HRCT images, airways remodelling, image analysis

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THE HRCT IMAGE ANALYSIS FOR QUANTITATIVE DESCRIPTION OF PERIPHERAL AIRWAYS REMODELLING

Airways remodelling is currently described as a process occurring before asthma becomes clinically manifest, which is confirmed by biopsy studies. The aim of this study was to test and validate image analysis methods to describe the changes such as peripheral airways remodelling in HRCT readings. Different methods of airways extraction from HRCT images were investigated including: manual identification of an airway region major axes on original and scaled images (using different interpolation techniques like pixel resize, bilinear interpolation and cubic convolution), manual extraction of the density profile through the major axes of an airway region, semi-automatic method using active contours and the Hough transform. Methods were tested with original images and artificially modified images by blurring and noise addition (Gaussian, Laplacian and salt-and-pepper). Results suggest that popular image magnification using cubic convolution is not suitable for accurate estimation of shape properties of small regions. Smart pixel resizing enables to delineate a region of inner and outer borders with subpixel accuracy reducing the total error of the wall thickness estimation. Additionally smoothing must be reduced to the minimum in the case of an active contour application.

1. INTRODUCTION

1.1. AIRWAYS REMODELLING

Perennial allergic rhinitis (PAR) is a very common disease frequently preceding bronchial asthma. Allergic rhinitis is a major risk factor for asthma [1, 2]. It is presently known that the inflammatory process in lower airways coexists with remodelling in some patients suffering from asthma [3]. Airways remodelling in asthma was described as the structural changes in the airways which can lead to the increase of functional abnormalities and decrease the degree of bronchial reversibility. This includes a reticular basement membrane thickness ("subepithelial fibrosis"), smooth muscle hyperplasia/hypertrophy, proliferation of fibroblasts, mucous gland hyperplasia, increase in globet cell in the epithelium, epithelium disruption, angiogenesis and changes in the adventitia. Thickening of the reticular basement membrane due to increased deposition of collagen I, III, V, fibronectin and tenascin is a characteristic feature of airway remodelling in asthma. Recent

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studies show that reticular basement membrane thickening in biopsy specimens correlates with whole bronchial wall thickening evaluated on high resolution computed tomography (HRCT) scans [6].

Airway remodelling is currently described as a process occurring before asthma becomes clinically manifest which is confirmed by biopsy studies showing features of subepithelial fibrosis and bronchial wall thickening in allergic children without symptoms of asthma. Based on the knowledge that asthma and allergic rhinitis are different manifestations of the same clinical syndrome we hypothesize that permanent changes visualized by HRCT method also occur in PAR patients.

The main aim of the research is to describe the changes such as peripheral airways remodelling in HRCT readings in PAR patients. This can be achieved by HRCT images analysis and calculation of quantitative peripheral airways shape descriptors. However the size of visible airways is very small (a few to several pixels) in HRCT images, so accurate indication of their inner and outer borders is very difficult.

1.2. SUBJECTS

98 subjects were enrolled in the study (43 females, 53 males), aged 18-64 years (mean age 31.6). Subjects were recruited among patients treated at Department of Allergology, Clinical Hospital No 1, Medical University of Gdansk according to the criteria of Executive Committee of Allergy Rhinitis and its Impact on Asthma (ARIA) and of Global Initiative for Asthma (GINA) and among volunteers. All subjects gave their informed consent for participation in the study, which was approved by the local ethics committee.

PAR group – PAR

48 patients with PAR treated for about 2.3 years were included in this group. They were aged 18 to 54 years (mean age 25.5), 14 female and 34 male. PAR was diagnosed on the basis of patient's medical history, physical and laryngological examination.

Asthma group – BA

30 patients with asthma participated in this study. They were aged 22 to 64 years (mean age 42.9), 18 female and 12 male. Patients were on the average treated for 9.3 years. The clinical severity of asthma was evaluated according to the criteria of the Executive Committee of Global Initiative for Asthma and presented as follows: 26% with mild asthma, 13% with moderate asthma and 61% with severe asthma. Etiological factors of asthma were not taken into account while classifying the patients for the study.

Control group – CG

20 volunteers without clinical symptoms of either PAR or asthma were enrolled as a control group. They were aged 18 to 52 years (mean age 29.4), 11 female and 9 male.

1.3. HRCT IMAGES

Modern HRCT reaches a limit of spatial resolution of approximately 100-300 micrometers using thin collimation <1 mm and dedicated image reconstruction algorithms. This level of resolution allows the imaging of lung anatomy at the level of the secondary pulmonary lobule. Given the limit of resolution of 300 microns, only certain normal

structures can be visualized in vivo. Since a bronchus is only seen when its wall is thicker than 300 microns, visualization is limited to the 8th bronchial generation which corresponds to 1.5 mm diameter bronchi. However the available HRCT system for our studies (General Electric HiSpeed system in Department of Radiology, Medical University of Gdansk) was unable to reach such a high spatial resolution. All acquired images are characterized by spatial resolution in the range 500-680 micrometers.

Standard CT scans were taken at 120kV, 140 mAs and at standard algorithm of reading with spiral option. Next CT of the chest was performed with a thin-section (1-mm collimation) technique and the following parameters: 120 kV, 180 mAs, matrix size 512x512. Both end-inspiratory and end-expiratory scans were obtained to observe “air-trapping”. The standard position of the subject was used. The measurements were taken in the right lung, which was divided into three fields: the upper field above the trachea, the middle field at the lung hilum and the lower field starting below the lung hilum. For the particular field 1 mm slices were taken at 3 mm intervals, 8 slices for each field were performed. For the upper field the scans were started at 1.5 cm above the tracheal carina, for the middle field 1.5 cm below the tracheal carina and for the lower field scans were started at a point 6 cm below the carina. From each field we chose one layer with best-visualized cross-section of bronchi and we evaluated 3 pairs of bronchus with the accompanying vessel. The bronchus-vessel pairs were selected from the central field located 5-6 cm from the mediastinal pleura at the level of the lung hilum, at end-inspiration.

All data were acquired in DICOM 3.0 format. Post processing was performed using Osiris [4] and our own software created in the Java programming language.

2. METHOD

The diameter of vessels and the external and internal diameter of bronchi were measured and the bronchial wall thickness was calculated. We evaluated the diameter of segmental or subsegmental bronchi and the adjacent vessels and changes in lung density on inspiratory and end-expiratory scans to detect “air-trapping” on secondary lobule level.

2.1. SHAPE DESCRIPTION

Shape description was based on bronchial wall thickness and the adjacent vessel area measurement [5][6]. As presented in fig. 1. the standard procedure requires to calculate external and internal diameters of bronchi, which leads to calculation of important bronchial wall thickness measures. These descriptors can be used for further studies in remodelling estimation (e.g., bronchi classification).

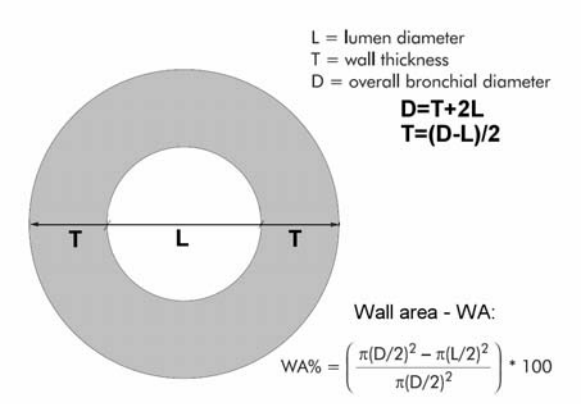


Fig. 1. Description of the wall thickness measurements

2.2. BRONCHI IDENTIFICATION

Calculation of bronchi descriptors requires identifying those bronchi which fulfill the following characteristics:

a) high SNR,

SNR calculated as a relation between bronchi wall density (in Hounsfield units – CT numbers) and the background (i.e., an average lungs area outside/inside bronchi).

b) circular orientation,

The disadvantage of thinner collimation is the lack of normal anatomic landmarks in the image. When the pulmonary vessels run perpendicular to the scan plane, an infinitely thin slice will contain nothing but dots. However if bronchi/vessels are not perpendicular presented bronchial walls are corrupted by projection distortions. We assumed that the maximum allowed relation of major to minor axes of the bronchi should not exceed 1.5.

c) number of bronchi/vessels pairs,

We assumed that at least 3 pairs in each measured field should be extracted and described.

2.3. BRONCHI REGION BORDERS EXTRACTION

The most important part of the quantitative description of bronchi shape parameters is a proper and accurate extraction of bronchi region borders. This task is difficult since the total area of the bronchial wall could be several pixels, and the wall thickness could be even one or two pixels wide. Thus it is crucial to test procedures, methods and other conditions that should be met to minimize the possible measurement error.

In fig. 2. the CT image with indicated bronchi/vessel pair is presented. The magnified region of the bronchi/vessel pair shows unclear bronchi/background border.

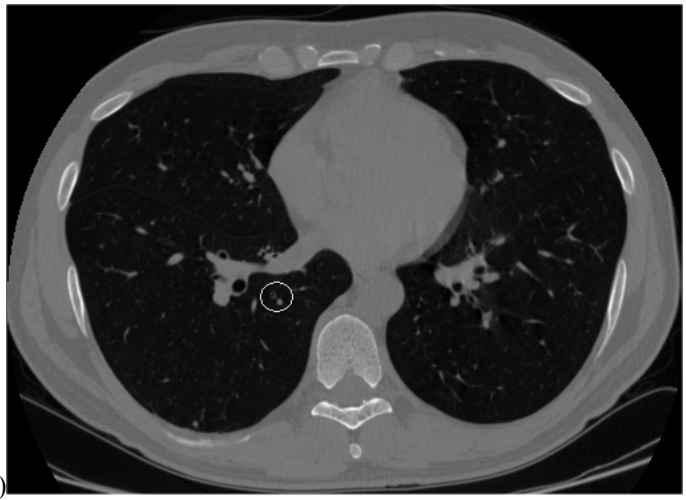
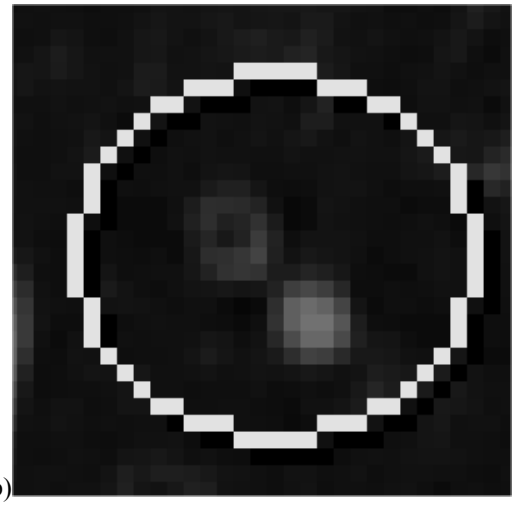
a)  b) 

Fig. 2. a) CT image with indicate bronchi/vessel pair.
b) Magnified (10 times with pixel resize by cloning) bronchi/vessel pair.

Bronchi region borders extraction requires:

1. It is impossible to delineate the bronchi/vessel pair in the original matrix size presentation of the image, so the magnification is a must.
2. Most medical workstations, to enforce smoothness of the image (radiologists do not like "stairs" effect), performed automatic interpolation, usually based on cubic convolution [7]. This method of interpolation is equivalent to low pass filtering using convolution with a proper filter mask. The filter mask depends on the cubic polynomial used for interpolation. Low pass filtering blurs the bronchi borders so the border extraction introduce additional (blur dependent) error. Low pass filtering is useful if the SNR is low (e.g., laplacian of gaussian) however we assumed, that the selected 3 pairs are characterized by high, local SNR, so smoothing is unacceptable.
3. Some medical workstations offer magnification with pixel resize (without smoothing) however delineation of the region borders is limited only to the resized, big pixels. Taking into account the partial volume effect, and limited spatial resolution it is required to measure the bronchial wall borders inside the resized pixel, especially for those pixels which are characterized by a transition density between bronchi wall and the background (fig. 3). This operation reduces the delineation error by a size of one pixel (in the wall border).

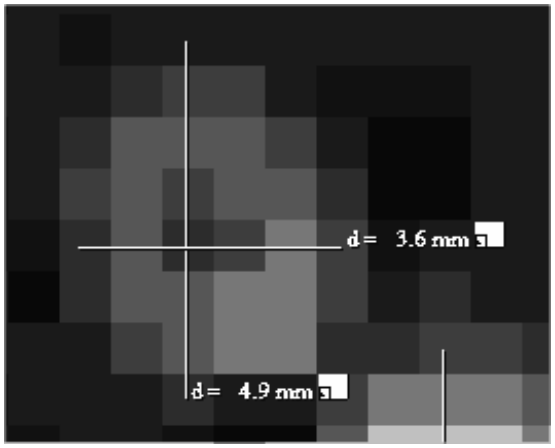


Fig. 3. Subpixel measurements of external diameters of bronchi

Most medical workstations are not calibrated, which leads to undefined transformation of image values to projected luminance. Taking into account that the measured images are characterized by matrix data in the 16 bits dynamic range (0-65535 levels) while the graphic mode enables only 256 grey shades, the presented image is a function of actually selected subset of data, scaling factors, and the monitor transfer function. This may lead to different presentation of the same data or different observation grey shades by observers. Elimination of those possible problems may be to use original image data (numbers) instead of the presented image (e.g., presented image may be an interface to data). In our studies we used several techniques based on original data:

a) density profiles,
b) active contours,
c) parametric description.

Density profiles

Using density profiles the image is treated as an interface to data allowing indication of density profile line (which starts before recognizable bronchi/vessel region and stops a few pixels after the region).

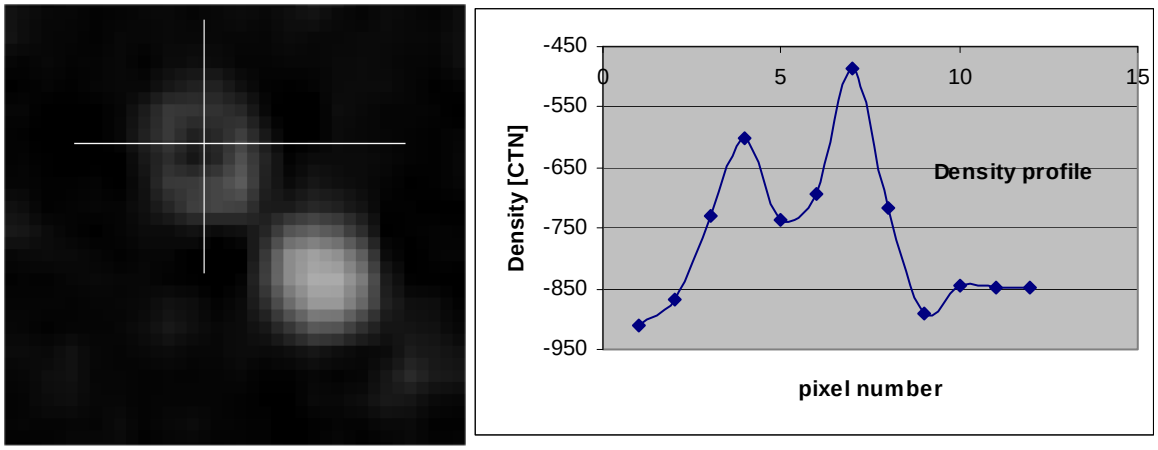


Fig. 4. Subpixel measurements of external diameters of bronchi.

Based on the extracted profiles (and known spatial resolution) it is possible to calculate bronchial region diameters as mid-points on the first ascending segment and the last descending segment of the profile.

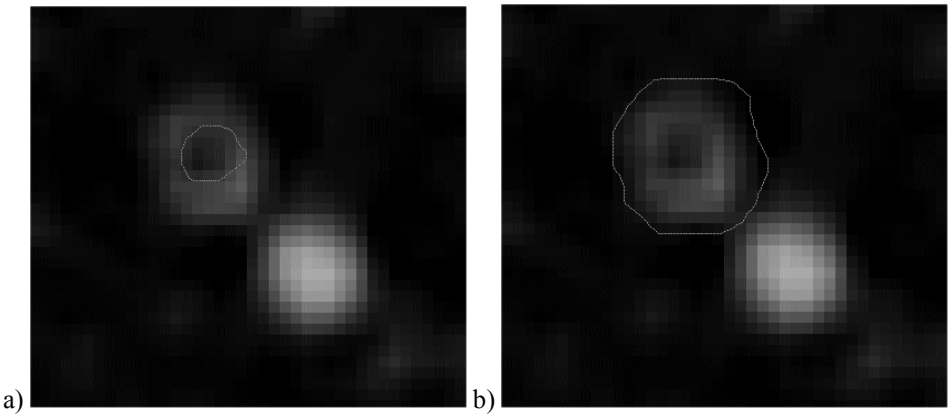
Active contours

The interesting feature of active contours is their possibility to fit the region borders, while initialized far away from those borders. After initialization the contour is iteratively fitted to the significant image region by minimizing the cost function, given as a contour energy function [8]

$$E_s = \sum_{i=0}^{N} E_i(v_i) + E_e(v_i) \qquad (1)$$

where: $E_i(v_i)$ - internal snake energy calculated based on first and second order derivative of the contour (smoothing the contour); $E_e(v_i)$ - external energy calculated based on the image properties (here the image gradient); this energy is related to the force that pulls the contour to the important image feature.

Using original data of the image it could be possible not to depend on subjective image presentation. In fig. 5 some results of active contours method are presented.



a) b)

Fig. 5. Final contours a) internal and b) external computed by active contour method.

An additional feature of the active contour method is extraction of the object area instead of major diameters of the region. This leads to the recalculation of bronchial wall thickness indexes based on difference between area enclosed by external and internal contours.

Parametric description.

The last evaluated method of original data based measurement of bronchial shape is parametric description. Parametric description assumed that the object can be described by a given model, here a circle or ellipse, and the parameters of those models. Having experimental data and the object model parameters could be found by data fitting procedure (minimizing fitting error e.g., RMS). In our study we used circular Hough transform and accumulation matrix for detection of most frequent parameters [9]. Hough transform

converts the image space (x,y) to the parametric space (for a given model). For a circle parametric description is given by:

$$(x-a)^2-(y-b)^2=r^2, \qquad (2)$$

(a,b) – coordinates of the circle centre; r-radius.

For a fixed radius r and for an edge pixel (x_1,y_1) the locus of points in parameter space is a circle centred at (x_1,y_1). Accumulation matrix is a discretised parametric space, where each matrix field is a pair of parameters (a,b). For every existing pixel (x_i,y_i) in the image space, there will be a circle in the parametric space. The circle is crossing many parameters (a,b). Each (a,b) crossing is registered (accumulation matrix field is incremented), so finally the highest number of counts for a given matrix field indicates the most probable circle with a given radius.

Initially, image is pre-processed leading to its binary version. Then circular Hough transform is applied, and based on accumulation matrix the maximal circle is searched for bronchi and vessel. The same operation is repeated for internal border of bronchi (search for a minimal circle).

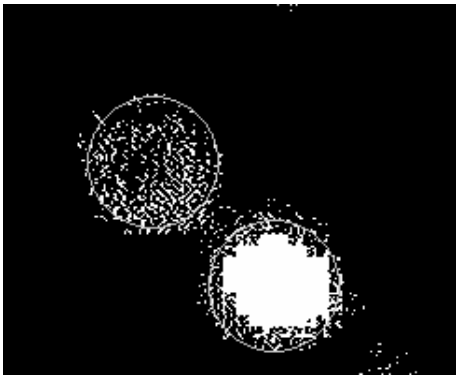
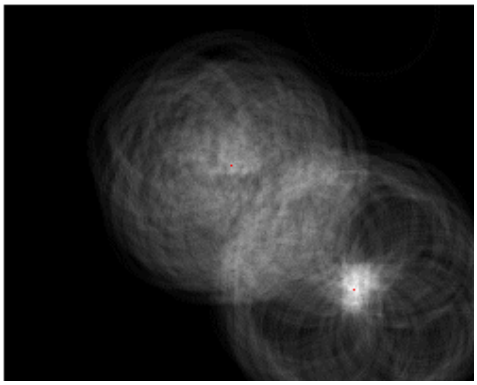
a)  b) 

Fig. 6. Circle detection using circular Hough transform a) binary image with detected circles, b) parametric space

Bronchial wall thickness indexes are recalculated based on difference between external and internal circles.

3. RESULTS AND CONCLUSION

Different methods of airways extraction from HRCT images were investigated. Total number of analyzed patient images exceeds 300. Additionally methods were tested with artificially modified images by scaling images (using different interpolation techniques like pixel resize, bilinear interpolation and cubic convolution), blurring and noise addition (Gaussian, Laplacian and salt-and-pepper). Results can be formalized as:

- cubic convolution as well as noise addition with the probability greater than 7% introduce unacceptable errors in bronchial wall extraction in the range 23% (WA) and higher;

- salt-and-pepper noise with the probability higher than 9% highly influence semi-automatic methods like active contours and Hough transform leading to the WA estimation error in the range 18% and higher;
- for small bronchial regions smart pixel resizing enables to delineate a region inner and outer borders with subpixel accuracy reducing the total error;
- analysis of density profiles allows faster WA calculation, since the image window modification (256 level subsets from 16 bits dynamic) is not required;
- in small image region analysis appropriate image magnification is extremely important (without smoothing interpolation); this requires to choose proper medical workstation software or options;
- medical workstation display should be calibrated daily, to ensure proper pixel grey shade presentation in case of image guided WA estimation;
- application of active contours or Hough transform does not improve the results obtained by analysis of density profiles; however those methods could be used in the future more automatic approach.

Preliminary results using WA analysis suggests that in PAR and asthma patients mean bronchial wall thickness in each of the evaluated fields of the right lung is significantly greater than in the Control Group (CG). There is no difference between bronchial wall thickness in PAR and asthma subjects in any of the examined fields. The mean values of the (bronchial wall thickness)/(bronchial diameter) ratio and (bronchial wall thickness)/(accompanying vessel diameter) ratio are statistically greater in PAR and asthma patients than in CG in each of the evaluated fields and the mean values for these ratios are significantly higher in asthma than in PAR patients in the lower field.

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