Chapter 7
From Black Box to Glass Box Interpretable AI for Lung Cancer Radiomics

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ABSTRACT

Lung cancer is the leading cause of cancer mortality, with deaths due to the disease anticipated to exceed 4.6M new cases and 3.5 million lives each year by 2050. AI-based radiomics tools can potentially analyze the levels of pixel distribution and identify hidden biomarkers related to tumor aggressiveness. However, clinicians are reluctant to adopt these methodologies due to the lack of transparency in the DL models, known as the "black-box" phenomenon. The chapter "From Black Box to Glass Box: Interpretable AI for Lung Cancer Radiomics" aims to facilitate the transition of AI-based applications from laboratories to clinics. The protocol for AI-enhanced radiomics is systematically described. The core focus is on enhancing transparency through explainable AI (XAI) techniques. AI designs should be transparent (glass boxes) and have the purpose of assisting clinicians rather than replacing them. The roadmap to success and excellence in the diagnosis and treatment of lung cancer is clear, with data-driven insights.

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1. INTRODUCTION: INTERPRETABLE RADIOMICS IN LUNG CANCER

Lung cancer is the deadliest and most difficult to treat (Sung et al., 2021) because of its aggressive and heterogeneous nature, progressive asymptomatic growth, and varying responses to therapy (Bade & Dela Cruz, 2020) (Herbst et al., 2018). Advancements have been made in diagnosing and treating tumors using radiomics (Gillies et al., 2016), a term that employs the "-omics" suffix commonly used in biomedicine to extract valuable information from large datasets (Lambin et al., 2017). Radiomics extracts measurable data from common medical images, such as CT scans and MRIs, uncovering hidden tumour patterns that reveal how the tumour behaves, without requiring invasive procedures (Aerts et al., 2014). These high-dimensional features may enhance diagnostic accuracy, predict outcomes, and optimize personalized treatment strategies (Kumar et al., 2012). The potential of radiomics increases even further when integrated with artificial intelligence (AI) technologies, particularly those based on deep learning (LeCun et al., 2015). These models can automate the identification of complex and highly tri-dimensional imaging features that human experts often miss (Esteva et al., 2021). However, one of the most critical problems remains: the "black box problem." Most AI systems provide no rationale for their predictions or insights (Samek et al., 2017). This issue renders the clinical implementation of such systems problematic because the absence of explanation makes them unreliable, impossible to interpret, and difficult to validate in practices (Holzinger et al., 2019). Addressing these concerns, the focus is gradually shifting towards more transparent and logical models, also known as 'glass box' systems, that clarify the reasoning behind their operations in a way that boosts confidence and trust (Rudin, 2019). Such systems are needed as trust is essential, particularly with radiomics in lung cancer and patient-centric care (Vellido, 2020). This introduction allows us to examine how radiomics with explainable AI can transform lung cancer care toward trust-based analytics.

1.1 Lung Cancer: A Persistent Global Health Burden

The magnitude of lung cancer's impact globally highlights the necessity for solutions. Data from GLOBOCAN 2022 shows that Lung cancer remains at the top of statistics. It is responsible for a significant portion of newly diagnosed cases and an even greater portion of deaths across the world. For example, 2.5 million new cases of lung cancer were diagnosed around the world in 2022, which came with an estimated 1.8 million deaths (Ferlay et al., 2024). The number of people who have lung cancer is alarmingly high compared to other forms of the disease. Different parts of the world see dissimilar rates of lung cancer due to different social factors