Published in final edited form as:

J Thorac Imaging. 2013 September ; 28(5): 284–290. doi:10.1097/RTI.0b013e318298733c.

Quantitative CT in COPD

David A Lynch and Mustafa L Al-Qaisi

Division of Radiology, National Jewish Health, 1400 Jackson Street, Denver, CO 80206, 303 270 2810, lynchd@njhealth.org

Abstract

Quantitative CT is increasingly used to quantify the features of COPD, specifically emphysema, air trapping, and airway abnormality. For quantification of emphysema, the density mask technique is most widely used, with threshold on the order of -950 HU, but percentile cutoff may be less sensitive to volume changes. Sources of variation include depth of inspiration, scanner make and model, technical parameters, and cigarette smoking. On expiratory CT, air trapping may be quantified by evaluating the % of lung volume less than a given threshold (e.g. -856 HU), by comparing lung volumes and attenuation on expiration and inspiration, or more recently by co-registering inspiratory and expiratory CT scans. These indices all correlate well with the severity of physiologic airway obstruction. By constructing a three-dimensional model of the airway from volumetric CT, it is possible to measure dimensions (external and internal diameters, and airway wall thickness) of segmental and subsegmental airways orthogonal to their long axes.

Measurement of airway parameters correlates with severity of airflow obstruction and with history of COPD exacerbation.

Introduction

COPD is now the third most common cause of death in the United States (after heart disease and malignancy) (1). Unlike heart disease and malignancy, mortality from COPD has increased progressively over the past 10 years. In the 2013 update, the Global Initiative for Obstructive Lung Disease (GOLD) group, defines COPD as follows: “COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients.” (2) The diagnosis of COPD is made on spirometry, by the presence of a post-bronchodilator FEV1/FVC ratio less than 0.70. The severity of COPD is commonly classified according to the GOLD staging system, where GOLD 1 is defined by FEV1 $\geq$ 80% predicted, GOLD 2 is FEV1 50-80% of predicted, GOLD 3 is FEV1 30-50% of predicted, and GOLD 4 is FEV1 $<$ 30 % of predicted. More recently the GOLD groupings have been further subdivided based on symptom severity, to provide an index of exacerbation risk (2). Although COPD is most commonly related to tobacco smoking, other risk factors include outdoor air pollution, occupational exposures, and indoor exposure to burning wood and other biomass fuels. (2)

While COPD is a convenient umbrella term, its routine use obscures the fact that the morphologic manifestations of this group of obstructive diseases vary widely, a fact that is

readily apparent to the clinical radiologist. Individuals with similar levels of physiologic impairment may have substantial, little, or no emphysema. Discrete subphenotypes of COPD include emphysema of varying morphologic appearance, large airway abnormality and small airway obstruction. Increasing awareness of the heterogeneity of COPD has led to increased use of CT to characterize COPD for purposes of genetic evaluation and identification of specific subgroups which may be amenable to therapeutic trials. While visual assessment is important in determining the presence and character of emphysema, there is increasing interest in the use of quantitative imaging to provide more precise estimates of the severity and distribution of emphysema, gas trapping and airway wall thickening. Several large cohorts of cigarette smokers have now been quite extensively characterized by CT, resulting in increased knowledge of the clinical correlates of quantitative CT parameters (3-5). The purpose of this paper is to present current knowledge regarding the use of quantitative CT for assessment of emphysema, gas trapping and airways abnormality that contribute to the clinical syndrome of COPD. Optimal CT acquisition techniques for COPD is covered elsewhere in this monograph (6).

Emphysema

Emphysematous lung destruction results in replacement of normal lung (which has a typical attenuation about -850 HU on inspiratory CT) by air-containing spaces, with CT attenuation close to -1000 HU. From the early days of CT, it was apparent that measurement of CT attenuation values could help quantify extent of emphysema. Müller et al. (7) were the first to describe and validate pathologically the density mask technique, in which CT pixels with attenuation below a certain threshold value (initially -910 HU) were defined as emphysema. Using a different approach, Coxson et al used CT to evaluate lung weight, gas and tissue volume, and estimated lung surface to volume ratios and surface area, and confirmed that these measures correlated with histological extent of emphysema (8). Bankier et al demonstrated that quantitative CT measurements correlated better with macroscopic measurements of emphysema than visual CT scoring (9). More recent evaluation with thin section CT using multidetector scanners showed that the highest correlation between QCT metrics and histology is found when the CT threshold is set at -960 or -970 HU (10). However, in the interests of balancing sensitivity and specificity, the threshold of -950 HU is now most commonly used (5, 11, 12) (Fig 1 a,b). An alternative approach to emphysema quantification, based on the frequency histogram of lung attenuation, evaluates the CT attenuation at a given percentile along the histogram (e.g. first or 15th percentile (12). There is some evidence that the percentile approach is more robust for longitudinal evaluation of emphysema, and less sensitive to change in lung volumes (13-15). Histologic correlation has shown that the optimal percentile value for this determination, measured on multidetector CT is the first percentile (10). However, because of concern regarding artifact from image noise and truncation artifact at the first percentile level, most studies have used the 15th percentile threshold (15, 16).

It is important to remember that the measurement of % low attenuation areas, while it correlates moderately well with histologic severity of emphysema, is not a direct measurement of emphysema. The term “% emphysema” is widely used to refer to such CT measurements, but is imprecise and may give rise to confusion. The annotations %LAA₋₉₅₀

(or %LAA₋₉₁₀, etc.) is preferred because it is more precise. The term RA950 is also sometimes used to indicate the relative area of lung less than -950 HU.

Since emphysema is a regionally distributed disease, it makes sense to determine the zonal or lobar distribution of emphysema. Most available QCT methods can divide each lung into upper, mid and lower zones of equal height or volume, and ratios between upper and lower lung LAA measurements can be computed. Newer methods can also permit segmentation of lobes to compute lobar volumes and extent of low attenuation areas.

To quantify the size of emphysematous spaces (Fig 1 c), several investigators have used the D value or alpha value. This represents the slope of the log-log plot of the cumulative frequency-size distributions of the %LAA₋₉₅₀. Mishima et al found that smokers with normal %LAA had lower D values than nonsmokers, suggesting that the D value might be a sensitive method for detecting early emphysema (17). However, Madani et al found that the D value did not correlate with macroscopic or microscopic indices of emphysema (18).

In evaluation of subjects with emphysema, one must minimize sources of variation. Major sources of variation in quantification of emphysema include variation in lung volume, technical CT parameters, and cigarette smoking. Madani et al showed that measures of emphysema changed significantly when scans were obtained at 100%, 90%, 80%, 70%, and 50% of vital capacity (19). However, the change between 100% and 90% of vital capacity was relatively slight. While several studies have used spirometers to standardize inspired lung volume (20, 21), such systems are not widely available, and the strong physiologic correlations obtained without lung volume control suggest that it may not be necessary. In the absence of a spirometer, careful coaching of the patient by the technologist is important to achieve total lung capacity.

Madani et al also showed in a different study that the %LAA₋₉₆₀ decreases with increasing slice thickness and with increasing tube current (22). Boedeker et al showed that differences in reconstruction algorithm have a large effect on measurement of low attenuation areas (23). In particular, the use of over-enhancing reconstruction algorithms resulted in a shift of 9.4% in CT measurement of emphysema, presumably because of increased image noise simulating emphysema. For this reason, a smooth reconstruction algorithm is generally used in quantitative CT evaluation of emphysema. The substantial variation in CT emphysema measures with technical factors emphasizes the importance of using a standardized acquisition technique. Use of the same technique is particularly important in longitudinal studies.

Several authors have shown that current smokers appear to have lower levels of emphysema than former smokers (24, 25). Even more intriguingly, the extent of “emphysema” appears to increase quite rapidly following smoking cessation, reflecting a fall in lung attenuation (26, 27). This effect is presumed to be due to a smoking-induced increase in inflammatory cells in the lung in current smokers, resulting in increased lung attenuation, so that partial volume averaging masks the areas of low-attenuation emphysema. Therefore smoking status should always be taken into account when assessing severity of emphysema by quantitative CT.

Several studies have evaluated the ability of CT to detect progression of emphysema on longitudinal evaluation. The main source of variation is related to change in lung volume. Correction for lung volume may be performed using a sponge model, where the % emphysema on the followup scan is corrected using the achieved lung volume on the baseline scan (28). Correction for lung volume reduces the variability in emphysema quantification by a factor of two (29). In a randomized controlled study of subjects with alpha-1 antitrypsin deficiency, change in 15th percentile CT density (corrected for lung volume) was found to be more sensitive as an index of progression than measures of physiology or health status (30). Combined analysis of two clinical trials of intravenous alpha-1 antitrypsin augmentation showed that this medication significantly reduces the decline in lung density in subjects with alpha-1 antitrypsin deficiency (31).

In subjects with smoking related emphysema, Gietema et al evaluated 157 subjects enrolled in a lung cancer screening study, who underwent repeat CT scans within 3 months, and found that the limits of agreement for percentage low attenuation areas < -950HU were from -1.3% to +1.1%, suggesting that CT can detect a change of 1.1% in extent of emphysema with 95% probability. Recently, Coxson et al found an average annual decline in lung density of 1.13g/L, after correction for lung volume, in a group of 1928 current and former smokers (5). The decline was more rapid in women than in men, and in current smokers than in former smokers.

Air trapping

End-expiratory CT, whether obtained at functional residual capacity or at residual volume, is an excellent way to assess gas trapping in COPD. Most studies have evaluated the presence of gas trapping by evaluating the % low attenuation at a threshold of -856 or -850 HU (LAA_{exp856} or LAA_{exp850}) (Fig 1 d,e). This value is chosen because it is the attenuation of normally inflated inspiratory lung, so the concept has been that expiratory lung should have higher attenuation than this. Murphy et al, in a study of 216 cigarette smokers showed that LAA_{exp850} provided remarkably high correlations ($r=0.85-0.90$) with FEV1/FVC ratio and with FEV1 % predicted (32). Schroeder et al (33) found similar levels of correlation in a study of 4062 COPDGen subjects with and without COPD. Quantitative CT evaluation of severity of emphysema and expiratory gas trapping provides a simple way to assign individual COPD subjects to subgroups characterized by predominant emphysema, mixed emphysema and gas trapping, and predominant gas trapping (Fig 2)

Other authors have used other indices of gas trapping, including the ratio of inspiratory to expiratory lung volume, inspiratory expiratory lung attenuation ratio, and the expiratory to inspiratory relative volume change of voxels with attenuation values between -860 and -950. Mets et al found that the inspiratory-expiratory lung attenuation ratio provided the strongest correlation with physiologic air trapping (34). The same group studied 1140 subjects enrolled in a lung cancer screening study, and found that a diagnostic model that included $LAA_{-950insp}$, ratio of inspiratory to expiratory lung volume, body mass index, smoking pack-years and smoking status permitted accurate diagnosis of COPD (35). As screening CT becomes more widely implemented for lung cancer detection, it is possible that routine expiratory CT may become part of the algorithm to permit detection of unrecognized COPD.

One of the challenges with evaluation of expiratory gas trapping in COPD is that a simple threshold measurement does not distinguish between gas trapping due to emphysema and small airways disease. Several authors have used deformation techniques to register the inspiration image to the expiration image, and calculate a voxel-by-voxel ventilation map, based on the change in CT attenuation between expiration and inspiration (32, 36, 37) (Fig 3). Galban et al with this technique generated a parametric response map, based on the assumption that voxels of lung with inspiratory CT attenuation less than -950 HU were emphysematous, while voxels that were greater than -950 HU on inspiration, but less than -856 HU on expiration represented non-emphysematous functional small airways disease (37) Murphy et al, using a similar technique, found that measures based on expiratory CT provided the best correlations with FEV1/FVC ratio and with presence or absence of COPD, while measures based on co-registered inspiratory and expiratory images provided better classification of the GOLD stage of COPD (32).

Airway abnormality

Radiologic evaluation of the airways is helpful in COPD to provide an index of bronchial inflammation and remodeling, to correlate with exacerbation and other symptoms, and to provide a window into abnormality of the small airways. There have been substantial recent advances in quantitative evaluation of the segmental and subsegmental airways. Currently available software permits multiplanar reconstruction of airway from thin section volumetric datasets, permitting measurement of luminal diameter and wall thickness to the level of subsegmental or subsubsegmental airways (Fig 4). Parameters available for evaluating the airway include absolute measures (bronchial luminal diameter or area, bronchial wall thickness or area, and total bronchial area), and relative measures (e.g. bronchial wall area %). A commonly used summary measure of bronchial wall area is the square root of wall area of a hypothetical bronchus of internal perimeter 10 mm, calculated from linear regression of all measured bronchi, referred to as Pi10 (38).

Nakano et al showed that there was a correlation between wall area of the small airways, measured using histology, and wall area of the large airways, measured using CT (39). Han et al showed that CT-quantified bronchial wall thickness and severity of emphysema were independently associated with exacerbation frequency, and could be used to define bronchial predominant and emphysema predominant subtypes of COPD (4). Grydeland et al showed that the Pi10 was independently related to symptoms of dyspnea, cough and wheezing in subjects with COPD (40). There are modest correlations between airway wall area % and physiologic impairment (33, 41). Additionally Washko et al (41) showed that on multivariate analysis, wall area % and peak airway attenuation appeared to be independent predictors of FEV1 % predicted.

Textural analysis

There is increasing interest in using more sophisticated textural analysis to evaluate smoking related lung injury, including emphysema. Ginsburg et al. showed that a texture-based approach could discriminate quite effectively between the lungs of never-smokers, smokers without emphysema and smokers with emphysema (42). This suggests that textural analysis

may be able to identify the early phase of smoking related lung injury, prior to the development of emphysema.

Concordance with visual evaluation

Although quantitative CT measures correlate with severity of visually assessed emphysema, the level of correlation is not strong. In the COPDGene workshop, where 58 observers independently scored CT scans of 294 subjects, agreement on pattern and extent of emphysema was poor to moderate, and concordance between visual and quantitative assessment of the presence of emphysema was only 75% (43). Gietema *et al* found that in those with less severe categories of emphysema, radiologists tended to visually underestimate extent of emphysema compared with quantitative measures, while in those with more severe emphysema, the radiologists tended to relatively overestimate emphysema extent. Thus, QCT and visual evaluation may provide complementary, independent assessments of severity of emphysema, particularly in those with less severe abnormality. Interestingly, although the presence of emphysema on visual assessment is associated with lung cancer (44, 45), quantitative CT measurement of emphysema has not been shown to be independently associated with lung cancer (46-48).

Summary

The density mask and percentile methods are well-validated measures of severity of emphysema. More recently, expiratory CT has become widely used in assessing severity of gas trapping, and correlates remarkably well with physiologic indices of airway obstruction. Quantitative assessment of COPD also requires evaluation of the airways, with wall area % and Pi10 the most widely used indices. Exciting new research directions include increased use of textural and local histogram methods to characterize emphysema, inspiratory-expiratory image registration to help distinguish gas trapping due to emphysema from small airways abnormality, and advances in our understanding of airway wall thickening due to inflammation and remodeling.

Acknowledgments

Disclosure

This work was supported by U.S. National Institutes of Health (NIH) COPDGene study, Award Numbers R01HL089897 and R01HL089856 from the National Heart, Lung, And Blood Institute (NHLBI). The COPDGene® project is also supported by the COPD Foundation through contributions made to an Industry Advisory Board comprised of AstraZeneca, Boehringer Ingelheim, Novartis, Pfizer, Siemens and Sunovion. Dr Lynch's institution and laboratory receives research support from the NHLBI, Siemens, Inc, Perceptive Imaging, Inc, and Centocor, Inc, Inc. Dr Lynch is a consultant to Perceptive Imaging, Inc, Boehringer Ingelheim, Inc, Genentech, Inc, Gilead, Inc, and Intermune, Inc.

Reference List

1. Centers for Disease Control. Deaths: Final Data for 2010. 2013. [cited 2013 Feb 23, 2013]; Available from: http://www.cdc.gov/nchs/data/dvs/deaths_2010_release.pdf
2. Global initiative for chronic obstructive lung disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2013. [cited 2013]; Available from: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf

3. Gietema HA, Schilham AM, van Ginneken B, van Klaveren RJ, Lammers JW, Prokop M. Monitoring of smoking-induced emphysema with CT in a lung cancer screening setting: detection of real increase in extent of emphysema. *Radiology*. 2007 Sep; 244(3):890–7. [PubMed: 17709835]
4. Han MK, Kazerooni EA, Lynch DA, Liu LX, Murray S, Curtis JL, et al. Chronic obstructive pulmonary disease exacerbations in the COPDGene study: associated radiologic phenotypes. *Radiology*. 2011 Oct; 261(1):274–82. [PubMed: 21788524]
5. Coxson HO, Dirksen A, Edwards LD, Yates JC, Agusti A, Bakke P, et al. The presence and progression of emphysema in COPD as determined by CT scanning and biomarker expression: a prospective analysis from the ECLIPSE study. *Lancet Respiratory Medicine*. 2013
6. Newell J, Sieren J, Hoffman E. Development of Quantitative CT Lung Protocols. *J Thorac Imaging*. 2013
7. Müller NL, Staples CA, Miller RR, Abboud RT. “Density mask”. An objective method to quantitate emphysema using computed tomography. *Chest*. 1988; 94(4):782–7. [PubMed: 3168574]
8. Coxson HO, Rogers RM, Whittall KP, D’Yachkova Y, Pare PD, Sciurba FC, et al. A quantification of the lung surface area in emphysema using computed tomography. *Am J Respir Crit Care Med*. 1999; 159(3):851–6. [PubMed: 10051262]
9. Bankier AA, De Maertelaer V, Keyzer C, Gevenois PA. Pulmonary emphysema: subjective visual grading versus objective quantification with macroscopic morphometry and thin-section CT densitometry. *Radiology*. 1999; 211(3):851–8. [PubMed: 10352615]
10. Madani A, Zanen J, de Maertelaer V, Gevenois PA. Pulmonary emphysema: objective quantification at multi-detector row CT--comparison with macroscopic and microscopic morphometry. *Radiology*. 2006 Mar; 238(3):1036–43. [PubMed: 16424242]
11. Regan EA, Hokanson JE, Murphy JR, Make B, Lynch DA, Beaty TH, et al. Genetic epidemiology of COPD (COPDGene) study design. *COPD*. 2010 Feb; 7(1):32–43. [PubMed: 20214461]
12. Heussel CP, Herth FJF, Kappes J, Hantusch R, Hartlieb S, Weinheimer O, et al. Fully automatic quantitative assessment of emphysema in computed tomography: comparison with pulmonary function testing and normal values. *European Radiology*. 2009 Oct; 19(10):2391–402. [PubMed: 19458953]
13. Dirksen A. Monitoring the progress of emphysema by repeat computed tomography scans with focus on noise reduction. *Proc Am Thorac Soc*. 2008 Dec 15; 5(9):925–8. [PubMed: 19056718]
14. Dirksen A, Friis M, Olesen KP, Skovgaard LT, Sorensen K. Progress of emphysema in severe alpha 1-antitrypsin deficiency as assessed by annual CT. *Acta Radiol*. 1997; 38(5):826–32. [PubMed: 9332238]
15. Stolk J, Dirksen A, van der Lugt AA, Hutsebaut J, Mathieu J, de Ree J, et al. Repeatability of lung density measurements with low-dose computed tomography in subjects with alpha-1-antitrypsin deficiency-associated emphysema. *Invest Radiol*. 2001 Nov; 36(11):648–51. [PubMed: 11606842]
16. Heussel CP, Herth FJ, Kappes J, Hantusch R, Hartlieb S, Weinheimer O, et al. Fully automatic quantitative assessment of emphysema in computed tomography: comparison with pulmonary function testing and normal values. *Eur Radiol*. 2009 Oct; 19(10):2391–402. [PubMed: 19458953]
17. Mishima M, Hirai T, Itoh H, Nakano Y, Sakai H, Muro S, et al. Complexity of terminal airspace geometry assessed by lung computed tomography in normal subjects and patients with chronic obstructive pulmonary disease. *Proc Natl Acad Sci U S A*. 1999 Aug 3; 96(16):8829–34. [PubMed: 10430855]
18. Madani A, Van Muylem A, de Maertelaer V, Zanen J, Gevenois PA. Pulmonary emphysema: size distribution of emphysematous spaces on multidetector CT images--comparison with macroscopic and microscopic morphometry. *Radiology*. 2008 Sep; 248(3):1036–41. [PubMed: 18710992]
19. Madani A, Van Muylem A, Gevenois PA. Pulmonary emphysema: effect of lung volume on objective quantification at thin-section CT. *Radiology*. 2010 Oct; 257(1):260–8. [PubMed: 20663967]
20. Fuld MK, Grout RW, Guo J, Morgan JH, Hoffman EA. Systems for lung volume standardization during static and dynamic MDCT-based quantitative assessment of pulmonary structure and function. *Academic radiology*. 2012 Aug; 19(8):930–40. [PubMed: 22555001]

21. Moroni C, Mascalchi M, Camiciottoli G, Bartolucci M, Falaschi F, Battolla L, et al. Comparison of spirometric-gated and -ungated HRCT in COPD. *Journal of computer assisted tomography*. 2003 May-Jun;27(3):375–9. [PubMed: 12794602]
22. Madani A, De Maertelaer V, Zanen J, Gevenois PA. Pulmonary emphysema: radiation dose and section thickness at multidetector CT quantification--comparison with macroscopic and microscopic morphometry. *Radiology*. 2007 Apr; 243(1):250–7. [PubMed: 17392257]
23. Boedeker KL, McNitt-Gray MF, Rogers SR, Truong DA, Brown MS, Gjertson DW, et al. Emphysema: effect of reconstruction algorithm on CT imaging measures. *Radiology*. 2004 Jul; 232(1):295–301. [PubMed: 15220511]
24. Grydeland TB, Dirksen A, Coxson HO, Pillai SG, Sharma S, Eide GE, et al. Quantitative computed tomography: emphysema and airway wall thickness by sex, age and smoking. *Eur Respir J*. 2009 Oct; 34(4):858–65. [PubMed: 19324952]
25. Camiciottoli G, Cavigli E, Grassi L, Diciotti S, Orlandi I, Zappa M, et al. Prevalence and correlates of pulmonary emphysema in smokers and former smokers. A densitometric study of participants in the ITALUNG trial. *European Radiology*. 2009 Jan; 19(1):58–66. [PubMed: 18690451]
26. Ashraf H, Lo P, Shaker SB, de Bruijne M, Dirksen A, Tonnesen P, et al. Short-term effect of changes in smoking behaviour on emphysema quantification by CT. *Thorax*. 2011 Jan; 66(1):55–60. [PubMed: 20978026]
27. Shaker SB, Stavngaard T, Laursen LC, Stoel BC, Dirksen A. Rapid fall in lung density following smoking cessation in COPD. *COPD*. 2011 Feb; 8(1):2–7. [PubMed: 21299472]
28. Bakker ME, Stolk J, Putter H, Shaker SB, Parr DG, Piitulainen E, et al. Variability in densitometric assessment of pulmonary emphysema with computed tomography. *Invest Radiol*. 2005 Dec; 40(12):777–83. [PubMed: 16304481]
29. Stoel BC, Putter H, Bakker ME, Dirksen A, Stockley RA, Piitulainen E, et al. Volume correction in computed tomography densitometry for follow-up studies on pulmonary emphysema. *Proc Am Thorac Soc*. 2008 Dec 15; 5(9):919–24. [PubMed: 19056717]
30. Dirksen A, Piitulainen E, Parr DG, Deng C, Wencker M, Shaker SB, et al. Exploring the role of CT densitometry: a randomised study of augmentation therapy in alpha1-antitrypsin deficiency. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology*. 2009 Jun; 33(6):1345–53.
31. Stockley RA, Parr DG, Piitulainen E, Stolk J, Stoel BC, Dirksen A. Therapeutic efficacy of alpha-1 antitrypsin augmentation therapy on the loss of lung tissue: an integrated analysis of 2 randomised clinical trials using computed tomography densitometry. *Respiratory research*. 2010; 11:136. [PubMed: 20920370]
32. Murphy K, Pluim JPW, van Rikxoort EM, de Jong PA, de Hoop B, Gietema HA, et al. Toward automatic regional analysis of pulmonary function using inspiration and expiration thoracic CT. *Med Phys*. 2012 Mar; 39(3):1650–62. [PubMed: 22380397]
33. Schroeder JD, McKenzie AS, Zach JA, Wilson CG, Curran-Everett D, Stinson DS, et al. Relationships between airflow obstruction and quantitative CT measurements of emphysema, air trapping and airways in subjects with and without COPD. *Am J Roentgenol*. 2013 in press.
34. Mets OM, Zanen P, Lammers JW, Isgum I, Gietema HA, van Ginneken B, et al. Early identification of small airways disease on lung cancer screening CT: comparison of current air trapping measures. *Lung*. 2012 Dec; 190(6):629–33. [PubMed: 23064488]
35. Mets OM, Buckens CF, Zanen P, Isgum I, van Ginneken B, Prokop M, et al. Identification of chronic obstructive pulmonary disease in lung cancer screening computed tomographic scans. *JAMA*. 2011 Oct 26; 306(16):1775–81. [PubMed: 22028353]
36. Barbosa EM Jr, Song G, Tustison N, Kreider M, Gee JC, Geftter WB, et al. Computational analysis of thoracic multidetector row HRCT for segmentation and quantification of small airway air trapping and emphysema in obstructive pulmonary disease. *Academic Radiology*. 2011 Oct; 18(10):1258–69. [PubMed: 21893294]
37. Galban CJ, Han MK, Boes JL, Chughtai KA, Meyer CR, Johnson TD, et al. Computed tomography-based biomarker provides unique signature for diagnosis of COPD phenotypes and disease progression. *Nat Med*. 2012 Nov; 18(11):1711–5. [PubMed: 23042237]

38. Grydeland TB, Thorsen E, Dirksen A, Jensen R, Coxson HO, Pillai SG, et al. Quantitative CT measures of emphysema and airway wall thickness are related to D(L)CO. *Respir Med*. 2011 Nov 10;105:343–51. [PubMed: 21074394]
39. Nakano Y, Wong JC, de Jong PA, Buzatu L, Nagao T, Coxson HO, et al. The prediction of small airway dimensions using computed tomography. *Am J Respir Crit Care Med*. 2005 Jan 15; 171(2): 142–6. [PubMed: 15516531]
40. Grydeland TB, Dirksen A, Coxson HO, Eagan TML, Thorsen E, Pillai SG, et al. Quantitative computed tomography measures of emphysema and airway wall thickness are related to respiratory symptoms. *Am J Respir Crit Care Med*. 2010 Feb 15; 181(4):353–9. [PubMed: 19926869]
41. Washko GR, Dransfield MT, Estepar RSJ, Diaz A, Matsuoka S, Yamashiro T, et al. Airway wall attenuation: a biomarker of airway disease in subjects with COPD. *J Appl Physiol*. 2009 Jul; 107(1):185–91. [PubMed: 19407254]
42. Ginsburg SB, Lynch DA, Bowler RP, Schroeder JD. Automated texture-based quantification of centrilobular nodularity and centrilobular emphysema in chest CT images. *Acad Radiol*. 2012; 19:1241–51. [PubMed: 22958719]
43. Barr RG, Berkowitz EA, Bigazzi F, Bode F, Bon J, Bowler RP, et al. A combined pulmonary-radiology workshop for visual evaluation of COPD: study design, chest CT findings and concordance with quantitative evaluation. *COPD: Journal of Chronic Obstructive Pulmonary Disease*. 2012 Apr; 9(2):151–9.
44. de Torres JP, Bastarrika G, Wisnivesky JP, Alcaide AB, Campo A, Seijo LM, et al. Assessing the relationship between lung cancer risk and emphysema detected on low-dose CT of the chest. *Chest*. 2007 Dec; 132(6):1932–8. [PubMed: 18079226]
45. Wilson DO, Weissfeld JL, Balkan A, Schragin JG, Fuhrman CR, Fisher SN, et al. Association of radiographic emphysema and airflow obstruction with lung cancer. *American journal of respiratory and critical care medicine*. 2008 Oct 1; 178(7):738–44. [PubMed: 18565949]
46. Gierada DS, Guniganti P, Newman BJ, Dransfield MT, Kvale PA, Lynch DA, et al. Quantitative CT assessment of emphysema and airways in relation to lung cancer risk. *Radiology*. 2011 Dec; 261(3):950–9. [PubMed: 21900623]
47. Wilson DO, Leader JK, Fuhrman CR, Reilly JJ, Sciurba FC, Weissfeld JL. Quantitative computed tomography analysis, airflow obstruction, and lung cancer in the pittsburgh lung screening study. *Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer*. 2011 Jul; 6(7):1200–5.
48. Kishi K, Gurney JW, Schroeder DR, Scanlon PD, Swensen SJ, Jett JR. The correlation of emphysema or airway obstruction with the risk of lung cancer: a matched case-controlled study. *European Respiratory Journal*. 2002 Jun; 19(6):1093–8. [PubMed: 12108862]

Figure 1.

Sixty-four year old cigarette smoker with severe COPD (GOLD Stage 4). (a) Coronal inspiratory image shows moderate upper lung predominant emphysema. (b) Density mask overlay identifies voxels with CT attenuation -950 HU, color coded by lung lobe. (c) Three dimensional representation provides an index of the size of the low attenuation clusters. (d) Coronal expiratory image shows gas trapping predominantly in areas of emphysema. (e) Density mask overlay of expiratory image identifies voxels with attenuation -856 HU, color coded by lung lobe.

Figure 2.

Scatterplot of 2619 subjects with moderate COPD (GOLD Stage 2: color coded green, and GOLD Stage 3: color coded blue) enrolled in the COPDGene study, with cutoff values based on normal subjects shows that 1% have predominant emphysema, 59% have mixed emphysema and gas trapping, 25% have predominant gas trapping, while 15% fall within the normal range for emphysema and gas trapping.

Figure 3.

Images from a 70 year old woman with GOLD Stage 2 COPD demonstrating registration of inspiratory and expiratory images, and subtraction. Top row: Segmented inspiration and expiration images. Second Row: Inspiration scan with density mask set at -950 HU and the corresponding expiration scan with density mask set at -850 HU. Third row: the registered inspiration image on the left has been deformed to match the original expiratory image on the right. Bottom row: Subtraction image, obtained by subtracting the value at inspiration from the value at expiration per voxel, and ventilation image, constructed based on the deformed inspiratory image and the expiratory image (32). Images courtesy of Dr Eva van Rikxoort, Radboud University Nijmegen Medical Centre

Figure 4.

(Same patient as Figure 1). (a) Automated airway segmentation provides a rendering of the central airway tree, with labeling of bronchial branches. (b) Curved planar reformation of bronchial pathway to right lower lobe posterior segmental bronchus (RB10). (c) Orthogonal cross section of RB10 facilitates cross-sectional measurement of bronchial luminal and wall parameters.