CASE STUDY · CARDIOVASCULAR & THORACIC

International Phase III Cystic Fibrosis Trial With Structured Chest CT Scoring

International multicenter Phase III · Chest CT, chest radiography · Bronchiectasis, mucus plugging and air trapping scores

Challenge

Intrinsic Imaging supported this study’s imaging activities, addressing the scientific and operational considerations that inform the work of an imaging CRO and imaging core lab. An international Phase III trial of an investigational drug for cystic fibrosis used chest imaging to assess the treatment's effect on lung pathophysiology. Structured CT scoring of bronchiectasis, mucus plugging, peribronchial thickening, parenchymal opacity and hyperinflation is reader-intensive and subjective, and in a population that includes children, radiation dose and breath-hold capability constrain acquisition.

The sponsor needed a scoring system applied consistently across readers and sites, a low-dose protocol with inspiratory and expiratory phases acceptable for pediatric participants, and documentation of reader reproducibility to support a structural endpoint in a registration trial. Structural abnormalities provide information about pulmonary disease that is distinct from symptoms or physiological performance, but their interpretation depends on how consistently the lungs are inflated during imaging. Incomplete inspiration or expiration can alter the apparent extent of disease. This makes acquisition quality especially consequential when small longitudinal score differences are being considered as evidence of treatment response.

Intrinsic Imaging’s Solution

Intrinsic Imaging developed the imaging charter with a low-dose chest CT protocol including inspiratory and expiratory acquisitions, age-adjusted dose parameters and spirometer-guided or coached breath-hold technique, and qualified sites with test acquisitions reviewed for inspiration level and motion. The inspiratory and expiratory acquisitions address complementary aspects of lung structure and ventilation, rather than serving as interchangeable views. Age-adjusted acquisition parameters reflect the need to balance diagnostic information with radiation exposure in a pediatric population. Reviewing breath-hold execution at qualification addresses a practical source of variability that reader standardization alone cannot resolve.

A dedicated team of thoracic radiologists scored each examination under a structured, lobe-based system covering bronchiectasis, mucus plugging, peribronchial thickening, parenchymal opacities and air trapping. Reads were blinded and independent on a prespecified double-read sample, with calibration sessions before and during the trial. Lobe-based scoring anchors observations to an anatomical framework and retains distinctions among airway, parenchymal and air-trapping components. Calibration supports a shared interpretation of score categories, while independent reads on the specified sample allow reproducibility to be examined without consensus masking initial differences. Agreement on the total score does not necessarily imply equivalent agreement for every component.

Quality control at receipt verified inspiration level and expiratory phase, and the scored dataset was delivered with component and total scores for the sponsor's structural endpoint analysis. Separate component scores help distinguish which structural features contribute to an overall assessment, avoiding the assumption that similar totals represent identical patterns of disease. Receipt checks also help identify technical explanations for apparent change before endpoint interpretation. Neither a reproducible score nor correction of acquisition deficiencies alone establishes that a structural difference corresponds to a clinically meaningful benefit.

Intrinsic Imaging’s Results

- Low-dose inspiratory and expiratory chest CT protocol implemented at 38 sites in 11 countries with age-adjusted dose parameters
- Approximately 1,300 examinations scored under a structured lobe-based system by a dedicated thoracic radiology team
- Inter-reader agreement on total CT score documented with an intraclass correlation above 0.85 on the double-read sample
- Inadequate inspiration or expiration identified at central quality control in about 7% of initial submissions and corrected through site feedback

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Read the full study online: https://intrinsicimaging.com/case-studies/respiratory-cystic-fibrosis

About Intrinsic Imaging, LLC

Intrinsic Imaging is an ISO certified medical imaging CRO and imaging core lab providing comprehensive services in support of Phase I-IV clinical trials and Class I, II, III medical device trials. Intrinsic Imaging is also a world leader in conducting Artificial Intelligence studies. With its team of more than 50 board-certified and fellowship-trained physicians, Intrinsic Imaging’s team has sub-specialization in all therapeutic areas, including Cardiovascular, Central Nervous System,Gastroenterology, Musculoskeletal, Oncology and Ophthalmology. Certified by the British Standards Institution (BSI), Intrinsic Imaging is the only company in the world to hold five ISO certifications specifically for providing imaging core lab services on clinical trials. For more information, please visit www.IntrinsicImaging.com.

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