volume collapsibility. Whole lung and left lower lobe collapsibility measures tended to have the highest correlations with PFT measures. Collapsibility of lung lobes and whole lung were also negatively correlated with the degree of air trapping between expiration and inspiration, as measured by mean lung density. All measured associations were statistically significant ($P < 0.01$).

Conclusion—Severity of COPD appears associated with increased collapsibility in the upper lobes, but change (decline) in collapsibility is faster in the lower lobes.

Keywords

lung volume; collapsibility; COPD; computed tomography; disease severity

INTRODUCTION

As a highly elastic organ functionally aimed at efficient oxygen exchange into the body and carbon dioxide discharge, the human lung comprises a variety of tissues, which include parenchyma, airways and vasculature, that is designed to perform extremely efficient gas exchange during the respiratory cycle, essentially extracting oxygen during inspiration and expelling carbon dioxide during expiration. Physiological functions of the lungs are

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intimately associated with lung anatomy. Diseases and/or abnormalities that affect the mechanical properties of the lungs are likely to prevent the lungs from functioning properly. For example, obstructed airways, thickened airway walls, destruction of air sacs, or air sacs losing their elastic quality will frequently lead to the development of COPD owing to a decrease in air flow into and out of the lungs [1]. Similarly, it is likely that the severity of lung dysfunction is reflected directly in the underlying elasticity and/or lung volume changes.

Because of its high spatial and temporal resolution, computed tomography (CT) has been widely used in routine clinical practice for in vivo investigation of pulmonary diseases. Previous studies have revealed a close relationship between quantitative CT findings and pulmonary function [6] as well as the nature and impact of various disease processes [11]. The quantitative CT methods most widely explored for COPD assessment are methods based on HU value thresholds applied to the CT images to identify specific regions of interest on the lung, often referred to as the “density mask” [12]. However, the ability of the threshold-based methods alone to detect and quantify the presence of COPD is reduced in the presence of co-existing abnormalities depicted on CT images as high-density lung regions, low-density air-trapping or fibrosis [12, 15]. Studies have analysed other CT features, such as the change in lung volume between paired inspiratory and expiratory images of COPD patients, to help categorise the type and severity of lung disease as well as assess lung function and/or response to therapy [16]. Kauczor et al [17] and Iwano et al [18] demonstrated that lung volumes estimated from inspiratory and expiratory CT examinations correlate with static lung volumes measured using spirometry. Yamashiro et al [1] found that lung volume collapsibility represented by the ratio of expiratory to inspiratory lung CT computed volume, correlates significantly with both pulmonary function tests and tissue density-based measures. Furthermore, surgical studies report that lung volume reduction surgery (LVRS) or bronchial valve treatment, used in severe cases of COPD, resulted in improved outcomes post-operatively as measured by pulmonary function tests [7, 20].

However, to date, studies on a relation between lung volume on CT examination and pulmonary function are limited in scope. To our knowledge, there are no reports on the correlation between regional (e.g. lobar) volume change on paired inspiratory/expiratory CT examinations and pulmonary function. Volume changes of individual lung lobes may differ as a function of the severity of disease (e.g. COPD). In this study, we assessed absolute and relative total lung and lobar volume changes using a large and diverse dataset acquired from COPD patients. The primary aim of the study was to assess whether total lung and specific lobar collapsibility correlate with severity of COPD as defined by a set of preselected pulmonary function measures.

MATERIALS AND METHODS

Study population

The subject population consisted of 180 consenting participants enrolled in an NHLBI Lung Tissue Research Consortium (LTRC) study that recruited subjects from multiple sites (Table 1). All available LTRC subjects that had inspiration and expiration CT examinations amenable for analysis were selected for this study across a range of airflow obstruction. Subjects were excluded if they had a known primary infectious disease, cystic fibrosis, berylliosis and/or pulmonary hypertension. The duration of a study visit was typically 4–6 h and subjects underwent spirometry and plethysmography tests, measurements of lung diffusion capacity, answered demographic and medical history questionnaires and CT exam. The CT exams were performed before surgery in all instances where the patient was determined to require surgery. Subjects were classified into COPD severity based on the five categories presented by the Global Initiative for Chronic Obstructive Lung Disease (GOLD)

[21]. Subjects not meeting the GOLD classification for COPD are classified as “none.” This study was approved by a University of Pittsburgh IRB-approved protocol (#0411036).

Acquisition of thin-section CT examinations

Computed tomography examinations used in this study were performed at multiple sites as part of the LTRC [22]. Six different systems were used: General Electric (GE) LightSpeed 16 (n=144), GE LightSpeed 16 Pro (n=23), GE LightSpeed VCT (n=2), GE LightSpeed Ultra (n=1), GE Discovery CT750 HD (n=1), and Siemens Sensation 64 (n=50). CT examinations were acquired without contrast material and with subjects holding their breath for less than 15 s at both end full-inspiration and (TLC) and end normal-expiration (FRC). The protocol varied slightly based on the CT manufacturer (Table 2), but were the same for the inspiration and expiration acquisitions for each participant. Images were reconstructed to encompass the entire lung field in a 512×512 pixel matrix.

Measurements of whole lung and lobe volumes

Automated computerised schemes were used to obtain total lung and lobar volumes from paired inspiratory and expiratory CT acquisitions. First, the entire lung volume was segmented using a three-dimensional (3D) adaptive border matching algorithm [23]. Pulmonary fissures were detected using computational geometry [29], and the surfaces of individual lobes were demarcated by representing the pulmonary fissures as implicit surface functions [23–25]. The results of the computerised segmentation were verified by visual inspection by image analysts and manually corrected when the computer failed to identify the lobes correctly (Fig. 1).

Lung and lobe volumes were computed from the CT images using the segmentation results by counting the voxels circumscribed by the lobe boundaries detected and multiplying by the voxel volume (mm^3). Two measures of dynamic volume collapsibility were computed: (a) the difference between paired inspiratory *(I)* and expiratory *(E)* CT volumes (or $I - E$) and (b) the difference between the inspiratory and expiratory CT volumes relative (fraction) of the inspiratory CT volumes [or (I-E)/I]. Note that the relative change in volume is a complement to the one used by Yamashiro et al [1]. In addition, we also computed the mean lung density (MLD) values for inspiratory (MLD_I) and expiratory (MLD_E) CT examinations for each individual lobe.

Statistical data analysis

Statistical analyses were performed using Matlab (MathWorks, Natick, MA, USA) and Excel (Microsoft Corp., Redmond, WA, USA). The mean values and standard deviation for the absolute and relative collapsibility of each lobe was computed for each COPD category from (none, GOLD I, GOLD II, GOLD III, GOLD IV). Spearman rank correlation was computed to estimate the association between the absolute and relative collapsibility of each lobe and

1. Residual volume (RV)/total lung capacity (TLC) ratio,
2. Forced expiratory volume at 1 s percentage predicted (FEV_1%),
3. Forced vital capacity percentage predicted (FVC%),
4. FEV_1/FVC ratio,
5. Diffusing capacity of the lung for carbon monoxide percentage predicted (DLco%), and
6. COPD severity category, as well as the association with mean lung density change (MLD_I - MLD_E) of individual lobes

A *P* value of 0.01 was used to declare a statistically significant association.

RESULTS

Assessment of lung volume collapsibility as a function of disease severity

Absolute lung collapsibility decreases monotonically in all lung lobes as GOLD category increases (Fig. 2). Both upper lobes (RUL and LUL) have lower absolute collapsibility across all GOLD categories compared with the lower lobes (RLL and LLL). As the right middle lobe (RML) is the smallest lobe, it has the lowest decline in collapsibility across COPD severity. The lower lobes (LLL and RLL) have the fastest rate of collapsibility decline with increasing GOLD classification, which was determined by the slope of the collapsibility decline from category "none" to GOLD IV. These lobes also have the largest absolute volume changes of all lobes. Thus, as severity of COPD increases, absolute collapsibility of the upper lobes is always smaller, and there is a faster decline in lower lobe collapsibility with increasing COPD severity. As the severity of COPD increases, relative lobe volume collapsibility decreased monotonically (Fig. 3). In addition, the upper lobes (RUL and LUL) have lower relative collapsibility for all COPD categories compared with relative collapsibility in the lower lobes (RLL and LLL). However, relative collapsibility of the lower lobes declines faster than that of all the other lobes.

Correlation between lung volume collapsibility and pulmonary function measures

In terms of absolute difference between inspiration and expiration, (*I-E*), the correlation between (*I-E*) and pulmonary function test (PFT) results is similar for all lobes and the whole lung (Table 3). As expected, there is a negative correlation between absolute change in volume and GOLD category.

The differences among individual lobes are more marked when we study the relative lobe collapsibility (Fig. 4) compared with simple collapsibility (Table 4). Across measures of lung function, namely FEV_1% predicted, FVC%, RV/TLC% and GOLD stage, the right lower lobe (RLL) and the left lower lobe (LLL) correlate more strongly with the functional measures of interest. We also note that relative collapsibility, which is scaled by the lobe volume, correlates more strongly with functional measures than absolute collapsibility. Finally, we note that for individual lobes there are no significant differences in the correlation between relative collapsibility and DLco% predicted.

Correlation between lung volume collapsibility and mean lung density change

The magnitude of absolute lung volume collapsibility (I-E) varies directly with the magnitude of change in mean lung density between inspiration and expiration (MLD_I-MLD_E) for each individual lobe (Table 5). The absolute lung volume difference between inspiration and expiration (I-E) was highly correlated with the MLD change (MLD_I-MLD_E) for all lobes (Fig. 5), although the magnitude of correlation is strongest for relative lung volume collapsibility and MLD change rather than absolute lung volume collapsibility and MLD change (Table 6). Among all lobes, the RUL and LUL had the strongest correlation coefficients over all GOLD stages.

DISCUSSION

The results of this study reveal that higher lung and/or lobe volume collapsibility is associated with better pulmonary function measure and decreased COPD severity. We found no material difference in the strengths of correlations for any individual lobe. With regard to relative collapsibility, the correlation between the lower lobes and lung capacity measures on PFTs was strongest when compared with the correlations for all the other lobes. The

lower lobes had greater collapsibility (both simple and relative) and a greater rate of collapsibility as COPD severity increased than the upper lobes, which is in part probably due to the lung biomechanics, but may also indicate that there are patterns of disease (e.g. emphysema) that are upper lobe-predominant. The upper lobe-predominant disease pattern was also supported by mean lung density changes between inspiration and expiration, which correlated well with collapsibility of individual lobes and was in general strongest for the upper lobes.

The results are in general agreement with a previous study that examined primarily total lung volume changes and used only a relative measure of collapsibility, E/I [1]. Our study expands on previous investigations by resolving the correlation between volume changes and pulmonary function at the level of individual lobes. Other studies examined how volumes, rather than changes in volumes, correlate with PFTs [17, 18] and a number of studies attempted to correlate inspiratory changes with pulmonary function using threshold-based approaches [6, 9, 26], but none has examined the behaviour of individual lung lobes. Our study also included a larger dataset than those used in previous studies.

The results of our study are consistent with findings by Kauczor et al [17], Iwano et al [18], and Yamashiro et al [19] that report correlation between lung volumes calculated from inspiratory and expiratory CT examinations and PFT measures. Our overall results are in general agreement with previous reports that state that upper lobe-predominant emphysema is associated with poorer overall lung function than lower lobe-predominant emphysema [26, 27]. However, other studies [28] have reported that in emphysema patients with alpha-1 antitrypsin deficiency, impairment in the lower lobes is associated with a greater degree of airflow obstruction. Our results may reconcile the seeming discrepancy in that although upper lobe collapsibility is lower across all severities of COPD, as severity increases a faster decline in collapsibility of the lower lobes was observed.

The results of this study may have implications in clinical practice. For example, analysis of lobe volume collapsibility may be informative in terms of which lobe to focus on during lung volume reduction surgery (LVRS) for emphysema or bronchial valve treatment, and what is the likelihood of a good prognosis. In fact, other quantitative CT measures, such as densitometric measures, have been correlated with good prognoses post-LVRS [29, 30, 31]. Another application of lung volume collapsibility analysis is in the selection of bronchodilators. Lung volume collapsibility may be interpreted as an indication of the degree of parenchymal damage, and some studies have recently reported that the efficacy of bronchodilators in COPD is influenced by the degree of parenchymal damage [8].

There are several limitations to the study. Firstly, we attempted to correlate global functional measures with global (i.e. total lung) as well as regional (i.e. lobar) changes in lung volume. This approach does not allow for analysis of the direct contribution of each lobe to overall pulmonary function. Secondly, the distribution of cases was not balanced in terms of disease severity (GOLD classification) in that we had no cases with truly mild disease in our dataset. However we believe that the conclusions of this study are not likely to be substantially affected by this limitation. Additionally, our cohort did include “healthy” controls because all subjects were part of the LTRC that was charge with collecting lung tissue, which was performed for a variety of reason mostly to treat lung cancer. Thirdly, subject breathing during CT was not controlled by any means of spirometric gating; such gating is rarely performed in clinical CT practice. Therefore, there is no reasonable way to determine a subject’s respiratory state or breathing effort during the CT data acquisition. We assume that any confounding factors related to the subjects’ respiratory state were mitigated by the fact that most subjects would make a reasonable effort to follow the breathing instructions and by the large number of subjects examined our study.

In conclusion, we showed that absolute and relative lobe volume collapsibility as measured on paired inspiratory/expiratory CT correlates significantly with measures of lung function. As the severity of COPD increases, the collapsibility of individual lung lobes decreases. Upper lobes tend to exhibit more severe disease, hence the lower collapsibility for COPD of all degrees of severity, while the collapsibility of lower lobes declines faster as the severity of COPD increases.

Acknowledgments

This work is supported in part by grants from the National Heart, Lung, and Blood Institute of the National Institutes of Health to the University of Pittsburgh under Grants and RO1 HL096613, P50 CA090440, P50 HL084948, R01 HL095397, U01 HL108642, RC2 HL101715 and the Bonnie J. Addario Lung Cancer Foundation.

Abbreviations

GOLD	global initiative for chronic obstructive lung disease
COPD	chronic obstructive pulmonary disease
TLC	total lung capacity
FEV	forced expiratory volume
LTRC	Lung Tissue Research Consortium
RV	residual volume
LVRS	lung volume reduction surgery
MLD	mean lung density
FVC	forced vital capacity
DLco	diffusion capacity for carbon monoxide
PFT	pulmonary function tests
CT	computed tomography
LUL, RUL, LLL, RLL, RML	right or left, upper or lower lobes

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Key points

- Inspiratory and Expiratory computed tomography allow assessment of lung collapsibility
- Lobe volume collapsibility is significantly correlated with measures of lung function.
- As COPD severity increases, collapsibility of individual lung lobes decreases.
- Upper lobes exhibit more severe disease, while lower lobes decline faster.

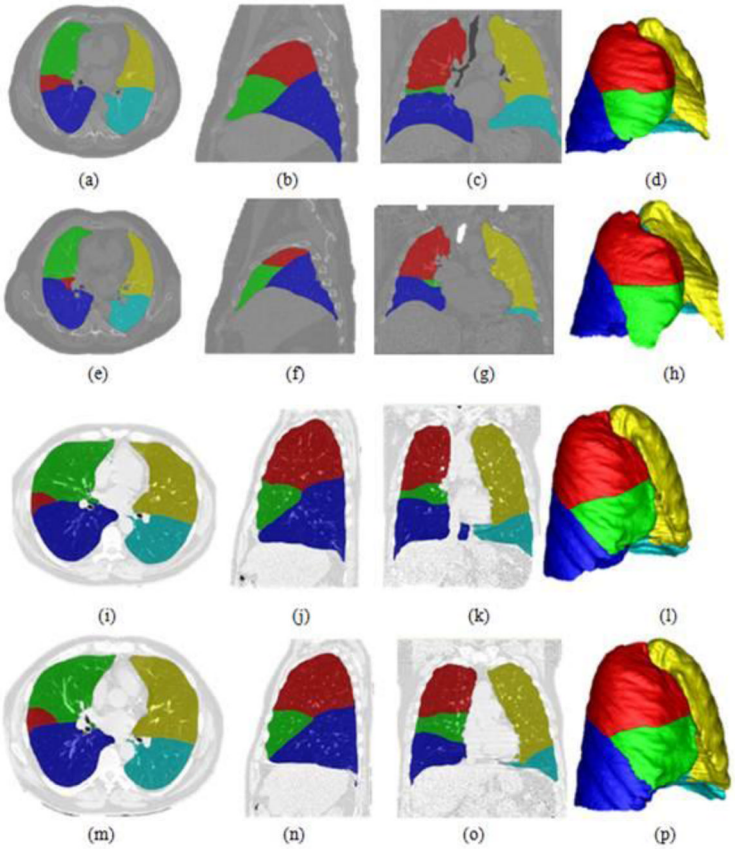


Fig. 1.

Examples of lobe segmentation results as outputted by the computerised scheme [23–25]. The images (a)–(h) were obtained from a single COPD patient classified as category “none”. Images (i)–(p) were obtained from a single COPD patient classified as GOLD category 4. The top rows in both grids represent inspiratory imaging and the bottom rows represent the corresponding expiratory imaging. Axial views (in column 1), sagittal views (in column 2), coronal views (in column 3) and 3D views (in column 4), are shown. We note that changes in lobe volumes between inspiration and expiration are more pronounced visually in the non-COPD patient (none) than that in the patient with high severity of COPD (GOLD 4)

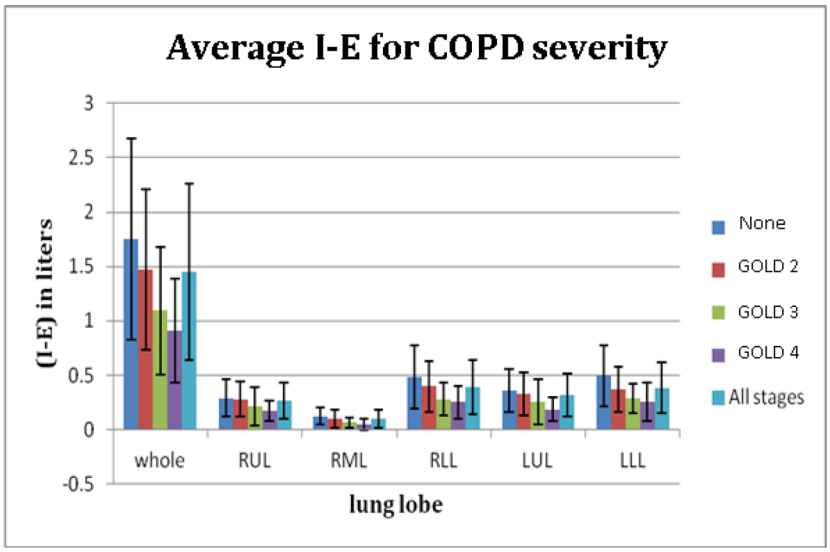


Fig. 2.

Absolute lobe volume collapsibility for individual lobes across GOLD categories. The error bars denote standard deviations

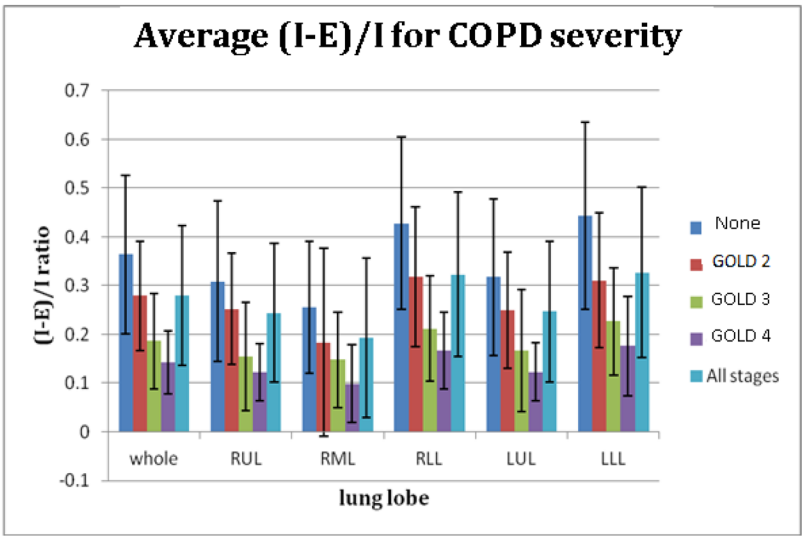
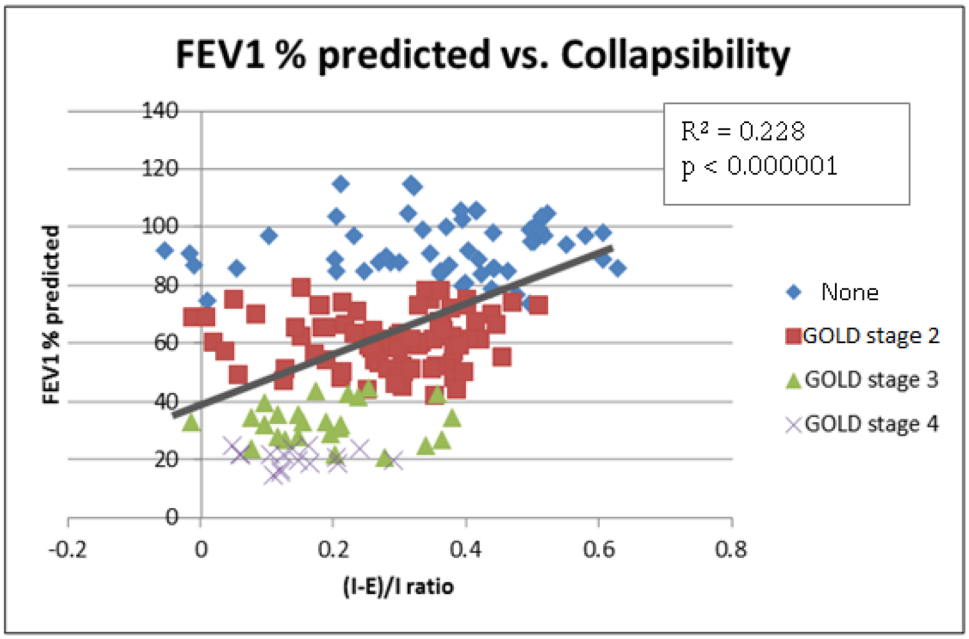
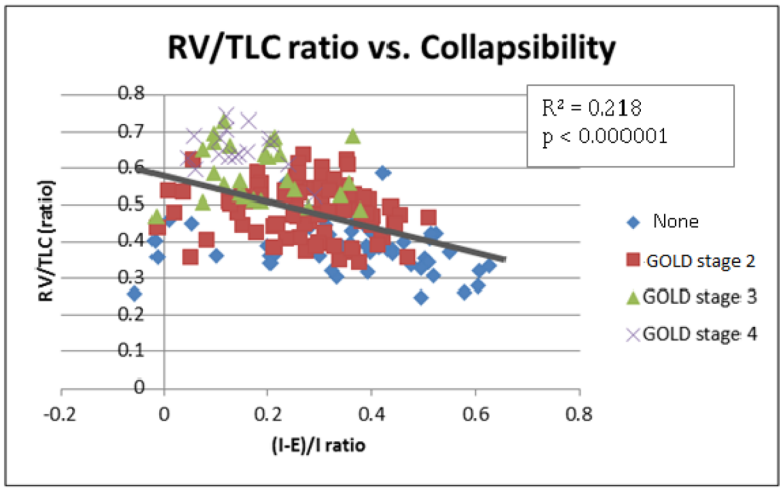


Fig. 3.

Relative lobe volume collapsibility for individual lobes across GOLD categories. The error bars denote standard deviations





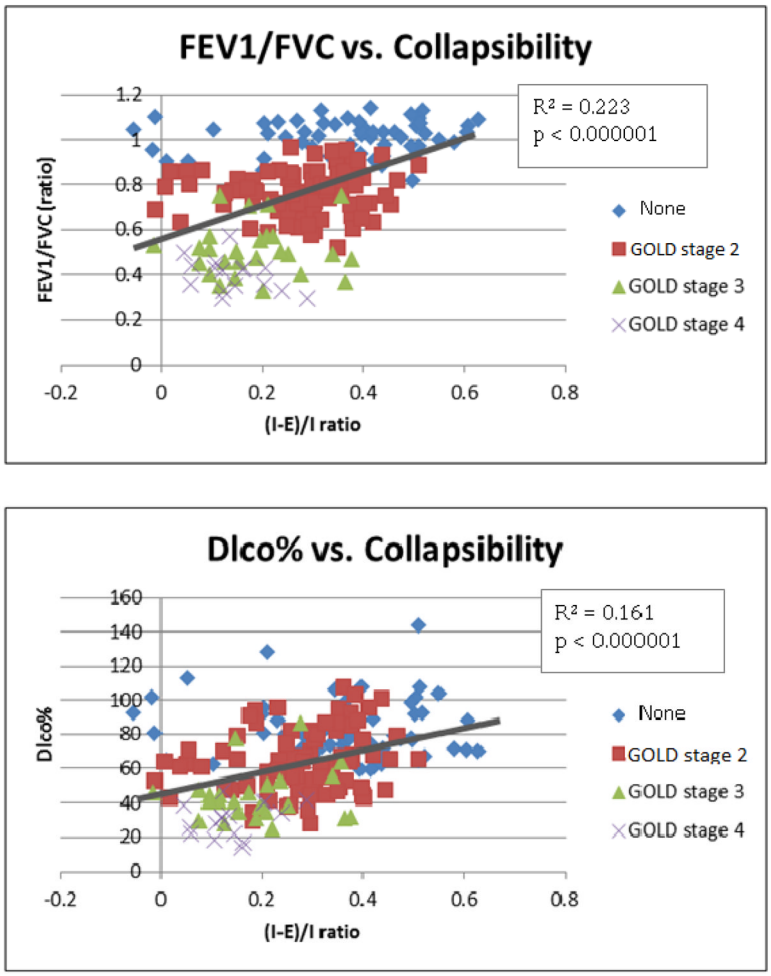
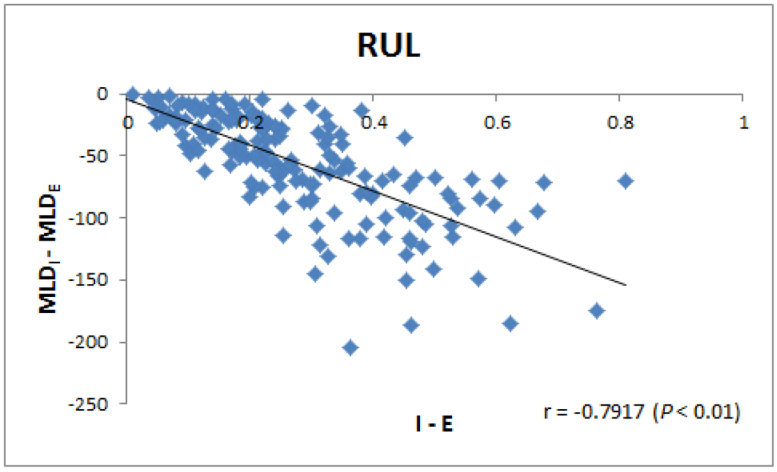
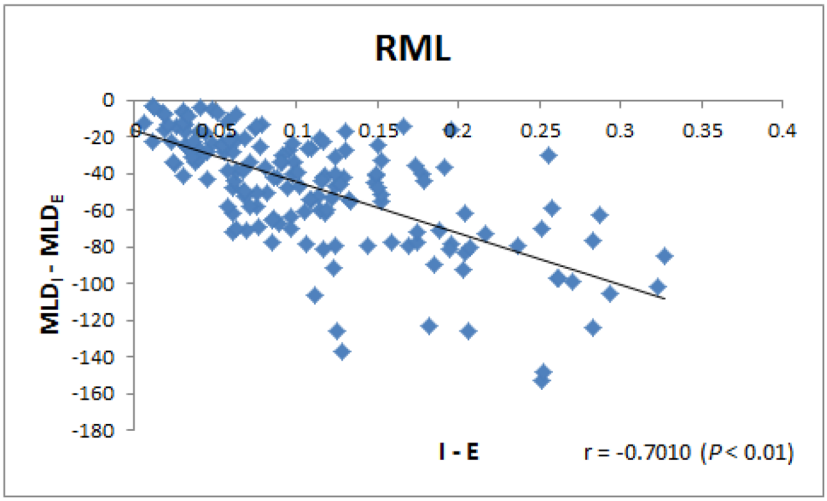
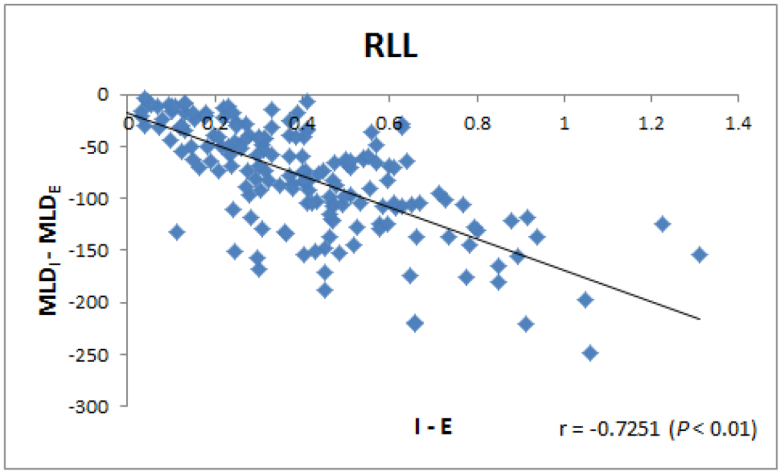


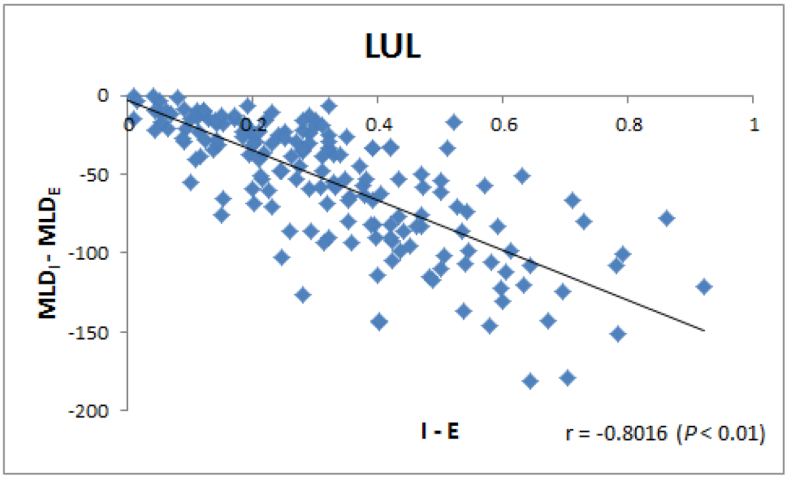
Fig. 4.

Selected scatter plots (a)–(d) showing the correlation between different pulmonary function measures and relative collapsibility









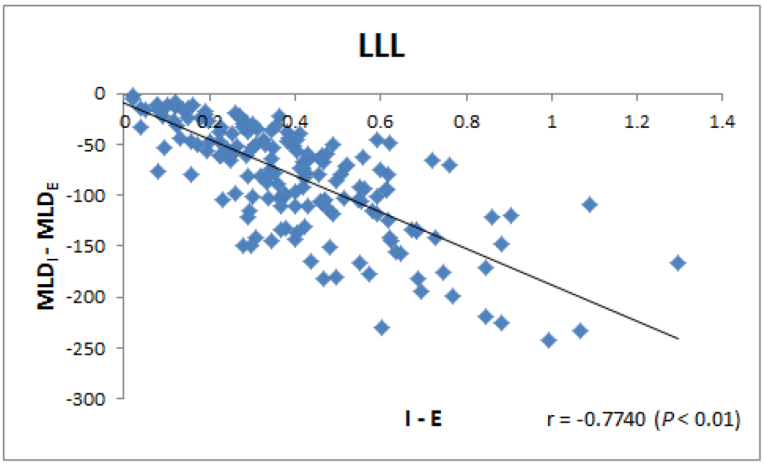


Fig. 5.

Relationship between the absolute lobe volume change and the CT-density change for each individual lobe. (a) RUL, (b) RML, (c) RLL, (d) LUL, and (e) LLL.

Table 1

Subject Demographics (n = 180)

Parameter	Mean (± std) or count (%)
Male/Female	93 (51.7%) / 87 (48.3%)
Age	65.6 (± 9.7)
Height (cm.)	168.7 (± 9.1)
RV/TLC %	48.5 (± 10.1)
FEV_1 %	63.0 (± 25.5)
FEV_1/FVC %	77.1 (± 22.0)
DL_{CO} %	64.0 (± 23.5)
GOLD category	
none	55 (30.6%)
I	0 (0.0 %)
II	83 (46.1%)
III	26 (14.4%)
IV	16 (8.9%)

Abbreviations: TLC – total lung capacity, RV – residual volume, FVC – functional vital capacity, FEV_1% forced expiratory volume in 1 s, percentage predicted, DL_{CO}% – diffusing lung capacity of carbon monoxide, percentage predicted

Table 2

CT protocol

CT manufacturer	General Electric (*n*=171)	Siemens (*n*=50)
Tube energy (kVp)	140	140
Exposure (mAs)	159.1 (28.7)	103.3 (28.6)
Auto-exposure	Off	On
Pitch	1.375	1.100
Reconstruction kernel	BONE	B46f
Section thickness (mm)	1.250	1.000
Reconstruction Interval (mm)	0.625	0.500
Pixel dimensions (mm)	0.527–0.891	0.527–0.781

Table 3

Correlation between lobe volume changes and specific PFT summary measures I-E

	Pulmonary Function Test Measurements					
	RV/TLC(%)	**FEV_1%**	**FVC%**	**FEV_1/FVC(%)**	**DLco%**	**GOLD stage**
RUL	−0.292	0.236	0.217	0.222	0.251	−0.243
RML	−0.300	0.263	0.176	0.300	0.401	−0.329
RLL	−0.325	0.272	0.236	0.248	0.342	−0.308
LUL	−0.307	0.254	0.264	0.204	0.267	−0.268
LLL	−0.373	0.318	0.275	0.303	0.307	−0.352
Whole Lung	−0.375	0.307	0.275	0.288	0.354	−0.348

RUL right upper lobe, RML right middle lobe, RLL right lower lobe, LUL left upper lobe, LLL left lower lobe

All rho values have $P < 0.01$

Table 4

Correlation between lobe volume changes and specific PFT measures (I-E)/I

	Pulmonary Function Test Measurements					
	RV/TLC(%)	**FEV_1%**	**FVC %**	**FEV_1/FVC(%)**	**DLco%**	**GOLD stage**
RUL	−0.439	0.429	0.325	0.426	0.394	−0.446
RML	−0.276	0.318	0.190	0.364	0.389	−0.368
RLL	−0.529	0.528	0.406	0.504	0.438	−0.543
LUL	−0.403	0.409	0.310	0.406	0.395	−0.432
LLL	−0.505	0.520	0.393	0.513	0.397	−0.533
Whole Lung	−0.481	0.492	0.362	0.493	0.437	−0.518

All rho values have $P < 0.01$

Table 5

Mean values of lobe volumes, lobe MLD, lobe volume change (I-E) and CT-density change (MLD_I-MLD_E).

	Variables					
	Volume (I)	**Volume (E)**	**MLD (I)**	**MLD (E)**	**I-E**	**MLD_I-MLD_E**
RUL	1.098(±0.364)	0.835(±0.350)	− 854.79(±41.04)	− 801.50(±66.52)	0.263(±0.168)	− 53.28(±42.29)
RML	0.477(±0.178)	0.378(±0.151)	−857.38(±29.19)	−813.06(±45.91)	0.098(±0.080)	−44.31(±32.44)
RLL	1.195(±0.391)	0.802(±0.321)	−825.30(±44.97)	−748.56(±71.00)	0.393(±0.252)	−76.74(±53.52)
LUL	1.275(±0.425)	0.961(±0.405)	−856.02(±39.08)	−802.70(±62.16)	0.314(±0.199)	− 53.31(±40.77)
LLL	1.155(±0.334)	0.772(±0.291)	−827.84(±43.95)	−749.34(±71.74)	0.383(±0.238)	−78.49(±55.61)

Unit: litre for volume related variables, and Hounsfield Unit (HU) for CT-density related variables.

Table 6

Correlation between CT-density change (MLD_I-MLD_E) and I-E, (I-E)/I, and E/I.

		Volume change variables		
		I-E	**(I-E)/I**	**E/I**
All	RUL	−0.7917	−0.9425	0.9425
	RML	−0.7010	−0.8234	0.8234
	RLL	−0.7251	−0.9214	0.9214
	LUL	−0.8016	−0.9358	0.9358
	LLL	−0.7740	−0.9259	0.9259
None	RUL	−0.7669	−0.9286	0.9286
	RML	−0.6985	−0.8202	0.8202
	RLL	−0.6266	−0.8737	0.8737
	LUL	−0.8280	−0.9159	0.9159
	LLL	−0.7610	−0.9107	0.9107
GOLD 2	RUL	−0.8297	−0.9497	0.9497
	RML	−0.6838	−0.8046	0.8046
	RLL	−0.8113	−0.9277	0.9277
	LUL	−0.8142	−0.9433	0.9433
	LLL	−0.8071	−0.9265	0.9265
GOLD 3	RUL	−0.8140	−0.9378	0.9378
	RML	−0.9056	−0.9371	0.9371
	RLL	−0.8244	−0.9617	0.9617
	LUL	−0.8313	−0.9535	0.9535
	LLL	−0.9022	−0.9480	0.9480
GOLD 4	RUL	−0.6446	−0.8676	0.8676
	RML	−0.0686 ($P = 0.795$)	−0.6127	0.6127
	RLL	−0.4608 ($P = 0.065$)	−0.8456	0.8456
	LUL	−0.6446	−0.8995	0.8995
	LLL	−0.2819 ($P = 0.272$)	−0.8113	0.8113

All rho values have $P < 0.01$ unless specified.