

 <p>UniSR Università Vita-Salute San Raffaele</p>	<p>APPLICATION TO ACT AS SUPERVISOR AND RESEARCH PROJECT PROPOSAL</p>	<p>MO 20-5 ed. 02 of 16/01/2026 PO 20 Page 5 of 11</p>
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PROJECT

Supervisor: Anna Palmisano

Title: Uncertainty-Aware Generative Modeling of Longitudinal Lung Nodule Evolution for Improved Risk Stratification

Curriculum: Clinical and Experimental Medicine

Link to the personal page of the University or relevant hospital site website: [_Palmisano Anna Università Vita-Salute San Raffaele_](#)-----

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Lung cancer remains the leading cause of cancer-related mortality worldwide, making early detection essential for improving survival. Low-dose CT screening has increased the detection of pulmonary nodules, but many lesions are indeterminate at baseline and require longitudinal surveillance to evaluate their evolution (7). Current computer-aided diagnosis methods based on deep learning mainly analyze single time-point images and therefore ignore the temporal dynamics of tumor growth. However, tumor progression is inherently heterogeneous, and clinically relevant decisions often depend on how a lesion evolves over time rather than on its baseline appearance. Although recent generative modeling approaches have shown strong potential in medical imaging (9,11), their application to modeling disease progression from longitudinal data remains limited. There is currently a lack of computational frameworks capable of learning temporal patterns of nodule evolution while explicitly modeling uncertainty in tumor growth.

Rationale and hypothesis

Modeling the longitudinal evolution of pulmonary nodules using probabilistic generative models could provide a more realistic representation of tumor progression than static image analysis (9,10,11). By learning distributions of plausible short-term nodule evolution conditioned on baseline imaging, such models may capture both the variability and uncertainty inherent in tumor growth. The hypothesis is that integrating uncertainty-aware synthetic longitudinal representations into malignancy prediction pipelines will improve early risk stratification compared with models relying solely on baseline CT scans.



Objectives and specific aims

The overall objective is to develop computational methods that model the temporal evolution of lung nodules from longitudinal CT data. The project will first construct and preprocess a curated longitudinal CT dataset with consistent nodule tracking while establishing baseline generative modeling benchmarks (4,5,6). It will then develop probabilistic generative architectures, including diffusion-based approaches adapted to 3D CT data, capable of producing plausible future representations of nodules while incorporating domain-informed constraints that preserve radiological realism (10,11). Finally, the work will evaluate the clinical utility of these generated longitudinal representations by integrating them into malignancy classification pipelines and measuring performance on previously unseen patient data.

Expected outcomes

The project is expected to produce a validated longitudinal imaging dataset, a novel uncertainty-aware generative framework for modeling nodule progression, and a systematic evaluation of its clinical relevance for lung cancer risk stratification. The results may demonstrate that incorporating generative temporal modeling improves predictive performance and supports earlier, more informed decision-making in lung cancer screening.

Skills that the student should acquire (max. 600 characters including spaces):

The student will acquire advanced skills in medical image analysis and machine learning, with a focus on generative and probabilistic modeling for longitudinal imaging data. Training will include 3D deep learning architectures, uncertainty modeling, and diffusion-based generative methods. The student will also develop expertise in curating and processing large-scale CT datasets, rigorous experimental design, and model validation in clinical contexts, while gaining experience in interdisciplinary collaboration with radiologists and scientific dissemination of research results.

References (max. 15)

1. Traverso A, Tiano D, Corvaglia A, Dimonte A, Draetta EL, Fabiani B, Scuri P, Barbieri S, Agazzi M, Arslan M, Celada D, Chiabrando F, Cibrario L, Cielo G, Colombo A, Contini S, Liberotti M, Montagna M, Ogliari FR, Palmisano A, Pisu F, Serra D, Varani D, Vignale D, Vitali AL, Zambello A, Chiapponi C, Denti M, Esposito A, Tacchetti C. Powering responsible artificial intelligence with high-quality real-world data: the S-RACE platform for scalable, multi-specialty clinical research. NPJ Digit Med. 2026 Jan 3;9(1):6. doi: 10.1038/s41746-025-02132-w. PMID: 41484225; PMCID: PMC12770359.



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2. van Genderen ME, Kant IMJ, Tacchetti C, Jovinge S. Moving Toward Implementation of Responsible Artificial Intelligence in Health Care: The European TRAIN Initiative. *JAMA*. 2025 May 6;333(17):1483-1484. doi: 10.1001/jama.2025.1335. PMID: 39928513.
3. Palmisano A, Vignale D, Boccia E, Nonis A, Gnasso C, Leone R, Montagna M, Nicoletti V, Bianchi AG, Brusamolino S, Dorizza A, Moraschini M, Veettil R, Cereda A, Toselli M, Giannini F, Loffi M, Patelli G, Monello A, Iannopollo G, Ippolito D, Mancini EM, Pontone G, Vignali L, Scarnecchia E, Iannacone M, Baffoni L, Sperandio M, de Carlini CC, Sironi S, Rapezzi C, Antiga L, Jagher V, Di Serio C, Furlanello C, Tacchetti C, Esposito A. AI-SCoRE (artificial intelligence-SARS CoV2 risk evaluation): a fast, objective and fully automated platform to predict the outcome in COVID-19 patients. *Radiol Med*. 2022 Sep;127(9):960-972. doi: 10.1007/s11547-022-01518-0. Epub 2022 Aug 29. PMID: 36038790; PMCID: PMC9423702.
4. Drè A, et al. The LUNA25 Challenge: Public Training and Development Set – Imaging Data (version 1.0.0). Zenodo; 2025. doi:10.5281/zenodo.14223624.
5. Drè A, et al. Benchmarking of Artificial Intelligence and Radiologists for Lung Cancer Screening in CT: The LUNA25 Challenge. In: *Medical Image Computing and Computer-Assisted Intervention (MICCAI) 2025 Proceedings*. 2025. doi:10.5281/zenodo.15094631.
6. Setio AAA, Traverso A, de Bel T, Berens MSN, van den Bogaard C, Cerello P, Chen H, Dou Q, Fantacci ME, Geurts B, et al. Validation, comparison, and combination of algorithms for automatic detection of pulmonary nodules in computed tomography images: the LUNA16 challenge. *Med Image Anal*. 2017;42:1-13. doi:10.1016/j.media.2017.06.015. PMID:28688735.
7. Ardila D, Kiraly AP, Bharadwaj S, Choi B, Reicher JJ, Peng L, Tse D, Etemadi M, Ye W, Corrado G, Naidich DP, Shetty S. End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography. *Nat Med*. 2019;25(6):954-961. doi:10.1038/s41591-019-0447-x. PMID:31110349.
8. Han C, et al. Synthesizing diverse lung nodules wherever massively: 3D multi-conditional GAN-based CT image augmentation for object detection. *arXiv [Preprint]*. 2019. doi:10.48550/arXiv.1906.04962.
9. Sun L, Chen J, Xu Y, Gong M, Yu K, Batmanghelich K. Hierarchical amortized GAN for 3D high-resolution medical image synthesis. *IEEE J Biomed Health Inform*. 2022;26(8):3966-3975. doi:10.1109/JBHI.2022.3172976. PMID:35522642; PMCID:PMC9413516.
10. Rombach R, Blattmann A, Lorenz D, Esser P, Ommer B. High-resolution image synthesis with latent diffusion models. *arXiv [Preprint]*. 2021. doi:10.48550/arXiv.2112.10752.
11. Kazerouni A, Aghdam EK, Heidari M, Azad R, Fayyaz M, Hacıhaliloglu I, Merhof D. Diffusion models in medical imaging: a comprehensive survey. *Med Image Anal*. 2023;88:102846. doi:10.1016/j.media.2023.102846. PMID:37295311.