Heterogeneity of Airways Obstruction in Asthmatic Patients Using High-Resolution Computed Tomography*

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The exact site of airways narrowing in asthma and chronic obstructive pulmonary disease is unknown. High-resolution computed tomography (HRCT) is a non-invasive imaging technique that can be used to measure the dimensions of an individual airway. This technique is very sensitive, and it has been demonstrated that bronchi as small as 2 mm in diameter can be accurately measured. High-resolution computed tomography has been used to measure the internal diameter of bronchi in dogs and humans.  

In this study, an original technique using HRCT was used to measure the internal size of the bronchi in normal human subjects and asthmatic patients in order to investigate variations in airway caliber during exercise challenge and β₂-agonist inhalation.

Subjects

Five healthy male subjects (17 to 32 years) and seven asthmatic patients (20 to 45 years) were studied. Asthma was defined according to the criteria set by the American Thoracic Society.

CT Scan

Measurement of Internal Size of Airways

Computed tomography scans of the chest were performed using a scanner (Somaton DR H, Siemens, Erlangen, Germany) in high-resolution mode according to the method of Mayo et al. Subjects were asked to take a full, deep inspiration and hold their breath as long as possible. A series of slices was performed during each full inspiration. Comparable slice levels were identified using anatomic landmarks such as airways or vascular branching.  

In order to analyze the size of the bronchi, a reconstruction of the image was obtained using a previously validated method. Bronchi were excluded from analysis if they were oriented in an oblique fashion, if branching occurred at the chosen level, or if artifacts were present. An index of airways roundness was determined using the method of McNamara et al.

Measurement of Internal Size of Bronchi

For the image of any bronchus the window width was set to the minimum value (2 Hounsfield units [HU]) in order to get a black and white representation of the bronchus. A region of interest (ROI) was drawn on the bronchus wall and the luminal area was calculated from the number of pixels in the ROI having attenuation values below the window level. This level, called the discrimination level, was determined as the highest window level which gives a closed circle as the representation of the bronchus for the two images. Therefore, a separate discrimination level was identified for each bronchus analyzed. The window level set for the baseline study was used for serial measurements on the same bronchus.

Study Design

Subjects underwent pulmonary function test (baseline) before the first CT scan was performed. The exercise challenge was performed in the CT scan room, and pulmonary function was measured serially at the end of the challenge, and after 1, 3, 5, 10, 15, 20, 25, and 30 min. Then, a second CT scan was immediately performed, and another pulmonary function test was conducted directly afterwards to confirm that there was no variation in pulmonary function during the CT scan. Subjects were given 200 μg of salbutamol by metered-dose inhaler, and a further pulmonary test was carried out 10 min later, immediately followed by a third CT scan.

Results

Using HRCT, it is possible to measure the internal size of the airways from segmental to sixth generation bronchi. From 7 to 36 bronchi were measured for each subject on three occasions (baseline, exercise challenge, and salbutamol). The luminal area ranged from 22 to 5,028 pixels (mean ± SD: 312 ± 962 pixels), corresponding to a mean area of 3.12 ± 9.62 mm² (ie, approximately 0.4 to 4 mm in luminal diameter).

The variation in airways size between the baseline and exercise challenge was minimal in all control subjects. There was a significant (p<0.004 to p<0.0001, Mann-Whitney U test) reduction in airways size in the four asthmatic patients who presented a decline of over 20% in FEV₁ (PD20FEV₁) (Fig 1). In these asthmatic patients, most if not all airways had a decreased caliber. On the other hand, three asthmatic patients had a decreased FEV₁ after challenge ranging from 5 to 11% and a mean reduction in airways size that was not significant. When individual airways were examined, it appeared that a few airways had an increased size after challenge, some airways did not present a variation in caliber whereas many airways had a decreased caliber.

After salbutamol inhalation, FEV₁ was unchanged in two normal subjects and one asthmatic subject and increased from 3 to 48% in all other subjects by comparison to baseline. On the other hand, there was a significant increase in airways size in all subjects tested. There was a significant correlation between the increase in FEV₁ value and the increase in airway caliber measured between exercise challenge and salbutamol.

Discussion

The technique used is original and is not directly derived from any previous study performed in either animals or in human subjects. Although the methods described are rel-

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shown that the method was observed. FEV₁ dropped from 75 to 68% of predicted after challenge and increased to 105% of predicted after salbutamol. Three of seven bronchi were obstructed at baseline. Ten bronchi of patient 2 have been visualized during the three examinations. FEV₁ dropped from 100 to 78% of predicted after challenge and increased to 102% of predicted after salbutamol. Although all bronchi had a reduced size after challenge, there was a large heterogeneity in the reduction of airway size.

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21711/)  
**Figure 1.** Internal size of airways of right lower lobe in two patients before challenge (baseline), after exercise challenge (challenge), and after salbutamol inhalation (B₂-agonist). A bronchus of 1 pixel at baseline or challenge was considered to be fully obstructed at these time points. Seven bronchi of patient 1 have been visualized during three examinations, and a large heterogeneity was observed. FEV₁ dropped from 75 to 68% of predicted after challenge and increased to 105% of predicted after salbutamol. Three of seven bronchi were obstructed at baseline. Ten bronchi of patient 2 have been visualized during the three examinations. FEV₁ dropped from 100 to 78% of predicted after challenge and increased to 102% of predicted after salbutamol. Although all bronchi had a reduced size after challenge, there was a large heterogeneity in the reduction of airway size.

Atively simple, care must be taken to carry them out precisely as indicated in a previous paper. In this paper it was shown that the measurement of the airways size was highly reproducible. There are some technical points to be discussed with such a method. It has already been shown that the slices were done at exactly the same level. The method of measurement of the airways size was found to avoid operator subjectivity. Finally, although the same window level had to be used for the serial measurements of the same bronchus, variable levels were used for the different bronchi, although some authors have used a single window level for all the bronchial measurements.

Heterogeneity of bronchial obstruction was observed after exercise challenge. Although PD20FEV₁ was only observed when the majority of bronchi had a decreased caliber during challenge, large variations in bronchoconstriction of individual airways were observed. Bronchi of a similar caliber at baseline and in the same area were found to present a variable decrement in their caliber during challenge from almost no change to complete obstruction. A greater heterogeneity was observed in patients who had a decrement in FEV₁ ranging from 5 to 11%. In such patients, some bronchi were even found dilated during challenge. After β₂-agonist inhalation, most bronchi of asthmatic patients presented an increase in caliber, and surprisingly, it was observed that some large bronchi were completely obstructed at baseline showing the inhomogeneity of the airways obstruction in asthma.

High-resolution computed tomography can therefore be used to appreciate changes in the caliber of individual airways and may help to improve the understanding of pulmonary physiology.

**References**


**New Method for Real-Time Measurements of Changes in Lumenal Area of Microsection Explants of Airways by Videomicroscopy**

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