Blog post CHUL – October 2024
Clinical challenges in the identification of lung cancer risk factors – the LUCIA consortium response

Identifying lung cancer risk factors presents numerous clinical challenges, primarily due to the multifactorial nature of the disease. While smoking remains the most prominent risk factor, a growing number of research indicates that genetic predispositions, environmental exposures (such as radon and asbestos), and occupational hazards also contribute significantly. However, distinguishing between these overlapping factors can be complex. Additionally, the latency period between exposure and cancer development complicates early detection and prevention efforts. The diversity in patient populations, with varying lifestyles and genetic backgrounds, further challenges the ability to create a one-size-fits-all approach to screening and risk assessment. Consequently, clinicians must rely on a combination of patient history, biomarkers, and evolving diagnostic tools to improve the accuracy of lung cancer risk identification.

The strength of the LUCIA project lies in our multidisciplinary consortium, which will work to explore these approaches together.

Advances in genetic research and imaging techniques are reshaping the identification and assessment of lung cancer risk factors, providing a more personalized approach to early detection and prevention. Imaging technologies, particularly low-dose computed tomography (LDCT), have revolutionized lung cancer screening by enabling the identification of early-stage nodules that may not be detectable through conventional methods. LDCT has significantly reduced lung cancer mortality in high-risk populations, particularly smokers, by facilitating early intervention. However, imaging still faces challenges such as distinguishing benign from malignant nodules, leading to false positives and unnecessary invasive procedures. Artificial intelligence (AI) and machine learning are increasingly being integrated into imaging analysis to improve accuracy, predict malignancy, and stratify patients based on their risk profiles.

On the genetic front, research has uncovered several mutations and genetic markers that predispose individuals to lung cancer, even in non-smokers. Mutations in genes such as EGFR, KRAS, and ALK are associated with increased cancer susceptibility and influence the tumor's behavior and response to targeted therapies. Identifying these genetic markers allows for personalized screening strategies, where individuals with a genetic predisposition can be monitored more closely. Further explorations evaluating the link between genes and lung cancer risk factors are of major importance to unveil the potential of an adequate personalized screening strategy.

In addition to imaging and genetic advances, volatile organic compounds (VOCs) are emerging as promising biomarkers in lung cancer detection. VOCs are metabolic chemical markers and certain profiles of these compounds have been linked to lung cancer. Studies have shown that lung cancer cells produce distinct VOCs that differ from those of healthy tissues, offering a non-invasive and potentially cost-effective screening tool. Breath analysis using VOC detection could provide an early warning system, especially in conjunction with other screening methods like LDCT and genetic testing. However, the clinical implementation of VOC-based

diagnostics is still in its early stages, with challenges related to the standardization of detection methods, environmental factors that affect VOC levels, and the interpretation of VOC patterns across different populations. Clinical partners involved in LUCIA will test several ways of measuring VOCs to assess their potential added value in the lung cancer screening strategy.

The integration of imaging, genetic, and VOC data into clinical practice remains challenging, and the reason why LUCIA aims to bring together all these investigational perspectives. Both imaging and genetic testing require careful interpretation and validation across diverse populations, while VOC analysis needs further refinement before becoming a mainstream diagnostic tool. Moving forward, combining imaging technologies, genetic profiling, and VOC biomarkers offers a promising path toward a more tailored and effective lung cancer screening strategy, but it requires continued refinement and validation in clinical settings.

The LUCIA project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement no. 101096473. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the Health and Digital Executive Agency. Neither the European Union nor the granting authority can be held responsible for them.