

**"VICTOR BABEȘ" UNIVERSITY OF  
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**ADVANCED MEDICAL IMAGING IN RESPIRATORY  
DISEASES: INNOVATIONS, OPPORTUNITIES AND  
CLINICAL APPLICATIONS**

**ABSTRACT**

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The Habilitation thesis entitled "Advanced Medical Imaging in Respiratory Diseases: Innovations, Opportunities and Clinical Applications" is the result of hard work after years of medical practice and scientific research. This is possible due to a perfectly combined path of the evolution of the medical career, the academic career, and the research performed and conducted. My research is based on two important directions: medical imaging in respiratory diseases and oncology research activity.

Firstly, I began my exploration of this field of research during my doctoral studies, graduating with a thesis entitled **"The Contribution Imaging in the Diagnosis of interstitial lung disease"**, which laid the foundations for their subsequent studies.

The first research direction included studies regarding lung ultrasound in lung fibrosis. On this topic, I have published several scientific studies, which I will present in brief:

- **Manolescu D**, Davidescu L, Traila D, Oancea C, Tudorache V. The reliability of lung ultrasound in assessment of idiopathic pulmonary fibrosis. *Clin Interv Aging*. martie 2018;Volume 13:437–49;
- **Manolescu D**, Oancea C, Timar B, Traila D, Malita D, Birsasteanu F, et al. Ultrasound mapping of lung changes in idiopathic pulmonary fibrosis. *Clin Respir J*. ianuarie 2020;14(1):54–63;
- Ciuca IM, Pop LL, Dediu M, Stoicescu ER, Marc MS, Manea AM, **Manolescu DL**. Lung Ultrasound in Children with Cystic Fibrosis in Comparison with Chest Computed Tomography: A Feasibility Study. *Diagnostics (Basel)*. 2022 Feb 1;12(2):376. doi: 10.3390/diagnostics12020376.

The first two articles are about idiopathic pulmonary fibrosis and the last one speaks about cystic fibrosis. The first pathology is a rare, progressive, idiopathic form of pulmonary fibrosis in adults. Cystic fibrosis is a systemic genetic disease of the child and by extension also pulmonary, which can also translate into young adulthood.

The first article is a literature review on lung ultrasound's reliability in assessing idiopathic pulmonary fibrosis. The most important messages from this study are represented by the conclusions:

1. LUS is a valuable tool for screening patients with IPF for several reasons, being a reliable non-invasive tool;
2. LUS can effectively differentiate between various ILDs based on the distribution and quantity of B-lines, allowing for the exclusion of inconsistent UIP patterns;

3. LUS could serve as a valuable tool for monitoring the treatment outcomes in IPF patients.

The second study aimed to evaluate the reliability of LUS in patients with IPF when compared to HRCT, using a simplified protocol covering 12 lung zones. It provides a cut-off of severity for monitoring treatment response by mapping lung changes and overlapping fibrotic scores which have a clinical impact.

The results prove that LUS represents a dependable imaging tool for mapping lung changes in idiopathic pulmonary fibrosis (IPF) without subjecting patients to radiation. In comparison with high-resolution CT (HRCT), LUS demonstrates a significant correlation in distribution. B-lines and the average thickness of the pleural line, identified as LUS markers of fibrotic interstitial syndrome, exhibit strong positive correlations with HRCT, forced vital capacity (FVC), and diffusing capacity of the lungs for carbon monoxide (DLCO).

The third one involved a cohort of individuals aged 6-18 years with typical cystic fibrosis, who were monitored in our cystic fibrosis center. This study aimed to evaluate the correlation between a newly developed LUS score and the lung clearance index (LCI), comparing it to the modified Bhalla CT score. The conclusions of this research revealed that LUS proves to be a reliable tool for monitoring lung disease in cystic fibrosis patients, particularly in cases of advanced lung disease and moderate-severe lesions. For the detection of early changes, LUS is not as consistent as CT, which remains the chosen method in imaging assessment. The study highlights that the LUS-CF score can serve as a valuable parameter for combined evaluation, complementing the diagnosis and monitoring of CF lung disease, particularly in children.

My research on the role of ultrasonography in pulmonary fibrosis has led me to conduct a series of comprehensive studies on this complex pathology.

Thus, in addition, I conducted, as coauthor, a study that aimed to assess cognition in patients with IPF in stable phase and to identify factors that modify clinical cognition: Tudorache V, Traila D, Marc M, Oancea C, **Manolescu D**, Tudorache E, Timar B, Albai A, Fira-Mladinescu O. *Impact of moderate to severe obstructive sleep apnea on the cognition in idiopathic pulmonary fibrosis. PLoS One. 2019 Feb 1;14(2):e0211455.* This study identified mild cognitive impairment in patients with idiopathic pulmonary fibrosis (IPF), particularly affecting visuospatial abilities, language, and working memory. Obstructive sleep apnea (OSA) is a potential predictor of cognitive deficits in IPF patients.

In close connection with the subject matter stemming from the first research trajectory I embarked upon subsequent to the completion of my Ph.D. studies, I

collaboratively authored a case report elucidating the correlation between idiopathic pulmonary fibrosis and autoimmune disease. The publication of the case report titled *Traila D, Marc MS, Pescaru C, Manolescu D, Fira-Mladinescu O. ANCA-associated vasculitis in idiopathic pulmonary fibrosis: A case report and brief review of the literature. Medicine (Baltimore). 2022 Mar 4;101(9):e29008* was a research demonstrated that autoimmune testing for antineutrophil cytoplasmic antibodies (ANCAs) should be considered a crucial component of both the diagnostic work-up and follow-up for IPF.

Secondly, medical imaging in the respiratory diseases section included topics like the role of lung ultrasound in other respiratory diseases, especially viral ones. In relation to this topic, we have disseminated the subsequent scholarly articles:

- Stoicescu ER, Ciuca IM, Iacob R, Iacob ER, Marc MS, Birsasteanu F, **Manolescu DL**, Iacob D. Is Lung Ultrasound Helpful in COVID-19 Neonates?-A Systematic Review. *Diagnostics (Basel)*. 2021 Dec 8;11(12):2296;
- Stoicescu ER, **Manolescu DL**, Iacob R, Cerbu S, Dima M, Iacob ER, Ciuca IM, Oancea C, Iacob D. The Assessment of COVID-19 Pneumonia in Neonates: Observed by Lung Ultrasound Technique and Correlated with Biomarkers and Symptoms. *J Clin Med*. 2022 Jun 20;11(12):3555;
- Stoicescu ER, Lovrenski J, Iacob R, Cerbu S, Iacob D, Iacob ER, Susa SR, Ciuca IM, Bolintineanu (Ghenciu) LA, Giornei-Hoffman A, Oancea C, **Manolescu DL**. COVID-19 in Infants and Children under 2 Years—Could Lung Ultrasound Score Be Correlated with Biomarkers and Symptoms? *Biomedicines*. 2023 Sep 24;11(10):2620.

The first scientific article aimed to evaluate the effectiveness of pulmonary ultrasound (LUS) in neonatal populations affected by COVID-19. Despite the limited number of publications focused on lung ultrasonography in neonates with COVID-19 pneumonia, these studies demonstrate the utility of LUS in the detection of lung lesions, this method opening the way to new directions of research with increased practical relevance.

The second article aimed to identify common changes detected through lung ultrasound (LUS) in neonates with COVID-19 pneumonia and establish correlations between LUS findings, infants' symptoms, and biomarkers in our paediatric infectious disease unit. The overarching goal was to demonstrate the efficacy of this imaging technique in diagnosing and assessing respiratory pathologies in newborns. This prospective study was carried out within the Neonatology and Neonatal Intensive Care Unit

(NICU), spanning from February 2020 to February 2022. Analysed data involved the largest number of newborns with SARS-CoV2 infection evaluated by ultrasound at the time of publication.

This study's findings suggest a strong and reliable correlation between the Lung Ultrasound Score (LUSS) and highly sensitive inflammatory markers, such as IL-6 levels and leukocyte counts. This correlation underscores the potential utility of LUSS as a valuable tool for monitoring inflammatory lung diseases. As advancements in this field continue to unfold, it is foreseeable that lung ultrasound may evolve into a non-invasive surveillance method for neonates and children grappling with pneumonia, offering a promising avenue for enhanced patient care and management.

The most recent paper (the third one in the list mentioned above) had the primary objective of identifying significant respiratory changes in infants and children below the age of two who had contracted SARS-CoV-2 using the lung ultrasound technique. The conclusions of this study have strengthened previously demonstrated results, suggesting the idea of widespread use of lung ultrasound in paediatric and adult respiratory pathologies.

Building upon the foundation of my prior research on ultrasonography in pulmonary fibrosis and other respiratory conditions, this foray into the realm of deep learning underscored the dynamic and evolving nature of my scholarly pursuits. It showcased a seamless continuity in my dedication to unravelling the complexities of lung diseases while embracing cutting-edge technology. Therefore, I have published as lead author or co-author the following studies:

- Trusculescu AA, **Manolescu D**, Tudorache E, Oancea C. Deep learning in interstitial lung disease-how long until daily practice. *Eur Radiol.* 2020 Nov;30(11):6285-6292;
- Broască L, Trusculescu AA, Ancușă VM, Ciocârlie H, Oancea CI, Stoicescu ER, **Manolescu DL**. A Novel Method for Lung Image Processing Using Complex Networks. *Tomography.* 2022 Jul 27;8(4):1928-1946
- Trusculescu AA, **Manolescu DL**, Broască L, Ancușă VM, Ciocârlie H, Pescaru CC, Vaștag E, Oancea CI. Enhancing Imagistic Interstitial Lung Disease Diagnosis by Using Complex Networks. *Medicina (Kaunas).* 2022 Sep 16;58(9):1288.

The initial paper in this thematic context was a review that endeavors to comprehensively examine the enhancements in interstitial lung disease (ILD) diagnosis facilitated by virtual artificial intelligence. This analysis places particular emphasis on convolutional neural networks (CNNs). We discussed the advancements in deep learning algorithms and their significance in the medical domain, particularly in the diagnosis of ILD. We emphasized the challenges and potential implementation pathways that could eventually make these technologies a part of routine clinical practice, aiding in the early detection of ILDs.

The second research provides a concise overview of the diagnostic processes performed by computers and humans, respectively. Furthermore, in this paper, a novel method utilizing complex networks to transform lung HRCT has been introduced. The methodology section thoroughly explains the algorithm's steps and the rationale behind selecting each parameter. All in all, the paper has successfully achieved its objective by illustrating how a complex network model can transform lung HRCT into a structured format that enhances the diagnosis of Diffuse Interstitial Lung Diseases (DILD) in both quantitative and qualitative aspects.

The last paper tests a complex network (CN) algorithm for image-assisted diagnosis for the possibility of obtaining relevant and novel DILD management data. The paper examines two hypotheses:

1. Hypothesis 1: States that the CN algorithm accurately characterizes quantitatively DILD progression.
2. Hypothesis 2: Advances that the CN algorithm allows early detection.

My transition into oncology research marked the second major research direction in my career, following the completion of my doctoral studies. This transition was a logical progression, driven by my clinical role as a radiologist and imaging physician at a pulmonology hospital. While my expertise initially was centred around radiology, my curiosity led me to delve deeper into the realm of lung cancer research, expanding beyond the confines of my radiology specialization.

Related to the lung cancer, during my academic career, I have published two studies:

- *Tanase, B.C.; Burlacu, A.I.; Nistor, C.E.; Horvat, T.; Oancea, C.; Marc, M.; Tudorache, E.; Mateescu, T.; **Manolescu, D.** A Retrospective Analysis Comparing VATS Cost Discrepancies and Outcomes in Primary Lung Cancer vs. Second Primary Lung Cancer Patients. Healthcare 2023, 11, 1745;*

- Tanase, B.C.; Burlacu, A.I.; Nistor, C.E.; Horvat, T.; Oancea, C.; Marc, M.; Tudorache, E.; **Manolescu, D.** Differential Outcomes of VATS and Open Surgery in Lung Cancer Patients with Antecedent Oncological Diagnoses. *J. Pers. Med.* 2023, 13, 1498.

The first study provides evidence short-term outcomes after VATS are comparable for primary and second primary lung cancer, but SPLC patients have longer operating times and hospitalizations. Additionally, the cost of VATS is significantly higher for second primary lung cancer patients.

According to the second study, patients with a previous history of cancer experience no significant difference in long-term outcomes between VATS and OS. However, VATS is associated with shorter surgical lengths, shorter hospital stays, and lower complication rates than OS, while maintaining good oncological results.

Regarding breast cancer, I published as co-author a literature review: *Iacob R, Manolescu DL, Stoicescu ER, Fabian A, Malita D, Oancea C. Breast Cancer—How Can Imaging Help? Healthcare. 2022; 10(7):1159.* We discussed their most important data and grouped the results as follows: mammography and tomosynthesis, ultrasound and elastography, MRI, ultrasound-guided biopsy, PET-CT, and PET-MRI in breast cancer. The conclusion was the correct use of the above-mentioned imaging techniques; all their newly derived methods can help with a better outcome for diagnosed patients.

Throughout my extensive and illustrious professional, medical, scientific, and academic career, I have actively engaged in a multitude of national and international congresses. My involvement extended to the presentation of research papers, encompassing both oral presentations and poster sessions. This commitment not only exemplifies my dedication to the realm of research but also underscores my enthusiasm for the widespread dissemination of research findings and knowledge. Furthermore, my scholarly activities have extended to participation in international and national congresses that have garnered global recognition. I achieved the first prize for my research at the European Network for Translational Research in Children's and Adult Interstitial Lung Disease. Until now, I have been invited lecturer at 7 international congresses, 25 national congresses. Also, I gave presentations and communications at 9 international congresses, 4 national congresses with international participation, and 62 national congresses.

The academic recognition of my publications in various ISI-rated international journals is underscored by a remarkable tally of 142 citations within the ISI Web of Science

system. This substantial citation count has culminated in a Hirsch index, or h-index, of 8, attesting to the influence and significance of my contributions in the field.

Throughout my academic career, I have actively contributed to the development of teaching materials in the field of radiology and medical imaging. I believe that high-quality educational resources play a crucial role in shaping the learning experience of students and enhancing their understanding of complex concepts. These cover a range of topics such as the role of the radiologist in diagnosing interstitial fibrosis, muscle dysfunction, pulmonary investigation methods, COVID-19's impact on infection pathology, and the application of artificial intelligence in lung diseases.

Currently, I am a primary physician in the specialty of Radiology and medical imaging. Since 2019, I have been the Laboratory Chief of Radiology and Medical Imaging at the 'Dr. Victor Babeș' Infectious Diseases and Pneumophysiology Clinical Hospital Timișoara. In 2020, I was honored to take on the role of the hospital's Medical Director. This position placed me at the helm of organizing, managing, coordinating, and controlling both medical and administrative activities within the hospital.