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Influence of inspiration level on bronchial lumen measurements with computed tomography

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Summary
Background: Bronchial dimensions measured in CT images generally do not take inspiration level into consideration. However, some studies showed that the bronchial membrane is distensible with airway inflation. Therefore, re-examination of the elasticity of bronchi is needed.
Purpose: To assess the influence of respiration on bronchial lumen area (defined as distensibility) in different segmental bronchi and to explore the correlations between distensibility and both lung function and emphysema severity.
Material and methods: In 44 subjects with COPD related to alpha-1-antitrypsin deficiency (AATD), bronchial lumen area was measured in CT images, acquired at different inspiration levels. Measurements were done at matched locations in one apical and two basal segmental airways (RB1, RB10 and LB10). Airway distensibility was calculated as lumen area difference divided by lung volume difference.
Results: Bronchial lumen area in the lower lobes (RB10 and LB10) correlated positively with FEV_1%predicted ($p = 0.027$ for RB10; and $p = 0.037$ for LB10, respectively). Lumen area is influenced by respiration ($p = 0.006$, $p = 0.045$, and, $p = 0.005$ for RB1, RB10 and LB10, respectively). Airway distensibility was different between upper and lower bronchi ($p < 0.001$), but it was not correlated with lung function.
Conclusion: Lumen area of third generation bronchi is dependent on inspiration level and this distensibility is different between bronchi in the upper and lower lobes. Therefore, changes in lumen area over time should be studied whilst accounting for the lung volume changes, in order to estimate the progression of bronchial disease while excluding the effects of hyperinflation.

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Chronic obstructive pulmonary disease (COPD) is defined by airflow limitation measured by the forced expiratory volume in 1 s (FEV_1),[1] but the limitation may be contributed by different pathologies such as emphysema and small airway disease, both of which can be measured separately with computed tomography (CT).[2] For the assessment of emphysema progression, lung densitometry is a well established sensitive and reproducible method.[3,4] The use of bronchial CT measurements for quantifying small airway diseases is steadily growing in studies dealing with COPD.[5–7]

Airway lumen dimensions obtained from CT lung images appear to be related to FEV_1 more directly than wall thickness. Although lumen area is measured in most studies, the results are not shown or discussed. Instead, wall thickness parameters are used to calculate correlation to lung function.[8,9] Under the assumption that the epithelial perimeter of airways does not change under different lung conditions,[10,11] parameters such as wall thickness and wall area are being used as a measure for airway size. However, studies on distensibility in strips of airway mucosa from guinea pigs[12] and with basement membrane perimeter measurements in human bronchial segments[13] showed that the mucosal bronchial membrane is distensible with airway inflation. Subsequently, Gunst[14] suggested that the utility of wall perimeter as a rigid marker for airway size should be re-examined.

Humans have different lung volumes depending on their height, weight and gender. This influences the size of the bronchi per subject. In addition, subjects show different amounts in volume change between TLC and FRC (dependent on effort and/or disease severity). As a consequence, bronchial CT morphometry may be influenced by lung volume and thus requires a normalization procedure, similar to those in lung densitometry studies,[4,15] in order to estimate progression in bronchial disease while excluding effects of hyperinflation. To study this influence of lung volume we performed bronchial measurements at matched locations in patients who were scanned by CT at different inspiration levels. Subsequently, we examined the distensibility in three segmental bronchi, defined as the response of bronchial lumen to changes in inspiration level, and explored the correlations between distensibility and both lung function and emphysema severity.

Material and methods

Patients

Subjects known with the diagnosis of COPD related to alpha-1-antitrypsin deficiency (AATD) were invited by letter to participate in the Repair study.[16] Forty-four Dutch subjects from this study underwent lung function testing and repeated CT scanning at baseline (untreated). The study was approved by the Ethics Committee of the Leiden University Medical Center and written informed consent was signed by all patients.

Lung function testing

Lung function tests were performed according to the ERS guidelines.[17,18] All tests were performed after nebulization of 5 mg of salbutamol and 500 mg of ipratropium bromide. The following tests were performed: spirometry with measurements of vital capacity (VC), forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC; and single-breath total lung diffusion capacity (carbon monoxide transfer factor – TLco and carbon monoxide diffusing coefficient – Kco).

CT scanning

Within 2 h after airway dilation, patients underwent two subsequent CT scans during the same visit, with a Toshiba Aquilion 16 detector row CT scanner (Toshiba Medical Systems Ltd., Tokyo, Japan), using the following parameters: 135 kVp; 40 mA; rotation time 0.4 s.; collimation: 16×1.0 mm; pitch factor: 1.4375, FOV 329–399 mm, and reconstruction filter FC03. Images were reconstructed with a slice thickness of 5 mm and a slice increment of 2.5 mm. No contrast media were used. Scans were made in supine position during breath hold, and were obtained in caudocranial direction to avoid artefacts due to breathing. The first scan was acquired at total lung capacity (TLC); the second scan was acquired at approximately functional residual capacity (~FRC) level.

Densitometry

Total lung volume and lung density was calculated with the software package Pulmo-CMS (version 1.3, Medis specials, Leiden, The Netherlands). The 15th percentile point (Perc15) and caudocranial locality were chosen as measures of emphysema severity and distribution, respectively.[15]

Bronchial measurements

Three 3rd generation bronchi were selected: the apical segmental bronchus of the right upper lobe (RB1), the posterior basal segmental bronchus of the right lower lobe (RB10), and the posterior basal segmental bronchus of the left lower lobe (LB10).

Within these bronchi, a measurement location was selected using the criteria that the bronchial wall was clearly visible, and that the inner and outer wall contour were approximately concentric. At the selected bronchus locations parallel measurements were performed in paired view in the TLC and corresponding ~FRC image (Fig. 1) using software developed at our institute (BBGui).

To identify the inner wall contour in the CT image, the user manually placed an initial contour within the bronchial lumen. Subsequently, the 2D image was super-sampled using a zoom-factor that was based on the approximate inner contour dimensions. The approximate inner contour was then refined automatically by using dynamic programming to find a closed contour, which follows the local maxima of the intensity gradient (corresponding to the transition from lumen to wall). A similar approach was used to identify the outer wall contour; this contour follows the outer bronchial wall and corresponds to the transition from bronchial wall to parenchyma. For each location on the inner wall contour, the corresponding location on the outer contour was found by a line search in the direction