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Interstitial lung diseases computer-aided imaging diagnosis, using complex networks

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Abstract

English:

The article aims to explore how a Complex Network (CN) computer-aided technique targeted for interstitial lung disease (ILD) approach can enhance the work of clinicians and if a CN-based computer-aided diagnosis can provide new data to help manage ILDs more successfully. The CN technique is used to evaluate the progression of the disease by analyzing relevant axial HRCT slices and dynamic CN evaluation using the relative speed for each layer. The article presents the results from a study of 65 patients with interstitial lung disease (ILD), comprising 18 females with a mean age of 59.35 years (ranging from 34 to 76). The initial clinical diagnosis was idiopathic pulmonary fibrosis (IPF) in 28 patients (43.07%), Non-Specific Interstitial Pneumonia (NSIP) in 11 patients, and other ILDs in the remaining patients. Each CT scan fulfilled the criteria for high-resolution CT with constant characteristics across the group. All patients underwent imagistic follow-up for at least 11 months, and additional data were provided for each investigation. The cohort was chosen based on concordant lung function decline and imaging evolution decline. The article concludes that the complex network approach provides both a qualitative visual map and quantitative metrics to enhance ILD diagnosis and progression tracking. The results suggest that a CN-based computer-aided diagnosis can provide new required data to manage ILDs more effectively. This approach may enable clinicians to make more precise conclusions regarding the structure of the analyzed lung area, which can help tailor disease management strategies to individual patient profiles.

Keywords

interstitial lung disease • imaging • complex network algorithm • HRCT computer-aided diagnosis • progression

Diagnosticul imagistic ajutat de computer al pneumopatiilor interstițiale difuze, folosind rețele complexe

Rezumat

Romanian:

Lucrarea își propune să exploreze felul în care o utilizarea unei tehnici asistate de computer, rețeaua complexă (Complex Network – CN) având ca țintă pneumopatiile interstițiale difuze (PID) poate îmbunătăți munca clinicienilor, și dacă un diagnostic ajutat de computer bazat pe CN poate ajuta la managementul mai bun al PID. Tehnica CN este folosită pentru evaluarea progresiei bolii prin analiza secțiunilor relevante de HRCT și evaluarea dinamică CN folosind viteza relativă pentru fiecare strat.
Articolul prezintă rezultatele unui studiu pe un grup de 65 de pacienți cu PID, 18 femei, cu o vârstă medie de 59,35 ani (între 34 și 76). Diagnosticul clinic inițial a fost fibroză pulmonară idiopatică la 28 de pacienți (43,07%), pneumonită nespecifică (NSIP) la 11, și alte PID la restul pacienților. Toate examenele CT au îndepălinit criteriile de înaltă rezoluție, cu caracteristici constante în tot grupul. La toți pacienții s-a făcut monitorizare timp de minim 11 luni și au fost furnizate date suplimentare pentru fiecare investigație. Cohorta a fost selectată pe baza concordanței între declinul funcțional și evoluția imagistică spre progresie.

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Lucrarea concluzioneaza că un abord bazat pe CN oferă atât o hartă vizuală calitativă cât și măsuri cantitative pentru a îmbunătăți diagnosticul PID și urmărirea progresiei. Rezultatele sugerează că un diagnostic ajutat de computer prin CN poate oferi informațiile necesare pentru un management mai eficient al PID. Această abordare poate sprijini clinicienii în formularea unor concluzii mai precise privind structura ariei pulmonare analizate, ceea ce poate ajuta la personalizarea strategiilor de management pentru profilul individual al pacienților.

Cuvinte-cheie

pneumopatii interstițiale difuze • imagistică • algoritm complex de rețea • diagnostic HRCT ajutat de computer • progresie

Introduction

Diagnosing and managing interstitial lung disease (ILD) is a complex and challenging process that requires a detailed evaluation of the patient's history, physical examination, thoracic imaging, and other testing. An accurate and specific diagnosis of the specific form of ILD is essential to provide the patient with useful prognostic information and to formulate an appropriate management plan that can relieve symptoms and restore or significantly improve quality of life [1,2,3,4].

The percentage of fibrosis among interstitial lung diseases can vary widely depending on the specific disease and its stage. In some cases, fibrosis may be a prominent feature, while in others, it may be minimal or absent. However, in many interstitial lung diseases, fibrosis is a key pathological feature that leads to impaired lung function and, in some cases, respiratory failure. The new guidelines [5] highlight the critical need for an early and accurate HRCT diagnosis to promptly introduce antifibrotic therapy for ILD management [6], [7]. For example, one of the most common forms of ILD is idiopathic pulmonary fibrosis (IPF), a progressive fibrosing intra-alveolar lung disease (PPF-ILD) with an abysmal prognosis and an elevated risk of premature mortality without treatment [2], [8]. The imagistic representation of end-stage parenchymal destruction in patients with interstitial fibrosis appears as honeycombing cysts, traction bronchiectasis, and architectural distortion. [9]. This fibrotic pattern is typically described as usual interstitial pneumonia (UIP), encountered in most patients with IPF, but could also be an advanced stage of other diseases, like hypersensitivity pneumonitis (HP), fibrotic non-specific interstitial pneumonia (NSIP), collagen disease ILDs, and others. [10,11].

Using current methods, clinicians face several challenges in diagnosing and tracking the progression of diffuse interstitial lung diseases (ILDs). These limitations include:

- Heterogeneity: ILDs are a group of lung diseases with varying causes, symptoms, and outcomes. This heterogeneity makes it difficult to diagnose and track the progression of these diseases accurately [1,2], [12,13].
- Overlap: ILDs can have overlapping features with other lung diseases, such as chronic obstructive pulmonary disease (COPD) and asthma. This overlap can lead to misdiagnosis and inaccurate tracking of disease progression [12].
- Interobserver variability: There can be significant variability in interpreting radiological images and lung function tests among different clinicians. This variability can lead to differences in diagnosis and tracking of disease progression [12].
- Diagnostic delay: The diagnosis of interstitial lung diseases, including ILDs, is often delayed by several years [13]. This delay can impact the accuracy of disease tracking and lead to poorer patient outcomes.
- Limited diagnostic approaches: Diagnosis of ILDs is often possible by exclusion alone, and laboratory-based in vitro methods, such as the drug lymphocyte stimulation test (DLST), have limitations [14], [15]. In addition, some studies used physician-reported diagnosis or radiological evidence of ILD to define cases without an assessment of clinical characteristics or exclusion of infection, and workup to exclude another competing diagnosis was not stated, minimal, or absent [16].

To overcome these challenges, combining computer enhancements and medical expertise is becoming a synergistic, more accurate diagnostic method [17],[18], [19],[20], [21]. In the last decade, the advancement of HRCT has made it the most crucial diagnostic tool, leading to a decrease in the need for biopsy due to high patient risk [2], [8]; therefore, any specific computer-aided diagnosis should include a form of image processing.

The HRCT imaging results are analyzed traditionally based on distinct textural patterns in the lung window's distribution and extent. Imagistic HRCT fibrosis progression is usually assessed visually based on the percentage of lung volume with fibrotic features in the upper, middle, and lower lung

areas. Side by side, adjacent HRCT sections of the initial and follow-up CT examinations are compared after adjustment for lung volume changes. Increased areas or severity of traction bronchiectasis and bronchiolectasis, novel ground-glass opacity with traction bronchiectasis, novel fine reticulation, augmented lobar volume loss, and new or increased honeycombing are the radiological features that must be carefully screened. Elevated levels of fibrotic features indicate progression [22]. It should be noted that the evaluation focuses on the picture's grayscale tones and geometrical structure and repeatedly pattern-matching, offering the ideal setting computer aided design (CAD) systems.

Due to the complexity of lung imaging, a completely autonomous CAD system is not yet possible, but there is a method based on expressive visual representations of data displayed as graphs that can help enhance various diagnostic features, like clinical and functional data, thoracic HRCT pathways, and disease networks form structures [23] and that can convey the influence that nodes assert over one another [24], [25]. This method is based on complex networks (CN) and can also be successfully used to pattern-match [26],[27].

In the imaging world, complex networks provide an innovative way to analyze lung imaging by representing the data as interconnected nodes, much like a map of roads. The nodes are pixels, and connections between pixels show similar lung tissue characteristics. This allows identifying patterns in lung damage from interstitial lung diseases (ILDs). The complex network maps out relationships between diseased areas and shows the "big picture view" of how disease manifests across the lung.

The CN algorithm [18], [19] takes CT scan samples, filters into pathological tissue types, and generates a network map for each. The connections between nodes in the network reveal insightful intricacies about disease progression. Metrics like node degree distribution mathematically characterize the networks, quantifying patterns not discernible by the eye. Differences between normal and ILD-affected networks are statistically significant.

In summary, the complex network approach provides both a qualitative visual map and quantitative metrics to enhance ILD diagnosis and progression tracking. This method extracts deeper insights from CT scans through an innovative network representation of lung imaging data.

This paper aims to explore how this complex network approach can enhance the work of clinicians and if a CN-based computer-aided diagnosis can provide new data to help manage ILDs more successfully.

Materials and Methods

From the dedicated „Dr. Victor Babes" Infectious Diseases and Pneumophthysiology Clinical Hospital Timisoara National Fibrosis Center database, we designated 65 ILD patients with multiple scans, exhibiting the most relevant and common ILD entities (IPF defined by usual interstitial pneumonia - UIP, non-specific interstitial pneumonia - NSIP, organizing pneumonia - OP, hypersensitivity pneumonitis - HP, and sarcoidosis). The inclusion criteria were: each patient was diagnosed by a minimum of three pulmonologists with five or more years of experience in ILD/IPF; each CT satisfies the criteria for HRCT, with constant characteristics across the group; all patients have imagistic surveillance for at least 11 months; additional data are provided for each investigation, including Diffusing Capacity of the Lung for Carbon Monoxide (DIco), Forced Vital Capacity (FVC), age, gender, and clinical outcome; all CTs are annotated with comprehensive CT descriptions prepared by center specialists following the multidisciplinary discussion (MDD). The study cohort was chosen based on a concordant decline in both lung function and imaging evolution. Exclusion criteria targeted patients refusing to return annually for imaging follow-up; patients with poor-quality HRCT images exhibiting artifacts or slices thicker than 1.5 mm; the presence of severe associated pathology, such as liver cirrhosis, neurodegenerative illness, neuropsychiatric disease, severe heart failure etc.; absence of freely expressed consent (observation sheet and/or lack of discernment).

All the scans were conducted on the same machine, General Electrics (GE) Healthcare Optima 520 16-slices, with 32-slices reconstruction, using a narrow slice width of 1.25 mm., and following the Radiology Working Group of the Pulmonary Fibrosis Foundation guidelines. This allowed for the same Houndsfield Units (HU) transformation scale to be applied based on the values defined in previous studies [28,29,30].

The CN algorithm processed the digital representation of the HRCT, a DICOM file [18], in multiple stages, as presented in Figure 1.

First, a manually selected area of interest is taken and split into 65X65 pixels squares, size depending on the machine settings, set to capture at least one entire secondary pulmonary

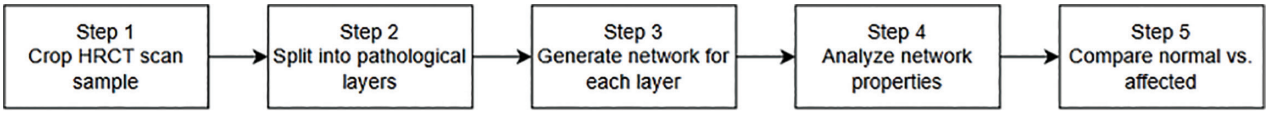


Figure 1. The CN algorithm workflow.

lobule and also to have a better algorithm run time (Step 1). After HU conversion, the sample is filtered into emphysema (E), ground glass opacity (GGO), and consolidation (C) layers (Step 2). The E has the same HU density as cysts, and C is considered equal to reticulation. Step 3 transforms pixels into nodes, connected based on proximity and density [31], [32,33]. Similar values are considered those with variations less than 50 HU units and closer than 4 px. These values are, again, machine-dependent but can be parametrized. Step 4 uses particular CN metrics, like degree distribution, to reveal disease patterns, and step 5 uses significant differences in network metrics to show pathology and quantify progression [19], directly impacting the disease management strategy.

Results

In this section, we present the results from a study of 65 patients with interstitial lung disease (ILD), comprising 18 females with a mean age of 59.35 years (ranging from 34 to 76). The initial clinical diagnosis was idiopathic pulmonary fibrosis (IPF) in 28 patients (43.07%), Non-Specific Interstitial Pneumonia (NSIP) in 11 patients, and other ILDs in the remaining patients. We report on the lung function tests of these patients, which revealed a mean Forced Vital Capacity (FVC) of 69.46% predicted and, a mean Diffusing Capacity of the Lung for Carbon Monoxide (DLCO) of 54.67% predicted, and a mean GAP-ILD starting score of 2.46. Each patient underwent a minimum of one follow-up imaging test, with an average of 2.09 examinations per patient.

The follow-up ranges are illustrated in Figure 2 (A), while the age distribution is presented in Figure 2 (B).

Figure 3 showcases the difference between the evaluation flow in the regular human assessment and the computer-guided one in a case of a non-specific usual interstitial pneumonia (NSIP). An ILD specialist scrolled the dynamic axial HRCT, compared the imaging findings, and manually selected the region of interest (ROI). Features of baseline (t_0 =2018) and follow-up (t_1=2019) are revealed. If in t_0, both superior and basal regions show fine reticulation, ground glass opacity, and honeycombing (HC, honeycombing) elements with subpleural distribution at the t_1, all these elements become more prominent, especially GGO and E layer.

The CN CAD crops an ROI from the same location, as specified by the ILD specialist, splits it into layers and generates the CN (b). The CN is rendered with a general, all-purpose layout named Forced Atlas, emphasizing the preferential attachment rules [34] typical in naturally generated networks.

In Figure 4 an IPF patient is presented. In 4 (a), relevant dynamic basal axial HRCT slices are followed: t_0 -2019 shows typical usual interstitial pneumonia elements(UIP) with subpleural, inferior distribution of reticulations and honeycombing features; t_1-2021 shows a possible GGO progression (depicted by patient worsening symptoms), and prejudicial fibrosis evolution with more architectural destruction and extension of HC surface (C layer evolution). The possible GGO is precisely the fine point, as a non-ILD specialist might neglect the structure and misdiagnose the imagistic exacerbation. The CN depicting the C layer has considerably increased the number of connections, from a few sparse clusters to a giant component-type network, interconnecting all the original clusters. Figure 4 (b) highlights the cluster component using mathematically generated community colors in the CN rendering. The GGO was significant, to begin with, yet its increase is not as much as the C, with the C doubling (see Ox scales in Figure 4c) and GGO increasing with a magnitude of ~50%, explaining the clinical exacerbation.

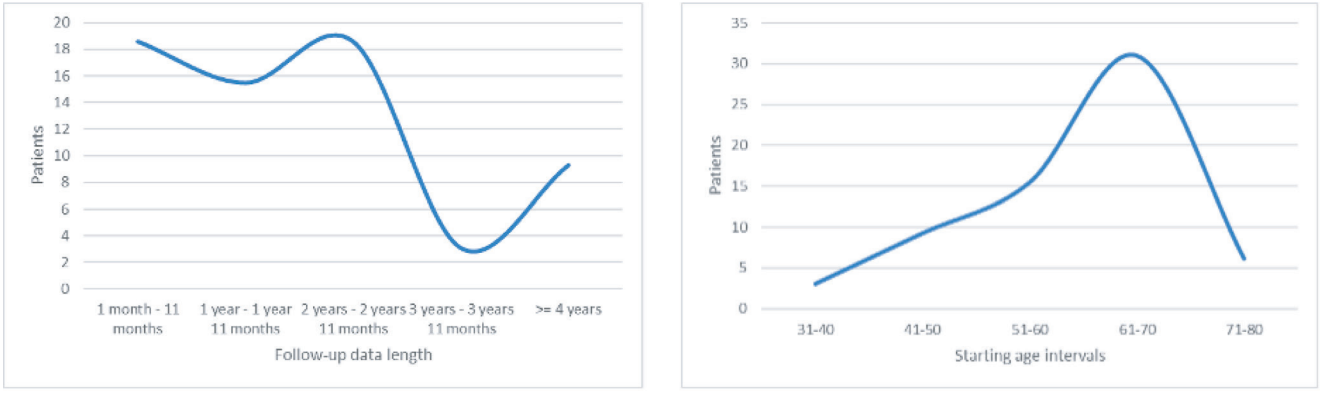
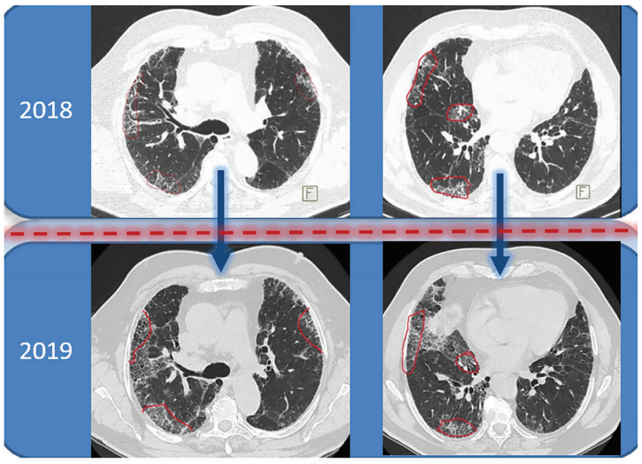
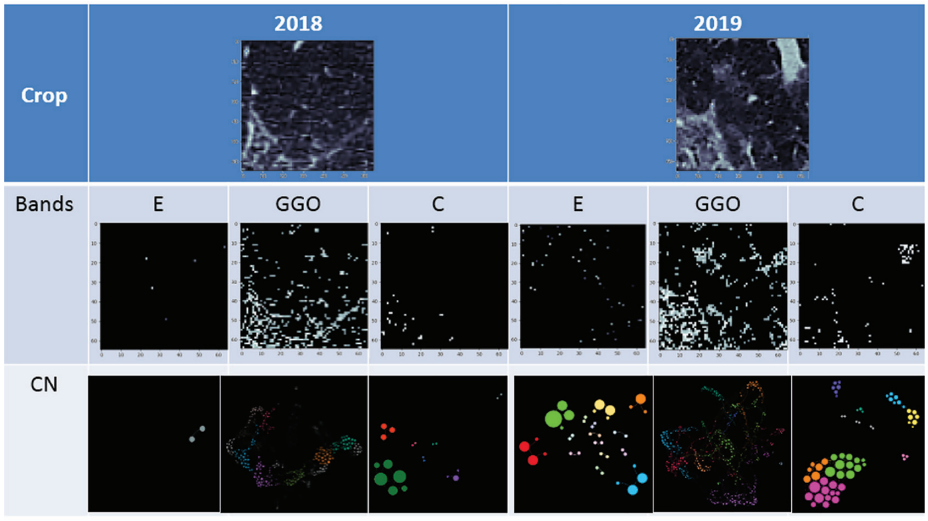


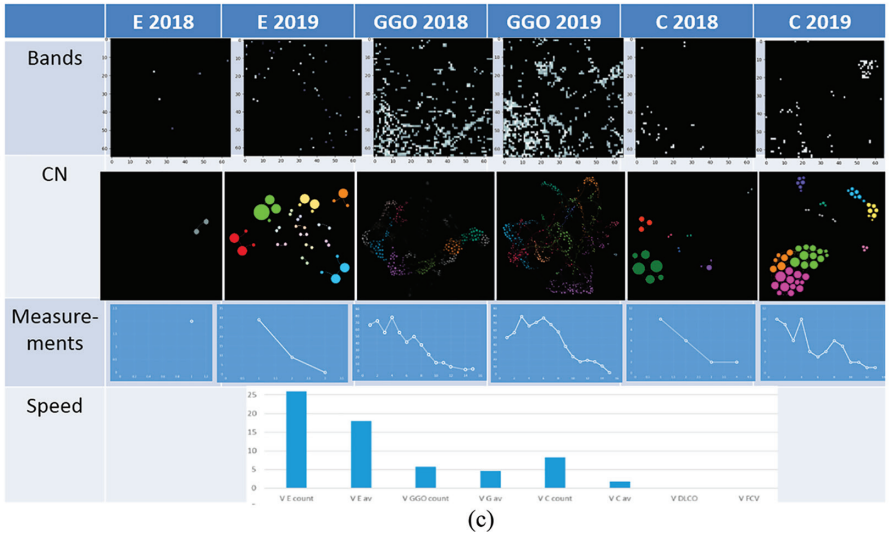
Figure 2. Characteristics of patients in the study group (A) Follow-up range distribution (B) Age distribution.



(a)



(b)



(c)

Figure 3. NSIP patient evaluation using the CN technique (a) Relevant axial HRCT slices showcasing progression (b) Region of interest selected from the same location, split into the three layers and the generation CN (c) Dynamic CN evaluation by using the relative speed for each layer.

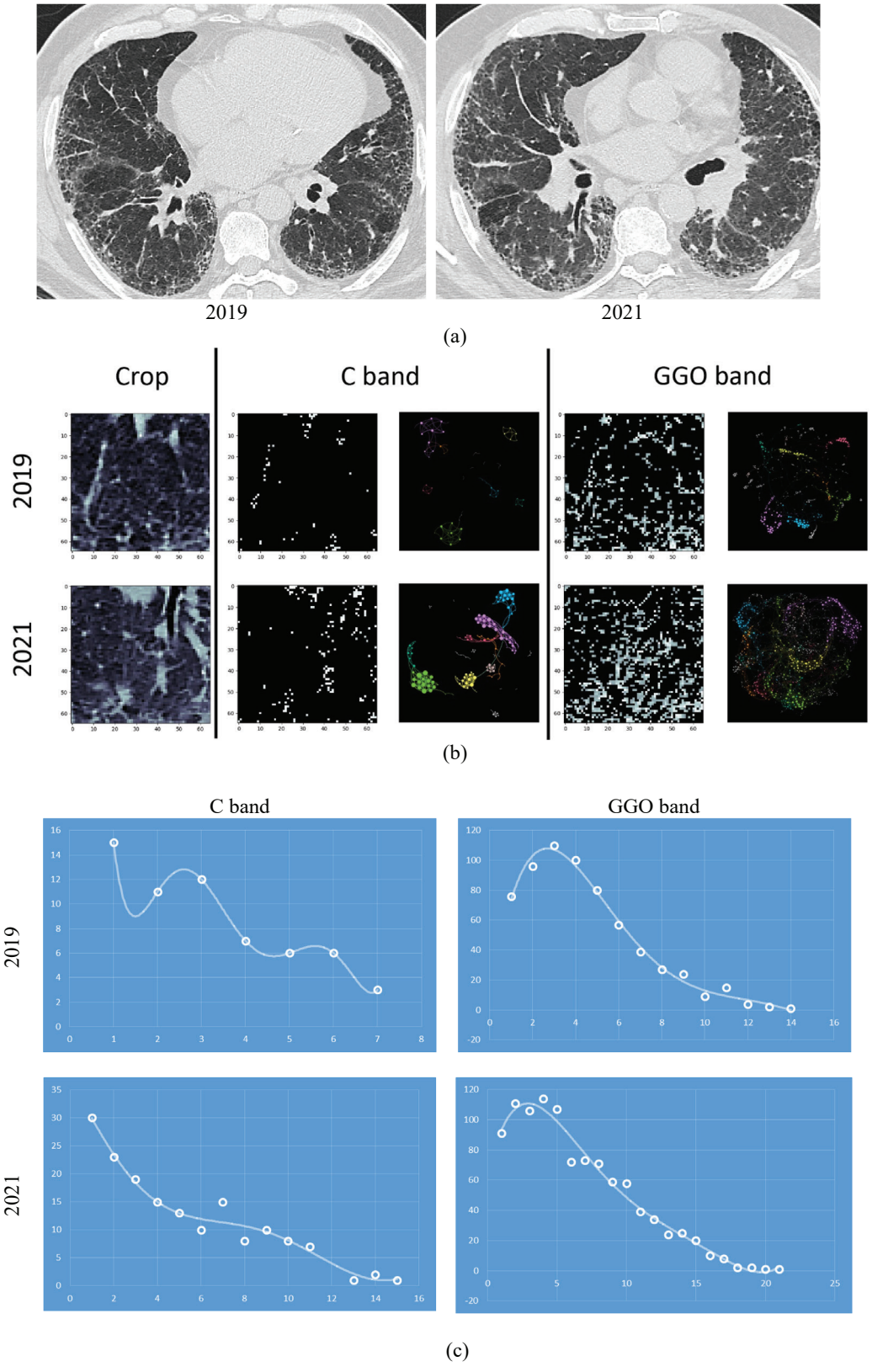
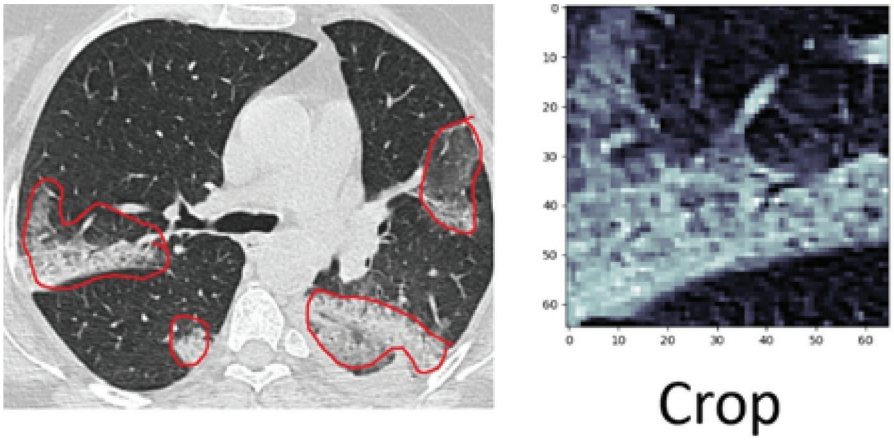
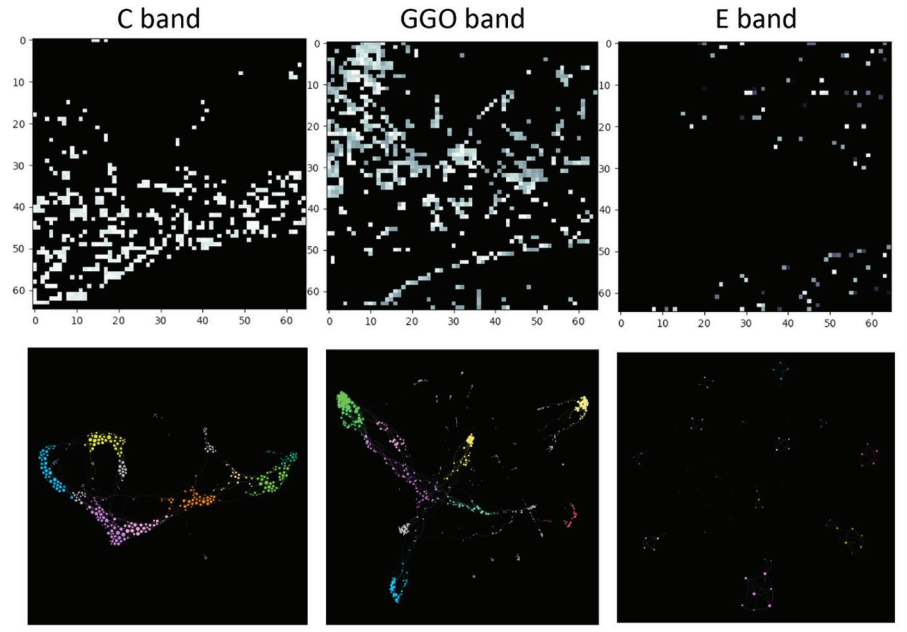


Figure 4. IPF patient – larger time gap (2 years). (a) relevant basal axial HRCT slices (b) Significant changes on the C and GGO bands (c) Degree distribution (lesion intensity) for the C and GGO bands.



(a)



(b)

(c)

Figure 5. Axial HRCT Organising Pneumonia(OP) patient – (a) relevant slice (b) CN on all three bands (c) Degree distribution plots (lesion intensity).

Figures 5 and 6 show typical Sarcoidosis (S) and Organising Pneumonia (OP) cases with their corresponding CN reflection of the original HRCT image on all three pathological bands. The S HRCT shows a perilymphatic micronodular pattern distribution, and the OP presents typical high attenuation multiple consolidation patterns.

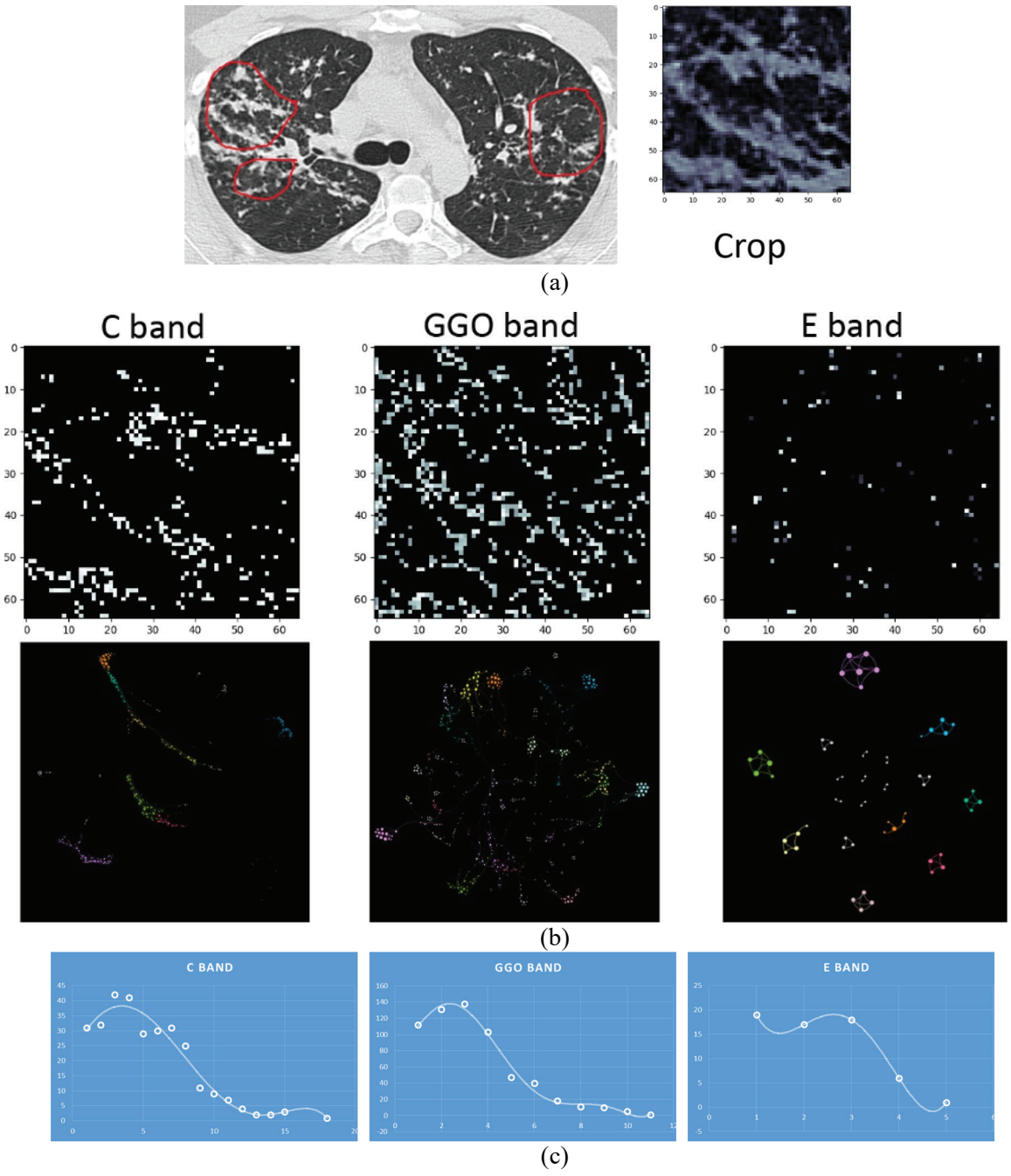


Figure 6. Axial HRCT Sarcoidosis patient (a) relevant slice (b) CN on all three bands (c) Degree distribution plots (lesion intensity).

Discussions

As demonstrated in studies focusing on interstitial lung disease [17], [21], [19], [28], [29] there is a strong correlation between the imaging features, lung function, and disease progression. This correlation was often unexpected and could not have been determined using traditional imaging interpretation alone.

For example, in Figure 3c, CN measurements reflect biological relevance. Each pathological band has a degree distribution that reflects lesion intensity and sparsity. Various elements of these measurements (the number of pathological entities, their average, and their peak intensity) can be used to compute a speed of change specific to each patient and investigation. In Figure 3c, this relative speed accentuated pathological decay on the E axis, correlated with NSIP evolution towards pulmonary fibrosis type, with increased honeycombing air cyst layers. It is essential to highlight that this change did not reflect immediately in the functional parameters of the lung (DLco, FCV). This minutia change detection allows for better management using early antifibrotic treatment.

The degree distributions in Figures 4c, 5c, and 6c show how abnormal, fibrotic trending ILDs present a polynomial distribution. The polynomial degree varies, as it should, and does not properly represent a criterion to identify the disease, as shown in [6]. The fact that biological changes as small as 2.96 mm are detected, due to the inherent nature of the CN algorithm, allows for the distribution to show alterations even in the beginning stages, such as in Figure 3c layer C 2018 and Figure 6c layer E.

The degree distribution can also quantify the progression of ILD. For instance, Figure 4c illustrates this for the GGO band. Despite the similarity in shapes, the curve for 2021 covers a range of 0-20 with a peak intensity of around 5, while the previous examination covers a range of 0-14 with a peak intensity of 3. This is a noteworthy observation because, even though the type of variation has not changed from a system perspective, the disturbance intensity has increased.

A caveat should be made regarding the danger of overfitting. The discussion around polynomial shapes and their degree should always take into account that there is a natural variation and should never favor a higher r^2 value over biological accuracy.

By utilizing computer-aided diagnosis, healthcare providers may gain new insights and data that can lead to more successful disease management strategies.

Conclusions

Complex networks have proved to be a proper technical and graphical equivalent of HRCT images due to their intrinsic visual structure as well as their ability to reflect the essence of the analyzed data.

A stand-alone CAD tool based on this technique can enhance the ILD approach in clinical settings and should be a priority to develop.

Authors contributions

1. First author and also a corresponding author: conceptualization;
2. Methodology; conceptualization;
3. Software design; investigation;
4. Validation process; image sample selection ,
5. Investigation;
6. Project administration; supervision.

Funding

None.

Institutional Review Board Statement

The study was conducted according to the Declaration of Helsinki's guidelines and approved by the local Ethical Commission of Clinical Hospital for Infectious Diseases and Pneumophthiziology Dr. Victor Babeș Timișoara (protocol code 11835/26.11.2021) for studies involving humans.

Informed Consent Statement

- Informed consent was obtained from all subjects involved in the study.
- No informed consent was necessary.

Data Availability Statement

Data used to support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflict of interest.

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