Fractal dimension of lung vessels negatively correlates with hemodynamics of patients

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Purpose

Pulmonary hypertension (PH) is a chronic disorder of the pulmonary circulation, marked by an elevated vascular resistance and pressure. This results in functional limitations, increased load on the right heart and ultimately right-heart failure [1]. PH is defined as a mean pulmonary artery pressure (mPAP) greater than or equal to 25 mmHg, which is determined during invasive right-heart catheterisation [2]. PH can result in decrease of volume of blood vessels [3]. One of the radiological features of PH is vascular pruning. This is due to vascular remodelling and loss of arterial branching. Quantitative assessment of pruning would provide a non-invasive method for PH diagnosis.

The purpose of this study is to examine the fractal properties of the lung vessels. A fractal is a self similar object over different scales [4]. An important feature of them is that their complexity can be measured by the fractal dimension (FD) which is a measure of space [5]. For calculation of FD an automatic lung vessel segmentation algorithm was developed.

In this study we determined the 3D fractal dimension of the segmented lung vessels from contrast-enhanced CT images of the thorax and compared it with the patient clinical parameters.

Methods and Materials

Patient population

The study was approved by the local ethics committee and written informed consent was obtained from all 18 patients. All patients undergoing right heart catheterization (RHC) at the Department of Pulmonology between May 2011 and June 2012 with indication for diagnostic CT were included. The CT examination was carried out within one and 18 days of RHC, with a median of one day. No change in therapy occurred during these time points. Patients with and without pulmonary hypertension were included. Exclusion criteria were renal insufficiency, known adverse reactions against iodinated contrast material, a recent diagnostic CT and pregnancy.

Examinations

RHC was performed on all patients for diagnostic or follow-up reasons by the same experienced medical personal. A 7-F quadruple-lumen, balloon-tipped, flow-directed Swan-Ganz catheter (Baxter Healthcare Corp., Irvine, California) was used in a transjugular approach without transparency.
A routine thorax CT examination was performed with a 128-slice dual-energy CT scanner (Somatom Definition Flash, Siemens, Forchheim, Germany). The images were reconstructed with 0.6 mm slice thickness using a medium-soft kernel (D30f), anonymised and transferred to an independent workstation. In this study we used the equally mixed images from both detectors.

**Vessel segmentation algorithm**

Fig. 1 on page 4 shows the flowchart of our fully automatic vessel segmentation method consisting of three steps: (1) preprocessing of the image that includes smoothing and extraction of the target processing regions, (2) enhancement of vessels inside the lung, (3) centerline extraction and connection.

In the preprocessing step the CT Image is smoothed using an edge preserving total variation based denoising [6]. Then the lung is segmented by grey level thresholding followed by morphological operations. Airways are segmented by detecting a point inside the bronchus and applying a region growing algorithm. Airway segmentation is needed to separate the lung segmentation into left and right lung, and to remove the airways from the target processing region (usually the bronchus runs along the pulmonary blood vessels and is attached to it; since the intensity contrast between the airway border and the vessels is low, incorrect segmentation of the blood vessels can occur).

The vessel-enhancement filter (VE-filter) is a Hessian based filter with an offset-medialness function (Fig. 2 on page 4a) [7]. After limiting the result of the VE-filter to the processing region (left and right lung, excluding the airways), a non-maxima suppression of the VE-filter response leads to disconnected centerline fragments (Fig. 2 on page 4b). To connect these centerline fragments and generate the vessel tree, a modified Dijkstra algorithm is used (Fig. 2 on page 4c) [8]. In Fig. 3 on page 5 a 3D rendering of the resulting centerlines is shown.

**Calculation of 3D FD with the box counting method:**

The fractal dimension of the connected vessel centerlines was calculated by applying a 3D extension of the well-validated box counting method [9]. Box counting consists of dividing the vessel centerline image into a grid of equal boxes with size $x^3$, and counting the number of boxes containing part of the vessel centerlines. This process was repeated for different box sizes (from one pixel up to 100 pixel side length). The fractal dimension is equivalent to the slope of a line fitted on a double logarithmic plot of the number of boxes against the box size $x$ (Fig. 4 on page 6). To account for limitations in resolution, only the linear part (Fig. 4 on page 6, red dots) was used for line fitting.

**Statistical analysis**
Statistical analysis was performed in GraphPad Prism (Version 5.04, GraphPad Software, Inc., La Jolla, California) with linear regression and Pearson correlation.

Images for this section:

![Flowchart of the automatic vessel extraction algorithm](image)

**Fig. 1:** Flowchart of the automatic vessel extraction algorithm
Fig. 2: An example thorax CT image superimposed with the vessel enhancement filter response in the lung vessels (a), non-maxima suppressed response (b, green lines), connected centerline (c, red lines)
**Fig. 3:** 3D rendering of the lung vessel centerlines (red lines). The airways are depicted in blue, whereas the heart and large thoracic vessels are red.
Fig. 4: Double logarithmic plot of the number of non-empty boxes (n) against the box size (delta). For linear fitting only the linear part of the data (red crosses) was used. The slope of the fitted line (green) corresponds to the fractal dimension.
Results

18 patients (female:male = 10:8) gave written informed consent to participate in the study. Patient characteristics are listed in Table 1 on page 8. There were no complications either during RHC or during CT examination.

The mean value of the 3D fractal dimension in our patient cohort was 2.265 (range 2.158-2.363, Table 1 on page 8), which is in good agreement with previously reported values from similar studies [9]. Despite our expectations, 3D fractal dimension showed no correlation with disease type (Fig. 5 on page 9). The same, lack of correlation could be observed in case of mean pulmonary artery pressure (mPAP) or cardiac output (CO) which are the main diagnostic parameters of PH (Fig. 6 on page 10). However, 3D fractal dimension showed correlation with other hemodynamic parameters determined during RHC (Fig. 7 on page 11). There was a negative correlation with arterio-venous difference in oxygen content (AVDO$_2$, Spearman $r = -0.49$). 3D fractal dimension showed a positive correlation with arterial saturation of oxygen (artSO$_2$, Spearman $r = 0.63$) and venous saturation of oxygen (venSO$_2$, Spearman $r = 0.59$).

One of the limitations of this study is the small number of patients, which allows only a preliminary conclusion, despite considering a wide range of diseases. A large scale prospective study would be necessary to determine the true benefits and constraints of this method. Further, because of the radiation exposure one cannot test the repeatability of the method. This would be necessary to determine its ability for use in disease monitoring and follow-up examinations.

Images for this section:
Table 1: Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (n=18)</th>
<th>No PH (n=5)</th>
<th>PH (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>59 (26-76)</td>
<td>59 (50-71)</td>
<td>59 (26-76)</td>
</tr>
<tr>
<td>Female : Male</td>
<td>10 : 8</td>
<td>3 : 2</td>
<td>7 : 6</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>30 (14-59)</td>
<td>18 (14-20)</td>
<td>38 (26-59)*</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>4.93 (3.0-7.8)</td>
<td>5.52 (4.3-7.8)</td>
<td>4.48 (3.0-5.7)</td>
</tr>
<tr>
<td>AVDO₂ (vol. %)</td>
<td>4.47 (2.4-6.4)</td>
<td>3.86 (3.3-4.3)</td>
<td>4.86 (2.4-6.4)*</td>
</tr>
<tr>
<td>art SO₂ (%)</td>
<td>95.35 (90-97.9)</td>
<td>96.89 (85.1-97.9)</td>
<td>94.2 (90-97.5)*</td>
</tr>
<tr>
<td>ven SO₂ (%)</td>
<td>70.76 (50.4-84.1)</td>
<td>74.7 (71.5-75.8)</td>
<td>67.8 (50.4-84.1)*</td>
</tr>
<tr>
<td>Fractal Dimension</td>
<td>2.265 (2.158-2.363)</td>
<td>2.302 (2.256-2.363)</td>
<td>2.254 (2.158-2.337)</td>
</tr>
</tbody>
</table>

Data are expressed as mean (range); PH = pulmonary hypertension; mPAP = mean pulmonary artery pressure; CO = Cardiac Output; AVDO₂ = arterio-venous difference in oxygen content; art SO₂ = arterial oxygen saturation; ven SO₂ = venous oxygen saturation; * = significant difference between patients with PH and without PH (p < 0.05)
**Fig. 5:** Distribution of 3D fractal dimension based on the disease type (iPAH = idiopathic pulmonary arterial hypertension, PAH = pulmonary arterial hypertension other than iPAH, PH = pulmonary hypertension, CTEPH = chronic thromboembolic pulmonary hypertension).
Fig. 6: (a) Correlation of 3D fractal dimension with mean pulmonary artery pressure (mPAP) and Cardiac Output (b). \( R = \) linear correlation coefficient, \( p = \) probability of non-significance

Fig. 7: (a) Correlation of 3D fractal dimension with arterio-venous difference in oxygen (AVDO2), arterial (b, art SO2) and venous (c, ven SO2) saturation of oxygen. \( R = \) linear correlation coefficient, \( p = \) probability of non-significance
Conclusion

3D fractal dimension is suitable to characterize the complexity of lung vascular trees. Our findings show that 3D fractal dimension is not suitable for the detection of pulmonary hypertension, but is a promising measure to determine certain hemodynamic parameters.

References


Personal Information