Semi-automatic Methods for Airway and Adjacent Vessel Measurement in Bronchiectasis Patterns in Lung HRCT Images of Cystic Fibrosis Patients

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Published online: 24 April 2018
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Abstract

Airway and vessel characterization of bronchiectasis patterns in lung high-resolution computed tomography (HRCT) images of cystic fibrosis (CF) patients is very important to compute the score of disease severity. We propose a hybrid and evolutionary optimized threshold and model-based method for characterization of airway and vessel in lung HRCT images of CF patients. First, the initial model of airway and vessel is obtained using the enhanced threshold-based method. Then, the model is fitted to the actual image by optimizing its parameters using particle swarm optimization (PSO) evolutionary algorithm. The experimental results demonstrated the outperformance of the proposed method over its counterpart in R-squared, mean and variance of error, and run time. Moreover, the proposed method outperformed its counterpart for airway inner diameter/vessel diameter (AID/VD) and airway wall thickness/vessel diameter (AWT/VD) biomarkers in R-squared and slope of regression analysis.

Keywords Airway and adjacent vessel measurement · Lung high-resolution computed tomography · Cystic fibrosis · Particle swarm optimization

Introduction

Cystic fibrosis (CF) is a genetic disorder that leads to pathological changes in several organs, among which the major cause of mortality is pulmonary dysfunctions [1]. So, the diagnosis and sequential follow-up of the lung complications very early in CF patients can improve their quality of life and prevent their death [2]. Pulmonary function test (PFT) and X-ray radiography are the common procedures to evaluate

lung changes in CF patients despite their low sensitivity to local and early changes in lung involvement [3]. Studies have shown high sensitivity of lung high-resolution computed tomography (HRCT) images in detecting lung disease severity in CF patients. HRCT images can be used to detect the presence and extent of structural lung damages such as air-trapping, bronchiectasis, and mucus plugging. Furthermore, quantification and characterization of the detected structural abnormalities in lung HRCT images are done by using the scoring

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systems [4]. The airway and vessel dimensions are used in scoring systems to evaluate the presence and extent of the CF patterns in lung HRCT images. So, the automatic extraction of airway tree and characterization of bronchiectasis airway and vessel in HRCT images can assist the radiologists to specify the severity of CF disease. In the field of airway tree extraction, some methods have been presented in 3D lung CT images such as region growing [5] [6], optimal graph construction method [7] [8] [9], front propagation [10], and classification approaches [11] [12]. In Kuhnigk et al. [5], a special region growing [13] was used for airway segmentation and a skeletonization method based on the thinning algorithm with respect to anisometric voxel size and boundary noise was utilized for graph representation of the bronchial tree. In Perez-Rovira et al. [9], the initial segmentation of vascular and airway tree was obtained by using Hessian eigen analysis and classification approach, respectively, and refined using an optimal surface graph-cut method. In Babu et al. [11], a Hessian matrix and 3D co-occurrence matrix were used as vessel enhancement filter and texture-based refinement, respectively. Then, the support vector machine (SVM) classifier was applied to correct the vessel tree segmentation. In Meng et al. [12], the Hessian analysis was employed for line-like structure enhancing and multiscale cavity-enhancement filter was utilized for airway tree detection. Finally, the SVM classifier was used to remove the false positive regions. Moreover, some methods have been proposed to characterize the airway and adjacent vessel such as thresholding [14] [15], full-width-half-maximum (FWHM) [16] [17], phase congruency [18] and model-based methods [19] [20]. In King et al. [14], an automated HRCT image analysis algorithm was developed to measure the airway lumen area, wall area, and orientation. The airway lumen area was specified by a threshold value around approximated center which was marked manually. Airway orientation was determined by measuring the displacement of center of airway lumen in adjacent slices and slice thickness. The airway wall area was estimated by using a score-guided erosion technique to determine the area within the outer airway border and its subtraction from the airway lumen area. These measurements were evaluated with an artificial phantom and an excised pig lung. In Mumcuoğlu et al. [15], a FWHM-based method was proposed to assess airway wall disease in children and infants with mild CF in lung CT images. The inner and outer airway walls were estimated by using the radial profiles that were originated from manually marked lumen center in all directions. In Nakano et al. [16], the airway wall thickness in CT images of 114 smokers was calculated and correlated with measurements of lung functions. The lumen area was identified using thresholding method and the airway wall thickness was determined by using the FWHM approach. In Saba et al. [19], the inner and outer airway wall locations were estimated initially by using the manually specified center and FWHM principle. Then, two

ellipses were fitted to the airway walls using the direct least squares method and the minor and major axes of ellipses were used to estimate the in-plane and tilt rotation angles. The parameters of the model were optimized by minimizing the difference between model and actual image. In Weinheimer et al. [17], a method was proposed for more objective measurement of the airway geometry in the 3D CT images. The wall thickness was estimated by using an integral-based closed form solution. This method was validated by using an artificial phantom and real clinical CT volumes. In Mumcuoğlu et al. [20], the threshold and model-based methods were improved to measure the airway dimensions and its paired vessel identified by a user on lung CT images from mild CF patients. The thresholding method was enhanced by including a regression-based correction to the conventional thresholding ones. The model-based method was developed as a 2D representation incorporating both the vessel and airway approximation in the same model. The model incorporated three ellipse-shaped regions for lumen, airway wall, and vessel and matched them to the original image via solving an optimization problem using Polak–Ribiera form of the conjugate gradient method [21]. In Estépar et al. [18], a phase congruency-based method was proposed for airway wall approximation. In this method, the airway wall was characterized based on the common points of intensity profiles along the radial direction of an airway for different reconstruction kernels. This method was independent from scanner specifications such as point spread function (PSF), reconstruction kernel, radiation dose, and airway model; however, it was sensitive to the airway size. In Nonomura et al. [22], the effect of global and sensory neuron-specific ablation of the mechanically activated ion channel Piezo2 on the respiratory death and distress was discussed in newborn mice. Also, the physiological function of Piezo2⁺ sensory neurons on innervation of airway organs was characterized in adult mice. In Sicard et al. [23], the Young's modulus of small human pulmonary arteries was characterized by atomic force microscopy (AFM) micro-indentation to investigate the effect of development, aging, and disease processes on the normal and pathological range of tissue stiffness.

In this paper, we propose a hybrid threshold and model-based method for vessel and airway characterization in lung HRCT images of bronchiectasis pattern in CF patients. After preprocessing, the enhanced thresholding method is applied to the HRCT image to obtain the initial model of the airway and vessel. The lumen area is approximated by using the Frangi filter [24] [25] and connected components labeling (CCL) [26] method. Then, the airway and vessel area border is specified by Canny's operator and CCL algorithm. Finally, the radial profiles from the center of the lumen approximate the initial model as two ellipses on the inner and outer airway boundary. Also, the initial model for the airway's adjacent vessel is approximated as an ellipse on its border. In the second stage, the model is matched to the actual image by solving

an optimization problem using the particle swarm optimization (PSO) method. PSO is a well-known evolutionary approach in complex optimization problems [27]. Unlike the other evolutionary computational algorithms in using the evolutionary operators, each individual in PSO flies with a dynamically adjusted velocity according to its own and swarms' flying experience [28]. This population-based algorithm converges quickly and is robust to problem nonlinearity.

The remainder of this paper is organized as follows: In the “Airway and Vessel Characterization in Bronchiectasis Patterns” section, the proposed hybrid method for characterization of airway and vessel in bronchiectasis patterns is presented. In the “Experimental Results” section, the performance of the proposed algorithm is evaluated on a dataset of lung HRCT images. Finally, the concluding remarks are given in the “Conclusion” section.

Airway and Vessel Characterization in Bronchiectasis Patterns

The flowchart of our proposed algorithm is shown in Fig. 1. It consists of three steps: (i) preprocessing, (ii) threshold-based method for approximating airway wall and vessel characteristics, and (iii) model-based evolutionary optimized approach for refining the extracted characteristics.

Dataset

In this study, we used 95 patches containing airway and vessel pair from HRCT lung images of 38 (14 female and 24 male) patients which were collected in Children's Medical Center at Tehran University of Medical Sciences [29]. The HRCT lung images were acquired using a multi-slice CT scanner ($\times 16$ LightSpeed, GE) with 80–120 kVp, 55–180 mA, 512×512 matrix, and 21.4–43.9-cm field of view. Moreover, the average voxel size and distance

between axial slices in our dataset were $0.63 \times 0.63 \times 1.2 \text{ mm}^3$ and 8 mm, respectively. The patches of size 17×17 pixels containing a paired airway and adjacent vessel were extracted and measured manually by two expert radiologists using the DiVision Lite (Marco imaging) software. Manual measurements were performed on magnified images in a blind design: The radiologists had no prior knowledge about the computer output nor did they have any knowledge about each other's results. The differences between radiologists' measurements arose from their experience and bronchiectasis pattern complexities. According to our experiments, the radiologist needed on average about 40 s to do measurement for each bronchiectasis pattern. For each patient, it depends on the disease severity and the number of patterns in the whole image volume. One sample of measurements performed by one of the radiologists on a magnified patch is shown in Fig. 2.

Preprocessing

The flowchart of our proposed algorithm is shown in Fig. 1. We use the Laplacian of Gaussian (LoG) [30] to enhance the edges of the airway and vessel as a preprocessing step. The Gaussian operator as a smoothing tool in LoG decreases the sensitivity of Laplacian operator to input noise [31, 32].

Threshold-Based Method

A new threshold-based method is proposed for preliminary airway and vessel segmentation and characterization in two-dimensional axial slices. Also, the obtained airway and vessel characterization is used to initialize the model-based method. In contrast to the earlier threshold-based method such as [14, 15], the score-guided erosion technique and FWHM-based approach are not used in our proposed algorithm. Indeed, our database suffers from varying contrasts between lung

Fig. 1 The flowchart of the proposed hybrid algorithm for airway and vessel characterization in bronchiectasis patterns. LoG, Laplacian of Gaussian, PSO, particle swarm optimization

Fig. 2 Radiologist measurements on a magnified patch. **a** Inner airway boundary. **b** Outer airway boundary. **c** Vessel boundary

airway, lumen, vessel, and lung parenchyma due to disease severity and airway/vessel generation. Therefore, we conducted toward approaches based on image enhancement. In the first step, the curvature patterns in the image are enhanced using Frangi filter [18] [19]. This filter computes the likelihood of an image to contain vessels by using the eigenvectors of the Hessian matrix [18]. Then, the CCL algorithm [20] is applied to the enhanced image in order to extract the lumen region. The resulted regions which are too small or far from the center of image are eliminated. Then, the region with minimum mean distance from the center of image is specified as the airway and vessel region. Finally, the lumen region is obtained by computing the difference between extracted airway and vessel region and its morphologically hole-filled version. Figure 3 shows the procedure for extracting the lumen region. The center of lumen is determined by the center of an ellipse fitted to the extracted lumen area.

In the second step, in order to extract the external boundary of airway, first, the external boundary of airway and adjacent vessel is found. For this purpose, the edge detection operator is applied to the hole-filled version of the airway and vessel region (e.g., the hole-filled version of airway and vessel regions in Fig. 3c). Then, the distance between the lumen center and the points on the external boundary of airway and adjacent vessel is computed (Fig. 4b). The boundary points corresponding to outlier

values of these distances specify partially the vessel area boundary. Therefore, the boundary pixels of the airway are specified by eliminating these pixels. Finally, two ellipses are fitted to the lumen area and boundary pixels of airway area as inner and outer boundaries of the airway, respectively. Figure 4 shows the procedure for approximating the inner and outer boundary of the airway region.

In the third step, the vessel center is manually determined and the radial profiles from this center are investigated to find their intersection with the approximated airway and adjacent vessel area boundary. The mean and standard deviations of distances between the vessel center and intersection points are used to determine the outliers. After eliminating the outlier intersection pixels, the remaining ones are considered as the vessel boundary points (Fig. 5a). Then, an ellipse is fitted to boundary pixels and the vessel center is determined. Figure 5 shows the result of the procedure for vessel boundary determination.

Model-Based Method

In this method, we consider a model for the airway and adjacent vessel and optimize its parameters by matching the model with the image via solving an optimization problem. The model is comprised of three ellipses corresponding to the inner and outer airway and adjacent vessel. The model parameters including the location, orientation, and elongation of the three ellipses are initialized using the results of the “[Threshold-Based Method](#)” subsection. As illustrated in Fig. 6, the model regions consist of the lumen, airway wall, parenchymal, and vessel. The lumen and vessel intensities are set to -996 HU [33] and 0 HU. The airway wall and parenchymal intensities are set to the mean of intensities of these segmented regions in the “[Threshold-Based Method](#)” subsection. Then, the model is

Fig. 3 The procedure for extracting the lumen region. **a** Input image. **b** Enhancement of edges by using Frangi filter. **c** Connected components labeled of (b). **d** Lumen region. **e** Inner airway boundary

Fig. 4 **a** Approximated external boundary of airway and adjacent vessel region. **b** Intersection of radial intensity profiles from the center of lumen and the boundary obtained in (a). **c** Boundary pixels of airway. **d** Inner and outer boundaries of airway

convolved with PSF to take into account the effect of scanner on the lung HRCT image.

In this model, each ellipse is described by five parameters including minor and major radii, coordinates of center, and angle of orientation. The vector of model parameters is

$$p = \{r_{min_{AWI}}, r_{maj_{AWI}}, r_{min_{AWO}}, r_{maj_{AWO}}, ang_{AW}, r_{min_V}, r_{maj_V}, ang_V\} \quad (1)$$

$r_{min_{AWI}}$ and $r_{maj_{AWI}}$ are the minor and major radii of inner airway, $r_{min_{AWO}}$ and $r_{maj_{AWO}}$ are the minor and major radii of the outer airway, and r_{min_V} and r_{maj_V} are the minor and major radii of vessel. Also, ang_{AW} and ang_V are the rotation angle of airway and vessel, respectively. The cost function to match the

image and model is defined as follows:

$$\min_P \sum_{i,j \in \delta} w(i,j) \cdot [I(i,j) - M(i,j)] \quad (2)$$

where I and M are the image and model intensity values, δ is the domain of the image pixels, and $w(i,j)$ is the contribution of pixel (i,j) in the cost function. The $w(i,j)$ minimizes the effect of other high-intensity structures on the segmentation. Figure 7 shows the soft threshold function $w_1(p)$ that computes for each pixel (i,j) . $P_{intensity}$ is appraised as the median intensity of parenchymal sub-region.

For each pixel (i,j) , $w(i,j)$ is specified as

$$w(i,j) = \begin{cases} 1 & 0 \leq r \leq r_{perimeter} \\ w_1(p) & r_{perimeter} \leq r \leq \alpha \cdot r_{perimeter} \end{cases} \quad (3)$$

where r is the radial distance between the center of airway to pixel (i,j) . $r_{perimeter}$ is specified by the boundary of ellipse fitted for perimeter of airway or vessel. Also, $\alpha > 1$ is a scaler which defines the parenchymal region [20].

In recent studies in a model-based approach [19] [20], the optimal parameters were obtained using linear optimization algorithms such as conjugate gradient method. However, their

Fig. 5 **a** Boundary pixels of vessel. **b** Boundary of vessel

Fig. 6 Model of airway and its adjacent vessel

Fig. 7 Contribution of pixel (i, j) in the cost function

performance was compromised by nonlinear properties and large dimensionality of the airway wall and vessel characterization problem. We solve the optimization problem in (2) by using PSO as a population-based stochastic optimization approach. The evolutionary computation approaches are appropriate for solving problems with no explicit analytical solution with reasonable running time [27] [34]. PSO converges quickly and is robust to problem nonlinearity and its space dimensionality. It can converge to the optimal solution in many

problems in which the gradient-based methods may fail [35] [36]. In PSO, a set of particles moves through the solution space to attend the function optima. The particle's experience and best experience of the swarm lead to adjust its position and velocity vector. In our problem, particle position is the vector of model parameters, $\mathbf{p}$. The position and velocity of particles in each iteration are adjusted as

$$\begin{aligned} \mathbf{v}^{k+1} &= \mathbf{v}^k + c_1 r_1 (\mathbf{p}_l^k - \mathbf{p}^k) + c_2 r_2 (\mathbf{p}_g^k - \mathbf{p}^k) \\ \mathbf{p}^{k+1} &= \mathbf{p}^k + \mathbf{v}^{k+1} \end{aligned} \quad (4)$$

where $\mathbf{v}^k$ is the velocity of the particle in the k^{th} iteration, r_1 and r_2 are the random numbers drawn from a uniform distribution $U(0, 1)$, c_1 and c_2 are the acceleration constants, $\mathbf{p}_l^k$ denotes the best solutions that the particles have achieved so far, $\mathbf{p}_g^k$ is the global best solution of all the particles, and $\mathbf{p}^k$ is the current position of the particles [37] [38]. The parameters vector $\mathbf{p}$ is initialized by the values obtained using the threshold-based method in the “Threshold-Based Method” subsection and the parameters variance that are set empirically. In our study, PSO considers the following: (1) the major radii of the inner airway are larger than

Fig. 8 Regression analysis of AID, AOD, and VD measurements using threshold-based (up) and model-based (down) methods versus the average of the two radiologists' measurements

Table 1 Results of the regression correction approach on AID, AOD, and VD measurements performed by the proposed methods along with regression function and maximum differences between it and $y = x$ line

		Regression correction			$y = ax + b$ (all data)	Maximum difference (%) between regression function and $y = x$
		Mean squared error (%)	Maximum error (%)	R^2		
Threshold-based method	AID	0.52	28.5	0.942	$x - 0.01$	24.08
	AOD	0.40	19.2	0.899	$1.02x - 0.11$	17.75
	VD	0.67	28.0	0.941	$0.97x + 0.05$	23.79
Model-based method	AID	0.54	28.5	0.942	$0.99x + 0.01$	23.98
	AOD	0.37	23.2	0.921	$0.94x + 0.22$	22.38
	V	0.65	28.8	0.959	$1.01x - 0.01$	27.58

the minor radii of inner airway and (2) the major radii of the outer airway are larger than the minor radii of the outer airway.

Our model-based method relies principally on the PSO method. At each iteration, a complexity of $O(n \times p + cof \times p)$, where n , p , and cof are the number of model parameters, population size, and cost of the objective function. On the other hand, our cost function's complexity is $O(N^2)$, where N^2 is the patch size. Therefore, the overall computational complexity of PSO in our application is $O(n \times p + N^2 \times p)$ or simply $O(N^2)$ per iteration. In our algorithm, the number of parameters is 8 and the maximum number of iterations is 200. The gradient descent-based method proposed by Mumcuoglu et al. [20] requires $O(N^2 \times q^2 + N^2 \times n)$ or simply $O(N^2)$ operations per iteration, where q^2 is the size of the window representing PSF of the imaging system. The number of parameters was 13 and the number of iterations was 10 in one reported experiment.

Experimental Results

The scoring system requires extraction of the following parameters from HRCT lung images of CF patients: the airway inner diameter (AID), airway outer diameter (AOD), vessel diameter (VD), AID/VD, and AWT/VD ratio. AWT is computed by half of the difference between AID and AOD. The acceleration constants in PSO are set to $c_1 = 2$ and $c_2 = 2$ [37] [28]. The parameters variance are set to $v_p = \{0.2686, 0.1352, 0.3001, 0.1951, \pi/12, 0.3686, 0.2686, \pi/12\}$. We use the regression analysis, R-squared, and mean and variance of error as the performance evaluation criteria. Regression analysis supplies a model for systematic bias in measurements [20] and R-squared is the square of correlation between the radiologist's measurement of the parameters f and modeled data values $\hat{f}$ by linear regression analysis [39].

$$R^2 = 1 - \frac{\sum (f_i - \hat{f}_i)^2}{\sum (f_i - \bar{f})^2} \quad (5)$$

where $\bar{f}$ is the mean values of f .

Fig. 9 Regression analysis of AID, AOD, and VD measurements performed by radiologist 2 versus radiologist 1

Evaluation

Figure 8 shows the regression analysis of AID, AOD, and VD measurements by using the threshold-based and model-based methods versus the average of two radiologists' measurements. In the threshold-based method, the slope of regression curve for AID, AOD, and VD measurements is close to 1, but R^2 criterion is not near to 1 especially in AOD measurement. Also, the distribution of points on the regression analysis shows the AID has been estimated better than AOD and VD.

The model-based method can improve the AID, AOD, and VD measurements. The regression analysis of measurements versus the average of two radiologists' measurements is shown in Fig. 8. The slope of regression analysis for AID, AOD, and VD is close to 1. Also, R^2 values are approximately acceptable except for AOD measurement.

We applied regression correction, leave-one-out training/testing method to evaluate the performance of the proposed threshold-based and model-based algorithms [20] [40]. In the training step, the parameters a and b of regression function $y = ax + b$ were obtained and used for correcting the test measurement (y) by the equation $x = (y - b)/a$, where x is the regression-corrected value. The regression-corrected measurement errors and R^2 values for the proposed threshold-based and model-based methods along with regression function and maximum difference between it and $y = x$ line are shown in Table 1. Regression-corrected MSE is less than 1% and R^2 is close to 1 in the proposed methods which demonstrates the validity of the linear regression.

Figure 9 shows the regression analysis of AID, AOD, and VD measurements performed by the two radiologists. The slope and R^2 values of AID and VD linear regression between radiologists are slightly worse than these criteria

in threshold-based and model-based methods versus the average of radiologists as indicated in Table 2. The slope of AOD regression analysis in threshold-based method is closer to 1 with respect to the slope of regression analysis between two radiologists.

According to CF disease's scoring systems, the AID/VD and AWT/VD ratios are biomarkers which specify the severity of the lung damages. Table 2 shows the slopes and R^2 values of linear regression for AID/VD and AWT/VD ratios. The first row concerns the linear relationship of AID/VD and AWT/VD between measurements performed by the radiologists ($p < 0.0001$). The second and fourth rows indicate the linear regression parameters of AID/VD and AWT/VD computed by the proposed methods versus the average of radiologists' measurements ($p < 0.0001$). The slope of linear regression in model-based method is better than that of threshold-based method for AWT/VD and is approximately the same for that in AID/VD. Our threshold-based method outperformed the threshold-based method in Mumcuoğlu's algorithm [20]. Moreover, the slope of linear regression in our model-based method is closer to 1 with respect to the slope of model-based Mumcuoğlu's algorithm [20]. The Bland–Altman plots of the difference between our results and average measurements of the radiologists are shown in Fig. 10.

The parameters of Bland–Altman relationship such as mean differences, standard deviation of differences, number of outliers, slopes, and R^2 are shown in Table 2. The number of outliers in threshold-based method is less than its value in Mumcuoğlu's algorithm [20]. Moreover, the slope of regression in Bland–Altman analysis is closer to zero for our methods with respect to Mumcuoğlu's algorithm [20].

Table 2 Slopes and R^2 levels for the linear regression and Bland–Altman analysis of the proposed methods versus the average of two radiologists' measurements. The results are also compared with the results reported in Mumcuoğlu et al. [20]

			Linear regression		Bland–Altman			
			Slope	R^2	Mean differences	Std of differences	Number of outliers	R^2 of regression
Radiologist 2 versus radiologist 1		AID/VD	1.17	0.87	−0.04	0.29	7	−0.24
		AWT/VD	1	0.70	−0.03	0.26	7	−0.19
Threshold-based method	Proposed algorithm	AID/VD	0.97	0.96	0.01	0.14	5	0.011
		AWT/VD	0.89	0.84	0.02	0.17	5	0.028
	Mumcuoğlu's algorithm [20]	AID/VD	0.71	0.91	0.00	0.14	9	0.090
		AWT/VD	0.38	0.57	0.00	0.08	13	−0.093
Model-based method	Proposed algorithm	AID/VD	0.96	0.93	0.01	0.17	6	0.004
		AWT/VD	0.92	0.81	0.00	0.19	6	−0.027
	Mumcuoğlu's algorithm [20]	AID/VD	0.74	0.97	−0.06	0.14	7	0.134
		AWT/VD	0.55	0.77	−0.03	0.07	6	0.054

Fig. 10 Bland–Altman analysis of AID/VD (top) and AWT/VD (bottom) ratios for the measurements performed by the radiologists and our threshold-based and our model-based methods

Conclusion

In this paper, we presented novel threshold-based and model-based methods for characterization of lung airway and

adjacent vessel. In the preprocessing step, LoG operator is used to enhance the edges in the image. In the threshold-based method, the inner and outer airway boundary is specified by using Frangi filter and connected component labeling.

The boundary of vessel is identified by using the intensity profiles from manually selected center of vessel. In the model-based method, the weighted difference between model and actual image as a cost function is optimized by PSO evolutionary algorithm. This population-based algorithm is robust to nonlinearity and size of the problem. Also, the run time of PSO is very low in comparison with that in classical optimization algorithms like gradient descent algorithm.

The results of our proposed algorithms to characterize the airway and adjacent vessel confirmed its outperformance in R^2 except in AOD parameter in threshold-based method. Also, our proposed methods outperformed Mumcuoğlu's algorithm in slope of regression analysis and in R^2 in AID/VD and AWT/VD biomarkers except in slope of regression analysis in threshold-based method for AID/VD parameter.

Funding Information The authors would like to thank the Iranian National Science foundation for its support of this work with the award number 95-45194.

Compliance with Ethical Standards

The ethical permission for retrospective use of HRCT lung images was provided by the local ethics committee of Tehran University of Medical Sciences, Tehran, Iran (approval number TR.TUMS.MEDICINE.REC.1396.4599).

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