Multidetector Row Computed Tomography to Assess Changes in Airways Linked to Asthma Control

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Key Words

Asthma control • Respiratory mechanics, physiology •
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Abstract

Background: In asthma, multidetector row computed tomography (MDCT) detects abnormalities that are related to disease severity, including increased bronchial wall thickness. However, whether these abnormalities could be related to asthma control has not been investigated yet. **Objective:** Our goal was to determine which changes in airways could be linked to disease control. **Methods:** Twelve patients with poor asthma control were included and received a salmeterol/fluticasone propionate combination daily for 12 weeks. Patients underwent clinical, functional, and MDCT examinations before and after the treatment period. MDCT examinations were performed using a low-dose protocol at a controlled lung volume (65% TLC). Bronchial lumen (LA)

and wall areas (WA) were evaluated at a segmental and sub-segmental level using BronCare software. Lung density was measured at the base of the lung. Baseline and end-of-treatment data were compared using the Wilcoxon signed-rank test. **Results:** After the 12-week treatment period, asthma control was achieved. Airflow obstruction and air trapping decreased as assessed by the changes in FEV₁ ($p < 0.01$) and expiratory reserve volume ($p < 0.01$). Conversely, LA and WA did not vary significantly. However, a median decrease in LA of $>10\%$ was observed in half of the patients with a wide intra- and intersubject response heterogeneity. This was concomitant with a decrease in lung density ($p < 0.02$ in the anteroinferior areas). **Conclusions:** MDCT is insensitive for demonstrating any decrease in bronchial wall thickness. This is mainly due to changes in bronchial caliber which may be linked to modifications of the elastic properties of the bronchopulmonary system under treatment.

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Introduction

One of the goals of asthma treatment is to achieve disease control and reduce chronic airway inflammation [1]. Indeed, inflammation, which is essentially characterized by edema, leads to airway remodeling, which is essentially characterized by subepithelial fibrosis [2]. Finally, these structural modifications are likely to contribute to the decline of lung function and can lead to chronic respiratory insufficiency [3]. Clinically, it has been demonstrated that inflammation is associated with symptoms and poor asthma control [1]. However, detecting persisting inflammation remains challenging [4–7]. Therefore, treatment efficacy remains based on the clinical features of the disease, including lung function abnormalities.

In asthmatic patients, computed tomography (CT) detects abnormalities that are related to airway inflammation and remodeling [8, 9]. Using CT, authors have noted an increase in lung density that may reflect inflammation in the lung and distal airways [10]. Others have observed an increase in the wall area (WA) of bronchi that is related to the duration and/or severity of the disease and correlated to the intensity of structural [11, 12] and functional [9, 13] changes. Recently, Niimi et al. [13] showed that in a population including a majority of moderate and severe asthma patients, the increase in WA responds partially to treatment by an inhaled corticosteroid [14]. However, whether patients in that group had uncontrolled disease was not mentioned and could be a confounding bias. Based on these results, the present study was designed to see whether modifications in airway geometry and lung density could be observed in a group of patients with poor asthma control but a homogeneous severity level.

Image acquisition was performed using multidetector row CT (MDCT), and analysis of bronchial dimensions was performed using a dedicated software (BronCare) [15]. This software makes it possible to create 3-dimensional reconstructions of the airway tree with quantification of the lumen area (LA) and WA orthogonal to the central axis of the bronchi and evaluation of the length (Lg) of the bronchi. Herein, we evaluated changes in airways using MDCT after the achievement of asthma control under inhaled treatment. The objective was to determine which changes in bronchial dimensions could be observed after disease control.

Material and Methods

This was a pilot, open-label, one-arm, 12-week study evaluating changes in airways before and after treatment with a salmeterol/fluticasone propionate combination (SFC; Seretide® or Advair®) of 50/250 µg [16, 17]. This treatment is a combination of an inhaled corticosteroid which aims to target inflammation and a long-acting β_2 -agonist which aims to target smooth muscle relaxation. The achievement of asthma control after 12 weeks with such a treatment has been proved [18]. The protocol, including the irradiation dose, was approved by the local Ethics Committee ('Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale'). All patients gave their written informed consent.

Patients

Twelve patients with poor asthma control – i.e. not fulfilling the criteria of asthma control defined by the GINA [1] – were recruited through a contracted research organization's database for voluntary asthmatics trials. Patients who were 18–40 years old and has a prebronchodilator forced expiratory volume in 1 s (FEV₁) >70% of the predicted value were included. Active smokers or previous smokers with a smoking history of ≥ 10 pack-years and patients suffering from any respiratory pathology that could also interfere with radiologic examination were not included. Treatment with corticosteroids (inhaled or systemic) within the 3 months prior to inclusion and treatment with long-acting inhaled β_2 -agonists, oral β_2 -agonists, or oral theophylline within 4 weeks prior to inclusion were not allowed.

Study Design

Patients entered a 12-week treatment period and received 1 inhalation of SFC twice daily. The treatment administration was performed within 2 weeks after inclusion (delay necessary to perform all baseline evaluations including the CT scan). Short-acting β_2 -agonists or any other bronchodilator therapy used as rescue were allowed. Seven visits were scheduled during the study. Clinical assessments were performed at the inclusion visit and at each following visit. A diary record card was filled out daily by patients who recorded their morning and evening peak expiratory flow rates, occurrence of asthma symptoms, and the number of puffs of rescue short-acting β_2 -agonist, allowing comparisons between baseline and the 12-week treatment period. Asthma control was assessed using the Asthma Control Questionnaire (ACQ) [19] at the inclusion visit, twice during follow-up visits, and at the end-of-the-study visit. MDCT acquisitions and lung function tests were performed before starting the study treatment and at the end of the treatment period.

Pulmonary Function Tests

Lung function measurements were performed at baseline and at the end of the treatment period, at least 6 h from short-acting bronchodilator use and 12 h after the last dose of treatment. FEV₁, maximal expiratory flow between 25 and 75% (MEF_{25–75%}), and forced vital capacity (FVC) were measured by a flow-volume loop. Lung volumes, including residual volume (RV), expiratory reserve volume (ERV), functional residual capacity (FRC), and total lung capacity (TLC), were evaluated by helium diffusion in the sitting position and by body plethysmography. The absence of significant air trapping was assessed by comparing the results obtained by helium diffusion to those obtained by plethysmography

Fig. 1. MDCT evaluation of the variations in bronchial dimensions (WA, LA, and Lg) before (**b–d**) and after (**e–g**) treatment at a subsegmental level using BronCare software. Three-dimensional automated segmentation of the lumen (**a**) and automatic 3-dimensional computation of the central axis of the airway tree (**b**, **e**) with selection of the bronchus under study [red arrows indicate

basilar subsegmental bronchus of the lateral bronchus of the inferior lobe (B9b)]. Cross-section image reformation of the bronchus perpendicular to the central axis (**c**, **f**) with automatic segmentation of the lumen (green area) and wall contour (red line) (**d**, **g**). Results show a decrease in LA on the second MDCT acquisition (after treatment) compared to the first one (before treatment).

[20]. Helium diffusion was also performed in the supine position at baseline in order to measure FRC in the position of MDCT acquisitions and to calculate the 65% TLC value used for these acquisitions. FEV₁ was measured before and after 400 µg salbutamol, permitting the calculation of the reversibility of FEV₁ (percentage of variation before and after salbutamol).

MDCT Protocol

Low-dose acquisitions were performed on a 16-channel detector row CT (GE LightSpeed 16; General Electric, Buc, France) at a controlled lung volume using a pneumotachograph (V2000; Sensormedic, Yorba Linda, Calif., USA). To ensure a comparable wash-out of the bronchodilator, CT examinations were performed at least 6 h from short-acting bronchodilator use and, for the second CT examination, at least 12 h after the last dose of treatment. Patients were instructed to perform a full inhalation followed by a slow exhalation. Acquisitions were made after interruption of the slow expiratory phase at 65% TLC according to a previously described protocol [10]. In order to limit the radiation dose delivered to patients, acquisitions were performed at the base of the lung with a slice thickness of 0.6 mm and low-dose irradiation parameters ranging from 100 kVp and 50–100 mAs according to the patient's morphotype, with a gantry rotation time of 0.5 s and a pitch of 1.3. This corresponded to a range of CT dose indexes of 2.54–6.36 mGy with a dose length product from 26 mGy·cm (an estimated effective radiation dose of 0.4 mSv) to 65 mGy·cm (estimated effective radiation dose of 1 mSv). Reconstruction was centered on the right middle and lower lobes using a lung kernel. The field of view was 18–20 cm with a 512 × 512 pixel matrix. Slice thickness was 0.6 mm with a reconstruction interval of 0.3

mm, corresponding to an extrapolated voxel size of 0.35 × 0.35 × 0.3 mm. The bronchi of the left lower lobe were not assessed because of cardiac motion artifacts.

Analysis of Airway Geometry and Lung Density

The evaluation of bronchial dimensions [LA, WA, WA% (defined as the ratio of WA to the total area of the bronchus), and Lg] was performed using BronCare software [15] for segmental and subsegmental bronchi of the middle and right lower lobe that fulfilled the validation criteria defined by Brillet et al. [15], including an LA > 4 mm². The different steps of the procedure are presented in figure 1. These validation criteria permitted limitation of the inaccuracy of bronchial segmentation with an overestimation of WA that could be observed when the bronchus was surrounded by vascular structures. For the evaluation of variations in bronchial dimensions, interactive selection of a given bronchial pair (before and after treatment) was performed on the 3-dimensional computation of the central axis by the same radiologist (P.Y.B.). This was based on anatomic landmarks, mainly the shape of the bronchus and the relationship between the bronchus and the adjacent vessels. The results of the segmentation as well as the location of the measurements were validated by 2 observers (P.Y.B. and C.I.F.).

Evaluation of the lung densities (Hounsfield Units; HU) was performed according to previously described methodology [10]. Regions of interest consisted of squares measuring 12–15 × 12–15 mm positioned in the periphery of the right lung in vessel-free areas. These regions included mainly alveolar units and distal conducting airways. Six areas were drawn in the anterior, lateral, and posterior part of the lung at 2 levels.

Table 1. Results of the diary record cards at baseline and during the 12-week treatment period (end of treatment)

	Baseline median (min–max)	End treatment median (min–max)	p value
Peak expiratory flow rate, l/min			
Morning	454 (370–636)	504 (394–697)	<0.001*
Evening	458 (385–649)	509 (398–692)	<0.001*
Absence of symptoms, %			
Days	60 (0–88)	99 (25–100)	<0.001*
Nights	100 (80–100)	100 (90–100)	0.156
Absence of short-acting bronchodilator use, %			
Days	70 (0–100)	99 (94–100)	<0.001*
Nights	95 (0–100)	99 (87–100)	0.039*

* $p < 0.05$ calculated using Wilcoxon signed-rank test was considered as significant.

Table 2. Results of the pulmonary function tests measured by a flow-volume loop (FEV₁, MEF_{25–75%}, FVC, FEV₁/VC, and FEV₁ reversibility) and body plethysmography (RV, ERV, FRC, and TLC) at baseline and at the end of the 12-week treatment period

	Baseline, median % predicted (min–max)	End of treatment, median % predicted (min–max)	p value
FEV ₁	92 (66–109)	98 (78–113)	0.007*
MEF _{25–75%}	58 (42–94)	79 (53–106)	0.007*
FVC	101 (81–126)	100 (81–126)	0.131
FEV ₁ /VC	94 (81–99)	101 (84–118)	0.007*
RV	109 (83–145)	100 (72–147)	0.006*
ERV	89 (53–123)	99 (81–122)	0.006*
FRC	105 (67–130)	107 (76–140)	0.252
TLC	99 (84–116)	93 (81–114)	0.33

* $p < 0.05$ calculated using the Wilcoxon signed-rank test was considered statistically significant.

Statistical Analysis

The statistical analysis was performed using SAS® version 8.02 (SAS Institute, Cary, N.C., USA). No data evaluating the effect of SFC on airways using CT was available in the literature, therefore no hypothesis was formulated for this exploratory pilot study. It was scheduled to include a total of 12 subjects in the study in order to obtain 8 patients with evaluable MDCT sets of data in the whole treatment period. Baseline and end-of-treatment bronchial dimensions, lung densities, and clinical and functional results were compared to the null hypothesis using a Wilcoxon signed-rank test (except when otherwise stated). For the selected bronchial pairs (before and after treatment), comparisons were also per-

formed for subgroups of bronchi: (i) segmental or subsegmental bronchi and (ii) LA on initial examination normalized to body surface (BS; mm²/m²) or <7. This cutoff was determined empirically, permitting the separation of bronchi into 2 groups equal in number. Data were therefore presented as medians and ranges (minimum–maximum values). $p < 0.05$ was considered statistically significant, taking into account that the variation of bronchial dimensions between values at baseline and at the end of treatment should exceed the 95% interscan variability of measurements. This variability was established using the Bland and Altman approach according to the methodology defined by Brillet et al. [21], giving thresholds of 1.6 mm², 2.71 mm², and 2 mm for LA, WA, and Lg, respectively.

Due to the design of the study, the type I error spending rate was not addressed.

Results

Patient Characteristics

The study population included 8 males and 4 females with a median age of 25.5 years (range 19–37). The median time between inclusion and SFC administration was 10 days (range 8–14). The patient population had poor asthma control with a median percentage of days without symptoms of 60% and a median percentage of days without short-acting β_2 -agonist use of 70%. The flow-volume curve analysis demonstrated a decrease in MEF_{25–75%} (58% predicted). Conversely, the FEV₁ value remained in the normal range. Body plethysmography and helium diffusion showed that FRC was in the normal range, although ERV (median of 89.5% predicted) was on the lower side and RV (median 109.5% predicted) on the higher side.

Clinical and Functional Response to Treatment

After the 12-week treatment period, the results of the diary record cards indicated that the asthma was controlled (table 1) with a change in the ACQ from 1.57 at baseline to 0.43 under treatment ($p < 0.001$). This was associated to a significant increase in FEV₁, MEF_{25–75%}, and ERV ($p \leq 0.007$; table 2) and to a significant decrease in RV ($p = 0.018$ compared to baseline). Conversely, no significant change in TLC or FRC was observed. Finally, a median (min, max) reduction of the reversibility of FEV₁ from 5.9% (–0.9, 13.9) to 1.0% (–3.2, 4.5) was noted ($p \leq 0.007$).

Changes in Bronchial Geometry under Treatment

Among the 12 patients included in this study, 10 fulfilled the complete MDCT protocol. The numbers of bronchi which matched the validation criteria and were included for statistical analysis are presented in table 3. No

Fig. 2. Percentage variation of the LA before and after treatment for each bronchus (diamonds). Results are presented for each of the 10 patients that completed the MDCT protocol and the median variation per patient is presented as a horizontal bar.

Fig. 3. Median pulmonary density changes (HU) before and after treatment in regions of interest drawn in the anterior, lateral, and posterior areas at the superior and inferior levels. Error bars represent the upper quartile limit. The difference was significant in the anterior areas of the lower level ($p = 0.016$). Ant = Anterior; Lat = lateral; Post = posterior; Sup = superior; Inf = inferior.

Table 3. Bronchial dimensions of segmental and subsegmental bronchi at baseline and at the end of the 12-week treatment period.

	LA, mm ²			WA, mm ²			WA%, %			Length, mm ²		
	baseline	end of treatment	p value	baseline	end treatment	p value	baseline	end of treatment	p value	baseline	end of treatment	p value
All bronchi	12.7 (9.6–19.8)	13.5 (8.1–17.1)	0.62	13.7 (11.2–15.3)	13.3 (10.6–14.7)	0.37	55 (50–59)	56 (51–60)	1	14.1 (11.3–15.9)	13.6 (10.8–15.4)	0.049*
Segmental	18.9 (11.2–29.5)	19.1 (10.3–25.2)	0.85	17.7 (12.8–20.2)	15.1 (11.7–18.7)	0.47	51 (50–56)	55 (52–60)	0.16	14.5 (10–15.8)	13.8 (10.8–15.6)	0.43
Subsegmental	10.5 (6.4–14.9)	10.1 (7.3–14.5)	0.32	12.7 (9.5–14.8)	12.6 (10.6–14.6)	0.85	56 (53–60)	55 (52–60)	0.19	13.7 (11.1–16.9)	13.3 (10.8–16)	0.06
LA/BS >7	18.5 (13.3–25.1)	19.4 (12.4–22.2)	0.62	17 (13.9–19)	16.1 (12.9–22)	0.85	48 (46–50)	46 (52–60)	0.92	13.9 (11.3–16.5)	13.8 (11–15.6)	0.38
LA/BS ≤7	8.8 (7.8–11)	9.1 (6.3–10.9)	0.77	12.2 (9.6–14.2)	11.6 (10–13.6)	0.16	58 (55–61)	55 (51–60)	0.62	14.8 (10.7–19.4)	13.9 (10–18.4)	0.02*

Data are presented as the median (min–max) values obtained for each patient for all bronchi ($n = 112$ for Lg and LA and $n = 74$ for WA and WA%) and for categories of bronchi.

* $p < 0.05$ was calculated using the Wilcoxon signed-rank test, but the variations under treatment were inferior to the interscan variability of measurements between successive acquisitions [personal data; 20, 34] so that results could not be considered significant.

statistically significant difference in bronchial dimensions (LA, WA, WA%, and Lg) was observed after treatment (table 3) in the whole population or in the different subgroups of bronchi compared to baseline measures.

The change in bronchial caliber under treatment was very heterogeneous for each patient (intrasubject) and between patients (intersubjects) (fig. 2). Indeed, 5 patients (50%) had at least a 10% decrease in LA, whereas 2 pa-

tients (20%) tended to dilate their bronchi. For WA, the median variations were inferior to 5%, except for bronchi with an LA/BS ratio ≤ 7 (-5.4% , $p = 0.16$; fig. 1).

Changes in Lung Density under Treatment

The median change in pulmonary density decreased in all areas (fig. 3) and was significant in the anterior areas of the lower level ($p = 0.016$).

Discussion

MDCT evaluation of bronchial dimensions is gaining interest in bronchial diseases. It provides an accurate evaluation of the bronchial caliber, as confirmed by comparisons with quantitative videobronchoscopy [22]. In recent studies, airway dimensions were obtained using volumetric CT, which allows measurement in a plane orthogonal to the long axis of the airways. Such an approach associates a 3-dimensional computation of the central axis of the tracheobronchial tree (leading to skeletonization of the airway tree) and a 2-dimensional segmentation of bronchial boundaries (leading to the quantification of LA and WA) [11, 15]. The bronchial segmentation is performed using an energy-driven contour estimation method which has proved to be as accurate as the full width at half maximum principle but induces less overestimation of LA for the smallest bronchi [21].

Our study is one of the very few to focus on the effect of asthma control on airway geometry and lung density. We focused on a homogeneous group of patients and applied inclusion criteria ensuring the exclusion of patients with a long history of asthma and severe disease and with nonreversible bronchial wall remodeling. Our results show that MDCT evaluation of bronchial dimensions at 65% TLC permitted the detection of some changes in bronchial caliber after treatment by SFC but not in bronchial wall thickness. This was associated with an improvement in clinical symptoms and pulmonary function tests and implied that the mechanical properties of the bronchopulmonary system had changed.

In our protocol, the MDCT acquisition pairs (before/after treatment) were performed at 65% TLC [10], a known volume predetermined experimentally by helium dilution in the supine position prior to the acquisition. The rationale of this protocol was based on the relation between lung volume and transbronchial pressure. Bronchi distend as the lungs are inflated, secondary to the transmission of pleural pressure to the lung and peribronchial space [23, 24]. At 65% TLC, the transbronchial pressure is minimized compared to full inspiration. Based on this assumption we would have expected to observe identical bronchial calibers before and after treatment. Surprisingly, this was not the case in our study as most bronchi changed caliber under treatment. In light of the clinical and functional results, we hypothesize that the change in LA values may be due to a change in bronchial hysteresis [25]. Based on the decrease in lung density and functional results evaluating distal lung function, our results suggest that the changes in the mechan-

ical properties of the bronchopulmonary system may be linked to a decrease in lung inflammation in the lung and distal airways. This conclusion can also be drawn in light of the histological findings using transbronchial biopsy techniques supporting the role of inflammation in distal regions of the lungs [26, 27] and evaluating the effect of inhaled treatment [6].

In comparison to the results of Niimi et al. [14], we did not observe any significant difference in WA between results obtained before and after treatment. Their study included a majority of moderate and severe asthma patients and did not take into account asthma control. The authors noted an 11% decrease in WA under treatment leading from 28.3 to 21.5 mm² ($p < 0.001$) for the apical bronchus of the right upper lobe. However, values remained higher than in the controls (17.6 mm²). Therefore, the authors hypothesized that the reversible part of bronchial wall thickening may reflect a decrease in bronchial inflammation [14] and that the thickened remaining part is linked to remodeling. Herein, patients were younger and had a less severe disease ensuring the existence of reversible inflammatory lesions. These 2 conditions may explain why the variation in WA under treatment measured using MDCT was mild, i.e. around 5%. Therefore, we conclude that the evaluation of WA lacks sensitivity for the direct detection of structural changes linked to bronchial inflammation and remodeling in our population of patients and, more generally, in patients with a recent history of asthma. This last point is also corroborated by the study of Siddiqui et al. [28] who observed no change in WA on CT performed at full inspiration in patients with mild-to-moderate asthma after 2 weeks of oral prednisolone. We hypothesize that longer treatment and follow-up periods as well as a large cohort of patient should be required for that kind of study in early stages of the disease.

Conversely to WA, the quantification of LA at 65% TLC may be an important endpoint in clinical studies, giving indirect information on airway inflammation and demonstrating the heterogeneity of airway response to treatment [29, 30]. Indeed, LA evaluation of proximal bronchi makes it possible to observe intrasubject – i.e. from one bronchus to another – and intersubject – i.e. between patients – variations between both MDCT acquisitions. Moreover, we could observe more prevailing changes in the smallest airways under study, whether they were subsegmental bronchi or bronchi with an LA/BS ratio ≤ 7 , and noted a high intra- and intersubject variability in LA variations (fig. 2) under SFC. Therefore, it would be interesting to determine in future studies how heterogeneity could be quantified and whether or not it

could be considered as a biomarker of asthma control. Indeed, we may hypothesize that asthma control should be associated to a more homogeneous distribution of bronchial calibers.

The main limitation of our study is the small number of patients, impairing the significance of the results obtained with MDCT and the power of the statistical analysis. For example, we could not conclude with regard to the significance of the changes in bronchial length (table 1; $p \leq 0.05$). Indeed, this result was inferior to our evaluation of the interscan variability of measurements of this parameter (personal data). However, as MDCT have few indications in asthma [31], limiting the irradiation in research settings is relevant [32, 33]. This was performed by limiting the number of patients involved and by decreasing the irradiation dose during acquisition. Using this low-dose protocol, thus minimizing any hypothetical risk of carcinogenesis due to repeated CT, we showed that the quantification of bronchial dimensions was feasible. However, in future clinical trials inclusion of a larger number of patients than in the present study will be required. Secondly, we could not demonstrate the respective roles of salmeterol and fluticasone propionate in the clinical improvement, and the changes in bronchial caliber could not be determined. In the light of our results, we hypothesized that the changes in the mechanical properties of the bronchopulmonary system through changes in the lung parenchyma-airway interdependence and pulmonary elastic recoil seemed the most prevailing factors responsible for the changes in LA under treatment [34, 35]. However, bronchial wall stiffness, bronchial hyperresponsiveness [29], and bronchial smooth muscle tone through the individual sensibility of patients to the inhaled β_2 -agonist [36] may also be involved. Therefore, it could be interesting to compare SFC to inhaled corticosteroids alone in order to distinguish the specific additional effect of salmeterol in patients naive to inhaled corticosteroids. This study should conclude on how the combination works and whether the 2 drugs have synergic effects. Third, the variations in lung density seem to

contrast with the report by Mitsunobu et al. [37] who observed low values of mean lung density in asthmatics. One explanation for this apparent paradox is overinflation associated with an evaluation of lung density at full inspiration in their study. Moreover, their population study is also different as it includes older patients with more severe disease. Therefore, we hypothesize that only the analysis at 65% TLC may demonstrate mechanical-property changes in the bronchopulmonary system as a consequence of the decrease in inflammation under treatment [10]. Finally, our results outline the great dependency of measurements to bronchial caliber using the combined 3-dimensional/2-dimensional approach applied here. We hypothesize that a fully 3-dimensional approach leading to an extraction and quantification of the bronchial wall volume should improve the sensitivity of measurements of bronchial remodeling [38]. Moreover, our results suggest that other parameters aside from WA should be considered for the evaluation of asthma control. These parameters would have to take into account the heterogeneity of bronchial geometry from one bronchus to another or along the bronchial axis [21]. Another interesting approach would be to compute fluid dynamics from the realistic 3-dimensional reconstructions of the lumen. Using this technique, De Backer et al. [39] demonstrated that measuring change in airway volume and airflow resistance was possible and correlated well with clinical improvement under treatment.

In conclusion, asthma control was associated with significant changes in pulmonary function tests and lung density at MDCT. However, even though no significant change was noted for bronchial dimensions, this technique seems to be an informative tool to demonstrate changes in airway caliber and is relevant for evaluating disease heterogeneity.

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