Characterization of Lung's Emphysema Distribution: Numerical Assessment of Disease Development

M. EMAM, J-F RENAUD de la Faverie, N. GHARBI
CNRS UMR 8162, Department of medical research,
Marie-Lannelongue Hospital – Paris-Sud University
(ORSAY), Le Plessis-Robinson, France.
mohamed.emam@u-psud.fr,
mo.mo.emam@gmail.com

M.I. El-GOHARY
Biophysics lab, Physics Department,
Faculty of Sciences, Al-AZHAR University,
Cairo, Egypt.

***Abstract*—Chronic Obstructive Pulmonary Disease (COPD) refers to a group of lung diseases that block airflow and make it increasingly difficult for you to breathe. Emphysema and chronic bronchitis are the two main conditions that make up COPD, but COPD can also refer to damage caused by chronic asthmatic bronchitis. Pulmonary emphysema is defined as a lung disease characterized by "abnormal enlargement of the air spaces distal to the terminal, non-respiratory bronchiole, accompanied by destructive changes of the alveolar walls". These lung parenchymal changes are pathognomonic for emphysema. Chronic bronchitis is a form of bronchitis characterized by excess production of sputum leading to a chronic cough and obstruction of air flow. In all cases, damage to your airways eventually interferes with the exchange of oxygen and carbon dioxide in your lungs. Habitual techniques of emphysema's diagnosis are based on indirect features, such as clinical examination; Pulmonary Function Tests (PFT) and subjective visual evaluation of CT scans. These tests are of limited value in assessing mild to moderate emphysema.**

Keyword- Digital image treatments, air density distribution and emphysema characterizations.

I. INTRODUCTION

Quantitative image analysis (QIA) goes beyond subjective visual assessment to provide computer measurements of the image content, typically following image segmentation to identify anatomical Regions of Interest (ROIs). Damage in lung airways eventually interferes with the exchange of oxygen and carbon dioxide in your lungs [1], and for the purpose of quantitatively characterizing different types of emphysema; we chose the classification of Weder [2] as the basis for our work. Commercially available picture archiving and communication systems focus on storage of image data. They are not well suited to efficient storage and mining of new types of quantitative data [3].
Image processing techniques allow a large and complex set of quantitative measures to be derived from images, particularly in a research setting. Commercially available Picture Archiving and Communication Systems (PACS) focus on storage of image data. They are not designed for efficient storage and mining of new types of quantitative data [3].

Examples of quantitative imaging can be found in lung cancer screening and assessment of emphysema lung disease. Lung cancer screening involves imaging of high-risk patients, such as long-time smokers, to search for lung nodules (tumors) that may indicate the presence of lung cancer [3-5]. Emphysema is another lung disease often associated with smoking, and imaging can be used to assess the extent and severity of the lung destruction, [6, 7]. The gray level energy of encoded image indicates how the gray levels are distributed. This quantitative statistical measure represents the gray level energy with 256 bins and its (PDF) refers to the Probability Distribution Functions, which contains image's histogram counts [8]. The mean of a sample of data is called the sample mean. When the Probability Distribution Function (PDF) of the data has a normal distribution, then as we collect more data, the sample means approach a limiting value that identified as the "right" value of the average, and is called the population mean. To apply the Mean Lung Density Method and the classical statistics, the intended system has to be devised in parts to be analyses individually to avoid many complicated result and in the most case many analogical results too. We have to make a tremendous effort to find or to choose the suitable statistical entries in order to segment the analyzed system; the CT image slices, as far as this review is concerned. The term segmentation appears usually as we make this kind of treatments [8, 9]. Given the advances in imaging modalities and image-analysis technology, radiologists are able to ask new clinical questions involving quantitative image data. For example, quantitative of emphysema done by using volume of gas per gram of lung tissue [7, 8] and changes in disease severity are being measured during evaluation of novel therapies [10, 11].

II. EMPHYSEMA CHARACTERIZATIONS

Generally, the diagnosis of emphysema is based on indirect features, such as clinical examination, pulmonary function tests, and subjective visual evaluation of computed tomography (CT) scans. These tests are of limited value in assessing mild to moderate emphysema [12]. Pulmonary emphysema is characterized by some pathognomonic changes in the affected lung; abnormal enlargement of the air spaces distal to the terminal, non-respiratory bronchiole,

accompanied by destructive changes of the alveolar walls.

As the detection of such changes during life, however, is difficult, so early and accurate diagnosis of emphysema is important for smoking cessation advice, evaluating the natural history of the disease, and disease phenotype as we improve our understanding of disease processes and therapeutic interventions [12].

III Detecting And Quantifying Emphysema

To detecting and quantifying emphysema from CT scans have been used. One approach involves assigning a grade or a rating to assess the presence of emphysema by visual examination of the hard copy scans [6, 7, 12, 13, 14]. In this approach, the visual assessments are compared with the subsequent pathological examination for emphysema, and the results have demonstrated a good correlation. However, such visual evaluations are time-consuming and limited by a wide range of interobserver variability and lack of sensitivity to early disease. The second approach directly analyzes digital data obtained from the CT scan [8, 12, 15-19].

This approach is objective and, therefore, not subject to interpreter bias. There are at least two computerized methods of identifying emphysema currently in use. Low Attenuation Areas (LAA) considered as a characteristic of emphysema. One technique identifies arias of low attenuation based on a single density index threshold or a range of density indices. Here, all areas having densities lower than the threshold (e.g., 910 Hounsfield Units (HU) or the lowest fifth percentile of the histogram) or falling within a given range of densities are considered to be emphysematous. The lowest fifth percentile of the histograms of emphysematous subjects has been shown to correlate well with the surface area of walls of distal air spaces per unit lung volume [8, 12].

The second method computes the mean lung density as a defining characteristic of emphysema. These studies have reported good correlation with some pulmonary function tests [12].

IV. Incompletely Clinical Judgment Problem

The diagnosis of COPD should be considered in any patient who has the following: symptoms of cough; sputum production; or dyspnoea; or history of exposure to risk factors for the disease [20]. Although COPD affects the lungs, it also produces significant systemic consequences. COPD is a preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking [20]. Spirometry should be obtained in all persons with the following history: exposure to cigarettes; and/or environmental or occupational pollutants; and/or presence of cough, sputum production or dyspnoea.

The diagnosis of COPD requires spirometry; a post-bronchodilator forced expiratory volume in one second (FEV1) [1] /Forced Vital Capacity (FVC) $\leq$ 0.7 confirms the presence of airflow limitation that is not fully reversible [20]. It is intended to be applicable to populations [21] and not to substitute clinical judgment in the evaluation of the severity of disease in individual patients. It is accepted that a single measurement of FEV1 incompletely represents the complex clinical consequences of COPD.

V. Macroscopic And Microscopic Lung Levels

The notion of "fractal dimension" provides a way to measure how rough fractal curves are. We normally consider lines to have a dimension of 1, surfaces a dimension of 2 and volumes a dimension of 3. However, a rough curve (say) wanders around on a surface; in the extreme it may be so rough that it effectively fills the surface on which it lies. Very convoluted surfaces, such as a tree's foliage or the internal surfaces of lungs may effectively be three- dimensional structures. We can therefore think of roughness as a decrease.

Whilst the topological dimension of a line is always 1 and that of a surface always 2, the fractal dimension may be any real number between 1 and 2. The fractal dimension D is most commonly estimated from the regression slope of a log-log power law plot. However, the definition of 'independent' and 'dependent' variables (required in least squares or regression analysis model) is not straightforward in such applications [22]. Fractal properties of the pulmonary vascular tree have been described in the adult lung [23-26]. Such mathematical properties permit the lung to be considered not only as a single compartment but also enable complex models of flow distribution in the pulmonary arterial tree to be performed, in order to better understand the effect of fractal arterial design on pulmonary vascular input impedance [27, 28].

Such models have led to a better understanding of the structure–function relationship in the pulmonary vascular tree [29-31]. Based on the self similarity of fractal structures, the mathematical relationship between dimensions of mother and daughter branches is relatively constant. Thus, complex fractal structures can be described by relatively simple mathematical rules. Recently there has been increasing interest in infant pulmonary circulation and its birth-related changes (e.g. Levine et al. study [32]). It is known that the increase in airway size in the parental period is linear and continuous with antenatal growth but slows after the first year of life [33]. Based on measurements taken from bronchograms airway growth during childhood seems to be proportional throughout the lung [34]. There is evidence that pulmonary arteries and airways grow and branch together resulting in a balance in the number of terminal arteries and alveoli [34-40].

In the same effort that has been done in this approach of analysis a study of U. Frey et al. [41] has shown that the infant

[1] Forced Expiratory Volume in a second.

pulmonary arterial tree showed relatively constant branching ratios, consistent with a fractal structure. Also, it has done mathematical evidence that proportionality of a growing fractal arterial structure remains constant. This simple mathematical rule of the arterial tree may be a very basic principle of this vascular structure [41].

The term fractal is a geometric concept related to, but not synonymous with, chaos, [42, 43]. A fractal is an object composed of subunits (and sub-subunits) that resemble the larger scale structure, a property known as self similarity. Mechanistically, these self-similar structures all serve a common physiological function: rapid and efficient transport over a complex, spatially distributed system. Various other organ systems contain fractal structures that serve functions related to information distribution (nervous system), nutrient absorption (bowel), as well as collection and transport (binary duct system, renal calyces).

The fractal concept can be applied not only to irregular geometric or anatomical forms that lack a characteristic (single) scale of length, but also to complex processes that lack a single time scale. Fractal (scale-invariant) processes generate irregular fluctuations on multiple time scales, analogous to fractal objects that have a wrinkly structure on different length scales.

Although both airway wall thickening and emphysema LAA correlated with measurements of lung function, stepwise multiple regression analysis showed that the combination of airway and emphysema measurements improved the estimate of Pulmonary Function Test (PFT) abnormalities [44].

Although the CT measurement of LAA correlates well with diffusing capacity, the relationship to measurements of airflow obstruction is less significant [45, 46] presumably because airflow obstruction is related to both loss of recoil and inflammatory narrowing of the airways.

As we seek to build a normative reference of the human and animal lungs for the purpose of detecting and quantitatively following disease [47, 48], there is a growing interest in subject-specific models of the pulmonary airway and vascular trees.

COPD is characterized by the presence of airflow obstruction caused by emphysema or airway narrowing, or both [49]. Low Attenuation Areas (LAA) on CT scans in vivo have been shown to represent macroscopic or microscopic emphysematous changes in the lungs of patients [50-52].

VI. Method And Database Description

The traditional methods which using the geometric feature based on the Euclidean space mathematical model and the gray level feature can hardly meet the requirement for the property of invariance in space when the random environments where the reality scene locate are more complex and irregular than that can be described by the conventional model [53].

In order to make a classification of emphysema heterogeneity, emphysema severity was calculated by developed software as the Ratio of Emphysema's Areas (REA) in the proceeded CT's image. Computerized Tomography examinations of 67 patients with emphysema were performed and the used software accurately assesses the extent of emphysema of a CT image.

Patients between January 2007 and May 2009, 67 patients underwent radiological preoperative evaluation of emphysema at the Marie-Lannelongue Hospital, "Le Plessis Robinson", France. The patients were referred with a clinical suspicion of emphysema and to determine whether they were suitable COPD candidates for LVRS. The median age was 62 years (34 to 79 years), and there were 38 women and 29 men.

All gathered examinations were taken from the internal system of medical images archive of the hospital in format JPEG [2]. The number of images/slices included in the measurements for this study differed between patients from 5 to 15 images/slices. This number depended on the number of all images/slices that have been taken of the lung and the final slice's area that decrease with increasing of number of its slice.

Computerized Tomography (CT) source images of lung are subjected by two phases of treatment in order to produce a fractal dimension of the air densities distribution. In the first phase, raw pixel values from source images, corresponding to all possible air densities, are processed by a presented program, developed in order to; construct an image which came from: a pre-processing analysis step of the source image. The produced image identifies values of air density within the airways tree, while eliminating all non-air-density values. During the second phase, in an iterative manner, a process of Resolution Diminution Iterations (RDI) takes place. In his phase every resolution reduction produces a new resultant histogram. A resultant histogram is composed of a number of peaks, each of which corresponding to a cluster of air densities. A curve is plotted for each resolution reduction versus the number of peaks counted at this particular resolution. It permits the calculation of the fractal dimension from the regression slope of log-log power law plot.

VII. Results Of Computational Techniques

Some preliminary studies have shown that image-analysis software that automatically searches CT images for lung nodules can be used to increase a radiologist's sensitivity in the detection of small lung nodules at an early stage when they may be more effectively treated [4, 54]. Systems can be used in the process of measuring nodule characteristics to assist in the diagnostic process [4], [55, 56]. Knowledge of the relationship between the structure and function [31-35] of the normal pulmonary arterial tree [27-30] is necessary to understand both normal pulmonary hemodynamics and the functional consequences of the vascular remodelling that

[2] Joint Photographic Experts Group is a group of experts on graphics and photography who developed a standard for compressing photographic data.

accompanies a pulmonary vascular disease. Presented tool tries to exhibit asymmetry and multi-fractal properties of the airways paths in the treated images. Fractals usually possess what is called self similarity across scales. That is, as one zooms in or out the geometry / image has a similar (sometimes exact) appearance. Applying the fractal analysis approach on the whole ROI data could be considered as a useful technique to obtain the fractal coefficient that reflects the degree of disorder in the whole of lung structure.

Attempted developed a method for make a classification of emphysema heterogeneity that offers a possibility to evaluate and assess emphysema's severity accurately and relatively in short time than the classical method.

The severity of emphysema was defined as an emphysema ratio (REA). The REA in this study was defined as the relative area of the lung tissue in each CT slice that was occupied by pixels which compose the first 5% in the extracted ROI. The images were analyzed using developed software. This software automatically recognizes the lungs, traces lung airways, and presents histogram of these attenuation values relatively to the all detected pixel values of the lung area occupied by pixels.

To design a model for computer-based classification of emphysema heterogeneity corresponding to the three types of emphysema distribution depicted in figure (1), the distribution of the REA in different parts of each lung was illustrated in a diagram with the position in the lung (from cranial to caudal) on the x-axis and the REA on the y-axis.

Diagram Illustrating REA for Each image/slice: The variation of REA between different parts of the lung was graphically illustrated in diagrams; Figures (2 - 5). The REAs for each lung were distributed along a straight line, which was determined by the least-square fit toolbox in MATLAB program.

As a simple measure of the variation of REA within each lung, we calculated the REA difference as the highest REA minus the lowest REA for each lung. To separate different types of emphysema we presumed that (1) a low value of REA difference represents homogeneous emphysema; (2) a high value of REA difference in combination with a low slope of the trend line represents intermediately heterogeneous emphysema; and (3) a high value of REA difference with a steep slope of the trend line represents markedly heterogeneous emphysema (either upper-lobe or lower-lobe dominance; Figures (2 - 5).

The slope of the fitted line was calculated, as a measure of the variation of the REA within each lung, the REA difference was calculated. A diagram was constructed with the absolute value of slope, on the x-axis and REA difference on the y-axis. This resulted in a diagram differentiating markedly heterogeneous, intermediately heterogeneous, and homogeneous emphysema. According to the criteria that gave mentioned above there are twenty one (21 patients) fulfilled the criteria of bilateral markedly heterogeneous emphysema, four (4 patients) patients fulfilled the criteria of bilateral intermediately heterogeneous emphysema, and sixteen patients (16 patients) fulfilled the criteria of bilateral homogeneous emphysema.

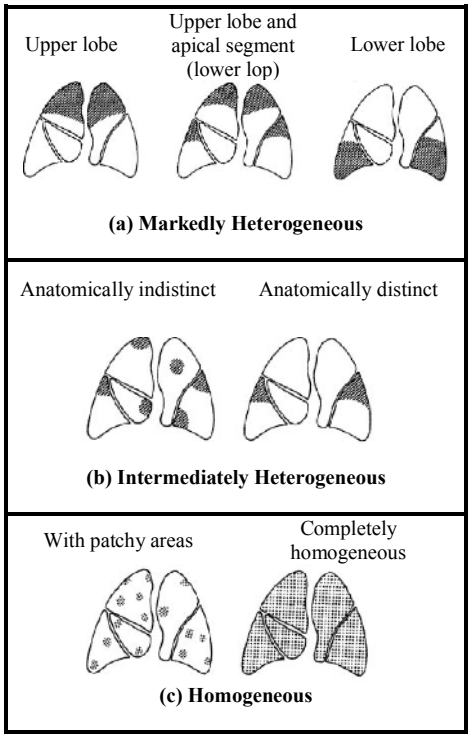

Fig. 1. Three major types of emphysema distribution: markedly heterogeneous (a), intermediately heterogeneous (b), and homogeneous (c) [2].

From the total number of the selected patients for this study (67 patients), there are twenty-six (26) patients have different types of emphysema in the right and left lung, Table I, which represent one of the most important output results of the developed tool based on the fractal analysis approach. It obviously shown that its powerfulness in assigning this huge percentage of patient whom will be suspected in different treatment or LVRS for each lung, although their two lungs were affected by emphysema. The presented method can make such classification of emphysema heterogeneity to help in choosing the proper treatment, curing process, or LVRS.

TABLE I
NUMBER OF DETECTED TYPES OF EMPHYSEMA IN RIGHT (RL) AND LEFT LUNG (LL)

LL-MHE	RL-MHE	21
	RL-IHE	3
	RL-HE	3
LL-IHE	RL- MHE	3
	RL- IHE	4
	RL- HE	2
LL-HE	RL- MHE	7
	RL- IHE	8
	RL- HE	16

- Markedly Heterogeneous Emphysema (MHE)
- Intermediately Heterogeneous emphysema (IHE)
- Homogeneous Emphysema (HE)

VIII. Conclusions

During the last few years, LVRS has received much interest as a palliative treatment in selected patients with severe pulmonary emphysema. The question "What is heterogeneous distribution of pulmonary emphysema?" was pointed out in an editorial by Austin [57].

This study presents a new accompaniment approach and image processing techniques to reveal the underlying fractal structure of airways tree paths of lung.

The present work is to investigate the powerful micro-level of fractal texture analysis that can assist in the diagnostic and interpretation of perfusion lung scans.

This method is based on fractal analysis, for describing emphysema by CT images. This technique allows for a surgically oriented classification into the categories that are; markedly heterogeneous, intermediately heterogeneous, and homogeneous emphysema.

The present study, enables separating the right and left lungs as well as the upper and lower lobes with predominant emphysema.

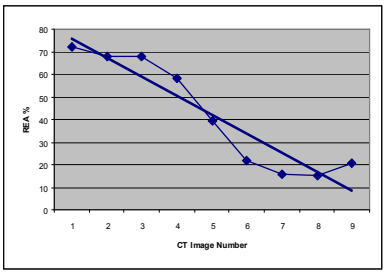

Fig. 2. Markedly heterogeneous emphysema with upper lobe predominance

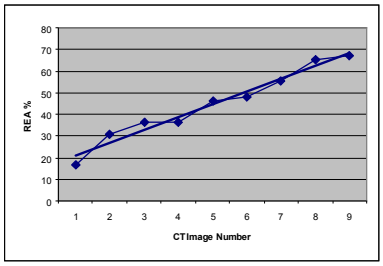

Fig. 3. Markedly heterogeneous emphysema with lower lobe predominance

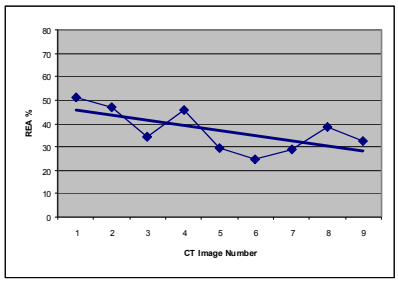

Fig. 4. Intermediately heterogeneous emphysema

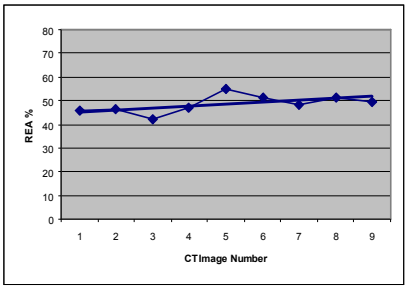

Fig. 5. Homogeneous emphysema

Acknowledgment

I would like to thanks Prof. Abdalla .S. Mohamed, Professor at department of Biomedical Engineering and systems, faculty of Engineering, Cairo University for his sincerely guide proposals that have added important understandings and many essential orientations to my work.

References

[1] Rabe KF, Hurd S, Anzueto A, et al. (2007). "Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: GOLD Executive Summary". Am. J. Respir. Crit. Care Med. 176 (6): 532–55. doi:10.1164/rccm.200703-456SO. PMID 17507545.

[2] Weder W, Thurnheer R, Stammberger U, et al. "Radiologic emphysema morphology is associated with outcome after surgical lung volume reduction". Ann Thorac Surg 1997; 64:313–320

[3] Matthew S. Brown, Sumit K. Shah, Richard C. Pais, Yeng-Zhong Lee, Student Member, IEEE, Michael F. McNitt-Gray, Member, IEEE, Jonathan G. Goldin, Alfonso F. Cardenas, and Denise R. Aberle. "Database Design and Implementation for Quantitative Image Analysis Research". IEEE Transactions on information technology in biomedicine, vol. 9, no. 1, march 2005.

[4] S. Sone, S. Takashima, and F. Li et al., "Mass screening for lung cancer with mobile spiral computed tomography scanner," Lancet, vol. 351, pp. 1242–1245, 1998.

[5] C. I. Henschke, D. I. McCauley, and D. F. Yankelovitz et al., "Early lung cancer action project: overall design and findings from baseline screening," Lancet, vol. 354, pp. 99–105, 1999.

[6] Muller, N. L., C. A. Staples, R. R. Miller, and R. T. Abboud. 1988. "Density mask: an objective method to quantitate emphysema using computed tomography". Chest 94:782–787.

[7] H. O. Coxson, R. M. Rogers, K. P. Whittall,Y.D,Yachkova, P. D. Pare, F. C. Sciurba, and J. C. Hogg, "The measurement of lung expansion with computed tomography and comparison with quantitative histology," J. Appl. Physiol., vol. 79, pp. 1525–1530, 1995.

[8] Mohanalin, Prem Kumar Kalra, Nirmal Kumar. "Tsallis Entropy based Microcalcification Segmentation". ICGST-GVIP Journal, ISSN 1687-398X, Volume (9), Issue (I), February 2009.

[9] Zhengmao Ye. "Objective Assessment of Nonlinear Segmentation Approaches to Gray Level, Underwater Images". ICGST-GVIP Journal, ISSN 1687-398X, Volume (9), Issue (II), April 2009.

[10] M. S. Brown, J. G. Goldin, R. D. Suh, M. F. McNitt-Gray, J. W. Sayre, and D. R. Aberle, "Automatic detection of lung micronodules in high resolution CT images—preliminary experience," Radiology, vol. 226, pp. 256–262, 2003.

[11] J. T. Mao, J. G. Goldin, J. Dermand, G. Ibrahim, M. S. Brown, A. Emerick, M. F. McNitt-Gray, D.W. Gjertson, F. Estrada, D. P. Tashkin, and M. D. Roth, "A pilot study of all-trans-retinoic acid for the treatment of human emphysema," Amer. J. Respir. Crit. Care Med., vol. 165, no. 5, pp. 718–723, 2002.

[12] American Thoracic Society. 1962. Chronic bronchitis, asthma, and pulmonary emphysema: a statement by the committee on diagnostic

standards for nontuberculous respiratory diseases. Am. Rev. Respir. Dis. 85:762–768.
[13] Kuwano, K., K. Matsuba, T. Ikeda, J. Murakami, A. Araki, H. Nishitani, T. Ishida, K. Yasumoto, and N. Shigematsu. 1990. "The diagnosis of mild emphysema—correlation of computed tomography and pathology scores". Am. Rev. Respir. Dis. 141:169–178.
[14] Dillon, T. J., R. L. Walsh, R. Scicchitano, B. Eckert, E. G. Cleary, and G. McLennan. 1992. "Plasma elastin derived peptide levels in normal adults, children and emphysematous subjects: physiological and CT scan correlates". Am. Rev. Respir. Dis. 146:1143–1148.
[15] Zhao, Y. and Lieber, B.B., 1994. "Steady inspiratory flow in a model symmetric bifurcation". ASME Journal of Biomechanical Engineering, 116:488-496.
[16] Sakai, N., M. Mishima, K. Nishimura, H. Itoh, and K. Kuno. 1994. "An automated method to assess the distribution of low attenuation areas on chest CT scans in chronic pulmonary emphysema patients". Chest 106:1319–1325.
[17] Kinsella, M., N. L. Müller, R. T. Abboud, N. J. Morrison, and A. Dy-Buncio. 1990. "Quantitation of emphysema by computed tomography using a "density mask" program and correlation with pulmonary function tests. Chest 97:315–321.
[18] Archer, D. C., C. L. Coblentz, R. A. deKemp, C. Nahmias, and G. Norman. 1993. "Automated in vivo quantification of emphysema". Radiology 188:835–838.
[19] Knudson, R. J., J. R. Standen, W. T. Kaltenborn, D. E. Knudson, K. Rehm, M. P. Habib, and J. D. Newell. 1991. "Expiratory computed tomography for assessment of suspected pulmonary emphysema". Chest 99:1357–1366.
[20] B.R. Celli, W. MacNee, and committee members. "Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper". Eur Respir J, ISSN 0903-1936, 2004; 23: 932–946.
[21] Celli B, Halbert R, Isonaka S, Schau B. "Population impact of different definitions of airway obstruction". Eur Respir J 2003; 22: 268–273.
[22] Smith, T.G., W.B. Marks, G.D. Lange, W.H. Sheriff and E.A. Neale. 1989. "A fractal analysis of cell images". J.Neurosci. Meth. 27: 173-180.
[23] Cumming, G., Harding, L.K., Horsfield, K., Prowse, K., Singal, S.S., Woldenberg, M.J., 1970. "Morphological aspects of the pulmonary circulation and of the airway. In fluid dynamics of blood circulation and respiratory flow". Neuilly-sur-Seine: North Atlantic Treaty Organization (AGARD Conf. Proc. No. 65), pp. 230–237.
[24] Horsfield, K., 1978. "Morphometry of the small pulmonary arteries in man". Circ. Res. 42, 593–597.
[25] Huang, W., Yen, R.T., McLaurine, M., Bledsoe, G., 1996. "Morphometry of the human pulmonary vasculature". J. Appl. Physiol. 81, 2123–2133.
[26] Singhal, S., Henderson, R., Horsfield, K., Harding, K., Cumming, G., 1973. "Morphometry of the human pulmonary arterial tree". Circ. Res. 33, 190–197.
[27] Bennett, S.H., 1994. "Modeling methodology for vascular input impedance determination and interpretation". J. Appl. Physiol. 76, 455–484.
[28] Bennett, S.H., Goetzman, B.W., Milstein, J.M., Pannu, J.S., 1996. "Role of arterial design on pulse wave reflection in a fractal pulmonary network". J. Appl. Physiol. 80, 1033–1056.
[29] Dawson, C.A., Krenz, G.S., Karau, K.L., Haworth, S.T., Hanger, C.C., Linehan, J.H., 1999. "Structure–function relationships in the pulmonary arterial tree". J. Appl. Physiol. 86, 569–583.
[30] Haworth, S.T., Linehan, J.H., Bronikowski, T.A., Dawson, C.A., 1991. "A hemodynamic model representation of the dog lung". J. Appl. Physiol. 70, 15–26.
[31] Krenz, G.S., Lin, J., Dawson, C.A., Linehan, J.H., 1994. "Impact of parallel heterogeneity on a continuum model of the pulmonary arterial tree". J. Appl. Physiol. 77, 660–670.
[32] Levine, G.L., Goetzman, W.B., Milstein, J.M., Bennett, S.H., 1994. "Irreversibility of birth- related changes in the pulmonary circulation. Pediatr". Pulmonol. 18, 368–373.
[33] Hislop, A., Haworth, S.G., 1989. "Airway size and structure in the normal fetal and infant lung and the effect of premature delivery and artificial ventilation". Am. Rev. Respir. Dis. 140, 1717–1726.
[34] Hislop, A., Muir, D.C., Jacobson, M., Simon, G., Reid, L., 1972. "Postnatal growth and function of pre-acinar airways". Thorax 27, 265–274.
[35] Elliot, F.M., Reid, L., 1965. "Some new facts about the pulmonary artery and its branching pattern". Clin. Radiol. 16, 193–198.
[36] Hislop, A., Reid, L., 1972. "Intra-pulmonary arterial development during fetal life-branching pattern and structure". J. Anat. 113, 35–48.
[37] Hislop, A., Reid, L., 1973a. "Pulmonary arterial development during childhood. Branching pattern and structure". Thorax 28, 129–135.
[38] Hislop, A., Reid, L., 1973b. "The similarity of the pulmonary artery branching system in siblings". Forensic Sci. 2, 37–52.
[39] Hislop, A., Wigglesworth, J.S., Desai, R., 1986. "Alveolar development in the human fetus and infant". Early Hum. Dev. 13, 1–11.
[40] Zeltner, T.B., Caduff, J.H., Gehr, P., Pfenninger, J., Burri, P.H., 1987. "The postnatal development and growth of the human lung". I. Morphometry. Respir. Physiol. 67, 247–267.
[41] U. Frey et al.2004. "Branching properties of the pulmonary arterial tree during preand postnatal development Respiratory Physiology & Neurobiology". 139, 179–189.
[42] Goldberger AL, Rigney DR & West BJ (1990) "Chaos and fractals in human physiology". Sci Am 262: 42-49.
[43] Bassingthwaighte JB, Liebovitch LS, West BJ. "Fractal Physiology". New York: Oxford University Press, 1994.
[44] Boulet, L.-P., M. Bélanger, and G. Carrier. 1995. "Airway responsiveness and bronchial-wall thickness in asthma with or without fixed airflow obstruction". Am. J. Respir. Crit. Care Med. 152:865–871.
[45] Nishimura, K., K. Murata, M. Yamagishi, H. Itoh, A. Ikeda, M. Tsukino, H. Koyama, N. Sakai, M. Mishima, and T. Izumi. 1998. "Comparison of different computed tomography scanning methods for quantifying emphysema". J. Thoracic Imaging 13:193–198.
[46] Nakano, Y., H. Sakai, S. Muro, H. Hirai, Y. Oku, K. Nishimura, and M. Mishima. 1999. "Comparison of low attenuation areas on CT between inner and outer segments of the lung in COPD patients: incidence and contribution to lung function". Thorax 54:384–389.
[47] Hoffman EA and McLennan G. "Assessment of the pulmonary structurefunction relationship and clinical outcomes measures: quantitative volumetric CT of the lung". Acad Radiol 4: 758–776, 1997.
[48] Hoffman EA, Reinhardt JM, Sonka M, Simon BA, Guo J, Saba O, Chon D, Samrah S, Shikata H, Tschirren J, Palagyi K, Beck KC, and McLennan G. "Characterization of the interstitial lung diseases via density- based and texture-based analysis of computed tomography images of lung structure and function". Acad Radiol 10: 1104–1118, 2003.
[49] Kitaoka H, Takaki J, Suki B. "A three-dimensional model of the human airway tree". J Appl Physiol 1999;87(6):2207–17.
[50] Gevenois, P. A., V. de Maertelaer, P. De Vuyst, J. Zanen, and J.-C. Yernault. 1995. "Comparison of computed density and macroscopic morphometry in pulmonary emphysema". Am. J. Respir. Crit. Care Med. 152:653–657.
[51] Gevenois, P. A., P. De Vuyst, V. de Maertelaer, J. Zanen, D. Jacobovitz, M. G. Cosio, and J.-C. Yernault. 1996. "Comparison of computed density and microscopic morphometry in pulmonary emphysema". Am. J. Respir. Crit. Care Med. 154:187–192.
[52] Gevenois, P. A., P. De Vuyst, M. Sy, P. Scillia, L. Chaminade, V. de Maertelaer, J. Zanen, and J.-C. Yernault. 1996. "Pulmonary emphysema: quantitative CT during expiration. Radiology" 199:825–829.
[53] A. CHANG Qing, B. Xiao D.Yao, C. Xi N.Ye, "A Fractal-based Feature Extraction Method for The Target Recognition of Infrared Image". GVIP 05 Conference, 19-21 December 2005, CICC, Cairo, Egypt.
[54] M. F. McNitt-Gray, E. M. Hart, N. Wyckoff, J. W. Sayre, J. Goldin, and D. R. Aberle, "A pattern classification approach to characterizing solitary pulmonary nodules imaged on high resolution CT: Preliminary results," Med. Phys., vol. 26, pp. 880–888, 1999
[55] S. J. Swensen, R.W. Viggiano, D. E. Midthun, N. L. Muller, A. Sherrick, K. Yamashita, D. P. Naidich, E. F. Patz, T. E. Hartman, J. R. Muhm, and A. L.Weaver, "Lung nodule enhancement at CT: multicenter study". Radiology, vol. 214, no. 1, pp. 73–80, Jan. 2000.
[56] Marsh DJ, Osborn JL, Cowley AW. "1/f fluctuations in arterial pressure and regulation of renal blood flow in dogs". Am J Physiol 1990;258:F1394-1400.
[57] Austin JH. "Pulmonary emphysema: imaging assessment of lung volume reduction surgery". Radiology; 212:1–3, 1999.