



Application of adjusted subpixel method (ASM) in HRCT measurements of the bronchi in bronchial asthma patients and healthy individuals

Grzegorz Mincewicz^{a,*}, Jacek Rumiński^b, Grzegorz Krzykowski^c

^a Department of Allergology, University Clinical Centre, Medical University of Gdansk, Gdansk, Poland

^b Department of Biomedical Engineering, Gdansk University of Technology, Gdansk, Poland

^c Department of Informatics, University of Gdansk, Gdansk, Poland

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ABSTRACT

Background: Recently, we described a model system which included corrections of high-resolution computed tomography (HRCT) bronchial measurements based on the adjusted subpixel method (ASM).

Objective: To verify the clinical application of ASM by comparing bronchial measurements obtained by means of the traditional eye-driven method, subpixel method alone and ASM in a group comprised of bronchial asthma patients and healthy individuals.

Methods: The study included 30 bronchial asthma patients and the control group comprised of 20 volunteers with no symptoms of asthma. The lowest internal and external diameters of the bronchial cross-sections (ID and ED) and their derivative parameters were determined in HRCT scans using: (1) traditional eye-driven method, (2) subpixel technique, and (3) ASM.

Results: In the case of the eye-driven method, lower ID values along with lower bronchial lumen area and its percentage ratio to total bronchial area were basic parameters that differed between asthma patients and healthy controls. In the case of the subpixel method and ASM, both groups were not significantly different in terms of ID. Significant differences were observed in values of ED and total bronchial area with both parameters being significantly higher in asthma patients. Compared to ASM, the eye-driven method overstated the values of ID and ED by about 30% and 10% respectively, while understating bronchial wall thickness by about 18%.

Conclusions: Results obtained in this study suggest that the traditional eye-driven method of HRCT-based measurement of bronchial tree components probably overstates the degree of bronchial patency in asthma patients.

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1. Introduction

The dynamics of bronchial remodeling is increasingly used during the process of clinically staging asthma [1]. Remodeling is routinely evaluated based on such parameters as internal and external diameters, the area of bronchial cross-section or bronchial lumen and their derivative indexes. Considerations on the dynamics of these parameters, while making diagnostic decisions, require measurement techniques which enable precise and reproducible assessment of the bronchial tree components. Recently, high-resolution computed tomography (HRCT) has gained increasing interest in this context.

Application of bronchial tree measurements based on HRCT scans was confirmed by several studies [2–5]. Optimization of the radiation beam parameters allows for the identification and

measurement of even the smallest bronchi along with recognition of existing pathologies, including wall thickening, bronchiectasis, mucus plugging, emphysema and atelectasis [6–9].

The low reproducibility of HRCT-based bronchial tree measurements is a crucial obstacle for clinical applications, since it impedes the evaluation of bronchial tree remodeling in consecutive measurement. This low reproducibility results mostly from the very subjective, eye-driven technique of bronchial tree measurement, with the precision of the latter strongly affected by the resolution of the CT scanner and the examiner's experience level.

Many attempts towards optimizing HRCT-based measurements have been undertaken, based on model systems and mathematical corrections. Unfortunately, all of these proposed solutions were derived from eye-driven measurements [9–15]. Recently, we described our experiences with a model system which included corrections of HRCT bronchial tree measurements based on the adjusted subpixel method (ASM). The idea behind this method is to make tomographic measurements both more precise and objective by replacing traditional line measurement with measurements

* Corresponding author. Tel.: +48 58 340 43 50; fax: +48 58 345 55 99.

E-mail address: info@medcare.pl (G. Mincewicz).

taken at the level of pixel subunits. We have further improved the precision of this type of subpixel method by implementing mathematical corrections. Our studies have given results that are highly precise in terms of measurements of both external and internal diameters of the bronchial tree model (Mincewicz et al., unpublished results).

The purpose of this study was to verify the clinical application of our proposed technique by comparing bronchial tree measurements obtained by means of the traditional eye-driven method, subpixel method and ASM in a group comprised of bronchial asthma patients and healthy individuals.

2. Patients and methods

Our study included 30 bronchial asthma patients receiving treatment at the Allergy Outpatient Clinic of the University Clinical Center, Medical University of Gdansk (Poland). The mean age of this group, which included 18 females and 12 males, was 42.5 years of age (range 22–64). Following criteria proposed by the Global Initiative for Asthma (GINA), the group members were classified accordingly and included 13 cases of mild asthma, 7 cases of moderate asthma and 10 cases of severe asthma. A minimum bronchial constriction reversibility of 15% was previously documented in every patient. The average duration of disease was 11.3 years (range 1–34), whereas average treatment time amounted to 2 years (range 0–9). Sixteen of the patients were qualified to the study at the time of diagnosis, and therefore they did not receive any anti-asthmatic treatment. The remaining patients were treated in accordance to GINA 2006 protocol. The average time between first symptoms of dyspnea and initial treatment in these patients was 9.3 years (range 1–34).

The control group was comprised of 20 volunteers (11 females and 9 males), aged 18–52 (mean age of 29.4), with no clinical and spirometric symptoms of asthma nor clinical symptoms of atopy. Other exclusion criteria for this group included: (1) administration of bronchodilators, teophylline preparations, cromones, intranasal, inhalatory, oral and systemic glucocorticoids and antihistaminic drugs, (2) FEV1 below 80% of the predicted value and FEV1 variability over 20% upon administration of short-acting bronchodilators, and (3) positive skin prick test to at least one allergen.

Exclusion criteria for both groups included: (1) history of chronic rhinitis, symptoms of which appeared or augmented after exposure to house dust, (2) chronic lung diseases: chronic obstructive pulmonary disease, tuberculosis, interstitial lung diseases, etc., (3) circulatory diseases: coronary heart disease, arterial hypertension, cardiac rhythm disorders, heart defects, etc., (4) other chronic diseases, including systemic diseases or gastric ulcers, (5) nasal diseases – other than allergic rhinitis, e.g. seasonal allergic rhinitis and conjunctivitis, intolerance to non-steroidal anti-inflammatory drugs, nasal polyps, and perforation of the nasal septum, (6) other allergic diseases, e.g. atopic dermatitis, (7) specific immunotherapy, and (8) pregnancy or lactation.

HRCT examinations were carried out using a Hi Speed (General Electric) scanner at the Department of the University Clinical Center, Medical University of Gdansk, with the following exposure parameters: 120 kV, 180 mA, 512 × 512 matrix, spiral option (pitch – 1.5). Tomographic scans were obtained during peak inspiration with layers every 30 mm. Bone algorithm was used to obtain bronchial images. In order to make this study maximally objective, both scan acquisition and interpretation were performed by the same radiological team. Measurements were taken of the right lung and divided into three fields (upper, medium and lower) according to Senéterre et al. [16]. The fields were distinguished using the lower edge of the tracheal bifurcation as a reference point. The upper field begun 1.5 cm superior to the tracheal bifurcation and

extended upwards. The medium field begun 1.5 cm below the tracheal bifurcation and extended downwards to a level 6 cm below the bifurcation. The lower field began 6 cm below the tracheal bifurcation and extended downwards. Eight HR layers, each 1 mm thick, were obtained in every field with a 3 mm distance between adjacent layers. One layer per field was selected for further measurements based on the quality of the transverse cross-sections of visualized bronchi. Three bronchi were measured in every selected layer, located within a central field that was 5 cm in diameter, and located 5–6 cm from the parietal pleura, at the level of the pulmonary hilus.

The lowest internal and external diameters of the bronchial cross-sections were measured in HRCT scans. Other parameters were calculated based on these measurements, including: (1) bronchial wall thickness, (2) total area of bronchial cross-section, (3) area of bronchial lumen, (4) area of bronchial lumen as a percentage of total bronchial area, and (5) area of bronchial wall thickness as a percentage of external bronchial diameter. Files with raw images recorded in DICOM (Digital Imaging and Communication in Medicine) format were used in this study and analyzed with the aid of Osiris software and original software written for the purpose of this study at the Department of Biomedical Engineering of the Gdansk University of Technology. Each measurement was determined in triplicate: (1) as a linear measurement by traditional eye-driven method, (2) using the subpixel technique, based on the division of scan pixels into lower subunits along with interpolation and bronchial border analysis by full width at half maximum of density profile (FWHM), and (3) by means of ASM, correcting measurements using the subpixel method by means of the following formulas resulting from non-linear regression:

(a) for external diameters

$$\text{real diameter} = 0.071625 \times (\text{measured diameter})^2 + 0.615151 \times \text{measured diameter}$$

(b) for internal diameters

$$\text{real diameter} = 0.000189 \times (\text{measured diameter})^2 + 1.711056 \times \text{measured diameter}$$

Measurements obtained by means of the eye-driven method, subpixel method and ASM were subjected to statistical analysis along with their derivatives. Arithmetic means were calculated for parameters determined by each method along with their standard deviations. Mean values of measurements determined in asthma patients and in control group were compared by means of the Mann–Whitney *U* test. The significance of inter-method differences was analyzed using the sign test. Calculations were performed using the Statistica 8 (StatSoft®, Poland) package, with statistical significance defined as $p \leq 0.05$.

3. Results

In the case of the traditional eye-driven method of measurement, significant differences were observed between asthma patients and healthy controls when it came to measurements of the internal bronchial diameter, area of bronchial lumen and area of bronchial lumen as a percentage of total bronchial area. These aforementioned values were significantly higher in controls, while bronchial wall thickness and its percentage ratio to external bronchial diameter were significantly higher in asthma patients (Table 1).

When measurements were determined using the subpixel method, the values of the external bronchial diameter, bronchial wall thickness and total bronchial area were significantly higher

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