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Measuring airway dimensions during bronchoscopy using anatomical optical coherence tomography

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ABSTRACT

Airway dimensions are difficult to quantify bronchoscopically because of optical distortion and a limited ability to gauge depth. Anatomical optical coherence tomography (*a*OCT), a novel imaging technique, may overcome these limitations. This study evaluated the accuracy of *a*OCT against existing techniques in phantom, excised pig and *in vivo* human airways.

Three comparative studies were performed: (i) micrometer-derived area measurements in ten plastic tubes were compared to *a*OCT-derived area; (ii) *a*OCT-derived airway compliance curves from excised pig airways were compared to curves derived using an endoscopic technique; and (iii) airway dimensions from the trachea to subsegmental bronchi were measured using *a*OCT in four anaesthetised patients during bronchoscopy and compared to CT measurements.

Measurements in plastic tubes revealed *a*OCT to be accurate and reliable. In pig airways, *a*OCT-derived compliance measurements compared closely with endoscopic data. In human airways, dimensions measured with *a*OCT and CT correlated closely. Bland-Altman plots showed *a*OCT diameter and area measurements were higher than CT by 7.6% and 15.1%, respectively.

Airway measurements using *a*OCT are accurate, reliable and compare favourably with existing imaging techniques. Using *a*OCT with conventional bronchoscopy allows real-time measurement of airway dimensions and could be useful clinically in settings where knowledge of airway calibre is required.

Keywords

Airway dimensions
Computed tomography
Interventional bronchoscopy
Optical coherence tomography
Quantitative bronchoscopy

INTRODUCTION

Bronchoscopy is a widely performed procedure with many indications. Several of these, such as airway stenosis, tracheomalacia, and the deployment of valves for endoscopic lung volume reduction, require knowledge of airway dimensions in order to optimise the interventions and/or to longitudinally assess disease progression. To date, bronchoscopists have relied on pre-procedure imaging, usually with computed tomography (CT), to quantify airway dimensions such as calibre or length of stenosis. CT has a proven capacity to provide such measurements, but it cannot be utilised during a procedure. This presents a major limitation when, for example, during a stenting procedure the bronchoscopist wishes to confirm the stenosis dimensions to ensure selection of an appropriate stent, as complications can arise from poorly sized stents [1, 2].

Whilst it is possible to derive quantitative information directly from the bronchoscopic images, two major impediments make doing so difficult. Firstly, bronchoscopes display 3D anatomy as a 2D image thereby limiting the ability of an observer to gauge depth. Secondly, the wide-angle lens at the tip of the bronchoscope, whilst employed to facilitate the widest possible view, results in image distortion particularly at the peripheries. Several techniques have been developed to permit quantification from bronchoscopic images [3-9]. However, these techniques entail complex correction algorithms, and for accurate calibration often require targets of known size (e.g., biopsy forceps or measuring devices) to be placed in the field of view.

This paper describes a novel imaging technique that addresses many of these problems. Optical coherence tomography (OCT) is a light-based imaging technique based on the principle of low-coherence interferometry. In its conventional form, OCT allows subsurface airway analysis to a depth of 2-3mm, providing an "optical biopsy" approaching histological resolution. Respiratory applications, focus on the detection of malignant and dysplastic epithelial changes [10, 11]. Anatomical OCT (*a*OCT) is a modification of conventional OCT designed to range over larger distances to permit real-

time macroscopic imaging of hollow organs [12]. Applications in the human upper airway demonstrate the in-vivo utility of this technique but it has yet to be validated in the tracheobronchial tree [13-16].

Our group has previously detailed the technical considerations of applying *a*OCT to the central airways [17]. The purpose of this paper is to validate *a*OCT for use in the human tracheobronchial tree.

METHODS

The accuracy of *a*OCT was systematically validated in plastic tubes, pig bronchi and human airways by comparing measurements made with *a*OCT to other established imaging techniques. The Human Research Ethics Committee at our hospital approved this study and patients provided informed consent. The animal study was approved by our institutional Animal Ethics Committee. Further details of the following methods can be found in an accompanying online repository.

Anatomical optical coherence tomography

The *a*OCT unit consists of a 1.3 mm wide fibre-optic probe housed within a plastic catheter (outer diameter 2.2 mm) as previously described [12-14, 17, 18]. The catheter is passed through the working channel of a standard bronchoscope and passed into an airway of interest. The probe rotates at 2.5Hz directing a broadband light beam (central wavelength 1310nm, bandwidth 32nm) perpendicular to the airway, thus building up a rotational scan of the internal airway lumen that is displayed on a monitor. The probe is capable of scanning over a radius of 36 mm with an optimal lateral resolution of 156 μm at a distance of 2.35 mm, although this varies with distance. A custom-built computer program enables the user to manually trace the internal lumen and diameter immediately post-acquisition. While rotating, the probe may also be mechanically retracted along an airway segment at 0.4mm/sec, to generate a volumetric dataset. We refer to this as a "pullback" scan.

Plastic tubes

A plastic airway phantom (online E1) consisting of 10 round tubes (diameters 2.6-50.0 mm) was constructed and the tubes were measured using internal micrometers (Bowers Metrology, West Yorkshire, UK) accurate to 0.01 mm. Three separate sites along each tube were imaged by one investigator using *a*OCT. The 30 images were then randomised prior to measurement of diameter and internal area (Ai). To evaluate intra-observer repeatability, measurements were repeated at three weeks. For inter-observer repeatability, a second investigator repeated the measurements. To assess the effect on measurement accuracy of the bends in the fibre-optic probe during bronchoscopy, in-vivo conditions were simulated by repeating the measurements through a bronchoscope inserted into a resuscitation mannequin (online E2).

Excised pig airways

A trachea and two bronchial segments were dissected from the lungs of an eight-week-old pig. Side branches were ligated with surgical silk and the segments (length approximately 60mm) were placed horizontally in a perspex chamber of Krebs solution at 37°C as described elsewhere [19]. The ends were cannulated one being connected to a reservoir containing Krebs solution, the height of which could be adjusted to vary the transmural pressure, thereby manipulating airway size (Figure 1).

The airway lumina were visualised using a videoendoscopy technique, whereby a rigid fibre-optic endoscope (SES1711D Olympus, Tokyo, Japan) was inserted into the airway through an outlet in the organ chamber (Figure 1) [19]. At the site selected for analysis, the mucosal surface was circumferentially stained with dye. Transmural pressures were increased in increments of 5cmH_2O from –15 cmH_2O to +30 cmH_2O then decreased back to –15 cmH_2O. Photographs of the dye-mucosa interface, depicting the inner airway perimeter, were captured and transferred to a PC workstation for

analysis of internal lumen area (Ai) using ImageJ software, version 1.38t [20]. The endoscope was then removed and the *a*OCT catheter was passed into the airway lumen and advanced to the dye ring where the measurements were repeated. The order of imaging (*a*OCT or endoscope) was randomised. We compared the two techniques by constructing airway compliance curves from the plot of transmural pressure against Ai. Compliance was described firstly from the slope of the curve between 0 and 10 cmH_2O (the region of maximal change) and secondly by fitting the positive pressure data with an exponential expression (also used to describe the non-linear elastic behaviour of the lungs), of the form $V = A - B \exp(-KP)$, where V is airway lumen area, P is transmural pressure and A, B and K are constants. The Colebatch shape factor K defines the non-linearity of the area-pressure curve, and is an index of distensibility independent of airway size [21].

To investigate the potential use of *a*OCT in the setting of tracheobronchial stenosis, immediately following measurement of airway compliance, a stenosis was simulated in the excised pig trachea by tying suture material around its centre. The *a*OCT probe was advanced through the tracheal lumen beyond the "stenosis" then mechanically retracted across the stenosis while recording continuously. This pullback scan was analysed using a 3D software viewer (VolView, Kitware, NY, USA), to measure stenosis dimensions .

In-vivo human airways

Subjects were recruited from patients scheduled for bronchoscopy who also required a chest CT as part of their medical care. The 64-slice scanner (Philips Brilliance CT 95089, Philips Medical Systems, Best, The Netherlands) scanned from the glottis to lung bases (220mA, 120Kvp, voxel size 0.625 × 0.625 × 0.625 mm and using a lung-enhanced reconstruction algorithm). On the same day a bronchoscopy was performed under propofol anaesthesia titrated to a depth sufficient to permit spontaneous breathing.

To ensure that scans were obtained at a similar lung volume during both the CT and bronchoscopy, impedance plethysmography bands (Respitrace 10.9230, Ambulatory Monitoring, Ardsley, USA) were positioned over the ribcage and abdomen and calibrated using an isovolume manoeuvre. The summed abdominal and ribcage signal is a measure of total chest wall displacement (lung volume change) and was used to monitor lung volume changes during CT and bronchoscopy [22]. During CT scanning, respiration was suspended at functional residual capacity (FRC) using the summed Respitrace signal to guide a voluntary breath-hold. FRC decreases during general anaesthesia [23]. To match FRC during bronchoscopy to the preceding CT, we noted baseline FRC using a period of quiet tidal breathing prior to anaesthetic delivery and, once stable anaesthesia had been achieved, applied positive-end expiratory pressure (PEEP) and pressure support to raise FRC back to baseline (online E3). In each subject, between 7 and 11 normal airway sites (from the trachea to the subsegmental airways) were imaged using *a*OCT over 6 respiratory cycles each, taking approximately 20 minutes.

After the bronchoscopy, Ai and short-axis diameter were measured from the *a*OCT and CT images and compared. CT images were analysed using Pulmonary Workstation 2.0 software (VIDA Diagnostics, Iowa City, USA), which reformats CT data into 3D images and calculates airway area and diameter perpendicular to the airways. At each site, measurements from three adjacent CT slices were averaged. For the *a*OCT images, measurements were performed at end-expiration (FRC) on three successive breaths and averaged.

Statistical analyses

The coefficient of variation of repeated Ai measurements from the plastic phantom was expressed as a percentage. Intra- and inter-observer repeatability coefficients were determined using the Bland and Altman method and a paired t-test compared compliance measurements derived using *a*OCT with the endoscopic technique [24]. Human airway dimensions measured by CT and *a*OCT were compared

using Bland-Altman plots [24]. Statistical analyses were performed using SPSS for Windows 15.0.0 (SPSS Inc, IL, USA).

RESULTS

Comparative Studies

(i) Plastic tubes

*a*OCT-derived Ai measurements in 10 plastic tubes (range 5.3-1963.5 mm^2) showed very close agreement to the micrometer Ai measurements (Figure 2) with the mean difference across the tubes being -0.1 ± 5.6 mm^2 (-0.3 ± 3.5%) with even scatter about the zero difference line. The coefficient of variation of repeated measurements was 0.8%. Measurements repeated through the resuscitation mannequin showed a small bias towards overestimating the Ai, and a paired t-test showed the difference of the means to be 2.1 mm^2 (95% confidence interval 0.7 – 3.5 mm^2, $p<0.01$). Bland-Altman plots of intra- and inter-observer variability demonstrated good agreement (Figure 3). The calculated intra- and inter-observer repeatability coefficients were 5.7 and 7.1 mm^2, respectively, which represent less than 2% of the mean area of all 10 tubes.

(ii) Excised pig airways

Three airways were dissected and four sites (A-D) were marked with dye (one bronchus was marked at two sites). Airway Ai ranged from 9.0-170.0 mm^2. At each site, ascending and descending limbs of the pressure/Ai curve were plotted using both endoscope and *a*OCT-derived Ai (Figure 4). Compliance curves for each technique were similar and the mean shape factor *K*, was not significantly different; mean K=0.11 (endoscopy) vs K=0.12 cmH_2O^{-1} (*a*OCT), 95% confidence interval for the difference of means -0.03 – 0.01, p=0.24. Compliance measured using the slope of the curve between

0 and 10 cmH_2O, was not different between techniques being 2.2 and 2.1 $mm^2cmH_2O^{-1}$ (95% confidence interval -0.3 – 0.2, p=0.64).

2D and 3D reconstruction of the tracheal stenosis is shown in Figure 5. At the narrowest point, the transverse dimensions measured 7.9 × 7.6 mm with a stenosis length of 23 mm.

(iii) In-vivo human airways

CT and *a*OCT measurements were obtained in 36 airway sites from six airway generations in four patients (Figure 6 and online E4). Ai ranged from 6.2–282.0 mm^2 and short-axis diameters from 2.3-16.9 mm. There was close correlation between CT and *a*OCT-based Ai and diameter measurements ($r = 0.99$, $p<0.001$, online E5). Bland-Altman plots showed *a*OCT measurements to be slightly greater than CT measurements by a mean of 6.2 ± 18.1 mm^2 for Ai (Figure 7A and 7B) and 0.4 ± 1.3mm for diameter (Figure 7C and 7D).

DISCUSSION

Despite a revolution in the field of thoracic imaging, the contemporary bronchoscopist still lacks a reliable tool to quantify endobronchial anatomy *during* a procedure. This paper describes a novel imaging technique, *a*OCT, in plastic tubes, excised pig and *in vivo* human airways. As *a*OCT operates independently of conventional bronchoscopic imaging, it overcomes the major limitation of bronchoscopic airway quantification – distorted images from which airway dimensions are difficult to derive requiring post-procedure analysis. The results of our validation studies indicate that *a*OCT is a suitable complementary bronchoscopic technique for real-time measurements of airway dimensions.

This study demonstrates the utility and accuracy of *a*OCT in three experimental settings. In plastic tubes, *a*OCT provided accurate and repeatable Ai measurements over a wide range of diameters.

Relative to micrometer measurements, Ai measured when the *a*OCT catheter was passed through a mannequin was greater, on average, by 2.1 mm^2. This may be due to bends imposed on the catheter/probe during in-vivo scanning causing torsion and uneven probe rotation. Regardless, the magnitude of this difference (representing <1% of the mean area of the 30 measurements), is clinically insignificant. Compliance measurements in excised pig airways using *a*OCT and an endoscopic technique were also similar, highlighting the potential for *a*OCT to determine physiological properties of airways, such as regional compliance during bronchoscopy. Lastly, comparison of *a*OCT to CT measurements in humans also showed close agreement. A strength of our approach was that great care was taken to control subject lung volume which can affect airway size [25]. Indeed, to our knowledge, amongst quantitative videobronchoscopy studies, this is the first such study to do so. However, whilst every attempt was made to standardise conditions during CT and *a*OCT scanning, the measurements were performed several hours apart making comparison of the exact site within the airway difficult. Simultaneous imaging would have been preferable but difficult to achieve as simultaneous bronchoscopy and CT scanning is complex and would cause CT image artefact.

While, as discussed above, there was close agreement between *a*OCT and CT, overall, *a*OCT yielded measurements of diameter and Ai that were 7.6% and 15.1% greater than CT measurements, respectively. This finding contrasts with the study by Coxson et al. who, using conventional OCT, found measurements of Ai in small airways (mean airway size 12.5 ± 6.1 mm^2) to be *less* when measured with OCT than CT, by an average of 31% [26]. The discrepancy is readily attributable to the higher CT lung volumes in the Coxson study (total lung capacity) relative to their bronchoscopic OCT images (tidal breathing during conscious sedation). With the use of impedance plethysmography bands, our study carefully controlled lung volume, allowing us to estimate FRC during CT scanning and approximate this lung volume during bronchoscopy.

We found the relative difference between CT and *a*OCT measurements greatest in smaller airways (Figure 7B and 7D). We have identified two mechanisms for this disparity. Firstly, it is possible that the presence of the *a*OCT catheter could mechanically increase small airway calibre leading to an overestimation of Ai although we only measured airways larger than the catheter with a partial air space evident between the two (Figure 6F). Secondly, CT partial volume averaging, which results in underestimation of Ai, is particularly evident in airways <2-3 mm in diameter and increases with the obliqueness of the imaging plane [27, 28]. Also, partial volume averaging may have been more significant in our study as we scanned at functional residual capacity rather than total lung capacity. This is less of a concern with *a*OCT where the "slice thickness" equivalence of an axial *a*OCT image in, for example, a 5mm-diameter airway is approximately 0.2 mm, as compared to 0.625 mm using modern CT scanners. Further, unlike CT, the *a*OCT probe lies within the plane of the airway and scanning occurs close to the airway axis, avoiding oblique imaging. Even in the largest airways, in which the relative size of the bronchoscope to airway lumen increases the likelihood of oblique scanning, an angle approaching 18° would be required to produce a 5% area error (online E6).

Potential applications

*a*OCT could prove beneficial in several bronchoscopic settings. The deployment of stents for airway stenoses requires pre-bronchoscopy imaging, usually with CT. This provides important information about the site, number and dimensions of stenoses. However, CT is usually performed at total lung capacity and scans are not always recent at the time of procedure. It is still, therefore, incumbent upon the bronchoscopist to estimate stenosis length and calibre which can be highly subjective. The ability to scan a stenosis and derive immediate quantitative dimensions would be highly advantageous for stent size selection. By virtue of real-time imaging, *a*OCT could also prove useful in the management of the malacia disorders where quantitative assessment of dynamic airway collapse is desirable. This

may be particularly useful in the setting of paediatric bronchology, where longitudinal assessment of tracheo-bronchomalacia is required, ideally without ionising radiation. Finally, measurement of airway size is required during endobronchial valve deployment for endoscopic lung volume reduction. This relatively new field might benefit from the capacity of *a*OCT to size airway diameters optimising valve selection.

Limitations

Although *a*OCT can image a wide range of airway sizes, the current prototype has limited subsurface detail and, therefore, cannot measure airway wall thickness. The catheter size could also be considered a limitation as the probe-catheter system limits the size of measureable airways to about 2.5 mm. This gets close to but does not image the small airways of greatest interest in asthma and chronic obstructive pulmonary disease. However, this technical limitation is temporary as smaller probes are in development.

Probe rotation speed was found to be adequate for scanning during normal breathing. Faster acquisition speeds would improve the capacity for 3D reconstructions to account for respiratory and cardiac motion. Despite this we have recently demonstrated the capacity to "gate" images to specific phases of the respiratory cycle[29]. Finally, as with any new technology, cost is a factor. Our device is a custom-built prototype making a unit cost difficult to estimate. Larger centres specialising in interventional procedures will likely be the first to realise the potential and benefit from this technique.

Conclusion

This paper demonstrates the accuracy and precision of anatomical optical coherence tomography in phantom, pig and human airways and demonstrates the capacity to reconstruct three-dimensional

images. An advantage of this technique over existing methods of bronchoscopic airway quantification is the ability to operate independent of the distorting effects of the bronchoscope. Such a tool could be of considerable value to the interventional bronchoscopist by improving assessment of disease severity and its progression, sizing dimensions of airway stenoses in preparation for stenting and for the deployment of endobronchial valves. Future studies examining the effectiveness of *a*OCT in these and other clinical settings will further define the optimal role of this emerging technique.

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CONFLICT OF INTEREST

JW, JA, RM, MP, DS, DH and PE are listed as inventors on a provisional patent application associated with clinical applications of anatomical optical coherence tomography.

PN, AW, SB, AC and HM have no competing interests to declare.

Figures:

Figure 1. Diagram indicating arrangement of the airway segments in the organ chamber. The endoscope or *a*OCT probe is inserted through the outlet channel into the airway lumen. Corresponding internal airway views are shown. Note that within the *a*OCT cross section the innermost circle is the reflection from the probe itself while the outer 2 circles are reflections from the inner and outer walls of the plastic catheter. The thickness of the white line in the *a*OCT view (the airway wall) represents penetration of light into the submucosal tissue. Modified from [19].

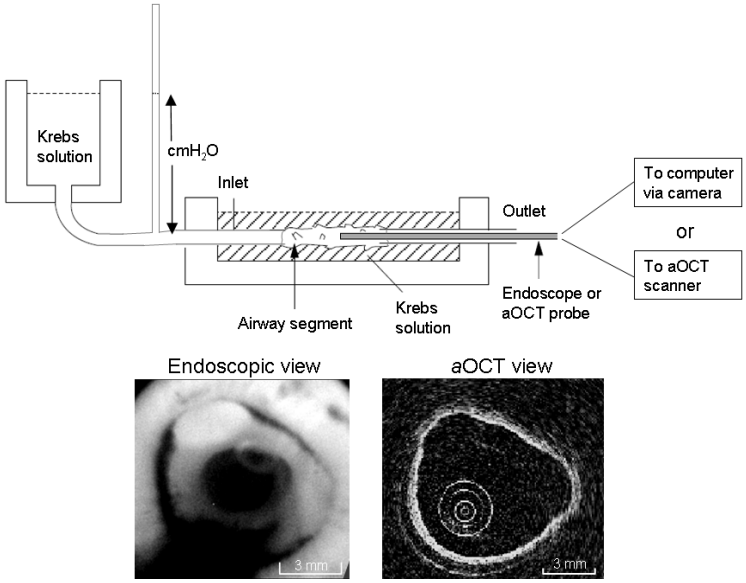


Figure 2. Absolute (A) and relative (B) accuracy of anatomical optical coherence tomography (*a*OCT) in plastic tubes with internal areas (Ai) in the range 5.3 – 1963.5 mm^2: Bland-Altman plots. Measurements obtained using an internal micrometer and an *a*OCT probe.

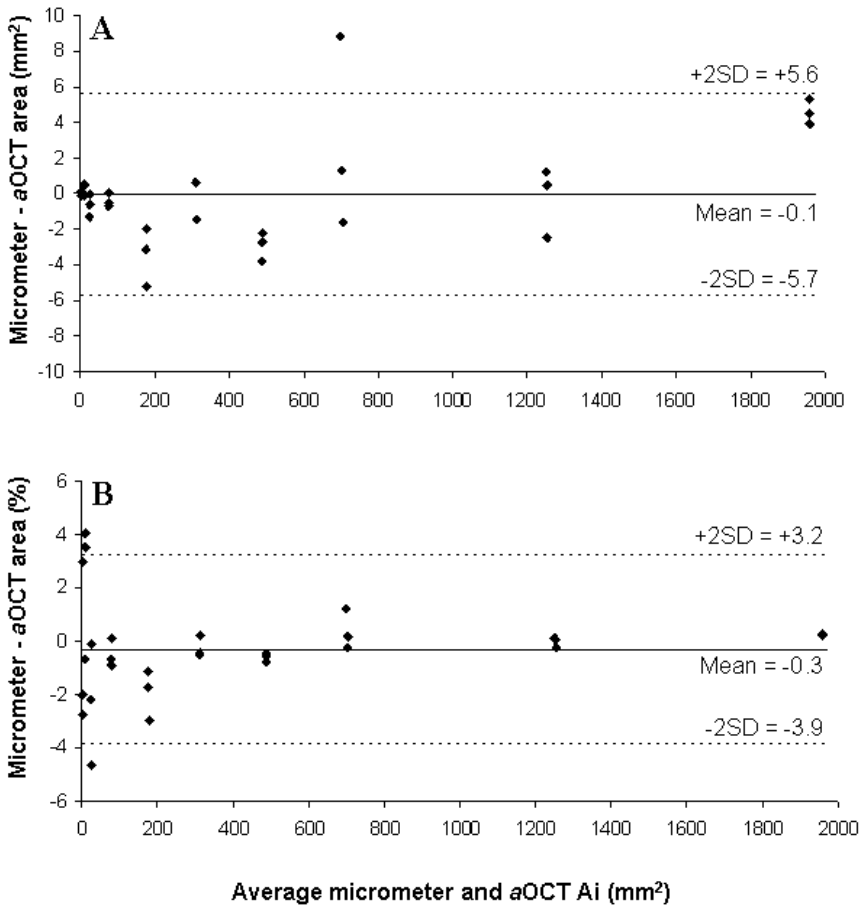


Figure 3. Intra-observer (A & B) and inter-observer (C & D) repeatability Bland-Altman plots for internal lumen area (Ai) using anatomical optical coherence tomography in plastic tubes.

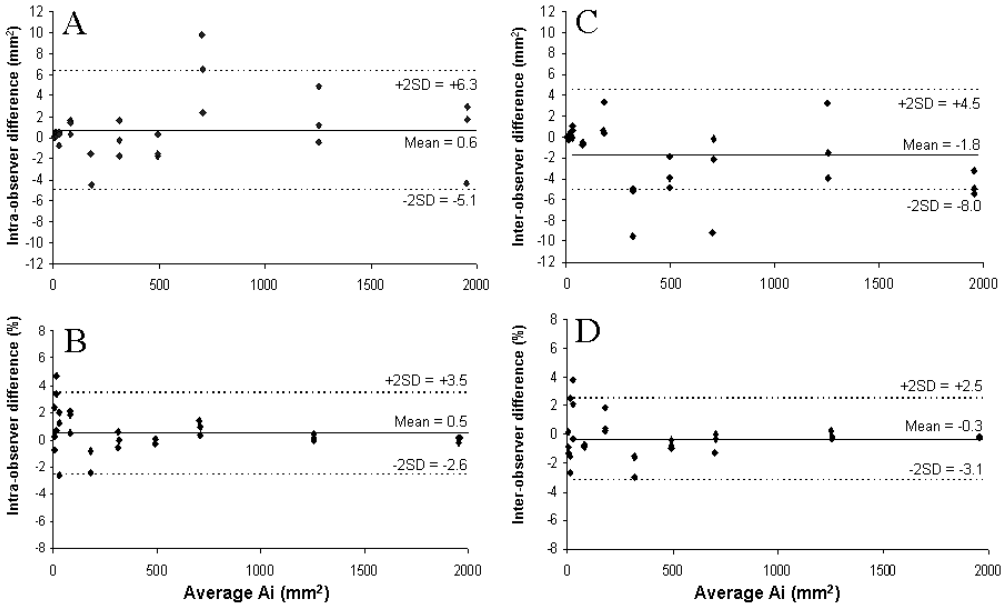


Figure 4. Compliance curves in pig airways at 4 sites A-D of differing internal lumen areas (Ai). Compliance was determined by plotting Ai derived from the endoscopic (dashed line) and anatomical coherence tomography (solid line) techniques against transmural pressure. Comparison of compliance using the Colebatch shape factor *K* applied to the ascending and descending limbs of the eight curves was not significantly different between the two techniques. Similarly, the mean slope of the curves between 0 – 10cmH_2O was not different.

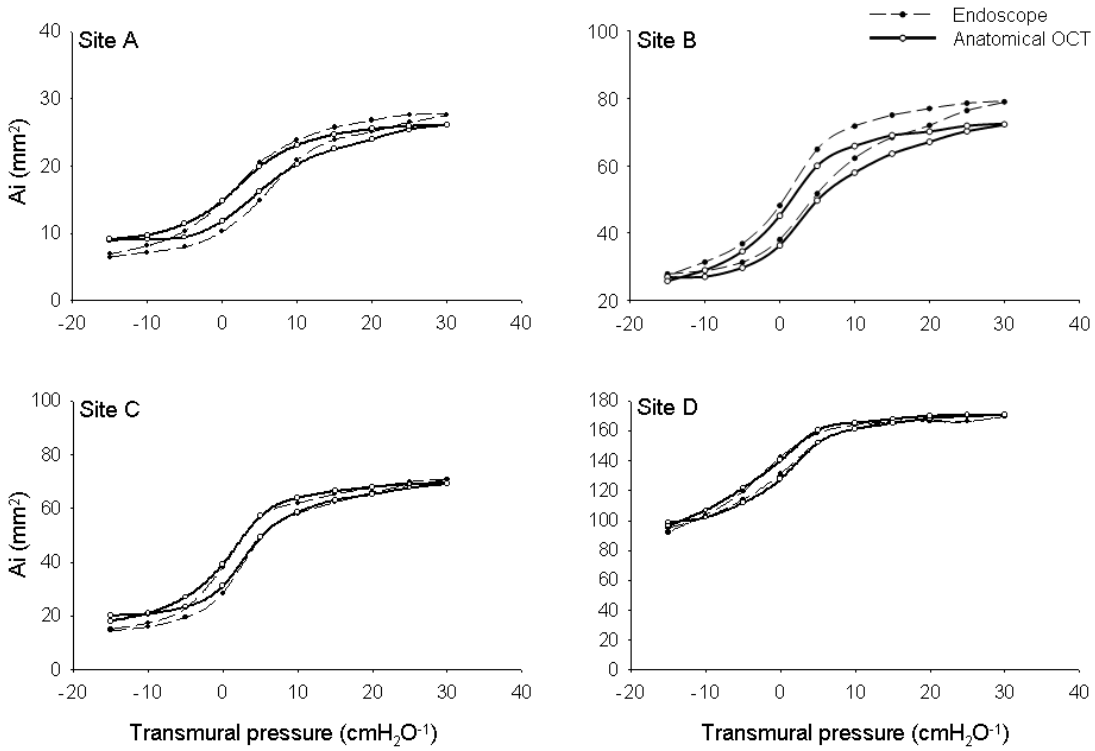


Figure 5. Simulated stenosis in an excised pig trachea (Panel A). 3D image generated from an anatomical optical coherence tomography "pullback" scan across the stenosis (Panel B). 2D reconstruction (Panel C) from which cross sections through the stenosis and the normal trachea are displayed in axial format (Panel D).

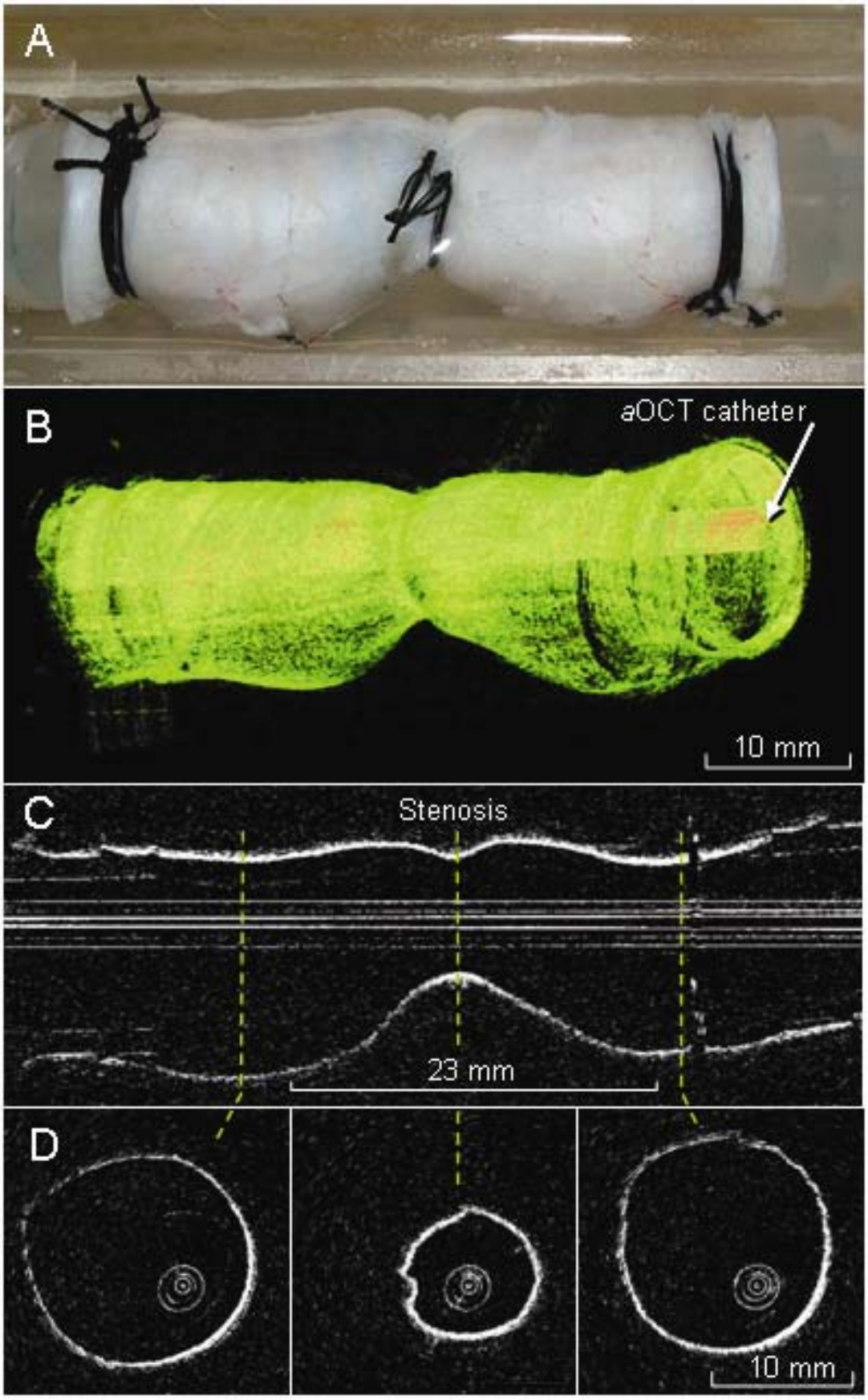

A
B
aOCT catheter
10 mm
C
Stenosis
23 mm
D
10 mm

Figure 6. CT images (top panel) and corresponding anatomical optical coherence tomography images (bottom panel) at: A. proximal trachea, B. left lower lobe and C. medial segment of the right middle lobe bronchus. The CT images, taken at functional residual capacity, demonstrate the internal and external airway wall perimeter as calculated using Pulmonary Workstation 2.0 software (VIDA Diagnostics, Iowa City, USA). Internal lumen area (Ai) measurements are shown for each technique.

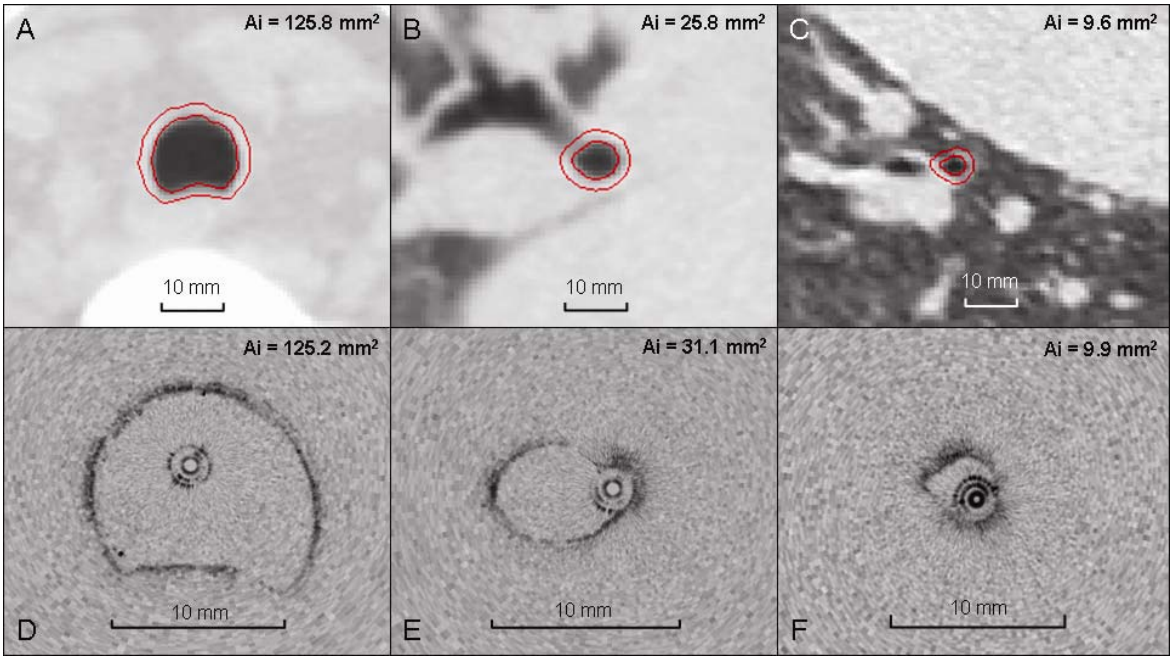
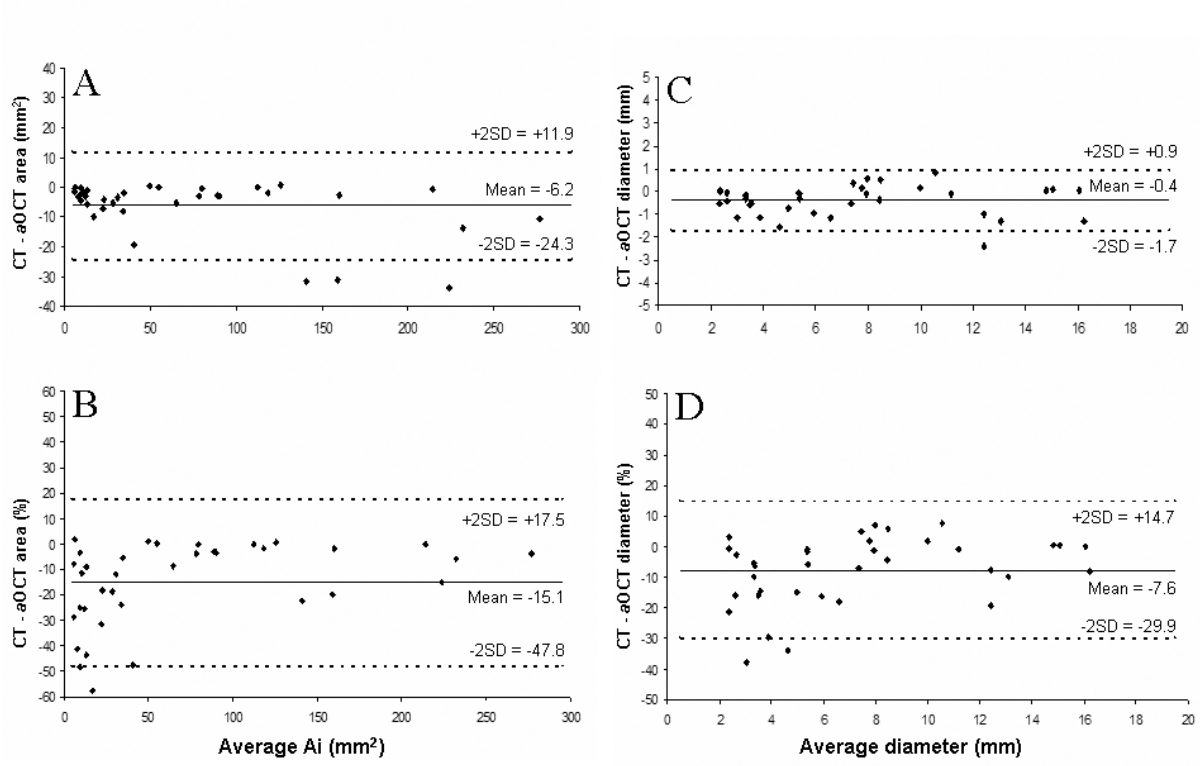


Figure 7. Absolute (A and C) and percent (B and D) measurement differences comparing human airway area (Ai) and short-axis diameter using computed tomography (CT) and anatomical optical coherence tomography (*a*OCT): Bland-Altman plots.



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