



Clinically-Suitable Multiomics Strategy Enhances the Malignancy Risk Prediction and Individual Management for Pulmonary Nodules

Mengmeng Zhao¹, Jiajun Deng, Chang Chen¹, Yunlang She¹

¹ Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University, Shanghai, China

Correspondence: langthoracic@tongji.edu.cn



IASLC 2026 World
Conference on Lung Cancer

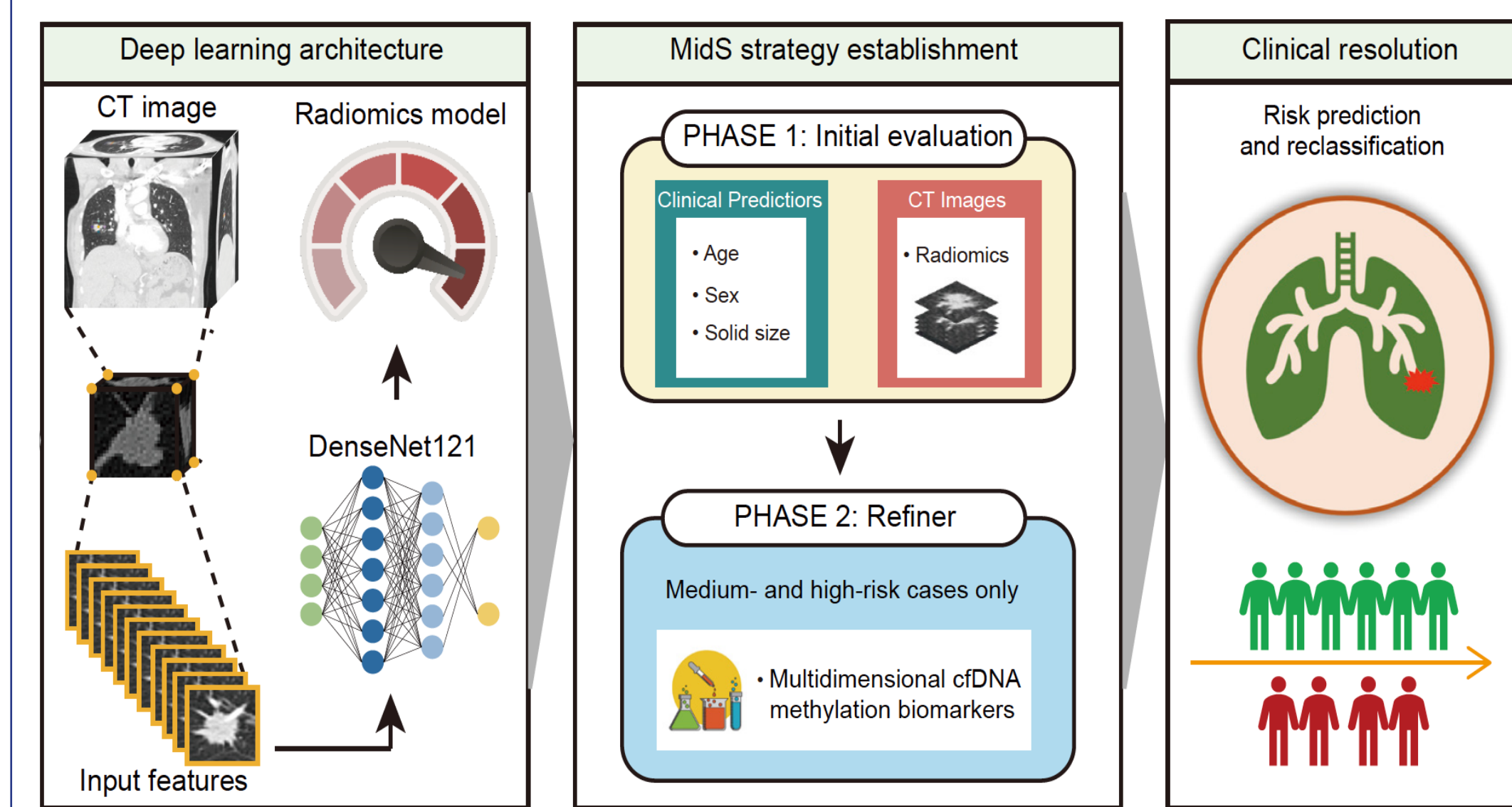
SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

- Multiomics biomarker has been a promising field in cancer detection.
- However, all reported multiomics models requested patients to provide the paired omics information, which might ignore clinical compliance, since the omics information frequently derived from high-throughput sequencing data.

METHODS

- chest CT images and cfDNA fragmentomic features of 2264 patients from 5 centers were enrolled.
- A MidS strategy was designed: malignant risk of lesions was initially identified by integrating clinical risk factors with radiomic features, and the malignant risk of the identified medium/high- cases was refined by an cfDNA-derived end motif model.



DISCUSSION AND CONCLUSION

Actionable Take Away Message

- The MidS strategy outperformed clinical and single-omics models for classifying the malignancy risk of nodules, reducing 52.0% of delaying treatment for lung cancer. It also prevented 9.1% of patients from unnecessary complex analyses, showing potential in saving clinical resources.

Future Direction for Research

- Our proposed MidS strategy provided a clinically suitable, cost-effective and noninvasive tool for precise diagnosis and management of pulmonary nodules.

REFERENCES & ACKNOWLEDGEMENTS

Most critical reference

- Veronesi G, Travaini LL, Maisonneuve P, et al. Positron emission tomography in the diagnostic work-up of screening-detected lung nodules. *European Respiratory Journal*. 2015;45(2):501-510.
- Chengdi Wang, Jun Shao, Yichu He, et al. Data-driven risk stratification and precision management of pulmonary nodules detected on chest computed tomography. *Nature Medicine*. 2024.
- Smith-Bindman R, Chu PW, Azman Firdaus H, et al. Projected Lifetime Cancer Risks From Current Computed Tomography Imaging. *JAMA Internal Medicine*. 2025.
- Zhao M, Xue G, He B, et al. Integrated multiomics signatures to optimize the accurate diagnosis of lung cancer. *Nature Communications*. 2025;16(1).
- Nicholson AG, Tsao MS, Beasley MB, et al. The 2021 WHO Classification of Lung Tumors: Impact of Advances Since 2015. *Journal of Thoracic Oncology*. 2022;17(3):362-387.
- He J, Wang B, Tao J, et al. Accurate classification of pulmonary nodules by a combined model of clinical, imaging, and cell-free DNA methylation biomarkers: a model development and external validation study. *The Lancet Digital Health*. 2023;5(10):e647-e656.
- Wang S, Meng F, Li M, et al. Multidimensional Cell-Free DNA Fragmentomic Assay for Detection of Early-Stage Lung Cancer. *Am J Respir Crit Care Med*. 2023;207(9):1203-1213.

Acknowledgement

This study was supported by National Natural Science Foundation of China (82603996, 92474114, 92259205, 82402371), Ningbo Top Medical and Health Research Program (No.2022030208), Central Guidance for Local Science and Technology Development Funds Project (2024FRD05), Tongji University Medicine-X Interdisciplinary Research Initiative (2025-0554-ZD-06, 2025-0554-YB-09), and Clinical Research Foundation of Shanghai Pulmonary Hospital (FKLY20016, fky2410, fky2508).

Artificial Intelligence (AI) Use Disclaimer

The multiple-phases multiomics strategy established in our study was developed via the deep learning and machine learning methods. In addition, all authors have to stated that there are no AI tools applied in this study.

RESULTS

- The MidS strategy achieved AUC of 0.901 in external test set for diagnosing lung cancer, with overall sensitivity of 88.6% and specificity of 83.6%.
- The MidS strategy showed superior performance to all clinical and single-omics models for classifying the malignancy risk of nodules.
- When compared with the Herder model, the MidS strategy might enable avoidance of delayed treatment for malignant IPLs in 52% of cases and reduce unnecessary invasive procedures by 0.5% for benign cases.
- It prevented 9.1% of low-risk patients from unnecessary complex analyses.

