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FROM IMAGE TO INSIGHT: A REVIEW OF DEEP LEARNING APPROACHES FOR CYSTIC FIBROSIS DETECTION IN COMPUTED TOMOGRAPHY

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Abstract

Cystic fibrosis (CF) is a genetic disease caused by mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. This disorder causes a wide range of clinical complications, primarily affecting the respiratory and digestive systems and extending its impact to other physiological areas. Early detection and careful monitoring are paramount to mitigate disease progression and improve the quality of life of individuals with CF. Computed tomography (CT), particularly high-resolution CT (HRCT), has become a key diagnostic method for detecting pulmonary manifestations of CF. However, manual analysis of CT images requires a high level of expertise and is time consuming. The combination of artificial intelligence (AI) and deep learning with CT imaging predicts significant advances in CF detection. Deep learning, a subset of AI, uses neural networks to analyse complex morphological patterns indicative of disease from large datasets. This review traces the journey from the earliest attempts to use artificial intelligence in CF detection to recent advances made using deep learning algorithms. By exploring various deep learning architectures and their integration into clinical practice, this review illuminates the potential of these new technologies to revolutionize CF detection using CT imaging. Automated and accurate analysis enabled by deep learning aims to reduce the diagnostic burden on radiologists, speed up the diagnostic process and pave the way for timely and personalized therapeutic interventions, which is in line with the ultimate goal of improving patient care.

Keywords

artificial intelligence, computed tomography, computer-aided diagnosis, cystic fibrosis, deep learning

1 Introduction

Cystic Fibrosis (CF) is a serious genetic disorder primarily impacting the respiratory and digestive systems. Originating from mutations in the CFTR gene, which encodes a crucial protein responsible for the regulation of chloride ion movement across cell membranes, CF leads to the accumulation of thick mucus secretions within the bronchial tree. This dysfunction causes recurrent respiratory infections and pancreatic insufficiency, marking a significant challenge in medical management. The prevalence of CF, notably among Caucasian populations, underscores its clinical importance, making early detection and meticulous monitoring crucial for effective disease management. Such vigilance is vital not only in alleviating disease progression but also in enhancing the life expectancy of those affected (Lukasiak, Zajac 2021).

In the realm of diagnostics, Computed Tomography (CT) plays an indispensable role in the detection and monitoring of cystic fibrosis. High-resolution CT (HRCT) in particular offers detailed images of pulmonary structures, enabling clinicians to identify characteristic CF features such as bronchiectasis, mucous impaction, and air trapping. Moreover, longitudinal CT assessments provide valuable insights into disease progression and the efficacy of therapeutic interventions, thereby equipping healthcare providers with essential information to tailor management strategies effectively (Linnane et al. 2008).

The integration of Artificial Intelligence (AI) and deep learning into medical imaging heralds a new era of diagnostic capability. Deep learning, a subfield of AI, employs intricate neural networks to analyse large datasets. In medical imaging, once trained on substantial datasets, these algorithms can identify complex morphological patterns indicative of various disease states. The application of AI and deep learning in CF detection through CT imaging offers a paradigm shift in diagnostic procedures. By facilitating automated and accurate analysis of CT scans, these technologies aim to reduce the diagnostic workload on radiologists, expedite the diagnostic process, and pave the way for timely, personalized therapeutic interventions. This aligns with the overarching goal of improving patient care, heralding a future where technology and medicine converge to enhance disease management and patient outcomes (Najjar 2023).

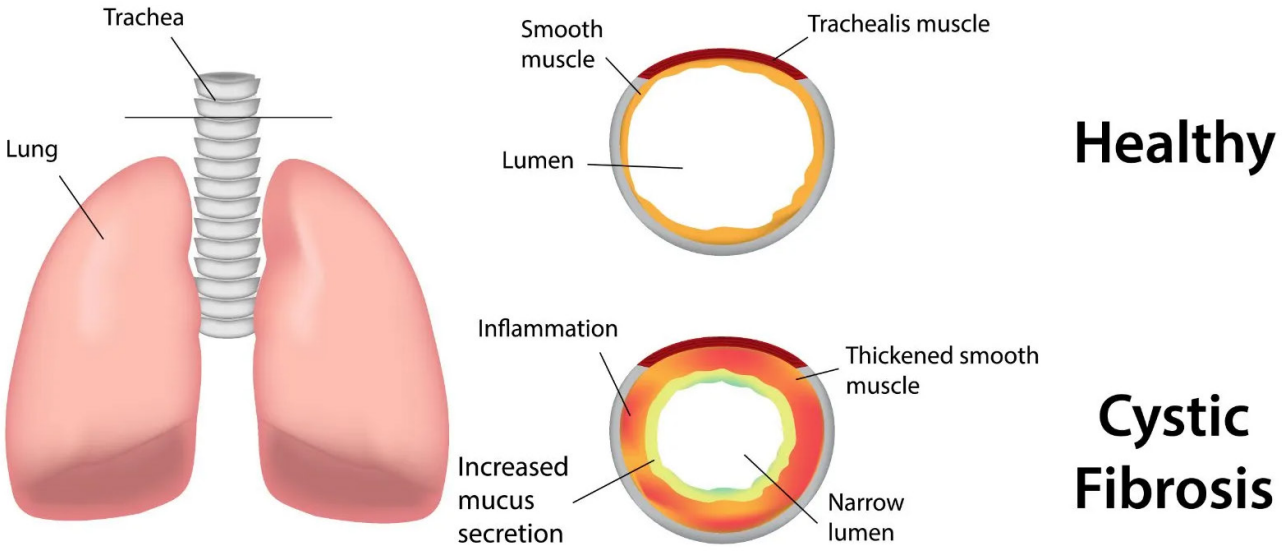

Figure 1 – Comparison of normal airway anatomy and pathological changes in cystic fibrosis. The left side shows a frontal view of the lungs and trachea, indicating a healthy airway structure. On the right, two transverse sections through the trachea are shown: the upper one illustrates a healthy airway with a well-defined lumen and smooth musculature, while the lower one illustrates a narrowed lumen, thickened musculature, excessive mucus and inflammation characteristic of cystic fibrosis.

2 Methodology of Literature Search

2.1 Database and Search Strategy

For this review, a comprehensive literature search was conducted on November 27th, 2023, using PubMed, a widely recognized database in the medical and scientific research community. The search strategy was carefully designed to capture relevant studies at the intersection of cystic fibrosis, artificial intelligence, and computed tomography. The specific keywords employed were: ("CFTR" OR "Cystic Fibrosis") AND ("Deep Learning" OR "Neural Networks" OR "artificial intelligence") AND ("Computed Tomography" OR "CT"). This combination of terms was chosen to ensure a broad yet focused retrieval of pertinent literature.

2.2 Inclusion and Exclusion Criteria

The initial search provided a total of 23 articles. To refine this pool of literature to the most relevant studies, we applied specific inclusion and exclusion criteria. The primary focus of this review was on studies directly related to cystic fibrosis. Therefore, we excluded articles that exclusively addressed non-CF bronchiectasis, as this condition, while similar, was not the primary subject of our study. Additionally, we excluded a study that focused on identifying gene targets for human splicing disorders, as it did not directly pertain to cystic fibrosis or its detection via computed tomography.

2.3 Final Selection of Studies

After applying these exclusion criteria, we narrowed down the selection to 19 studies that directly aligned with our research focus. These studies encompassed a range of approaches and findings related to the application of artificial intelligence in the detection and monitoring of cystic fibrosis using CT imaging. The final set of articles was deemed comprehensive and relevant for the purposes of this review, offering a broad perspective on the current state of research in this area.

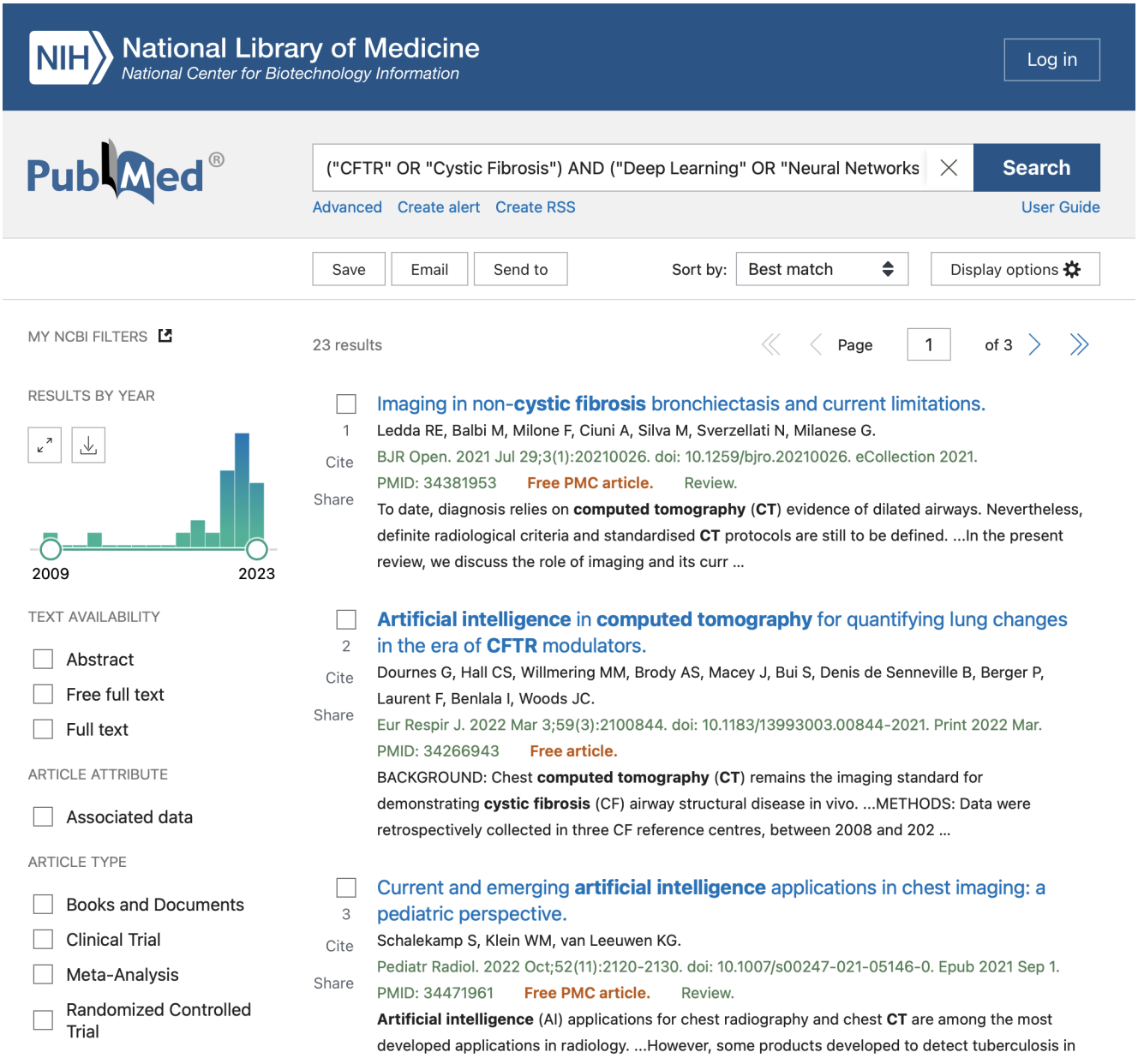

Figure 2 – Search results

Author	Year	DOI	Summary
Mumcuoglu	2009	10.1109/IEMBS.2009.5332413	A computerized method for assessing airway and vessel dimensions in paediatric CT lung images.
Bauer et al.	2012	10.1016/j.compmedimag.2012.08.001	An automated approach to model airway trees from porcine lung micro-CT scans, accurately representing airway morphology in cystic fibrosis studies.
Singh et al.	2018	10.1371/journal.pone.0204155	Designing a deep learning algorithm effectively to detect multiple abnormalities, including cystic fibrosis, in chest X-rays.
Truog	2019	10.1002/hast.1041	A discussion on the evolution of medical diagnosis from physical examination to image-based analysis, highlighting the increasing reliance on AI to manage the growing deluge of data.
Zucker et al.	2020	10.1016/j.jcf.2019.04.016	Evaluating a deep convolutional neural network model for automated Brasfield scoring of chest X-rays in cystic fibrosis patients, with comparable accuracy to pediatric radiologists.
Crowley et al.	2021	10.1097/MCP.0000000000000828	A review of pulmonary imaging techniques in cystic fibrosis, highlighting the transition from chest radiography to CT, ultra-low-dose CT and MRI, with a focus on reducing radiation exposure and improving diagnostic accuracy through deep learning algorithms.
Ram et al.	2021	10.1371/journal.pone.0248902	Evaluating a convolutional neural network model for quantifying air trapping in expiratory CT scans of cystic fibrosis patients, demonstrating effectiveness compared to traditional threshold-based methods.
Garcia-Uceda et al.	2021	10.1038/s41598-021-95364-1	A fully automated airway segmentation method for thoracic CT scans, based on a 3D U-Net architecture, validated on datasets including cystic fibrosis patients and showing high accuracy and generalizability.
Schalekamp et al.	2022	10.1007/s00247-021-05146-0	A review of AI applications in thoracic radiology, highlighting over 40 AI products for chest X-ray and CT, with a focus on adults but noting potential paediatric applications, including software under development for detecting early cystic fibrosis changes on chest CT.
Dournes et al.	2022	10.1183/13993003.00844-2021	Evaluating a fully automated scoring system for assessing CF severity using chest CT, demonstrating good accuracy, reproducibility, and correlation with clinical outcomes, especially in evaluating treatment effects with lumacaftor/ivacaftor.
Aliboni et al.	2022	10.1097/RTI.0000000000000588	Evaluating a convolutional neural network for automatic detection and classification of bronchiectasis types in CT images, demonstrating high accuracy in distinguishing between healthy tissue and bronchiectasis with reduced interobserver variability.
Ciet et al.	2022	10.1183/16000617.0173-2021	A consensus of CF experts highlights the need for guidelines on imaging in cystic fibrosis, advocating for routine CT and MRI use, and considering AI for quantitative analysis, but finds limited evidence for lung ultrasound.
Beswick et al.	2022	10.1513/AnnalsATS.202101-057OC	ETI therapy in cystic fibrosis patients showed substantial improvements in sinus CT opacification and productivity loss, along with meaningful enhancements in sinonasal quality of life and health utility, with most benefits appearing quickly and persisting throughout the study.
Pusterla et al.	2022	10.1002/mrm.29184	Evaluating a recurrent neural network to segments pulmonary lobes in MRI images of pediatric cystic fibrosis patients, demonstrating potential for automated lung segmentation in various MRI examinations.
Chang et al.	2022	10.3760/cma.j.cn112137-20220413-00790	The use of AI in identifying airway mucus plugs via chest CT has improved efficiency and accuracy in respiratory diseases like cystic fibrosis, COPD, and bronchial asthma, marking a significant advancement in clinical applications.

Chen et al.	2023	10.1016/j.jcf.2023.05.013	An automated bronchus and artery analysis showed that 48-week treatment with inhaled hypertonic saline positively impacted bronchial lumen and wall thickness in children with cystic fibrosis, compared to isotonic saline, without affecting the progression of bronchial widening.
Ciet et al.	2023	10.1007/s00247-022-05522-4	A review on imaging for cystic fibrosis highlights advancements like AI image analysis and photon-counting detector CT, enhancing the effectiveness of chest radiography and CT while minimizing radiation exposure.
Lv et al.	2023	10.1136/thorax-2023-220021	An AI-based algorithm effectively analyzes bronchus-artery pairs in chest CT scans of cystic fibrosis patients, allowing for automatic detection and monitoring of bronchial wall thickening and widening.
Blaskovic et al.	2023	10.3390/cells12192375	A new protocol using synchrotron X-ray tomography and machine learning effectively analyzes lung airspaces, revealing structural changes in cystic fibrosis-like lung diseases and emphysema in mice.

Table 1 – Search results and brief summary of articles 3 Key Outcomes

3.1 Early Applications in Paediatric Radiology

The initial exploration of artificial intelligence (AI) in the realm of pediatric radiology for cystic fibrosis (CF) detection has shown promising potential. A key focus in this field is on harnessing AI to identify early signs of CF-related changes in chest CT scans of pediatric patients. This is particularly important given the early onset of airway (AW) inflammation and structural damage in CF, often occurring even in asymptomatic infants and children.

In Mumcuoglu (2009), a computerized method was developed to assess AW and vessel (V) dimensions from axial CT lung images. This method, utilizing a full-width-half-max (FWHM)-based automatic AW and V size measurement approach, allows for rapid, efficient, and accurate evaluation of the airway structures in infants and children with CF. What makes this method stand out is its minimal requirement for user input, only needing an approximate center marking of AW and V by an expert. Mumcuoglu's study tested this method on a small patient population of 4 infants and 4 children with mild CF-related lung disease. The results demonstrated a good correlation with measurements made by experienced observers and with spirometric measurements. This indicates the potential of the method as a useful tool for early detection and assessment of airway disease in pediatric CF patients, which is crucial for timely intervention and management.

3.2 Evolution into Deep Learning Approaches

Recent advancements have taken a significant leap forward, utilizing deep learning algorithms to quantify lung alterations pertinent to cystic fibrosis via computed tomography. This shift towards deep learning is pivotal as it facilitates automated volumetric quantification of CF-related changes in the lungs. Such advancements could potentially augment, or even replace, the conventional visual scoring systems which are not only time--consuming but also require extensive training and often suffer from a lack of high reproducibility (Dournes et al. 2022).

Garcia-Uceda et al. (2021) presentsa fully automatic airway segmentation method for thoracic CT scans, utilizing a 3D U-Net architecture. Their approach simplifies the processing of large 3D image patches, sometimes encompassing entire lungs, in a single network pass, enhancing both efficiency and robustness. This method has been rigorously validated across diverse datasets, including those with paediatric CF patients, proving its high accuracy and generalizability—even achieving one of the highest sensitivity scores in the EXACT'09 test set while maintaining good specificity.

Similarly, Pusterla et al. (2022) have introduced an innovative workflow using a recurrent neural network (RNN) for pulmonary lobe segmentation in MR images, trained on chest CT datasets. Their method converts CT-based segmentations to match 2D MRI data, indicating a significant advance in the use of MRI in paediatric CF patients. The RNN achieved impressive accuracy, with Dice similarity coefficients and Hausdorff distances indicating high agreement with manual segmentations. This suggests a promising future where AI can provide automated, accurate lobe segmentation across various lung MRI examinations and quantitative analyses.

3.3 Algorithm Development and Performance

In the realm of algorithm development, there have been notable strides in creating models capable of automating the volumetric quantification of cystic fibrosis-related lung changes. For instance, certain algorithms can now assess an entire lung, potentially improving upon the conventional visual scoring systems. The aim is to develop algorithms with high reliability in identifying and quantifying hallmark CF features like bronchiectasis, mucous impaction, and air trapping in CT images (Rea et al. 2023).

Bauer et al. (2012) introduced an automated approach to model airway trees from porcine lung micro-CT scans, which is vital for studying lung diseases that affect airway morphology. Their method, which automatically identifies tubular airway-like structures and groups them into a connected airway tree, was validated on a dataset that included subjects with cystic fibrosis, demonstrating high accuracy with few false positives.

Ram et al. (2021) evaluated a convolutional neural network model for quantifying air trapping in expiratory CT scans. Their method compared favourably to other quantitative air trapping measures and showed consistency with clinical scores, suggesting its utility for monitoring disease progression in cystic fibrosis patients.

Aliboni et al. (2022) provided an automatic tool for the detection and classification of bronchiectasis through convolutional neural networks. Their study showed the networks' ability to accurately detect and classify bronchiectasis disease, presenting an important advance for the quantitative analysis of radiologic severity and distribution of bronchiectasis subtypes.

Lv et al. (2023) aimed to validate an artificial intelligence-based algorithm to assess dimensions of all visible bronchus-artery pairs on chest CT scans from patients with CF. Their method, which fully automated the segmentation of the bronchial tree

and measurement of bronchial and arterial dimensions, showed no significant differences compared to manual analysis and was able to detect and monitor the progression of bronchial wall thickening and widening.

3.4 Architectural Choices in Deep Learning

The choice of deep learning architecture plays a critical role in diagnostic accuracy. While the specific architectures employed in recent studies are not always detailed, common architectures in medical imaging include Convolutional Neural Networks (CNNs), Recurrent Neural Networks (RNNs), and variants like U-Net for segmentation tasks. The selection of architecture significantly influences the algorithm's performance in terms of accuracy, sensitivity, and specificity (Zhou et al. 2021).

The study by Zucker et al. (2020) serves as a prime example of how a Deep Convolutional Neural Network (DCNN) can be leveraged to automate and possibly improve upon traditional diagnostic scoring systems like the Brasfield score used for assessing chest radiographs in CF patients. In their study, a comprehensive dataset of 2058 chest radiographs from CF patients was used to train and validate the DCNN model, with a significant subset reserved for testing against the ground-truth scoring performed by board-certified paediatric radiologists.

3.5 Validation and Benchmarking for Clinical Utility

To evaluate the clinical utility of these AI algorithms, validation on separate datasets and benchmarking against established diagnostic standards is essential. This process is crucial for understanding the performance metrics of the algorithm, particularly its precision in identifying CF-related abnormalities with minimal false positives and negatives (Szczesniak et al. 2018).

In this regard, Dournes et al. (2022) embarked on validating a fully automated artificial intelligence (AI)-driven scoring system for assessing the severity of CF lung disease using chest CT scans. They gathered a comprehensive dataset from three CF reference centres, which spanned over a decade and included patients across a broad age range. The AI algorithm employed three 2D convolutional neural networks, trained to semantically label various pathological features characteristic of CF on CT scans. The clinical validity of their method was meticulously assessed using a group of patients undergoing treatment, comparing AI-driven volumetric quantifications with both visual imaging scoring and pulmonary function tests. The proposed system demonstrated good pixelwise similarity to ground-truth labels, as indicated by the Dice coefficient, and showed moderate to very good correlations with the visual imaging scoring system.

3.6 Comparative Studies and Architectural Performance

Comparative studies, although not extensively available in the literature, are critical for understanding the efficacy of different deep learning architectures in CF detection through CT images. These studies could focus on various metrics including diagnostic accuracy, computational efficiency, and integration into clinical workflows (Suganyadevi et al. 2022).

Singh et al. (2018) contributed to this area of research by designing a deep learning algorithm aimed at detecting multiple thoracic abnormalities, including CF, in chest X-rays. The study underscores the shift from manual examination of radiographs by experts to more advanced computer-aided methods, which promise enhanced accuracy, speed, and automation. Singh et al.'s work involves a technical evaluation and synthesis of various computer-aided chest pathology detection systems, focusing on those developed in the past five years.

3.7 Integration in Clinical Practice and Its Implications

The integration of AI technologies, such as Thirona's PRAGMA-AI algorithm, into clinical practice is beginning to streamline the analysis of CT scans. This integration is a testament to how AI technologies are gradually finding their place in clinical settings, aiding in rapid and precise analysis, which is crucial for timely CF management. The benefits extend to real-time analysis, reducing radiologists' workload, and enhancing the accuracy and consistency of diagnoses (Humphries et al. 2021).

Crowley et al. (2021) offer a comprehensive review of the pulmonary imaging techniques used in CF, underscoring the superiority of radiological imaging over pulmonary function testing in detecting structural changes in the lungs. The review brings to light how chest CT has largely superseded radiography for initial assessment and surveillance of CF lung disease, with an emphasis on the advent of techniques that utilize less ionizing radiation, which is crucial given the need for recurrent imaging in CF patients from an early age.

Schalekamp et al. (2022) delved into the AI applications specific to thoracic radiology, noting the existence of over 40 certified AI products for chest radiography or CT. The review provides an overview of current AI applications and discusses the potential paediatric applications, signifying a significant step towards personalized and precise paediatric care.

Ciet et al. (2023) investigated the importance of imaging in the non-invasive assessment of CF lung disease. Through a collaboration of experts, they scrutinize the challenges and advances in imaging techniques, aiming to offer evidence-based recommendations for both clinicians and radiologists. The systematic review culminates in consensus statements calling for international guidelines to optimize the timing and selection of imaging modalities in CF, tailored to each clinical scenario. The review acknowledges the indispensable role of CT and MRI in routine monitoring and anticipates that AI-driven image analysis could further revolutionize clinical practice by providing rapid and reliable quantitative assessments of disease status.

3.8 Addressing Ethical and Regulatory Challenges

Despite these advancements, challenges in data privacy, algorithm transparency, and validation remain. Addressing these concerns is vital for the seamless integration of AI in CF detection and monitoring. Ensuring patient data security, algorithmic transparency to build clinician trust, and rigorous validation processes are key to overcoming these hurdles and fostering the successful adoption of AI in healthcare.

Truog (2019) offers a profound discussion on the evolution of medical practice, from a discipline grounded in physical examination to one increasingly reliant on image-based analysis and, by extension, on AI. The shift from direct patient contact to remote diagnostics is both a metaphor and a literal example of the distance AI can create between the patient and the physician. The tactile connection to the patient, which was historically central to medical diagnosis, is being supplanted by a reliance on technological interfaces. This transformation has profound implications, not only for the patient-doctor relationship but also for how clinicians perceive and interpret medical data.

Chang et al. (2022) highlighted the advantages of AI in identifying airway mucus plugs, a significant indicator in diseases like asthma and CF. AI's ability to augment clinical evaluations of chest CT scans represents a major leap in diagnostic accuracy and efficiency. However, the use of AI to interpret medical images, while improving precision, also introduces concerns about the over-reliance on technology, the potential for misinterpretation, and the need for oversight to prevent errors that could have severe implications for patient health.

4 Conclusion

This review provides a comprehensive overview of the emerging intersection of artificial intelligence (AI), computed tomography (CT) and cystic fibrosis (CF) diagnostics. We follow the journey from the origins of CF as a genetic disorder to the state-of-the--art applications of AI in medical imaging, and examine how this technological leap is shaping the future of CF treatment. The studies included in this review highlight the progressive stages from early applications in paediatric radiology to complex algorithmic designs that are pushing the boundaries of diagnostic accuracy.

Our investigation underscores how deep learning has evolved to play a key role in enhancing the diagnostic acumen of clinicians. By leveraging AI's ability to process and analyse large datasets, it has been possible to automate the volumetric quantification of CF-related lung changes, reducing the workload of healthcare providers and opening the way to more timely and individualized patient care. The development and performance of these algorithms, highlighted by strategic architectural decisions in deep learning, has demonstrated the potential to extend and in some cases surpass traditional CF detection and monitoring methods.

Validation and comparison with established clinical standards were critical to determine the clinical utility of these AI-based methodologies. Benchmarking studies are deepening our understanding of the performance of the architecture and providing insights that drive continuous improvement of these systems. The integration of these technologies into clinical practice heralds a new era of efficiency and accuracy in patient care, where real-time analysis and reduced workload for radiologists will become the norm.Alongside these advances, however, we face the ethical and regulatory challenges that arise with the introduction of AI in healthcare. At the forefront of these considerations remain data protection, transparency of algorithms and the need for rigorous validation processes. Addressing these challenges is essential to ensure the responsible integration of AI into healthcare settings, maintain trust between patients and providers, and ensure the seamless adoption of these technologies.

In conclusion, the integration of AI with CT imaging in CF represents a promising area full of opportunities to revolutionize patient outcomes. As we continue to witness the transformative impact of AI on the field of medicine, it is essential to encourage an environment in which innovation is balanced with ethical responsibility, ultimately improving the quality and length of life of people affected by cystic fibrosis.

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