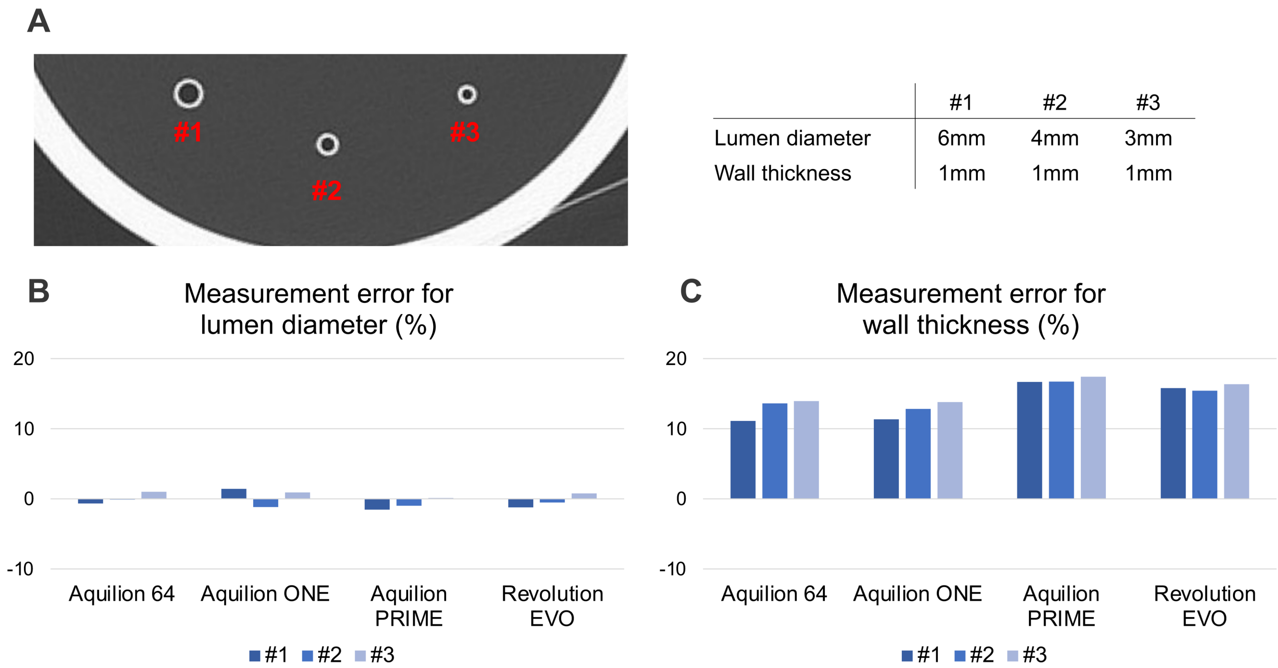
Supplementary materials:

Title: Computed tomography morphological assessments of central airways in interstitial lung abnormalities and idiopathic pulmonary fibrosis

Contents:

Supplementary Figure S1 CT scan of airway phantom tubes to evaluate the accuracy of lumen diameter and wall thickness measurements

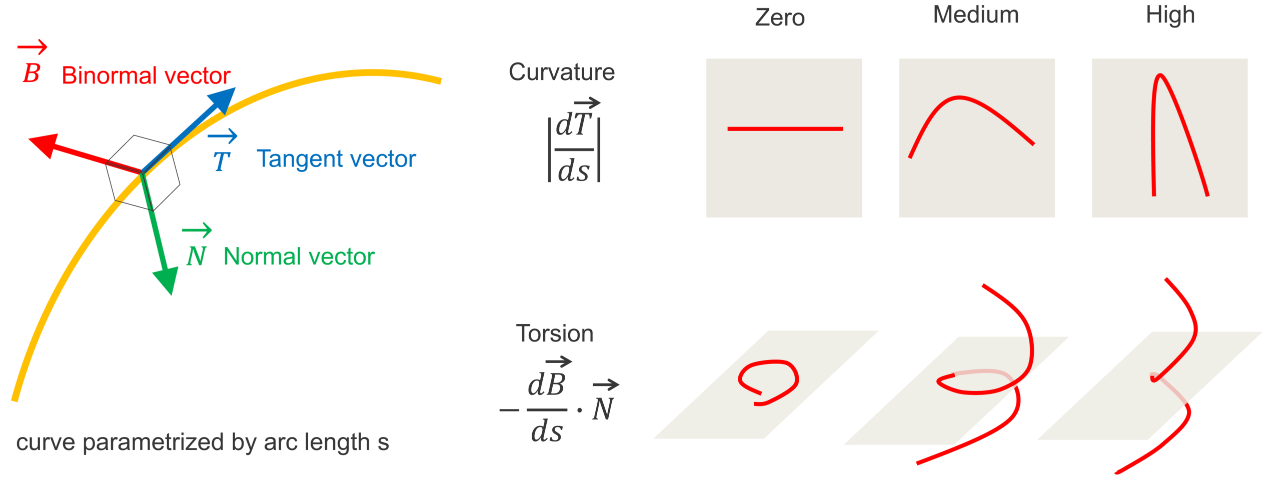


(A) Phantom tubes mimicking airways were scanned with all four scanners to validate the accuracy of segmentation. The lumen diameter ranged from 3 mm to 6 mm, while the wall thickness was 3 mm for all the tubes.

(B) The measurement error of the segmented lumen diameter was <2% for all four scanners.

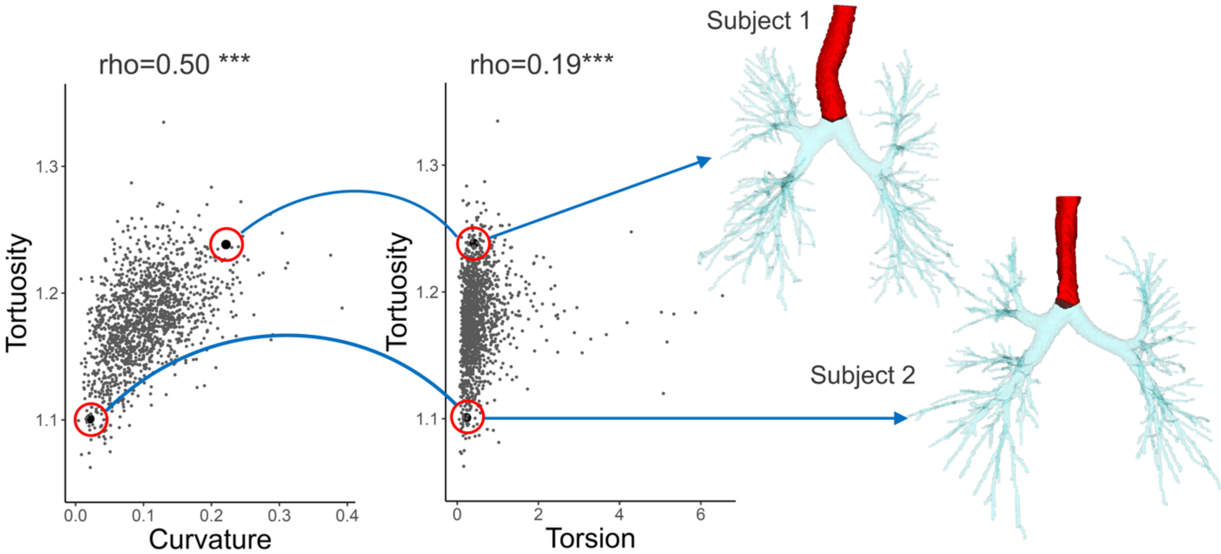
(C) The measurement error of the segmented wall thickness ranged from 11.1 to 17.5%. The wall thickness exhibited consistently higher values.

Supplementary Figure S2 Curvature and torsion



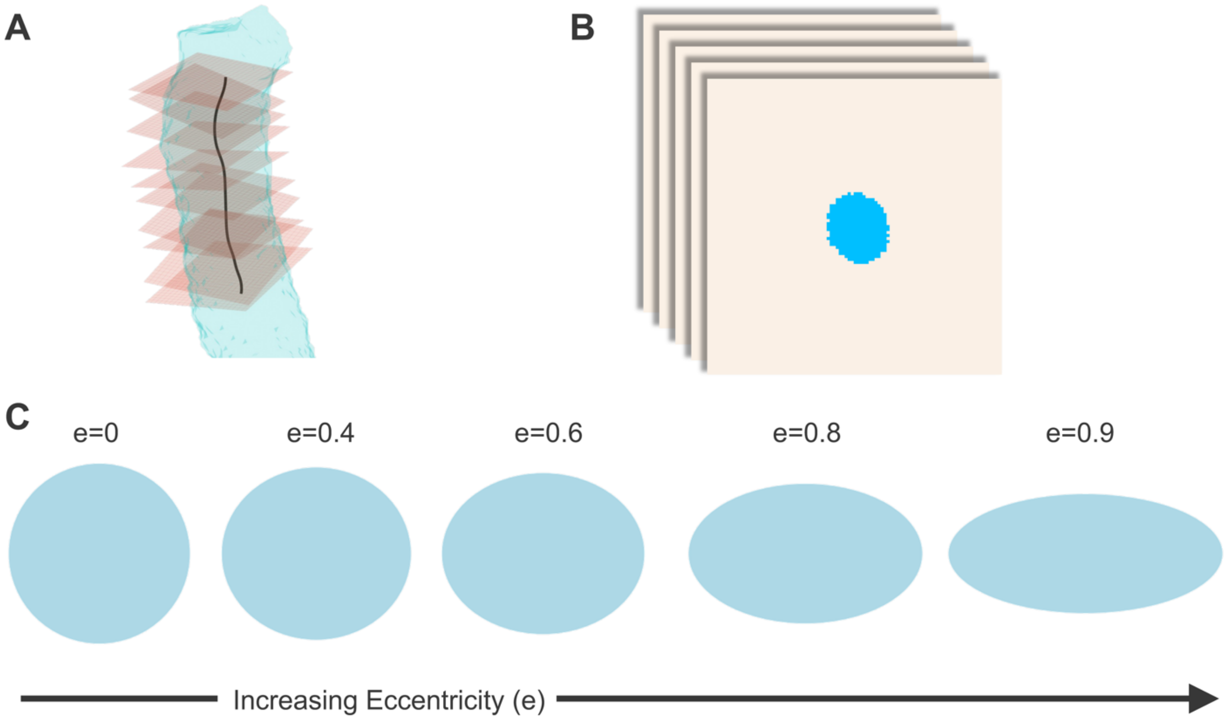
Curvature represents the two-dimensional steepness of a curve, describing how the tangent vector changes. Torsion represents the three-dimensional twisting of the curve, indicating how the plane formed by the normal and tangent vectors changes. To compute these metrics, the curve was parameterized by the arc length s. At each point on the curve, three orthogonal unit vectors were determined: the tangent vector, the normal vector, and the binormal vector. Curvature was mathematically defined as the magnitude of the derivative of the tangent vector with respect to s. Torsion was defined as the negative dot product of the derivative of the binormal vector and the normal vector. For this analysis, the absolute value of torsion was used to evaluate the degree of three-dimensional twisting. Since the normal vector and the derivative of the binormal vector are parallel and the normal vector has a magnitude of 1, torsion is essentially determined by the magnitude of the derivative of the binormal vector. Since the edge of the centreline can be affected by the adjacent bronchus, 15% at both ends of the centreline were trimmed. Ten points along the centreline of the trachea were sampled, and a spline curve was fitted through these points. The curvature and torsion were then calculated as the mean values across the ten sampled points.

Supplementary Figure S3. Correlation of torsion and curvature with tortuosity



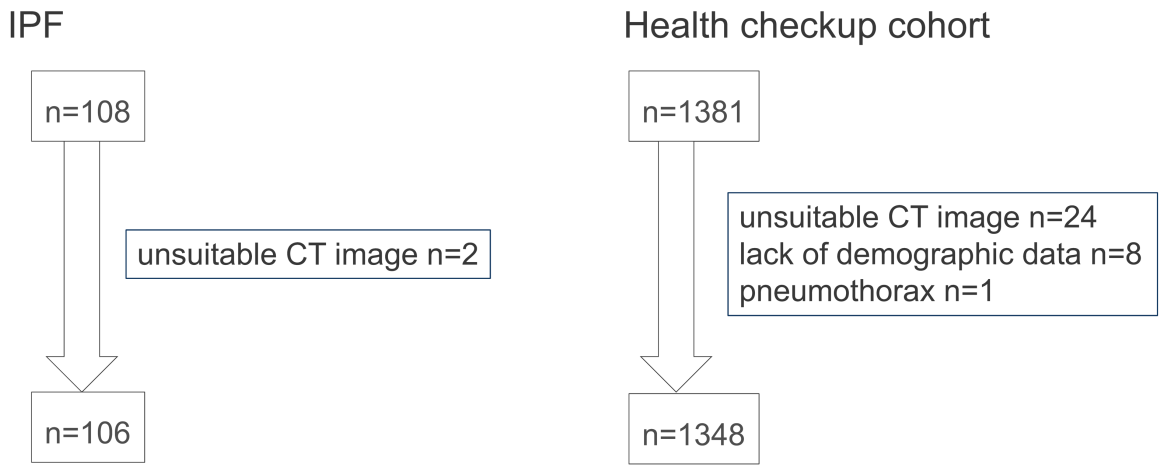
The correlation of torsion and curvature with tortuosity was evaluated in the all subjects (n=1454). Two representative cases with different tracheal tortuosity, curvature, torsion values are presented here (tortuosity / curvature / torsion = 1.24 / 0.22 / 0.41 in subject 1 vs. 1.10 / 0.021 / 0.23 in subject 2). Spearman's correlation coefficient (rho) is shown in each graph, and its significance is indicated as follows: *** p<0.001

Supplementary Figure S4 Eccentricity Measurement



Eccentricity refers to the deviation of the airway's cross-section from a true circle. It ranges between 0 and 1, where 0 is the representation of a true circle and a value near 1 represents a very elongated ellipse. Eccentricity is essentially the ratio of the focus of an ellipse to its longest diameter. A cross-section of the airway perpendicular to the centreline was made at 10 locations, and the mean of these cross-sections was used as the eccentricity of the trachea.

Supplementary Figure S5. Patient flow of each of the two cohorts



Supplementary Table S1 Subanalysis of multivariable models of differences in airway parameters excluding subjects suspected of other airway diseases

	ILA - (Control)	ILA +	IPF
n	1119	42	80
LA^{extra}	Ref	0.17 [-0.13, 0.47]	0.54 [0.30, 0.78]***
LA^{intra}	Ref	0.38 [0.08, 0.68]*	0.77 [0.53, 1.01]***
WA^{intra}	Ref	0.42 [0.14, 0.69]**	1.61 [1.39, 1.83]***
Tortuosity	Ref	0.01 [-0.30, 0.32]	0.30 [0.05, 0.55]*
Curvature	Ref	-0.23 [-0.54, 0.08]	0.31 [0.05, 0.56]*

The association between each airway parameter and the presence of ILA or IPF was evaluated in multivariable regression models excluding subjects suspected of other airway diseases. Subjects who were likely to have COPD (FEV_1/FVC <0.7 with smoking history) or asthma (history of asthma on the questionnaire) were excluded from health checkup cohort. Furthermore, patients with combined pulmonary fibrosis and emphysema (CPFE) were also excluded from IPF cohort. In this study, CPFE (the presence of emphysema in IPF) was defined as more than 5% of lung volume occupied by regions with emphysema-like hyperlucent regions identified by AIQCT. Models were adjusted for age, height and smoking history (current smoking, smoking duration and daily tobacco consumption). Values are expressed as standardized estimate [95% confidence interval]. Significant differences are indicated as follows: * p<0.05, ** p<0.01, *** p<0.001.

Supplementary Table S2. Subanalysis of multivariable models of differences in airway parameters limiting to subjects with a history of smoking

	ILA - (Control)	ILA +	IPF
n	905	44	100
LA^{extra}	Ref	-0.05 [-0.34, 0.24]	0.68 [0.47, 0.90]***
LA^{intra}	Ref	0.35 [0.06, 0.64]*	0.85 [0.64, 1.07]***
WA^{intra}	Ref	0.40 [0.13, 0.67]**	1.48 [1.28, 1.68]***
Tortuosity	Ref	0.07 [-0.23, 0.38]	0.23 [0.01, 0.46]*
Curvature	Ref	-0.09 [-0.40, 0.21]	0.36 [0.14, 0.59]**

The association between each airway parameter and the presence of ILA or IPF was evaluated in multivariable regression models limiting to subjects with a history of smoking (current and past smokers). Models were adjusted for age, height and smoking history (current smoking, smoking duration and daily tobacco consumption). Values are expressed as standardized estimate [95% confidence interval]. Significant differences are indicated as follows: * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Supplementary Table S3. Subanalysis of multivariable models of differences in airway parameters with and without subpleural fibrotic ILA.

	Subpleural fibrotic ILA - (Control)	Subpleural fibrotic ILA +	IPF
n	1322	26	106
LA^{extra}	Ref	0.11 [-0.26, 0.48]	0.75 [0.54, 0.96]***
LA^{intra}	Ref	0.50 [0.13, 0.88]**	0.88 [0.67, 1.09]***
WA^{intra}	Ref	0.44 [0.10, 0.78]*	1.58 [1.39, 1.77]***
Tortuosity	Ref	0.02 [-0.37, 0.41]	0.22 [0.01, 0.44]*
Curvature	Ref	-0.05 [-0.44, 0.34]	0.35 [0.13, 0.57]**

The associations between each airway parameter and the presence of ILA or IPF were evaluated in multivariable regression models. Health checkup subjects were divided into subjects with and without subpleural fibrotic ILA. The models were adjusted for age, height and smoking history (current smoking, smoking duration and daily tobacco consumption). Values are expressed as standardized estimate [95% confidence interval]. Significant differences are indicated as follows: * $p<0.05$, ** $p<0.01$, *** $p<0.001$.