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Imaging of cystic fibrosis lung disease in paediatrics with computed tomography: A focus on radiation exposure

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Abstract

Thoracic CT is the gold standard imaging method in the diagnosis, assessment and management of lung disease. In the setting of cystic fibrosis (CF), CT demonstrates increased sensitivity compared with pulmonary function tests and chest radiography, and findings correlate with clinical outcomes.

Increased understanding of the aetiology of CF lung disease indicates that even asymptomatic CF infants can have irreversible pulmonary pathology. Surveillance and early diagnosis of lung disease in CF is important for the preservation of lung parenchyma and to optimise long-term outcomes.

CF is associated with increased cumulative radiation exposure due to the requirement for repeated imaging from a young age. Radiation dose optimisation, important for the safe use of CT in children with CF, is best achieved in a team environment where paediatric radiologists work closely with paediatric respiratory physicians, physicists and radiography technicians to achieve the best patient outcomes.

Despite the radiation doses incurred, CT remains a vital imaging tool in children with CF. Radiologists with special interests in CT dose optimisation and respiratory disease are key to appropriate use of CT in paediatric imaging. Paediatric radiologists strive to minimise radiation dose to children whilst providing the best assessment of lung disease possible.

Key Words

Cystic fibrosis; computed tomography; paediatric imaging; cystic fibrosis lung disease; child; adolescent

List of Abbreviations:

CF: cystic fibrosis

CT: computed tomography

Background

Though radiological imaging has been responsible for considerable advancements in medical diagnosis and treatment, paediatric imaging poses specific challenges. The clinical presentation of some pathologies can vary in children compared with adults; diseases are frequently encountered at an earlier stage, hence providing the opportunity to intervene earlier in an effort to slow disease progression and improve clinical outcomes. Paediatric radiologists play an important role in tailoring imaging assessment to the specific needs of their patients, whilst cognisant of the often subtle early features of the pathologies encountered. The roles of paediatric radiologists, and radiologists with special interest in radiation dose reduction techniques, in the management of children with cystic fibrosis (CF) is a good example of this.

CF is the most common life-shortening autosomal recessive genetic disorder across the Western World, affecting an estimated 1 in 2,000 – 3,000 Caucasian new-borns [1]. Fortunately, effective treatment options are improving. Genomically-guided medicine provided Ivacaftor (Kalydeco; Vertex Pharmaceuticals, MA, USA), the first disease modifying drug in CF [2]. Approved for use in CF patients with the *G551D* mutation, Ivacaftor improves lung function, reduces sweat chloride levels and facilitates weight gain [3]. The Food and Drug Administration of the United States subsequently approved Lumacaftor/Ivacaftor combination therapy (Orkambi; Vertex Pharmaceuticals, MA, USA) for CF patients, aged 12 years and older, homozygous for *Phe508del* mutation [4]. In Ireland, Ivacaftor is now available for children from 1 year of age and Orkambi from 2 years of age. These developments have provided the potential to significantly improve quality of life for CF patients.

Ireland has the highest worldwide incidence of CF [1]. Across a 17-year study period, there has been a 5.9-fold increase in the use of all computed tomography (CT) imaging in CF patients [5], prior to the advent of genomically targeted therapy. Prevalence of the *G551D* mutation in patients at our CF centre is 23% [6]. We have previously reported improvements in the severity of lung disease in CF, using ultra-low dose CT imaging for follow up examination, post initiation of Ivacaftor treatment. Early and sustained improvements in CF lung disease have increased our reliance on the use of ultra-low dose CT in the monitoring of response to treatment (Fig. 1, 2, 3).

This review article explores imaging in CF, with a focus on the use of CT in children with CF. The importance of, and options available for, inclusion of dose optimisation into regular practice will be particularly emphasised.

Pathological Changes Observed in CF Lung Disease

Even in the absence of overt respiratory symptoms, airway inflammation, infection and structural damage exist in children with CF. Studies evaluating the use of limited slice high-resolution CT in infants and young children with CF confirm that these individuals have more dilated airways, with thicker walls compared with controls. Structural alterations in the CF lung begin during the years of infancy and early childhood [7].

Bronchiectasis is by definition irreversible, even in children with CF. It is observed in many asymptomatic infants shortly after CF diagnosis, and predates those abnormalities detected by more traditional means, including spirometry and chest radiographs [8]. Bronchiectasis is evident on CT imaging in 30-40% of children with CF aged 3-4 years [8], and in up to 80% of young CF children by the age of 5 years [9].

Given developments in therapy and improvements in prognosis, repeated imaging of the CF lung now plays an increasingly important role in the monitoring of both disease progression and effectiveness of therapeutic interventions.

Imaging in Paediatric CF Lung Disease

Pulmonary complications remain life limiting in the CF population. Whilst pulmonary function testing is one of the key investigations in the assessment and monitoring of CF patients, CT images demonstrate increased sensitivity; many patients with significant lung disease identifiable on CT maintain normal pulmonary function tests [10]. Over 2 years of follow up of 48 children, with re-evaluation by way of pulmonary function tests and high-resolution CT, lung damage progression was evident on thoracic imaging, whilst pulmonary function tests had remained stable or even improved.

Traditional spirometry pulmonary function tests are difficult to accurately perform in preschool children as they struggle to meet the quality control criteria defined in spirometry guidelines, thus limiting the availability of sensitive outcome measures of CF lung health in this cohort. Whilst other forms of preschool pulmonary function tests such as multiple breath washout are available, they are not accessible in many clinical paediatric CF centres as a result of manpower and technical challenges. Pulmonary function tests are frequently non informative as to the early development of CF lung disease, and often under estimate the full extent of disease [11]. Quantification of CF bronchiectasis utilising CT bronchiectasis scores is more sensitive for evaluating the degree of lung destruction compared with pulmonary function tests [12].

Though useful in the setting of an acute exacerbation of lung disease to guide clinical management, chest radiographs are too non-specific and insensitive for detailed evaluation of early CF pulmonary disease [13]. Thoracic CT offers increased sensitivity [10] for the diagnosis, assessment and monitoring of bronchiectasis and its associated complications in children with CF.

The ability of CT to accurately follow declining lung function has implications for CF management. CT has potential to facilitate informed management decisions including timing of escalation of drug therapy, and when lung transplantation might be necessary [14]. Clinical trials are increasingly using CT to gauge treatment response to antibiotics and gene therapy in CF cases [15].

Quantitative evaluation of radiological imaging has improved objectivity and reproducibility when compared with traditional qualitative analysis. When focused primarily on asthma and chronic obstructive pulmonary disease imaging studies, quantitative analysis of CT scans has demonstrated both good accuracy and correlation with functional tests [16]. Recent studies have further confirmed that airway quantitative analysis can detect changes in CF patients [17]. In individuals with severe airflow obstruction, quantitative analysis is beneficial in CF disease severity assessment, facilitating the study of increased numbers of bronchi, and increasing the sensitivity of bronchiectasis detection [18].

Radiation Exposure in Children with CF

CF patients will proceed to an average of 3.2 thoracic CT scans (range 0-13) during their lifetime [19]. As a result, they have cumulative effective doses in excess of the general population. A 6-fold increase in the use of CT scanning in CF patients has been reported over the last 15 years [5], likely

due to a variety of factors, including increased availability of CT, rapid acquisition time and a high sensitivity and specificity for CF pulmonary disease.

Annual cumulative effective dose from medical imaging has been steadily increasing over the last 30 years. Mean annual effective dose for CF patients has increased consecutively from 0.39 mSv to 0.47 mSv, and then to 1.67 mSv, per person per year over the last three decades, respectively [5]. Comparably, in a French context, mean cumulative effective dose in a cohort of CF patients was 19.5 mSv (range 2.24-78.5 mSv) [19].

In view of cumulative radiation exposure, the frequent imaging required in children with CF is a concern. Average age at first CT Thorax has fallen dramatically in recent years, from 20 years for patients born pre 1980, to 1.9 years for patients born post 1997 [19]. Thoracic imaging frequently commences during infancy, as the earliest CF radiological changes, mucous plugging, can be detected using CT imaging. Although CF is a life limiting disease and therefore the risk of radiation-induced cancer is reduced, CF life expectancy continues to improve. Median age of death from CF is rising, with an increase of 0.543 life years per year across the US, England and Wales between 1972-2009. As such, there is an ongoing requirement to design and implement strategies aimed at reducing the effective doses incurred by patients undergoing CT without sacrificing diagnostic capabilities.

With children most susceptible to potential radiation induced malignancy, the need to justify CT imaging and the requirement to use the lowest radiation dose achievable has never been greater. This is particularly relevant for those children with CF, due to early illness onset and an increased risk of high cumulative radiation exposure throughout their lifelong illness. Radiologists must aim to limit radiation exposure as far as possible, whilst maintaining optimum quality of pulmonary imaging studies.

As demonstrated in the “Image wisely” and “Image gently” campaigns, a three-tiered approach to radiation protection is advised: the as low as reasonably achievable principle, justification of the imaging procedure and dose limitation.

CT Radiation Dose Reduction Strategies

A number of scanning parameters affect CT associated radiation dose including: tube current, tube voltage, scanning length, collimation, table speed, table pitch, gantry rotation time and shielding.

Image noise is inversely related to X-ray beam energy and is a significant predictor of image quality. Whilst alterations to tube current and tube voltage have direct effects on radiation dose, they also affect image noise.

Reduction in tube current is the most practical means of reducing CT radiation dose. A 50% reduction in tube current results in a 50% dose reduction [20]. As this process increases image noise, it must be validated prior to clinical use. High-resolution CT images of lung parenchyma obtained at 40 mAs yield anatomic detail equivalent to that achieved at 400 mAs, without a significant difference in subjective image quality [21].

Tube voltage affects both image noise and tissue contrast by virtue of the quantity of radiation administered. In abdominal CT, the majority of scans can be optimally performed at 120 kVp instead of 140 kVp, producing a 20%-40% reduction in radiation dose [22]. However, scanning parameters must be guided by individual patient characteristics, including body mass index, when attempting to

reduce radiation dose. This is particularly important when imaging children, and has been addressed by the development of individualised weight-based protocols.

Patient positioning relative to the isocenter affects both patient dose and image noise [23]. Optimisation of image quality and radiation dose is achieved in part by positioning the patient at the isocenter of the CT gantry. Patient centering within the CT scanner is typically achieved through adjustment of the patient and table position, by the radiograper, with the assistance of laser guides. Additional necessary adjustments can be performed once the initial scout images have been obtained. Potential for centering error increases with more complex CT examinations; isocenter misalignment has been demonstrated to be greater during CT colonography compared with abdominopelvic CT or CT-Kidneys, Ureters, Bladder [24]. Going forward, automated patient centering solutions demonstrate potential for improved patient positioning.

In helical scanners, table speed, pitch and beam collimation are intertwined parameters which contribute to image diagnostic quality. Faster table speed produces a higher pitch, and whilst scanning at a higher pitch is more dose effective, image quality can be compromised. Technological advances have resulted in sixty-four slice scanners acquiring whole body scans in less than 10 seconds, and static organ imaging in 1 second. Importantly, radiation exposure decreases with decreased tube rotation time.

Further technological advances aimed at dose optimisation include automatic exposure control. Automatic tube current modulation, a type of automatic exposure control, works on the basis that pixel noise on CT scanning is attributable to quantum (random) noise in the image projections. Quantum noise projections can be standardised, so that a minimum desired level of noise is achieved and dose efficiency is improved, by constantly modifying tube current in accordance with the anatomic region being scanned [20]. For example, patients may be administered a higher dose over the region of the liver where attenuation is greater, though a lower dose in the chest where lung attenuation of the X-ray beam is less than in the abdomen. There are important caveats however; foreign objects, including metallic devices, will elicit increased radiation dose, and the adequacy of exposure control is heavily reliant on data from the planning scout acquisition radiograph. Automatic tube current modulation produces dose reduction with only minimal compromise to image quality; mean dose reduction of 22.3% for CT scanning of the neck, thorax and abdomen in children, without loss of image quality, has previously been reported [25].

Though reductions in CT radiation dose are to be welcomed, drawbacks include reduced image quality and increased image noise. This needs to be compensated for, in order that image quality is not detromentally affected. Whilst standard CT scanners reconstruct images using filtered back projection, algorithms utilising iterative reconstruction have been produced to reconstruct image data using a system of models to improve image noise. Iterative reconstruction isolates noise from CT images obtained at reduced exposure, maintaining image quality and interpretability [26], thus producing considerable radiation dose reduction whilst preserving satisfactory image quality when compared with traditional filtered back projection. Iterative reconstruction operates on list-mode data as opposed to histogrammed projection data and can produce images following one pass through the scan [27]. This creates a shorter scanning time, and produces a reduction in CT Thorax associated radiation exposure almost to levels approaching that of a chest radiograph [28].

Iterative reconstruction techniques significantly decrease subjective and quantitative image noise on both standard and reduced dose thoracic CT. Without compromising image quality, dose reductions of up to 80% for thoracic CT can be achieved using adaptive statistical iterative reconstruction (GE Healthcare, MI, USA) [29]. In practice, this strategy can be applied when imaging children with CF, as significant reductions in radiation dose can be achieved, without major compromise in image quality.

More advanced forms of iterative reconstruction use “pure” iterative reconstruction such as model-based iterative reconstruction. Pure iterative reconstruction produces high quality images, with dose

reductions in excess of 80% expected [30]. Model-based iterative reconstruction enables ultra-low dose thoracic imaging, with maintenance of image quality at doses approaching that of a chest radiograph [31]. As an example, Figure 1 compares images obtained with standard high-resolution CT, with low dose CT images reconstructed with model-based iterative reconstruction producing significant reductions in radiation dose exposure. The prolonged processing time of iterative reconstruction limits its value in some practices. However, in the context of the paediatric CF population, with outpatient imaging performed for evaluation of chronic disease, the benefit of reduced radiation dose far outweighs the time required for image reconstruction.

When applied to thoracic imaging in CF patients, iterative reconstruction has facilitated contiguous/spiral chest imaging at plain chest radiography doses. This improves scanning time and obviates the need for recurrent patient breath-holds, which has potential for error in the setting of sequential imaging. Contiguous CT scanning through the chest enables 3D reconstruction which facilitates more comprehensive characterisation of distribution of lung changes, offers the potential for more robust comparison with previous chest imaging examinations, and can provide the facility for virtual bronchoscopy. Thoracic CT images reconstructed with adaptive statistical iterative reconstruction can remain diagnostically satisfactory when obtained at 40 mAs/3.5 mGy [32]. Downsides to datasets reconstructed with iterative reconstruction include the waxy impasto texture of the image, which is not to the liking of every radiologist.

Additional methods of radiation dose reduction are on the horizon. Scientists are looking towards artificial intelligence as a means of improving many aspects of medical imaging. Furthermore, manufacturers are investing heavily in this area. A recent product of this investment has been the use of artificial intelligence for the purpose of dose reduction by the removal of image noise from low dose CT datasets acquired using filtered back projection (TrueFidelity; GE Healthcare, MI, USA). In addition to reducing image noise, these low dose datasets have the benefit of maintaining a more familiar image ‘feel’ or texture compared with iterative reconstruction images.

Dose optimisation aims to produce a diagnostic image with the least amount of radiation possible. Secondary to the high inherent contrast and low radiation absorption of the lung, thoracic CT is highly suited to dose optimisation protocols [33]. In assessing the use of low dose protocols for thin-section CT in the evaluation of CF, research has concluded that low dose thin-section CT is an appropriate option for accurate evaluation of pathological changes in the CF lung, even at doses appoaching that of a chest radiograph [34]. Thin-section protocols show promise for use in children with CF, as an effective dose reduction of 26% can be achieved without compromising image quality [35]. Given the potential for high cumulative exposure to radiation, modified low-dose CT protocols must be considered for children with a known CF diagnosis.

The majority of CF CT thoracic protocols include both inspiratory and expiratory images. Structural changes, including bronchiectasis and peribronchial thickening are best observed with end-inspiratory images. End-expiratory CT scans are useful in the assessment of trapped air [36], an early feature in the identification of CF lung disease [37]. In evaluating a cohort of CF patients which did not include children aged less than 6 years, end-inspiratory and end-expiratory CT scores have been found to correspond closely [38]. Should low-dose (0.4 mSv, 110 kV) end-expiratory CT alone be sufficient to assess for CF related structural abnormalities, a reduction in CT radiation dose of up to 75% could be expected, whilst maintaining high inter-observer correlation of CF CT scores. Of note however, trapped air and bronchiectasis remain the more commonly reported structural abnormalities in the young CF population. Though end-expiratory CT is optimum in the evaluation of trapped air, the detection of bronchiectasis, present in at least one-third of young CF patients, is significantly different depending on the use of either end-inspiratory or end-expiratory images across a cohort of patients aged 1.4-3.6 years [39]. Such functional type assessments of the lung

would be better performed using alternative imaging techniques, such as magnetic resonance imaging, where possible.

Limiting Radiation Exposure

Radiation exposure must be considered when selecting diagnostic imaging studies. In essence, the optimal method for reducing radiation dose is to avoid unnecessary CT imaging, and instead seek alternative imaging modalities that either reduce or avoid radiation exposure.

Thoracic imaging accounts for 46.9% of total cumulative effective dose in CF patients [5]. This is followed by abdominopelvic imaging, responsible for a surprisingly high 42.9% of cumulative effective dose. Though increased utilisation of CT imaging for the evaluation of abdominal complications in CF may account for these figures, it may also signal a trend to image the thorax, abdomen and pelvis together routinely, as opposed to chest only. Close observation of these changing trends in radiation exposure among CF patients is required.

Additionally, there is often a tendency to image beyond the defined region of interest. As a consequence, scanning length increases, with patients receiving unnecessarily increased radiation doses. Furthermore, radiosensitive structures often lie adjacent to the beam pathway. Adequate shielding is vital, particularly for the paediatric population whose organs are inherently more radiosensitive. In shielding regions of the body not directly in the path of the X-ray beam during CT with lead protection, thyroid and breast radiation doses are reduced by an average of 45% and 76%, respectively. In the particularly vulnerable CF population, where an intrinsic risk of malignancy is coupled with repetitive ionising radiation exposure, this is of heightened importance. It is essential for referring physicians to be mindful of these issues when requesting CT scans, and for operators to restrict CT examinations to the anatomical area that requires investigation.

Advances in the use of magnetic resonance imaging for the assessment of lung disease in the setting of CF have shown great progress. Whilst CT is considered the gold standard examination for evaluation of CF lung disease, magnetic resonance imaging has potential in the monitoring of disease progression and response to treatment. Though superior in the assessment of functional change such as alterations in pulmonary perfusion, magnetic resonance imaging is less sensitive for detection of small airways disease compared with CT [40]; peripheral morphological changes including discrete small airway mucous plugging and peripheral bronchiectasis without bronchial wall thickening are poorly visualised. Furthermore, air trapping, in addition to mosaic perfusion, a frequent CT finding in CF patients, is challenging to diagnose on magnetic resonance imaging. New advances in the use of magnetic resonance imaging for evaluation of CF include the use of inhaled agents such as hyperpolarised helium [41] or xenon. These agents provide functional information regarding gas exchange. Obvious limitations for inclusion into regular practice include availability, cost and time for acquisition.

The responsibility of ensuring that the immediate benefits of CT are likely to outweigh the long-term risks is multidisciplinary. Radiologists, radiographers and referring clinicians should consider all available options prior to proceeding to CT imaging. This can be of particular importance outside specialist paediatric centres; Larson *et al* demonstrated that only 15% of paediatric CT studies were performed in paediatric centres [42]. CT is utilised much more frequently outside specialist paediatric centres, where radiological and technical dose reduction expertise in the creation, assessment and validation of low dose imaging techniques may be more readily available.

CT Radiation Dose Tracking

Patient radiation dose tracking, an initiative that automatically records all medical radiation exposures received by patients, has been developed. Data can be included in individual radiology reports and medical files, and can be used to calculate lifetime cumulative exposures.

Whilst no regulations are yet established to record and monitor cumulative lifetime radiation exposure, the scope to develop a CT dose record incorporated within personal health records is potentially practice changing. As an individual, dose records identify those patients at risk of high cumulative radiation doses. Through programmes of continuous radiation dose monitoring, with secondary corrective actions, a significant reduction in dose length product has been demonstrated across both paediatric and adult populations [43].

Furthermore, radiation dose tracking can encourage adoption of best practices among medical institutions that utilise ionising radiation. Maintenance of a dose index register, and sharing of data between facilities, allows institutions to compare their performance with peers regarding the radiation dose used for common imaging examinations [44]. This practice has been encouraged by the American College of Radiology who, in 2011, launched a dose index registry. This offers a valuable tool for institutions to benchmark their radiation doses for medical imaging, and to highlight areas where improvements could be made. Additionally, data inclusion into registries will assist in advancing epidemiological research.

CF Scoring Systems in Radiology

Thought to have good correlation with pulmonary function, the Brasfield scoring system is a CF scoring system based solely on conventional chest radiograph findings [45]. Subsequent acknowledgement of the potential benefit of CT in the evaluation of CF pulmonary disease led to publication of the Bhalla scoring system in 1991, the first high-resolution CT scoring system for CF [35]. Various further scoring systems have followed, with more recent CT studies inclusive of expiratory images, thought to reflect small airway disease typical of early stage CF lung disease [15]. The Australian Respiratory Early Surveillance Team for CF, in collaboration with colleagues in Rotterdam, have developed the PRAGMA-CF CT score, a reproducible outcome measure for evaluating the severity of CF lung disease in children younger than 6 years [46]. Across almost all scoring systems, mucous plugging and bronchiectasis are allocated highest weighting, recognising these as hallmark features of CF [47].

Scoring systems are sensitive in the detection of early CF related pulmonary disease and well suited to monitoring disease progression. Furthermore, in demonstrating a dissociation between pulmonary function tests and CT score in around half of patients, longitudinal studies have confirmed that CT scoring provides additional information on the progression of CF lung disease not detected by pulmonary function tests [10,12]. We have observed that there is a requirement for an updated version of these scoring systems, capable of better reflecting subtle changes in CF related lung disease demonstrated on CT post initiation of new disease modifying medications, which currently are not accounted for by traditional scoring systems.

CT Image Quality in Children

As a significant proportion of CF patients are children, compliance with scanning methods can be difficult to achieve. A strong positive correlation between age and ability to cooperate with breath holding commands for CT studies has been demonstrated, such that from the age of 5-6 years, the majority of children will be in a position to follow necessary instructions [48]. For children less than 5 years of age, sedation may be necessary if multiple scans are to be avoided secondary to movement or inability to comply with instructions. When the lowest milliamperage settings are applied during high-resolution CT scanning, cooperation has a crucial role in reducing streak artefact, and thereby determining overall image quality. Rogalla *et al* described acceptable image quality of helical thoracic CT scans in children using 25mAs [49]. Lucaya *et al* further demonstrated that although artefact incidence is greater in 34mAs images compared with 50mAs images, in a cohort of cooperative children scanned with 34mAs, artefact is limited to a few slices [48]. Slight differences, including subtle distortion of peripheral structures and fissures, were evident on comparing scans obtained with 34mAs and 180mAs settings.

Diagnosis of Cystic Fibrosis in Adults

Newborn screening for CF is a well established public health strategy, with a gradual uptake in national CF newborn screening programmes across Europe in recent years. Prior to widespread rollout of newborn screening programmes, just under 8% of CF patients were diagnosed in adulthood [50]. Adult screening for CF is not routine, with diagnostic testing conducted in cases clinically suspicious for CF. Indeed, the majority of diagnostic testing in adults, accounting for 39% of cases, is triggered by pulmonary symptoms. Combination pulmonary/gastrointestinal symptoms prompt 22% of tests [50].

Those individuals receiving a late CF diagnosis typically experience fewer complications, with reduced hospitalisations as a result. Severity of pulmonary disease at diagnosis is highly variable, with up to 30% of patients having normal chest radiographs [50]. 50% of patients will maintain a forced expiratory volume in one second (FEV1) of greater than 87% of predicted value.

Across a cohort of ten CF patients first diagnosed in adult life, two had normal high-resolution CT thoracic scans [51]. Features reflecting early pulmonary disease were evident in all other cases. Though the severity of pulmonary disease seen in CF patients receiving a diagnosis as adults is typically less than those who obtain a diagnosis as infants, the extent of bronchiectasis can be pronounced [52]. These patients will have commonly received prior diagnoses of asthma, chronic bronchitis or emphysema. Only occasionally will patients receive diagnoses of apparent single-organ manifestations, including idiopathic pancreatitis, with minimal involvement of the respiratory tract.

Health Information

The United Nations Scientific Committee on the Effects of Atomic Radiation has reported uncertainty in relation to the health effects of low dose radiation. At doses less than 100 mSv, the risk of radiation induced cancer is thought to be too small to be distinguishable from other risk factors for cancer development [53]. However, a retrospective cohort study evaluating the risk of leukaemia and brain tumours associated with CT scans performed during childhood observed that in the 10 years following first CT scan undertaken in patients younger than 10 years, one excess case of leukaemia and one excess case of a brain tumour per 10,000 head CT scans occurred [54].

In clinical practice, dialogue surrounding risk is difficult. Conversations regarding medical radiation even more so; precise calculation of both the probability of harm and potential severity of that harm is almost impossible. Only approximations of radiation dose can be provided to patients prior to scanning. Furthermore, data regarding radiation induced malignancy is population based as opposed to individual calculated risk. Given the latency of radiation induced cancer is 10-20 years, the effects may not become apparent for decades, if at all.

Increased media reporting on the potential risks of low dose ionising radiation from medical imaging have made this a complicated process for parents. This is compounded by the relatively high volume of inaccurate information relating to CT associated radiation exposure found on Internet searches [55]. Assessment of Internet searches for information regarding radiation safety demonstrated that the information provided is only accurate on two thirds of webpages. This highlights the need for communication and education of children and their parents with regard to imaging techniques, their benefits and downsides.

Based on current available evidence, data regarding diagnostic radiation carcinogenesis remains too indeterminate to justify a formal consent process [56]. Until this is further delineated, it will remain impossible to undertake a risk benefit calculation with sufficient certainty to warrant informed consent. Instead, a move from informed consent to informed decision making is to be encouraged, permitting patients, and parents of paediatric patients, to make a decision based on the known, whilst always being aware of the potential unknown. This will promote the decision making process as a path towards fostering patient involvement, as opposed to fulfilling administrative requirements or taking precautions against liability.

Conclusion

Children with CF require lifelong radiological imaging and CT is likely to continue to play an important role. Given the increasing life expectancy for this patient cohort, control of cumulative radiation exposure is now of utmost importance. Dose optimisation strategies, including improvements to CT protocols and patient-specific dosing guidelines, are necessary to minimise radiation exposure in children. Development of ultra-low dose CT protocols with model based iterative reconstruction has facilitated pulmonary imaging at radiation doses similar to those used in chest radiography, and artificial intelligence has the potential to further advance research in this area. Ongoing image optimisation is vital to ensure that the beneficial effects of CT can be realised at the lowest radiation dose possible, with minimisation of potential for undesired ill effects. Future improvements in dose reduction strategies must continue to balance image quality with diagnostic acceptability.

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Figures

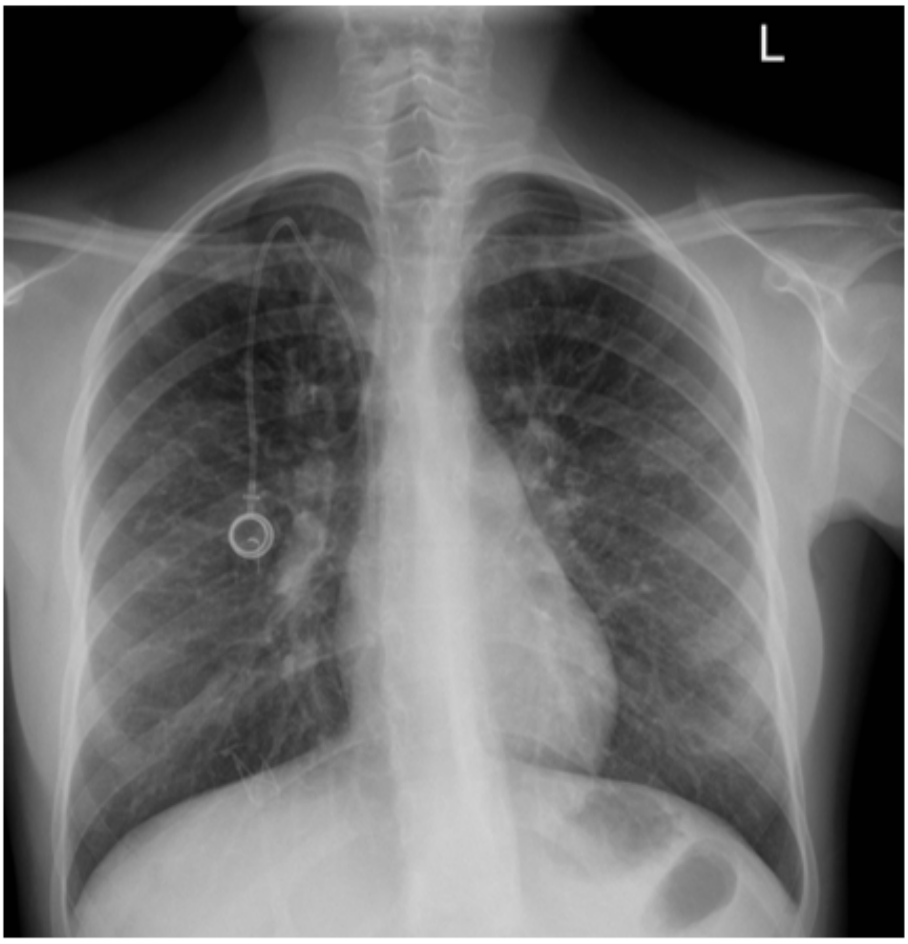
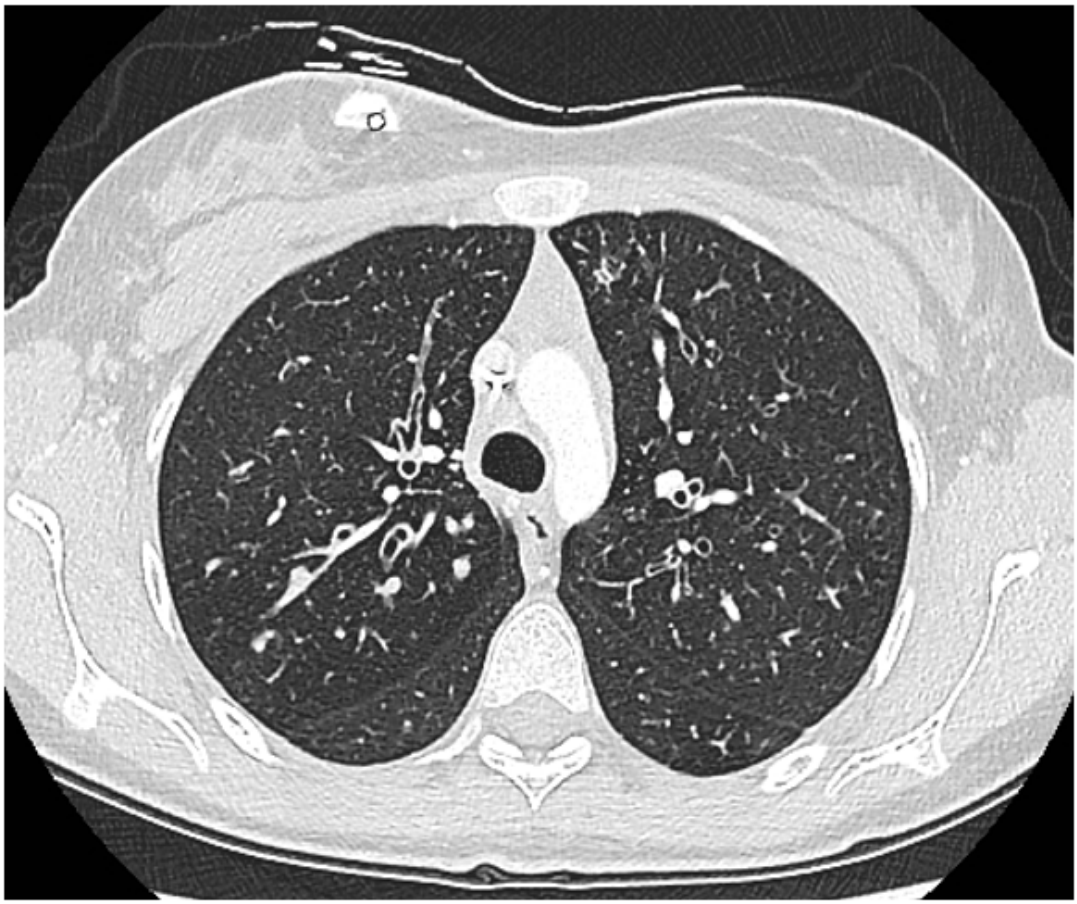


Fig. 1 (a)



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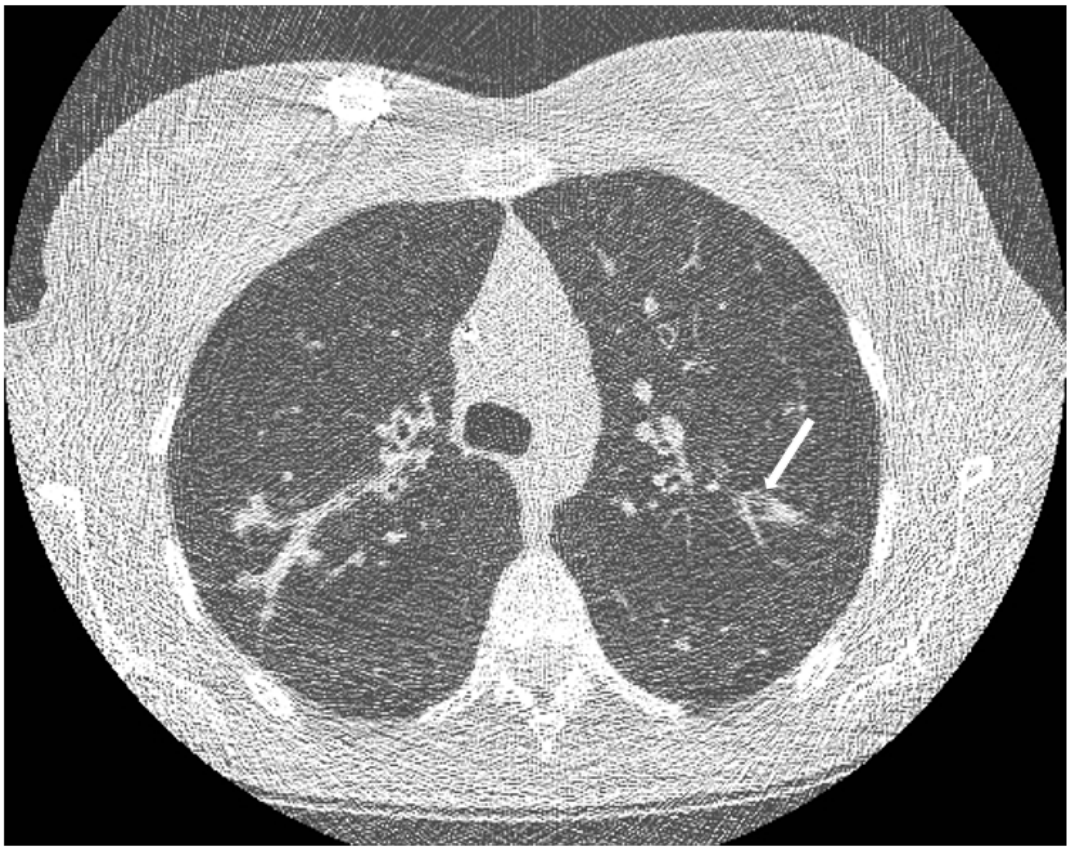

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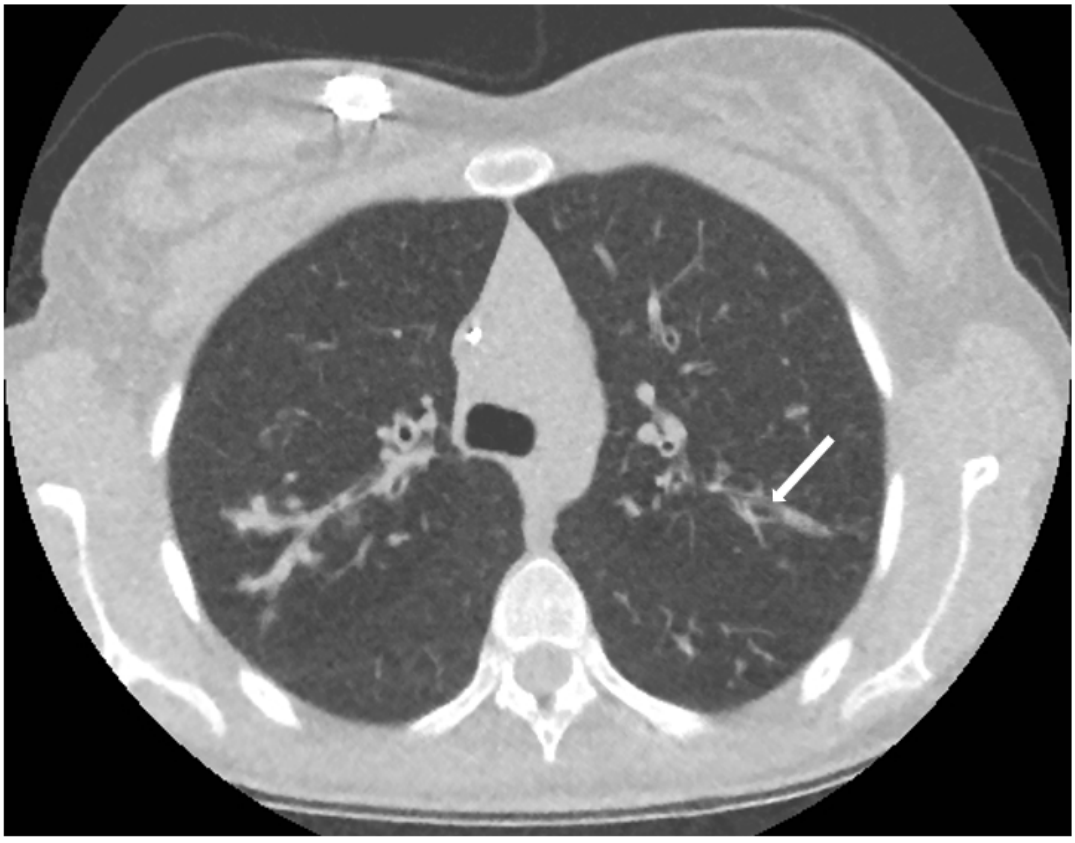

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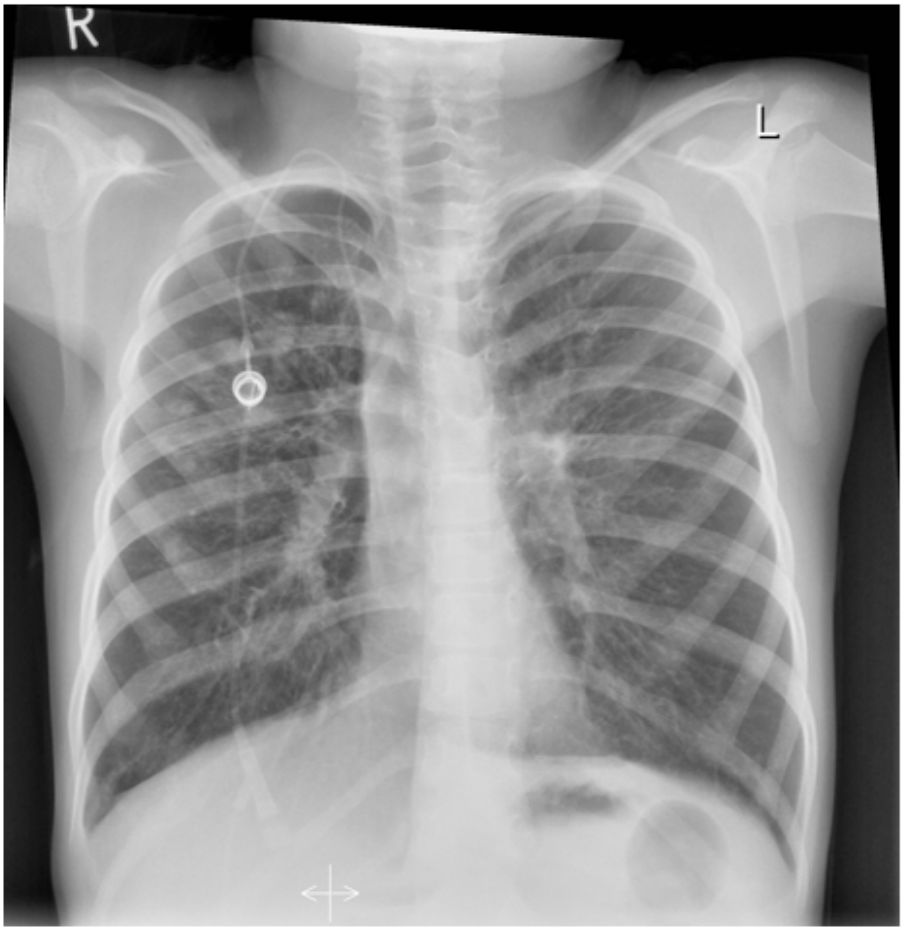

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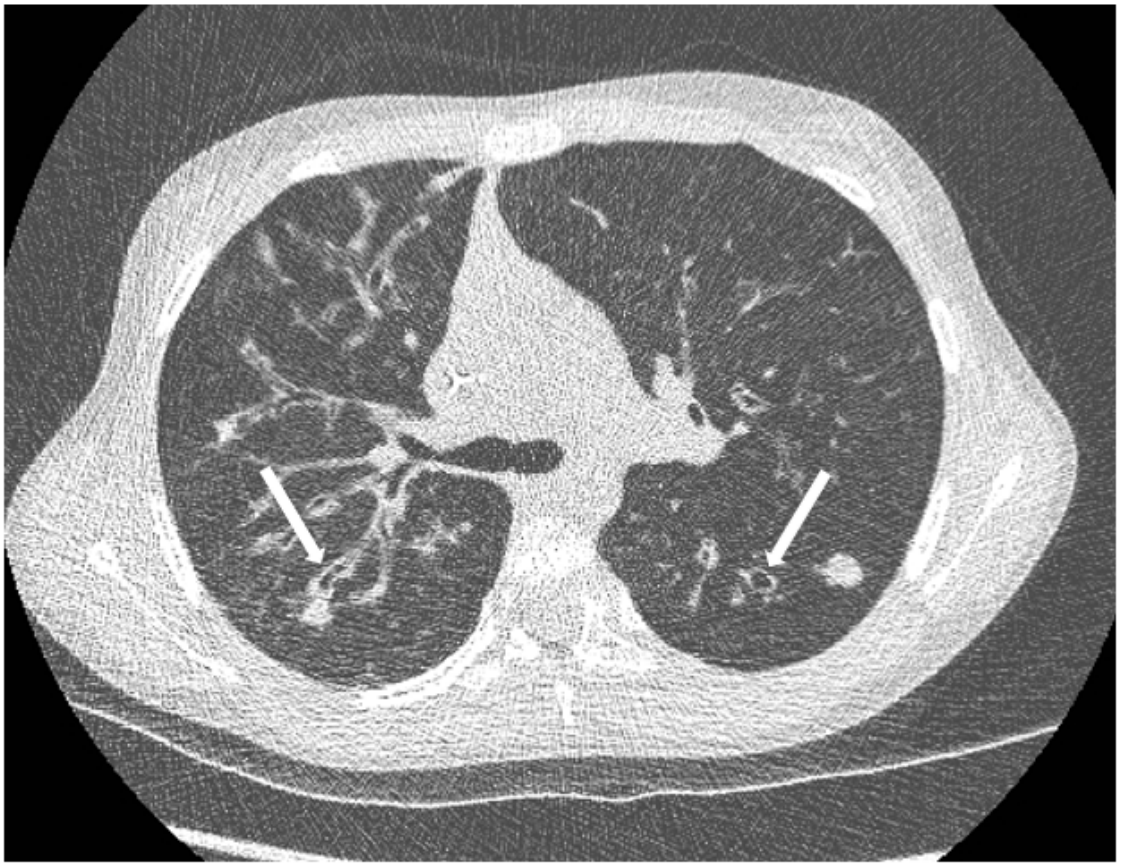

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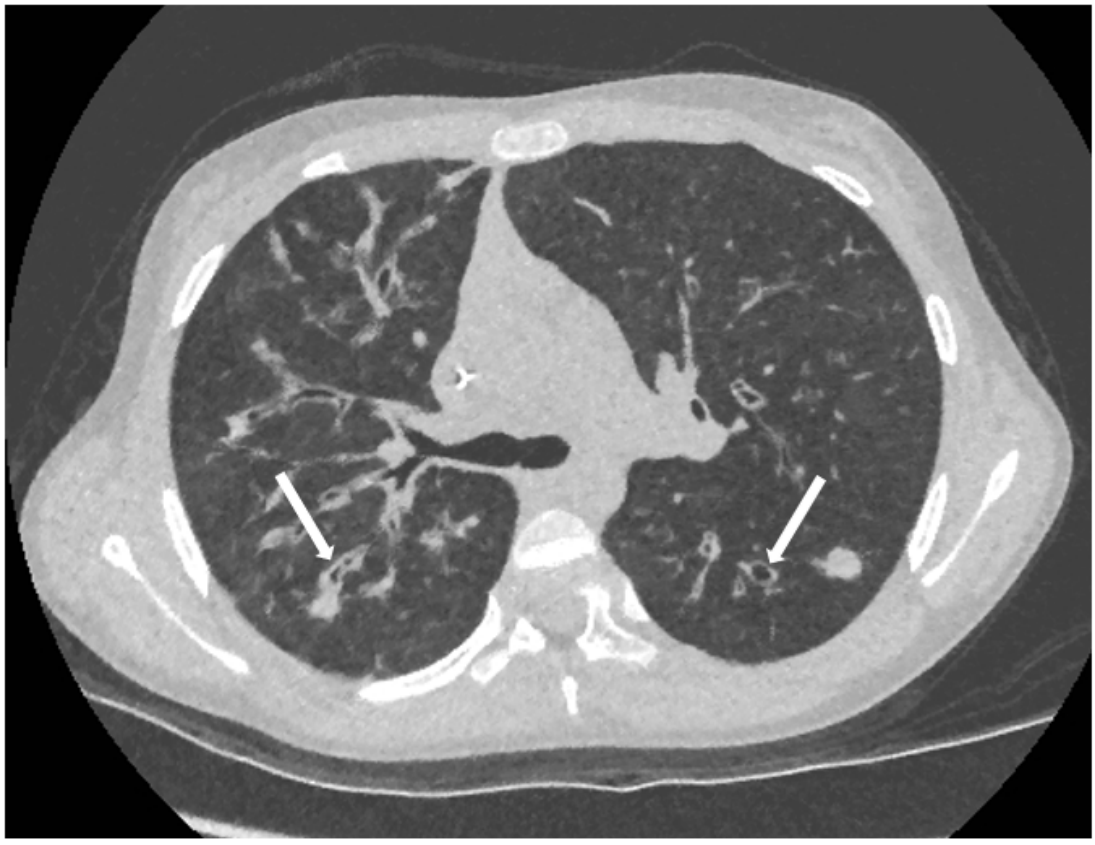

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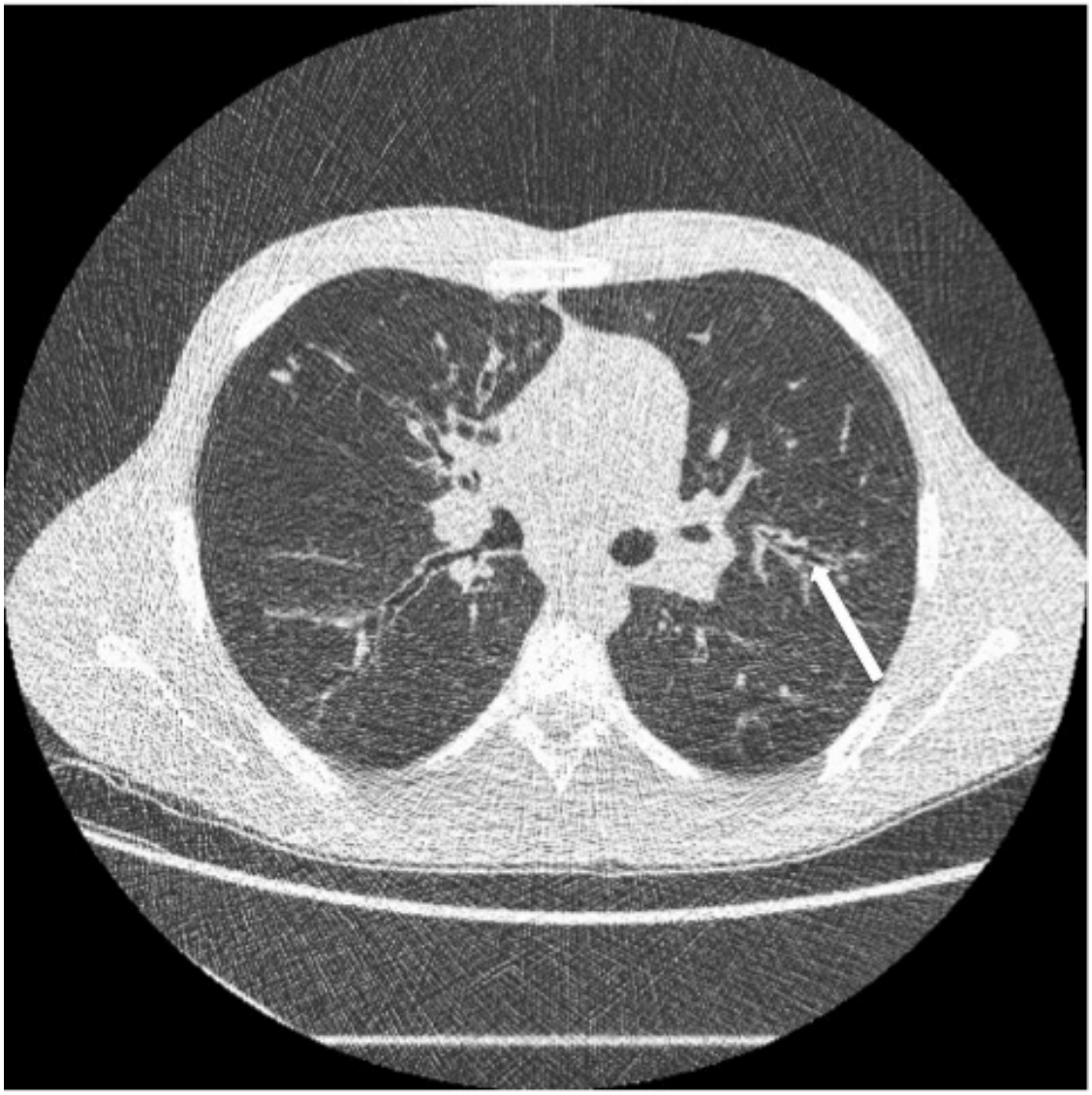

Fig. 3 (a)

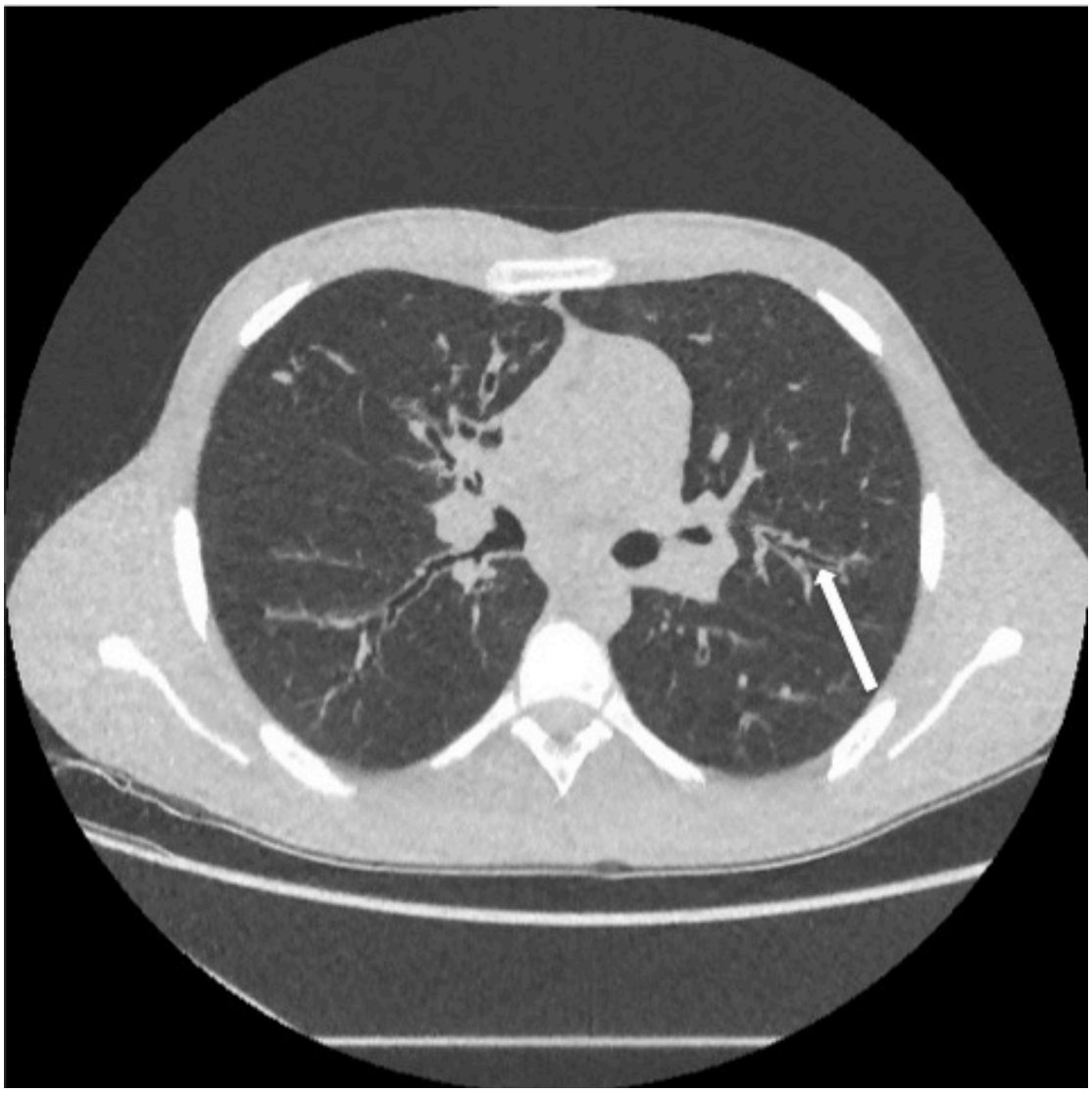

Fig. 3 (b)

Legends

Fig 1: Radiology images in a 16-year-old female child with CF, receiving treatment with Lumacaftor/Ivacaftor combination therapy (Orkambi; Vertex Pharmaceuticals, MA, USA).
Chest radiograph **(a)** demonstrates bilateral airway thickening and dilatation, consistent with CF bronchiectasis. There is an implanted central venous catheter present.
CT **(b-d)** axial slices, taken above the level of the carina for comparison, demonstrating established bronchiectasis with significant mucous plugging; **(b)** CT Thorax with contrast demonstrating features of CF with excellent image quality. Total examination dose length product for CT Thorax was 119.66 mGy-cm; **(c)** Ultra-low dose CT Thorax in the same patient, now aged 17 years, reconstructed using filtered back projection. Poor image quality is demonstrated. Total examination dose length product of 4.31 mGy-cm; **(d)** The same ultra-low dose CT Thorax, this time reconstructed using model based iterative reconstruction, Veo (GE Healthcare, MI, USA), 3 mm axial slice. Total examination dose length product of 4.31 mGy-cm. Image quality is inferior to that of the conventional dose examination, but sufficient for diagnosis even when obtained at doses similar to a chest radiograph. Peripheral regions of bronchiectatic change are well demonstrated (arrows), and mucous plugging is evident.

Fig 2: Radiology images in a 9-year-old female child with CF, receiving treatment with Lumacaftor/Ivacaftor combination therapy (Orkambi; Vertex Pharmaceuticals, MA, USA).
Chest radiograph **(a)** demonstrates bilateral airway thickening, consistent with CF bronchiectasis. The central venous catheter is appropriately positioned.
Ultra-low dose axial CT **(b-c)** images, taken at the level of the carina for comparison. Airway thickening, mosaic attenuation, mucous plugging and mid to upper zone predominant bronchiectasis are demonstrated (arrows). Total examination dose length product of 5.15 mGy-cm. Images reconstructed with **(b)** filtered back projection; and **(c)** model based iterative reconstruction, Veo (GE Healthcare, MI, USA). Image quality is far superior on the images reconstructed with model based iterative reconstruction. In particular, the quantity of image noise has been markedly reduced on the image reconstructed with model based iterative reconstruction.

Fig 3: Ultra-low dose CT images in a male CF patient, aged 17 years, receiving treatment with Lumacaftor/Ivacaftor combination therapy (Orkambi; Vertex Pharmaceuticals, MA, USA).
CT axial sections **(a, b)** taken below the level of the carina for comparison, demonstrating bilateral cystic bronchiectatic changes (arrows) and bronchial wall thickening. Total examination dose length product was 5.95 mGy-cm. Images reconstructed with **(a)** filtered back projection; and **(b)** model based iterative reconstruction, Veo (GE Healthcare, MI, USA), 3mm axial slice, at the same radiation dose. Image quality is far superior on the data reconstructed using model based iterative reconstruction, facilitating more confident radiological assessment.