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Image Analysis for Cystic Fibrosis: Automatic Lung Airway Wall and Vessel Measurement on CT Images

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Abstract— **Cystic Fibrosis (CF) is the most common lethal genetic disorder in the Caucasian population, affecting about 30,000 people in the United States. It results in inflammation, hence thickening of airway (AW) walls. It has been demonstrated that AW inflammation begins early in life producing structural AW damage. Because this damage can be present in patients who are relatively asymptomatic, lung disease can progress insidiously. High-resolution computed tomographic imaging has also shown that the AWs of infants and young children with CF have thicker walls and are more dilated than those of normal children. The purpose of this study was to develop computerized methods which allow rapid, efficient and accurate assessment of computed tomographic AW and vessel (V) dimensions from axial CT lung images. For this purpose, a full-width-half-max based automatic AW and V size measurement method was developed. The only user input required is approximate center marking of AW and V by an expert. The method was evaluated on a patient population of 4 infants and 4 children with different stages of mild CF related lung disease. This new automated method for assessing early AW disease in infants and children with CF represents a potentially useful outcome measure for future intervention trials.**

I. Introduction

Cystic Fibrosis is the most common lethal genetic disorder in the Caucasian population, affecting about 30,000 people in the US [1]. Normal regulation of the movement of ions such as chloride and sodium is disrupted due to a defective transmembrane protein called cystic fibrosis conductance transmembrane regulator. As a result, thick, immobile mucus builds up in the airways, leading to obstruction and infection. The result of these pathological changes is chronic progressive lung disease and eventual death [2].

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Lung inflammation begins early in life [3-4] and produces both structural and functional changes in the airways of infants and young children with this disease [5-6]. Because this damage can be present in patients who are relatively asymptomatic, lung disease can progress insidiously [5-6]. In 2004, Long et al. used high-resolution computed tomographic (HRCT) lung imaging to show that the airways of infants and young children with CF have thicker walls and are more dilated than those of normal children [5]. Airway (AW) dimensions were measured manually by using the electronic caliper tool on a PACS workstation, which is a tedious, time-consuming and subjective process. Thus, this technique is impractical for any large clinical study attempting to use the quantitative measurement of AW characteristics to detect early AW disease.

The purpose of this study is to develop computerized methods, which allow rapid, efficient and accurate assessment of CT AW and vessel (V) dimensions from axial CT lung images.

Many lung-CT image analysis studies and tools have been reported in the literature [8-11]. The 2D and 3D AW wall estimation problem has also been investigated extensively. Among the methods developed, the most well-known approaches are: full-width-half-max (FWHM) based [12], ellipsoidal modeling [13] and phase congruency [10] based methods. One of the main challenges in AW wall estimation is the fact that AW wall thickness is close to CT resolution limits. Secondly, the surrounding high intensity parenchymal tissue and vessel structures create a challenge. In this study, a FWHM-based method is employed for automatic AW estimation problem, to address these challenges. One of the contributions of this study is the proposed AW wall axis estimation method, which is a precursor to the subsequent estimation of AW inner and outer interfaces. The only user input required is an approximate center marking of AW and V by an expert.

Section II explains the method developed to measure the AW wall and V interfaces automatically, as well as the evaluation methods employed. Experimental results are presented in Section III.

II. AIRWAY AND VESSEL SHORT-AXIS DIAMETER MEASUREMENT METHOD

A CT lung image with three labeled AW-V pairs are shown in Figure 1 (red and green points show the center of AW and V respectively). HRCT scans were performed by using a General Electric Hi Speed Advantage CT scanner (General Electric Medical Systems, Milwaukee, Wisc) with 1.25-mm slice thickness, 400-1000 millisecond scan time, 80-120 kVp, 60-80 mA, bone algorithm, 512 X 512 matrix, and the smallest possible field of view (15-25 cm). Four equally spaced images of the lung were obtained at four anatomical levels: (1) at the top of the aortic arch; (2) 1 cm below the carina; (3) at the lower edge of the left hilum; and (4) 1 cm to 2 cm above the top of the diaphragm.

HRCT images from 8 patients (4 infants and 4 children) with varying degrees of early CF related lung disease were selected for evaluation. A total of 88 AW-V pairs satisfying the above rules were assessed. (This is a pilot project to develop the algorithm and the 8 patients were deliberately selected to span the range of disease severity levels seen in these age groups. This was thought best for testing the algorithm across variations in age and disease.)

A. Airway short-axis diameter measurement method

Figure 2 gives flowchart of the algorithm. Since AW and V diameters are mostly only a few pixels wide (Figure 1), a sub-pixel accuracy is desired in the measurements. It is also observed that average AW wall CT intensity is observed to vary significantly. The algorithm starts by fine-tuning the center coordinates of AW by searching the local minimum (of a weighted average of pixel values) in half-pixel steps within a 1-pixel radius. Next, radial intensity profiles (polar coordinate transformation) from the center are obtained by bilinear interpolation (Figure 4). To eliminate the effect of image noise, radial profiles are smoothed in angular direction. On each profile, first positive peak (whose CT value is higher than air) is taken to correspond to the AW wall axis. Our algorithm starts by estimating this axis, followed by inner and outer boundary estimations of AW wall. To find the first positive peak, the zero crossing of the first derivative can be searched [7]. However, if there is surrounding parenchymal tissue/vessel, at these radial angles from center of AW, the peak moves out from the AW wall towards this high intensity structure (Figure 3). We propose that such cases can be detected by observing the peak intensity, which gets higher in such cases. For those radial directions whose peak intensity is 35% higher than the median peak intensity, first smoothing is applied (to the radius value), and then the radius value is decreased in proportion to the excess peak value (beyond 1.35*median), followed by another smoothing (Figure 3). The proportionality constant is experimentally determined. Next, the inner interface of the AW wall is estimated as the 75% cutoff point between peak intensity and AW intensity. The radius (interface) is clipped at 1.35*median and smoothed.

The estimation of AW outer wall is more challenging due to surrounding parenchymal tissue and V structures. In our current algorithm, we compute the outer wall as a point outward from the estimated AW axis of 80% of the distance between estimated AW axis and the inner interface.

Finally, post-processing (as in inner interface estimation) is also applied. Using the estimated inner and outer interfaces, minimum short-axis diameters are computed.

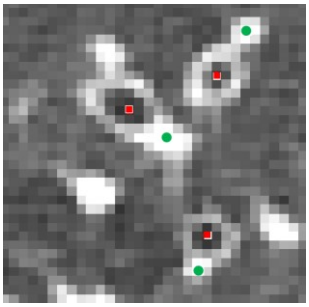

Fig. 1. A portion of a CT lung image with three labeled AW and V pairs (red and green dots show the centers of AW and V respectively).

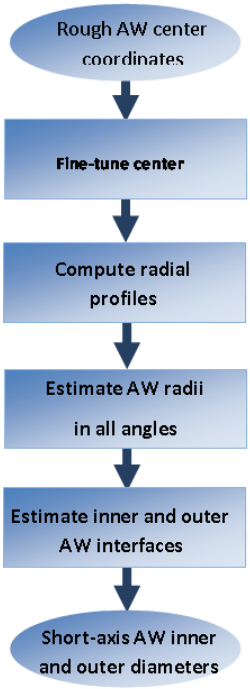

Fig. 2. Flowchart of the overall AW wall measurement algorithm.

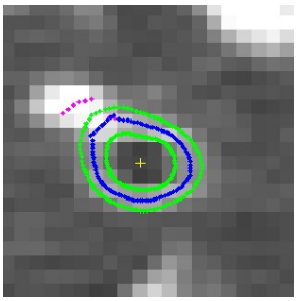

Fig. 3. An AW-V pair. Overlayed are the automatically computed AW wall axis (blue) and inner / outer walls (green). Also shown in purple is the preliminary computed AW wall axis by simple peak detection (before the correction method applied described in the text).

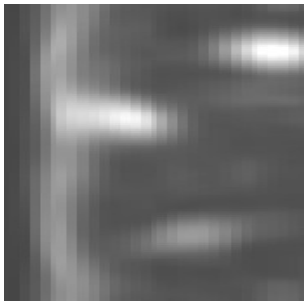

Fig. 4. AW in Figure 3 plotted in polar coordinates (radially sampled) to work in 1D profiles cast from AW center. Left most vertical high intensity region corresponds to the AW wall.

B. Vessel wall short-axis diameter measurement method

The vessel wall estimation method is similar to the AW wall estimation method. Vessel wall is estimated at the 75% cutoff point of peak vessel intensity (Figure 5).

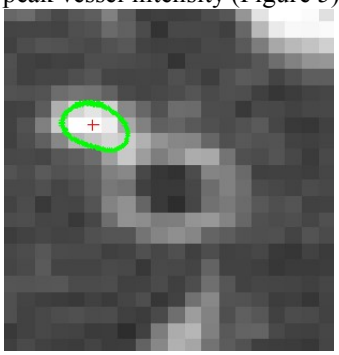

Fig. 5. An AW-V pair. Overlayed is the automatically computed V wall (green).

C. Evaluation of the measurements

All clearly visible segmental and sub-segmental airway/vessel pairs (bronchus and accompanying pulmonary artery within 1 mm of each other) that had a rounded cross-sectional circumference (ratio of long axis to short axis diameter <1.5) were measured manually by 3 expert observers using electronic calipers available in the General Electric Medical Systems Advantage Windows 3.1 workstation. For each airway/vessel pair, the shortest axis of the airway outer diameter (AOD), airway inner or lumen diameter (AID), and adjacent pulmonary artery or vessel diameter (VD) was measured [5]. From these measurements, the airway wall thickness (AWT) was derived (AWT = [AOD – AID]/2). Airway lumen diameters that measured <0.5 mm were considered too near the limits of line pair resolution of the scanner to be measured accurately and were thus excluded. Next, the key textbook rule of thumb ratios [5] are computed, which are AWT/VD and AID/VD.

Forced expiratory flow (FEV) and forced vital capacity (FVC) are standard spirometric measures used clinically (not image based) to assess pulmonary function. In the 4 infants, FVC and FEV in 0.5 seconds were measured using the raised volume rapid thoracic compression method, and percent predicted values calculated from the normative data of Jones et al [15]. In the 4 children FVC and FEV in 1 second were measured during voluntary spirometry and percent of predicted values calculated based upon the normative data of Eigen et al [16].

III. EXPERIMENTAL RESULTS

Evaluations of the algorithm are shown in Figures 6-12. Figure 6 shows the inter-observer variability between assessments of overall mean patient AID/VD ratios made by three experts using electronic calipers and algorithmically derived mean patient ratios. Figure 7 and Figure 8 show good correlation of AID/VD ratios between algorithmic and manual measurements. Figure 9 and Figure 10 show some overestimation in the lower range of AWT/VD ratios. Figure 11 and Figure 12 show that the global patient mean airway measurements are clinically meaningful in relationship to individual patient radiologist scoring and lung function. We have also measured the average time it takes to do manual vs. automatic measurement of one AW-V pair, which are ~30 sec vs. ~1.5 sec respectively. (Algorithm is developed on MATLAB [14].)

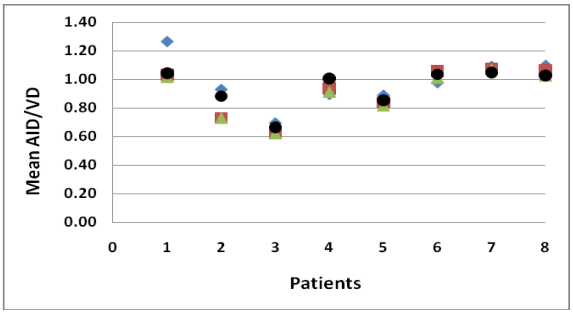

Fig. 6 Mean AID/VD ratio plots for 8 patients. Algorithmic estimates are in black. Red, blue and green are caliper measurements by three expert observers.

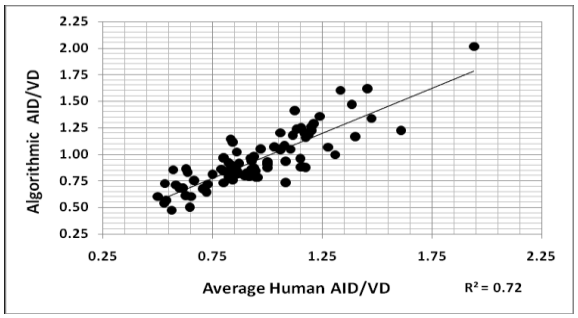

Fig. 7. Regression plot of AID/VD ratios of algorithm vs. manual measurements (averaged among three expert observers) of 88 AW-V pairs.

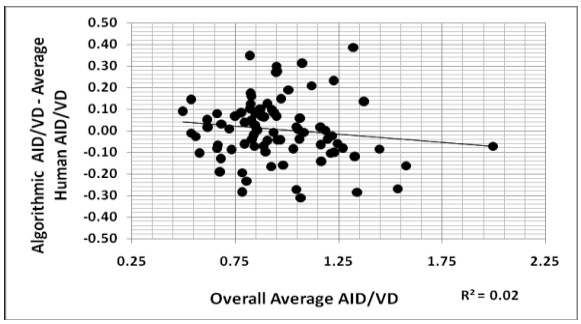

Fig. 8. Bland-Altman plot of AID/VD ratios: algorithm - manual measurement (averaged among three expert observers) for 88 AW-V pairs.

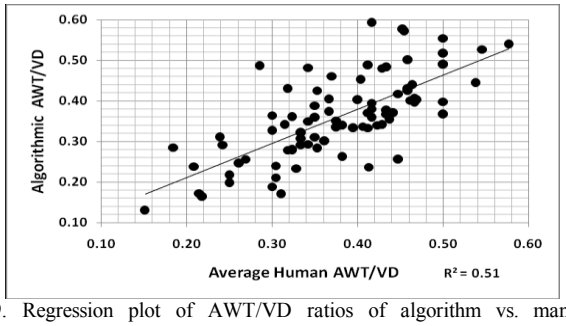

Fig. 9. Regression plot of AWT/VD ratios of algorithm vs. manual measurement (averaged among three expert observers) for 88 AW-V pairs.

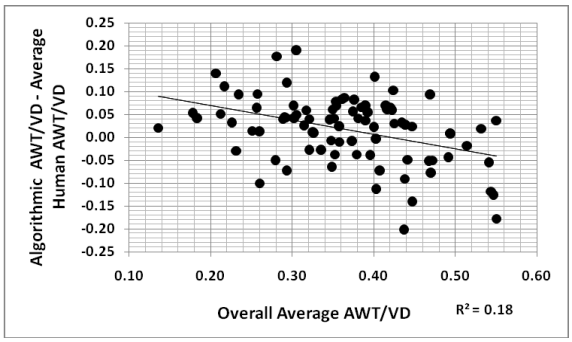

Fig. 10. Bland-Altman plot of AWT/VD ratios: algorithm - manual measurement (averaged among three expert observers) for 88 AW-V pairs.

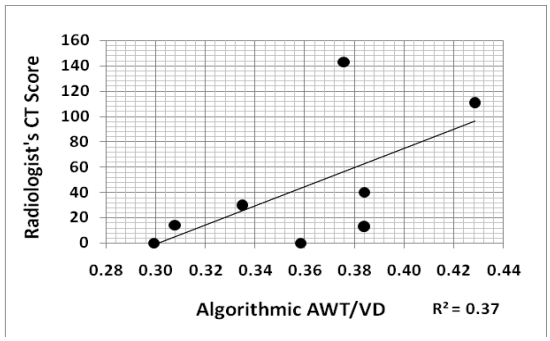

Fig. 11. Radiologist's score versus mean algorithmic AWT/VD ratio for 8 patients.

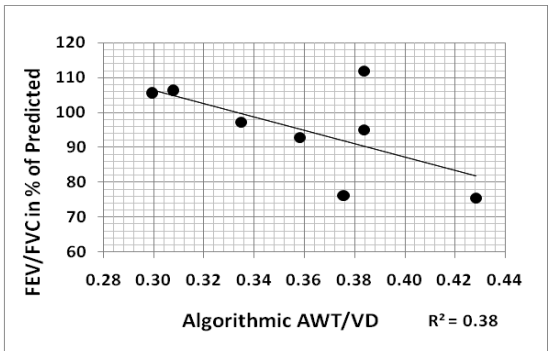

Fig. 12. FEV/FVC in % of predicted versus mean algorithmic AWT/VD ratios for 8 patients.

IV. CONCLUSION

In this pilot study, a FWHM-based estimation method is developed to measure AW and V wall short-axis diameters. Our initial evaluations with a data set of eight patients demonstrated a good correlation with the measurements made by experienced observers using electronic calipers (except some overestimation in the lower range of AWT/VD ratios) as well as with the spirometric measurements. This pilot study will proceed by making evaluations on a larger population.

We have also employed ellipsoidal fitting to the both estimated inner and outer interfaces by using MATLAB signal processing toolbox [14]. However, the results were found to be inferior. In the future, we are planning to investigate derivative-based, ellipsoidal modeling or the recently popular phase congruency based approaches.

Automatic detection of AW-V pairs in 2D CT scans is a component of this study to be investigated in the future to make it completely independent of expert knowledge.

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