Adjusted subpixel method enables optimisation of bronchial measurements in high-resolution CT

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Objectives: The purpose of this paper is to present a new technique of high-resolution computed tomography (HRCT) bronchial measurement, which was worked out in our centre and is based on a mathematically adjusted subpixel method (ASM).

Methods: This study used a bronchial tree model comprising two polyvinyl chloride/rubber pipes with various densities placed in a larger plastic object. External and internal diameters of both pipes corresponded to the sizes of structures that are usually evaluated in HRCT scans (*i.e.* the bronchus with accompanying blood vessel). The model was subjected to repeated HRCT measurements of the external and internal diameters of model pipes using a subpixel technique and ASM.

Results: Significant differences were observed between mean values of external and internal diameters of model pipes determined by means of subpixel method or ASM, with the latter being the ones that resembled real diameters of the model pipes more closely. Mean external diameters of the larger and smaller model pipes determined by ASM differed from the real diameters by 0.23% and 0.57%, respectively. The internal diameter of the larger pipe was on average 25.96% larger, whereas the internal diameter of the smaller pipe was 48.05% smaller than the real diameter.

Conclusion: The technique of non-linear prediction of HRCT bronchial measurements described in this paper raises attractive prospects in its clinical application owing to potential improvements in the objectivity and reproducibility of bronchial wall measurements.

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High-resolution CT (HRCT) has recently gained increasing attention as an evaluation method of bronchial remodelling in asthma patients [1]. The efficiency of HRCT has been proven by numerous studies [2–5]. Optimisation of the radiation beam parameters enables identification of structures down to 100–200 µm in size and allows for evaluation of even the smallest bronchi (1.5–2 mm in diameter) [6]. Because of the aforementioned characteristics, HRCT is useful in the diagnosis and evaluation of many pathologies, including bronchial wall thickening, bronchiectasis, mucus plugging and emphysema or atelectasis [7–11].

Owing to its many advantages, HRCT is likely to become the standard tool for disease evaluation in patients with difficult/refractory asthma [12–15]. However, a number of constraints are associated with the application of this otherwise valuable method. The first constraint is the lack of clearly defined clinical criteria for asthma evaluation in HRCT scans [16]. Among the proposed criteria, disease-related changes in bronchial wall thickness and bronchial lumen diameter seem to be the most reasonable. However, repeating and comparing measurements obtained at different time points is often frustrated by the low

reproducibility of HRCT-based measurements. This problem results mostly from the wide use of eye-driven, non-standardised techniques of measurements.

A number of attempts towards optimising HRCT measurements have been undertaken, mostly based on model systems and mathematical corrections. However, all of the proposed solutions are based on eye-driven measurements [10, 17–22]. The purpose of this paper is to present a new technique of HRCT bronchial measurement, which was worked out in our centre and is based on a mathematically adjusted subpixel method (ASM).

Methods and materials

This study used a bronchial tree model which was designed and prepared at the Department of Biomedical Engineering of the Gdansk University of Technology (Poland). The model comprised two polyvinyl chloride/rubber pipes with various densities (1620 and 460 HU for larger and smaller pipe, respectively) placed in a larger plastic object. External and internal diameters of both pipes corresponded to the sizes of structures that are usually evaluated in HRCT scans (*i.e.* the bronchus with accompanying blood vessel; Figure 1). Repeated measurements of the model tubes were taken with the aid of an electronically scaled calliper (0.01 mm precision) in order to provide the standard against which further CT measurement was made.

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Figure 1. Transverse cross-sections and spatial relationships of the bronchial tree model used in this study: (a) schematic presentation and (b) high-resolution CT image.

The model was subjected to repeated measurements using the Hi Speed CT scanner (GE Healthcare, Waukesha, WI; 1 mm collimation, 120 mAs, 120 kVp) at the Department of Radiology of the University Clinical Center of the Medical University of Gdansk or on the Somatom Sensation 40 scanner (Siemens Healthcare, Munich, Germany; 1.5 mm collimation, 80–128 mAs, 60–120 kVp) at the Department of Roentgenodiagnostics at the Oncology Center, Maria Skłodowska-Curie Memorial Institute in Gliwice. 80 measurements were performed using each of these aforementioned systems. A reference lung window (window length = −500, window width = 1400) was used, and the model was placed at an angle of 90° in relation to the scanning surface. External and internal diameters of larger and smaller model pipes were measured repeatedly.

Files with raw images recorded in DICOM (Digital Imaging and Communication in Medicine) format were used in this study and analysed with the aid of the Osiris software and original software written for the purpose of this study at the Department of Biomedical Engineering of the Gdansk Technical University.

All measurements were determined by 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).

ASM was used to increase the precision of FWHM-based measurements, using the following correction:

$$\text{real diameter} = (\alpha \times \text{measured diameter} + \beta) \times \text{measured diameter} \quad (1)$$

The values of α and β parameters were estimated based on consecutive measurements of model pipes, using the following regression formula:

$$\text{real diameter} = \left[(\alpha \times \text{measured diameter} + \varepsilon)^2 + \beta \right] \times \text{measured diameter} + \varepsilon \quad (2)$$

where ε was a variable with normal distribution, expected value equal to zero and unknown variance σ^2 .

The proposed model was based on the following non-linear regression formula:

$$\text{measured diameter} = \frac{1}{\left\{ 2\alpha \times \left[(\beta^2 + 4\alpha \times \text{real diameter})^{1/2} - \beta \right] + \varepsilon \right\}} \quad (3)$$

The following estimators were calculated based on the above formula: (i) for external diameters $\alpha=0.071625$ and $\beta=0.615151$; (ii) for internal diameters $\alpha=0.000189$ and $\beta=1.711056$.

The resulting correction coefficients enabled modification of empirical measurements using the following

Table 1. Statistical characteristics of external and internal diameters of model pipes (in mm), determined by means of subpixel method or by adjusted subpixel method (ASM)

Measurement	Model	Subpixel method		ASM		<i>p</i> -value ^a
		Mean ± SD (mm)	95% CI (mm)	Mean ± SD (mm)	95% CI (mm)	
Larger pipe						
External diameter	4.8	4.95 ± 0.28	4.89 to 5.02	4.81 ± 0.37	4.73 to 4.89	<0.001
Internal diameter	1.9	1.40 ± 0.31	1.33 to 1.47	2.39 ± 0.53	2.28 to 2.51	<0.001
Smaller pipe						
External diameter	1.7	2.21 ± 0.20	2.16 to 2.25	1.71 ± 0.19	1.67 to 1.75	<0.001
Internal diameter	1.4	0.43 ± 0.21	0.38 to 0.47	0.73 ± 0.35	0.65 to 0.81	<0.001

CI, confidence interval; SD, standard deviation.

^aSign test ($p \leq 0.05$).

formulas. For external diameters:

$$\text{real diameter} = 0.071625 \times (\text{measured diameter})^2 + 0.615151 \times \text{measured diameter} \quad (4)$$

For internal diameters:

$$\text{real diameter} = 0.000189 \times (\text{measured diameter})^2 + 1.711056 \times \text{measured diameter} \quad (5)$$

Measurements obtained with the subpixel method and ASM were subjected to statistical analysis. Arithmetic means along with 95% confidence intervals and standard deviations were calculated for each measured parameter. The significance of intermethod differences was analysed using the sign test. Calculations were performed using the Statistica 8 package (StatSoft, Tulsa, OK), with statistical significance defined as $p \leq 0.05$.

Results

Significant differences were observed between mean values of external or internal diameters of model pipes determined by means of subpixel method or ASM (Table 1).

In the case of the larger pipe, mean values of the external diameter determined by the subpixel method and by ASM differed from the real diameter by 3.21% and 0.23%, respectively. The external diameters of the smaller pipe determined by the subpixel technique and by ASM differed by 29.83% and 0.57%, respectively, compared

with the real diameter. The internal diameter of the larger model pipe was on average 26.40% lower than the real diameter, when determined by the subpixel method. The same parameter determined by ASM was on average 25.96% larger than the real diameter. Mean internal diameters of the smaller model pipe were lower than the real diameter by 69.64% and 48.05% for the subpixel method and ASM, respectively. Deviations of measurements from real values when using the subpixel technique and ASM-based measurements of the model pipes are expressed as direct values and presented in Table 2.

No significant differences were observed between measurements taken with the aid of two different CT systems.

Discussion

According to current literature, radiographic measurements of bronchi that are smaller than segmental ones are problematic [23]. Size determination (*e.g.* of bronchial diameters) based solely on eye-driven evaluation of structures visible on the computer screen is associated with markedly lower precision [22, 24, 25]. Precision of CT-based measurements depends upon at least four variables: (i) window selection and calibration of computer screen, (ii) finite spatial resolution of an image, (iii) diffusion of borders of examined structures due to data acquisition and reconstruction and (iv) orientation of examined bronchus/vessel in relation to the cross-section (scan) surface. In the case of eye-driven measurements, human factors also have a significant impact, reflecting the experience of the examiner.

Table 2. Deviations (in mm) from real values of the external and internal diameters of model pipes determined by subpixel technique and adjusted subpixel method (ASM)

	Subpixel method		ASM		
Measurement	Mean $\pm$ SD (mm)	95% CI (mm)	Mean $\pm$ SD (mm)	95% CI (mm)	<i>p</i> -value ^a
Larger pipe					
External diameter	0.15 $\pm$ 0.28	0.09 to 0.22	0.01 $\pm$ 0.37	−0.07 to 0.09	<0.001
Internal diameter	−0.50 $\pm$ 0.31	−0.57 to −0.43	0.49 $\pm$ 0.53	0.38 to 0.61	<0.001
Smaller pipe					
External diameter	0.51 $\pm$ 0.20	0.46 to 0.55	0.01 $\pm$ 0.19	−0.03 to 0.05	<0.001
Internal diameter	−0.97 $\pm$ 0.21	−1.00 to −0.93	−0.67 $\pm$ 0.35	−0.80 to −0.59	<0.001

CI, confidence interval; SD, standard deviation.

^aSign test ($p \leq 0.05$).

This model system-based study proves that the precision of measurements of bronchi and accompanying vessels may be increased by applying the subpixel technique. This is 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 [26]. Application of the subpixel technique instead of linear measurement makes the determination more objective and increases its reproducibility compared with the traditionally used eye-driven method. Moreover, our repeated measurements of the model structures were the basis for determination of a coefficient that corrected the measurement bias. In the case of the external pipe diameters, this produced an unprecedented accuracy of 100%.

Attempts towards the improvement of the precision of HRCT bronchial measurements, including the application of various models of the bronchial tree, are already described in the literature. Previously tested model systems included cadaver lungs (bovine and canine), water-embedded Plexiglas blocks with calibrated holes of various diameters and calibrated glass or plastic pipes embedded in sponge. The significant limitation of all of the aforementioned studies is the fact that their measurements are not based on a fully objective eye-driven technique [10, 17–22, 25, 27, 28].

Application of a bronchial model comparable in size with human bronchi is an unquestionable advantage of this study. Both the external and internal diameters of the model pipes were selected to resemble bronchial sizes obtained in HRCT images, also helping to evaluate the resolution abilities of CT scanners.

The angle between the scan surface and the long axis of the examined structure is an important factor responsible for the precision of tomographic diameter measurements of bronchial tree components. If this angle differs from 90°, bronchial cross-sections on CT images have ellipsoid shapes with at least two different diameters. This may result in a further decrease in the reproducibility of bronchial measurements performed by means of HRCT. Therefore, in previous model studies, the ratio of the largest diameter of measured structures to the perpendicular diameter was lower than 1.5:1 [22]. In this study, we used a scan surface that was perpendicular to the model. Consequently, the obtained cross-sections of model pipes were of circular shape. Nevertheless, during the preparation of our model we also evaluated the variability of subpixel measurements resulting from changes in the angle between the scan surface and the long axis of the model. These experiments revealed that the highest precision of parameter analysis is obtained when the smallest diameters of ellipsoids visible on tomographic scans are measured. Measurements taken in this manner were the ones that resembled real diameters of the model pipes (e.g. the external diameters of the larger pipe determined by ASM at 45° were nearly 100% larger than the real diameter and the diameter determined by ASM at 90°).

In the case of the external diameters of the model pipes analysed in this study, and particularly for the larger pipe, a nearly absolute consonance was obtained between the determined parameters measured by ASM and the real measurements. However, the ASM-determined internal diameters of the model pipes—although

closer to the original ones than those determined by the subpixel technique alone—were still significantly smaller. This deviation probably resulted from significant differences between the density of the internal border of the bronchial wall and the air density inside the bronchial lumen. Consequently, the densities of border voxels are averaged and the measurement precision is decreased. The possibility of eliminating this bias requires further studies—perhaps with the application of pixel subunits smaller than voxels.

Conclusion

In spite of the aforementioned constraint, the technique of non-linear prediction of HRCT bronchial measurements described in this paper raises attractive prospects in its clinical application. Improvements in the objectivity and reproducibility of bronchial wall measurements may become the basis for unified clinical criteria in asthma outcome evaluations carried out by HRCT scans.

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