Author/s:
Tadd, K;Morgan, L;Rosenow, T;Schultz, A;Susanto, C;Murray, C;Robinson, P

Title:
CF derived scoring systems do not fully describe the range of structural changes seen on CT scans in PCD

Date:
2019-04-01

Citation:
Tadd, K., Morgan, L., Rosenow, T., Schultz, A., Susanto, C., Murray, C. & Robinson, P. (2019). CF derived scoring systems do not fully describe the range of structural changes seen on CT scans in PCD. Pediatric Pulmonology, 54 (4), pp.471-477. https://doi.org/10.1002/ppul.24249.

Original Article: PCD, PIG, NEHI, ChILD, and Rare Diseases

CF derived scoring systems do not fully describe the range of structural changes seen on CT scans in PCD. [1]

Katelyn Tadd [(1)]

Lucy Morgan [(4,5)]

Tim Rosenow 0000-0003-3727-5131 0000-0003-3727-5131 [(6,7)]

André Schultz [(6,7)]

Clarissa Susanto [(4)]

Conor Murray[(6,7)]

Philip Robinson 0000-0001-6129-9075 0000-0001-6129-9075 [(1,2,3)]

Departments of Respiratory and Sleep Medicine, Royal Children's Hospital, Melbourne Australia [(1)], Department of Paediatrics University of Melbourne [(2)], Murdoch Children's Research Institute, Melbourne [(3)] and Department of Respiratory Medicine, Concord Hospital, Sydney [(4)], School of Medicine, University of Sydney[(5)], Division of Paediatrics, School of Medicine, The University of Western Australia, Perth, Australia [(6)], Telethon Kids Institute, The University of Western Australia, Perth, Australia [(7)]

Corresponding author:

A/Professor Phil Robinson,
PCD diagnostic service,
Respiratory and Sleep Medicine,
Royal Children's' Hospital,
Melbourne, Australia
Email: phil.robinson@rch.org.au

Key words: Primary Ciliary Dyskinesia, Cystic Fibrosis, CT scans, bronchiectasis.

Running Title: Chest CT changes in Primary Ciliary Dyskinesia.

[1] This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi:10.1002/ppul.24249

Abstract

Background

Structural lung changes seen on computed tomography (CT) scans in Cystic Fibrosis (CF) and Primary Ciliary Dyskinesia (PCD) are currently described using scoring systems derived from CF populations. This practise assumes lung damage in the 2 conditions is identical, potentially resulting in a failure to identify PCD-specific changes. Our study addresses this assumption.

Methods

58 CT scans from 41 PCD patients (age 2 – 48 years) were examined and the presence and extent of abnormalities common in CF; bronchiectasis, bronchial wall thickening, atelectasis, mucous plugging, and air trapping noted. Further assessment of the PCD scans by an experienced chest radiologist identified several unique PCD specific changes.

Results

Bronchial wall thickening was the commonest abnormality seen in PCD. All abnormalities were present more often in middle and lower lobes than in upper lobes ($p < 0.001$). Bronchiectasis, mucus plugging, atelectasis and air trapping were present more often in PCD than in the historic CF cohorts which formed the basis of 2 CF scoring systems ($p<0.05$). Extensive tree-in-bud pattern of mucus plugging, thickening of interlobar and interlobular septa, and whole lobe atelectasis were seen significantly more frequently in PCD than CF.

Conclusions

Structural changes identified on CT scans in PCD are not identical to those previously described in CF patients and suggest assessment of PCD structural changes on CT should not use CF derived scoring systems.

Introduction

The spectrum of structural changes seen on chest computed tomography (CT) scans from patients with Primary Ciliary Dyskinesia (PCD) and Cystic Fibrosis (CF), both

significant causes of bronchiectasis, have been the basis of several previous publications. (1-9) Validated scoring systems have been developed from populations of patients with CF and have been used to describe structural changes in patients with CF and extrapolated to populations of patients with PCD (1,2,3). This practice inherently assumes that the underlying pathophysiology and progression of the two diseases are closely similar if not identical. Several clinical features of PCD would however suggest that this assumption may not be appropriate. A high proportion of children diagnosed with PCD have evidence of neonatal respiratory distress. In a large study by Mulloweney some 60% of children with PCD presenting with neonatal respiratory distress were shown to have upper lobe collapse early in life on plain chest X-ray (10). Such findings are rare in patients with CF diagnosed early in life through new born screening (11). In addition, reports of CT scan findings from older patients with PCD almost universally note the relative sparing of the upper lobes even in established disease (7,8,12). Sparing of the upper lobes is not a feature of established Cystic Fibrosis lung disease (13).

Despite these clinical and radiological differences the majority of previous reports of structural lung disease in PCD have utilised CF derived scoring systems to describe the nature of the changes. In 2007, Jain et al reported the spectrum of structural changes seen on CT scans from 26 children with PCD using a modified Brody score (9). Santamaria et al (12) in 2008 also used a modified Brody score to evaluate structural lung disease in 20 patients with PCD while Magnin et al examined structural changes on CT scans in 20 adolescents with PCD using a modified Brody and Bhalla scoring system(6). To date no assessment of PCD structural lung changes has commenced with an open consideration of the range of structural changes seen in PCD.

The differences in clinical manifestations of lung disease between PCD and CF have lead us to postulate that, to accurately describe the full spectrum of PCD lung disease, scoring systems derived from CF populations may not be ideal. This present study aimed firstly to compare the lobar frequencies and distributions of CF described structural changes in a set of CT scans from a group of patients with PCD. We then further aimed to examine in detail the range of structural changes seen in a series of CT scans from patients with PCD without consideration of previously reported changes from CF studies to determine if such scans may show PCD specific changes. We postulated that the findings would be significantly different between the 2 conditions and may suggest the need for consideration of a PCD specific scoring system.

Methods

The study was conducted in two complimentary parts. In the first part of the study CT scans of patients with PCD were assessed for the frequency and lobar distribution of the previously described structural changes of CF including bronchiectasis, bronchial wall thickening, mucous plugging, atelectasis and air trapping. These results were then compared directly to the results described separately by Bhalla and Brody in their original papers describing the development of their CF scoring systems. In a further part of the study the set of PCD scans were assessed by an experienced paediatric pulmonary radiologist for structural changes unique to PCD or which were significantly more common than reported in previous series from patients with CF.

Study population & image acquisition

This was a retrospective study of 41 patients with PCD aged between 2 and 48 years who had undergone at least one chest CT scan at a time of clinical stability.

Scans were obtained from the three tertiary centres in Australia with a dedicated diagnostic and clinical PCD unit; the Royal Children's Hospital Melbourne, Concord Hospital Sydney, and Princess Margaret Hospital for Children Perth. The study received ethical approval as a multisite study from The Royal Children's Hospital Melbourne Human Research Ethics Committee (HREC). Ethics approval number 35214A. The project also received governance authorisation at the Melbourne Children's Campus (incorporating The Royal Children's Hospital, Murdoch Children's Research Institute and the University of Melbourne (Department of Paediatrics).

All available scans were deemed eligible for inclusion, provided the patient had a definitive diagnosis of PCD according to diagnostic criteria recently summarised by Shapiro (14). Patients over 5 years of age required at least 2 of the major clinical symptoms of PCD: unexplained neonatal respiratory distress, laterality defects, evidence of a chronic upper or lower airway suppurative disease – productive cough or recurrent sinusitis/coryza. In addition, patients had at least two of the following: low nasal NO (<100 ppb), presence of bi-allelic PCD-causing genes, ultrastructural ciliary abnormalities on electron microscopy, or ciliary waveform abnormalities recognised in PCD seen on high speed video-microscopy. Patients less than 5 years of age had similar requirements but without nasal NO measurement.

Due to the retrospective and multi-centre nature of this study, CT scanners and protocols varied. In Perth scans were performed using a Siemens Definition FLASH Dual Source 64 slice scanner. Scans from the Sydney unit were performed on a Siemens definition 1st generation dual source scanner while scans in Melbourne were performed on a Siemens Somatom Sensation 16 scanner . All patients were reported as clinically stable at the time of scanning, the scans being performed as

part of an annual (or less frequent) review process. Each scan was considered to be an individual unit, and longitudinal data was not analysed separately. For each scan, age, sex, date of birth, date of scan and type of scan (HRCT or volumetric) were noted. All personal identifying information was removed from the CT scans before assessment, and scans were viewed on Radiant DICOM Viewer (Medixant Pty Ltd, Poland).

In the first part of the study, the PCD scans were assessed for structural changes as described by two of the most frequently used CF scoring systems, the Bhalla and Brody scores (4,6). The relative frequencies and lobar distributions of the changes were described. Several patients had more than one CT scan available for assessment. In this part of the study only the most recent scan from each patient was considered. The primary observer for this part of the study was K.T. Scans were also reviewed by an experienced paediatric respiratory physician (P.R.) with experience in CT scoring (4,11,16,17,18). Both researchers reviewed scans separately, blinded to the patients' identities. An Intraclass Correlation Coefficient (ICC) was derived to assess inter-observer variability. A randomly selected subset of 20 scans was reviewed twice by P.R. one week apart to determine intra-observer reliability. Again, further ICC was calculated based on the 2 results. In general ICC 0.4 - 0.6 is considered moderate, 0.6 - 0.8 good and above 0.8 excellent (15).

In a further part of the study the PCD scans were assessed by C.M., a paediatric pulmonary radiologist with extensive experience in reporting paediatric chest CT scans (11,15,16). The radiologist was asked to comment on any findings which in his opinion were 1) seen more frequently in PCD than in CF or 2) were seen in PCD and not in CF. All the scans were then analysed for these findings with tabulation

including number of lobes and number of patients where the findings were present in at least one lobe.

Incidence of structural changes typically associated with CF in PCD CT scans

All CT scans were assessed for the presence and extent bronchiectasis, bronchial wall thickening, atelectasis, mucous plugging, and air trapping, as these abnormalities previously reported by Brody and Bhalla as common in CF, form the basis of subsequent CF scoring systems. If present, each abnormality was designated as mild-moderate if the extent was <50% of the lobe, and moderate-severe ≥50% of the lobe. CT changes were annotated for all 5 lobes of the lung, with the lingula classified as an additional sixth lobe (12).

Bronchiectasis was identified when the outer edge bronchus-artery cross-sectional area ratio was greater than 1, or the bronchus was non-tapering as it approached the pleura, assessed subjectively (12). Bronchial wall thickening was identified when airway walls were thicker than healthy airways, assessed subjectively. Mucous plugging was identified when there was a high-density occlusion seen in an airway, or tree-in-bud appearance in small airways. Trapped air was identified on expiratory images only as an area of reduced signal intensity compared to healthy lung (12).

Situs solitus was defined as normal thoraco-abdominal asymmetry. Dextrocardia was noted in patients where the apex of the heart was seen on the right. As is custom in PCD literature, in patients with dextrocardia we considered the lung in which the middle lobar bronchus and the corresponding middle lobe were identified on the CT scan as the right lung (12).

Statistical analysis.

The Chi-squared tests was used to assess the presence of each abnormality in the upper and middle-lower lobes; the extent of each abnormality when present by number of lobes affected as well as between the right and left sides of the lung; and the presence of abnormalities in PCD compared to CF. P-values less than 0.05 were considered significant. All analyses were performed using Stata Version 13 (*StataCorp* 2013, College Station, TX: StataCorp LP). Inter and intra observer variability were assessed using an interclass correlation.

Results

58 CT scans from 41 patients with proven PCD were included. The mean age at the time of scan was 13 years (range 2-48 years). There were 14 patients from the Royal Children's Hospital, 12 from Concord Hospital, and 15 from Princess Margaret Hospital. Sixteen patients (40%) were male and twenty-six (44.8%) had dextrocardia. Thirty-nine scans (67.2%) were volumetric. There were 52 expiratory scans, 16 (27.6%) of which were volumetric. (Table 1).

Incidence of CF structural changes in PCD CT scans

The most recent scan for each patient was used in this part of the study (41 scans). Bronchial wall thickening was the commonest abnormality, occurring in all scans (n=41, 100%) and in 229 of 246 lobes (93%). Bronchiectasis was present in 36 of the 41 scans (88%) and 206 lobes (83.6%). Mucous plugging was seen in 37 scans (91.4%) and 169 lobes (68.7%). Atelectasis was noted in 38 scans (94%) and 179 lobes (72.7%). Air trapping was present in 33 of 39 expiratory scans (85%), and in 130 of 234 lobes (55.4%) (Table 2). All patients had some abnormality in at least one lobe, and there were no significant differences between the right and left lung for any abnormalities.

Comparisons between lobes are shown in Table 3. All abnormalities were present significantly more often in the middle and lower lobes compared to the upper lobes. When present, all abnormalities were significantly more extensive (i.e. severe) in the middle and lower lobes compared to the upper lobes (Table 3).

Incidence of CF structural changes in PCD compared to original CF reports

Bronchiectasis, mucous plugging, bronchial wall thickening, atelectasis and air trapping were compared to results from Brody (6) and Bhalla (4); as these features form the basis for each respective scoring system (Table 4) Bronchiectasis, mucus plugging, atelectasis ($p<0.001$) and air trapping ($p=0.005$) and bronchial wall thickening ($p=0.04$) were all present significantly more often in the PCD cohort than the Brody or Bhalla CF cohorts.

Inter-observer reliability was good (ICC 0.68). There was excellent intra-observer reliability (ICC 0.88).

Unique PCD based structural changes on CT scans

Review of the 58 PCD scans identified several structural changes uncommon to CF. Commonly seen was dextrocardia and extensive tree-in-bud pattern of mucus plugging. Other findings uncommon to CF were bronchoceles or nodules, thickening of interlobar and interlobular septa, and atelectasis mostly seen as collapse of whole lobes (as opposed to small sections of segmental or sub-segmental atelectasis). Dextrocardia was not considered further.

Twenty nine patients (70% of study group) showed evidence of extensive mucous plugging and tree in bud changes in a total of 78 lobes (32% of all lobes). 26 patients (63%) showed evidence of partial atelectasis in 42 lobes (17% of all lobes). Inter-

lobar septal thickening was found in 21 patients (51% of patients) in 29 lobes (12% of all lobes).

Discussion

This present study has highlighted that lung disease seen on chest CT scans differs between CF and PCD both in the incidence and locality of common changes. In addition, several structural changes were found to be common to PCD than to CF including extensive tree-in-bud pattern of mucus plugging, bronchoceles or nodules, thickening of interlobar and interlobular septa, and whole lobe atelectasis. CF derived scoring systems applied to CT scans from patients with PCD will therefore not include information regarding these unique changes.

The variation in CT findings between CF and PCD is perhaps not unexpected given differences in underlying disease pathophysiology. CF is associated with impaired functioning of the CFTR protein causing disturbances in electrolyte transport across the epithelial surface and resultant changes in airway surface liquid osmolality and mucus rheology (19, 20,21). Primary ciliary dysfunction is not considered a part of the basic underlying pathophysiology of CF. In comparison, defective electrolyte transport across the epithelial surface is not considered a primary element of PCD pathophysiology, instead impaired cilial function is the primary defect of this condition. These underlying differences in pathophysiology may reflect the different features of CF lung disease compared to PCD lung disease and include the relative preponderance of neonatal lung disease in PCD particularly involving the upper lobes, previously described by Mulloweney and the relative sparing of the upper lobes in established PCD lung disease, both features not frequently seen in CF lung disease (10).

Several previous investigators have described structural changes in PCD using CF derived scoring systems. Jain *et al* used a modified Brody score to describe the range of structural changes seen on CT scans in 26 children with PCD (9). While they reported the previously described changes commonly seen in CF including bronchiectasis and bronchial wall thickening, they also described the relative sparing of the upper lobes from structural disease, particularly bronchiectasis. Santamaria et al in 2008 also used a modified Brody score to describe structural changes on CT scans of 20 patients with PCD (12). Bronchiectasis was seen in 80% of cases while peribronchial thickening (80%), mucus plugging (75%) and parenchymal changes (65%) were also seen commonly. In comparison to a group of age matched CF patients, the total HRCT scan score in PCD was significantly lower. In 2012 Magnin *et al* examined structural changes on CT scans in 20 adolescents with PCD using a modified Brody and Bhalla scoring system (6). Bronchiectasis and peribronchial thickening were the commonest structural changes noted. CT scores were negatively correlated to measurements of lung function. Similar findings were described by Cohen-Cymberknoh et al in 2014 when lung function and CT changes were assessed, using the Brody score, in children with PCD and 2 groups of CF patients (12). No previous report has outlined the range of structural changes seen in a collection of scans from PCD patients descriptively particularly concentrating on whether there may be different structural features to those previously reported in CF.

We elected to compare the PCD structural changes seen in our scans with those reported by Bhalla and Brody as these changes were derived from populations of patients not diagnosed by new born screening. While CF currently is generally diagnosed through newborn screening, with interventive therapy commenced early in life, no such newborn screening is available for PCD. As a result the diagnosis of

PCD usually occurs after a patient presents with clinical manifestations of the underlying condition such as chronic cough and other clinical features of suppurative airway disease. Hence, we felt it was more appropriate to compare findings from our PCD group with findings described from a group of CF patients diagnosed prior to widespread newborn screening many of whom may have had similar clinical presentations due to underlying lung disease.

Several previous reports have attempted to correlate CT scan findings with those of lung function or type of ultra-structural defect seen on electron microscopy (22). These relationships were not investigated in this present report as we, like Brody and Bhalla had previously reported with CF derived scans, wanted to examine the spectrum of structural changes found in PCD as a separate body of work. This project opens up the opportunity to further explore the relationships between the structural and functional decline in PCD. It is possible that some previous investigators have failed to identify any relationship between lung function and radiological changes because of the use of a CF derived scoring systems as opposed to a PCD derived system.

One limitation of this study was that scans were collected retrospectively, which did not enable lung volume control, standardisation of radiation dose, or imaging protocols. While the majority of scans were volumetric it is possible that structural changes were under-reported in those scans performed as HRCT. While any under reporting may influence the quoted frequency values of the structural changes they will not likely result in failure to detect any unique structural change. Any attempt to construct a PCD specific scoring system for CT scans would ideally utilise a prospective study allowing for standardised scanning protocols. The recent development of more quantitative CF scoring systems such as the PRAGAMA-CF

score may also provide more detailed information than the qualitative scoring systems such as the CF Brody and Bhalla scores (15).

In conclusion our study has shown that PCD, as a progressive suppurative lung disease, manifests not only different frequencies and localisation of structural damage when compared to CF but also manifests several unique changes uncommon to CF including extensive tree-in-bud pattern of mucus plugging, bronchoceles or nodules, thickening of interlobar and interlobular septa, and whole lobe atelectasis. CF derived scoring systems in failing to take these unique PCD changes into account, potentially limit the utility of using these scoring systems to examine lung disease in PCD and its consequences.

Acknowledgements

PR, LM, KT, devised the study protocol and were involved in preparation of the manuscript. Data analysis was performed by KT and PR. AS provided data and contributed to the writing of the manuscript. TR provide necessary training for KT prior to the start of the study and also provided manuscript comment.CM reviewed all scans and provided data on specific PCD changes and reviewed the manuscript. CS reviewed the manuscript and helped with data collection.

References

1. Bhalla M, Turcios N, Aponte V, Jenkins M, Leitman B, McCauley D, et al. Cystic fibrosis: scoring system with thin-section CT. Radiology. 1991;179(3):783-8.

2. Brody AS, Klein JS, Molina PL, Quan J, Bean JA, Wilmott RW. High-resolution computed tomography in young patients with cystic fibrosis: distribution of abnormalities and correlation with pulmonary function tests. Journal of Pediatrics. 2004;145(1):32-8.

3. Brody AS, Kosorok MR, Li Z, Broderick LS, Foster JL, Laxova A, et al. Reproducibility of a scoring system for computed tomography scanning in cystic fibrosis. Journal of Thoracic Imaging. 2006;21(1):14-21.

4. Loeve M, van Hal PTW, Robinson P, De Jong P, Lequin M, Hop W, et al. The spectrum of structural abnormalities on CT scans from patients with CF with severe advanced lung disease. Thorax. 2009;64(10):876-82.

5. Kennedy MP, Noone PG, Leigh MW, Zariwala MA, Minnix SL, Knowles MR, et al. High-Resolution CT of Patients with Primary Ciliary Dyskinesia. American Journal of Roentgenology. 2007;188(5):1232-8.

6. Magnin ML, Cros P, Beydon N, Mahloul M, Tamalet A, Escudier E, et al. Longitudinal lung function and structural changes in children with primary ciliary dyskinesia. Pediatric Pulmonology. 2012;47(8):816-25.

7. Irving SJ, Ives A, Davies G, Donovan J, Edey AJ, Gill SS, et al. Lung clearance index and high-resolution computed tomography scores in primary ciliary dyskinesia. American Journal of Respiratory & Critical Care Medicine. 2013;188(5):545-9.

8. Cohen-Cymberknoh M, Simanovsky N, Hiller N, Hillel A, Shoseyov D, Kerem E. Differences in disease expression between Primary Ciliary Dyskinesia and Cystic Fibrosis with and without Pancreatic Insufficiency. CHEST 2014; 145(4):738–7449.

9. Jain K, Padley SP, Goldstraw EJ, Kidd SJ, Hogg C, Biggart E, Bush A. Primary ciliary dyskinesia in the paediatric population: range and severity of radiological findings in a cohort of patients receiving tertiary care. Clinical Radiology. 2007; 62(10):986-93.

10. Mullowney T, Manson D, Raymond K, Stephens D, Shah V, Dell S. Primary Ciliary Dyskinesia and Neonatal Respiratory Distress. PEDIATRICS Volume 134, Number 6, December 2014

11. Sly PD, Brennan S, Gangell C, de Klerk N, Murray C, Mott L, Stick SM, Robinson PJ, Robertson CF,Ranganathan SC. Lung disease at diagnosis in infants with cystic fibrosis detected by newborn screening. Am Jnl Resp Crit Care Med 2009; 180:146-152.

12. Santamaria F, Montella S, Tiddens HA, Guidi G, Casotti V, Maglione M, de Jong PA. Structural and functional lung disease in primary ciliary dyskinesia. Chest 2008; 134(2):351-7.

13. Mott LS, Park J, Gangell CL, de Klerk NH, Sly PD, Murray CP, et al. Distribution of early structural lung changes due to cystic fibrosis detected with chest computed tomography. Journal of Pediatrics. 2013;163(1):243-8.e1-3.

14. Shapiro AJ, Zariwala MA, Ferkol T, Davis SD, Sagel SD, Dell SD, Rosenfeld M, Olivier KN, Milla C, Daniel SJ, Kimple AJ, Manion M, Knowles MR, Leigh

MW. Diagnosis, monitoring, and treatment of primary ciliary dyskinesia: PCD foundation consensus recommendations based on state of the art review.Pediatr Pulmonol. 2016 Feb;51(2):115-32

15. Rosenow T, Oudraad MC, Murray CP, Turkovic L, Kuo W, de Bruijne M, et al. PRAGMA-CF. A Quantitative Structural Lung Disease Computed Tomography Outcome in Young Children with Cystic Fibrosis. Am Jnl Resp Crit Care Med. 2015;191(10):1158-65.

16. Stick S, Brennan S, Murray C, Douglas T, von Ungern-Sternberg B, Garratt L, Gangell C, De Klerk N, Linnane B, Ranganathan S, Robinson P, Robertson C, Sly P. Bronchiectasis In Infants And Preschool Children Diagnosed With Cystic Fibrosis Following Newborn Screening J Peds 2009;155(5) 623-8.

17. Widger J, Ranganathan, S, Robinson P. Progression of structural lung disease on CT scans in children with Cystic Fibrosis Related Diabetes. Jnl of Cystic Fibrosis. 2012, 12(3) 216-221

18. Loeve M, Hop W, de Bruijne M, van Hal P, Robinson P, Aitken M, Dodd J, Tiddens H. Chest Computed Tomography scores are predictive of survival in CF patients awaiting lung transplantation. Am Jnl Resp Crit Care Med 2012; 185(10) 1096-1103.

19. Boucher RC. Evidence for airway surface dehydration as the initiating event in CF airway disease. J Intern Med. 2007;261(1):5-16.

20. Button B, Cai LH, Ehre C, Kesimer M, Hill DB, Sheehan JK, et al. A periciliary brush promotes the lung health by separating the mucus layer from airway epithelia. Science. 2012;337(6097):937-41.

21. Henderson AG, Ehre C, Button B, Abdullah LH, Cai LH, Leigh MW, et al. Cystic fibrosis airway secretions exhibit mucin hyperconcentration and increased osmotic pressure. J Clin Invest. 2014;124(7): 3047-60.

22. Davis SD; Ferkol TW; Rosenfeld M; Lee HS; Dell SD; Sagel SD; Milla C; Zariwala MA; Pittman JE; Shapiro AJ; Carson JL; Krischer JP; Hazucha MJ; Cooper ML; Knowles MR; Leigh MW. Clinical features of childhood primary ciliary dyskinesia by genotype and ultrastructural phenotype. Am Jnl Resp Crit Care Med 2015; 191(3):316-2.

Table 1:

Sex	**N (%)**
Female	25 (61%)
Male	16 (39%)
Location	

Melbourne	14 (34%)
Perth	15(37%)
Sydney	12(29%)
Age (years)	
Median and IQR	13 (9-21.25)
Range	2-48
Situs Status	
Solitus	24 (60%)
Dextrocardia	16 (40%)

Table 1 Patient demographics. The patient population of this study included 41 patients with a diagnosis of Primary Ciliary Dyskinesia from the 3 tertiary Australian centres with a dedicated diagnostic and clinical PCD service; the Royal Children's Hospital Melbourne, Concord Hospital Sydney, and Princess Margaret Hospital, Perth.

Table 2:

	Number of scans (n)	% of total scans (%)	Number of lobes (n)	% of total scans (%)
Bronchiectasis	36	87.9	206	83.6
Bronchial wall thickening	41	100	229	93.4
Mucous plugging	37	91.4	169	68.7
Atelectasis	38	94.8	179	72.7
Air trapping	33	85	130	55.4

Table 2. Presence of abnormalities by lobe in CT scans in PCD.

Table 3

	Upper lobe changes (n)	Middle-/Lower lobe changes (n)	p value	95% confidence interval
Bronchiectasis	32/58	52/58	**<0.001**	**0.195-0.495**
Bronchial wall thickening	40/58	58/58	**<0.001**	**0.191-0.429**
Mucous Plugging	25/58	53/58	**<0.001**	**0.336-0.610**
Atelectasis	27/58	54/58	**<0.001**	**0.322-0.610**
Air trapping	21/52	41/52	**<0.001**	**0.211-0.558**

	Upper lobes with severe changes (n)	Upper lobes with any change (n)	Middle-Lower lobes with severe changes (n)	Middle-Lower lobes with any change (n)	p value	95% confidence interval
Bronchiectasis	8	49	73	161	**<0.001**	**0.0161-0.419**

Bronchial wall thickening	4	70	62	189	**<0.001**	**0.019-0.357**
Mucous Plugging	1	35	56	147	**<0.001**	**0.026-0.448**
Atelectasis	0	41	44	168	**<0.001**	**0.195-0.328**
Air trapping	4	33	31	105	**.0450**	**0.033-0.316**

Table 3a: Statistical analyses of findings in PCD scans.

1: Comparison of presence of abnormalities between the upper and middle-lower lobes as seen in PCD cohort. All abnormalities are distributed significantly less in the upper lobes compared to the middle-lower lobes.

2: Comparisons of extent of severe abnormalities between upper and middle-lower lobes in PCD cohort. When present all abnormalities are significantly worse in the middle-lower lobes. Worse is defined as the lobe being more than 50% affected by the structural change.

Table 3b:

	PCD scans with any change (n)	Total PCD scans (n)	CF scans with any change (n)	Total CF scans (n)	p value	95% confidence interval
Bronchiectasis	51	58	35	60*****	**<0.001**	**0.0146-0.446**
Bronchial wall thickening	58	58	13	14^{+}	**P=0.040**	**-0.635-0.206**
Mucous Plugging	53	58	9	60*****	**<0.001**	**0.648-0.879**
Atelectasis	55	58	2	14^{+}	**<0.001**	**0.614-0.997**
Air trapping	45	52	38	60*****	**P=0.005**	**0.088-0.385**

Table 3b: Statistical analyses of findings in PCD CT scans vs CF scans from original Brody and Bhalla descriptions.

Comparison between presence (in any lobe) of features of PCD compared to CF cohorts described in original Brody (*****) and Bhalla ($^{+}$) studies. Abnormalities are present in significantly different proportions in the PCD cohort compared to the CF cohorts in all parameters.

	PCD scans with change (n)	CF scans with change (n)	p value	95% Confide interval
Bronchiectasis	51/58	35/60	<0.001	0.146-0.44
Bronchial wall th	58	13/14	0.04	-0.635-0.20
Mucous plugging	53/58	9/60	<0.001	0.648 – 0.8
Lobestasis	55	2/14	<0.001	0.614-0.99
Air Trapping	45/52	38/60	0.005	0.088-0.38

	Mucous plugging	Inter-lobar thickening
Patients	29 (70%)	21 (51%)

Table 4.

Table 4: Frequency of structural changes seen in PCD scans compared to frequencies for the same changes reported by Brody and Bhalla in CF.

Table 5:

Table 4: Relative incidence of PCD specific structural changes as assessed by an experienced paediatric radiologist.

Lesions were assessed as being either more frequent in PCD than in CF or not frequently seen in CF.

Figure 1:

Representative images depicting structural changes in lung disease on computed tomographic scans in Primary Ciliary Dyskinesia. *A,* Bronchial wall thickening, seen diffusely through middle and lower lobes, examples *(arrows).* B Bronchiectasis, seen diffusely through lower lobes examples *(arrows).* C, Large mucous plugs in left lower lobe *(arrows).* D, Tree-in-bud mucous plugging diffusely throughout right and left lower lobes, seen as multiple small opacities *(within circles).* E, Septal thickening of the right oblique fissure *(arrow).* F, Complete collapse of the right middle lobe *(arrow).* G, Air trapping *(arrows* seen as lower density areas on expiratory images compared to the higher density normal lung. Note dextrocardia in images *A, C, D, G*