Virtual Human Twins in Lung Health: A Comprehensive *In Silico* Screening Approach

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Background & Purpose

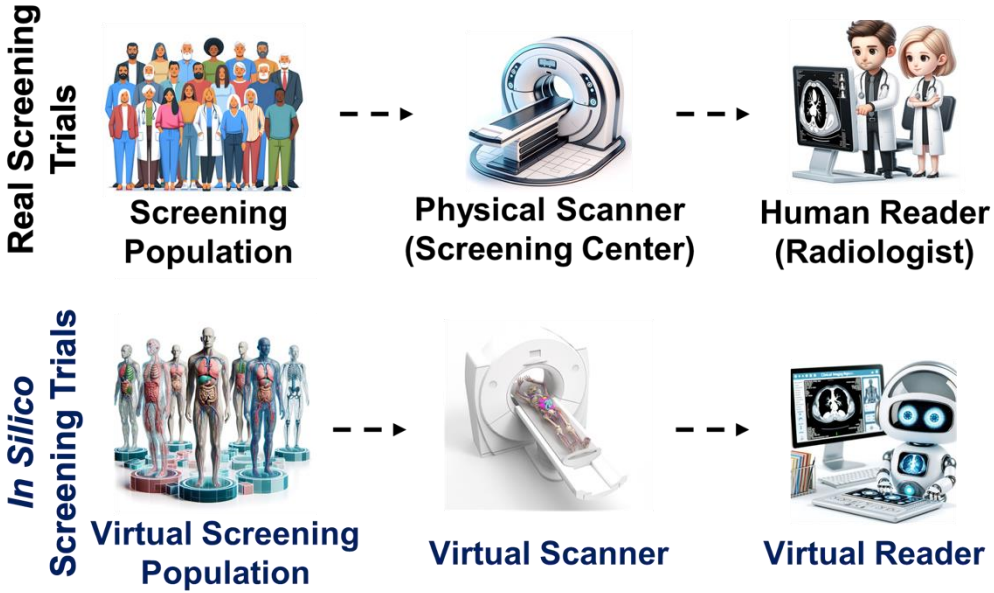
- **Challenge**: Limitations of traditional lung cancer screening (cost, time, FPR).

- **Purpose**: To enhance lung cancer screening via ***In silico*** trials, simulating the entire imaging and diagnostic process.

Aberle, *NEJM*(2011)

In Silico Screening Trial

- In silico imaging trials, provide a computational substitute for clinical trials.
- Proposed platform mimics essential components of imaging process:
  - virtual patients
  - virtual scanners
  - simulated readers



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Tushar, *arXiv:2404.11221* (2024), SPIE *Phy. Medl*(2024)

Methods

- **Virtual Cohort**: 294 virtual patient models, with 512 digitally inserted nodules.
- **CT Simulation**: Verified software for imaging, MCR toolkit for standard protocol adherence (**DukeSim**).
- **Virtual Reader**: 3D AI model (**CT AI-reader**) for nodule detection and cancer diagnosis.
- **Statistical Labeling**: Radiomics-informed **benign/malignant** nodule probabilities.
- **Statistical Analysis:** Performance was evaluated using **AUC with 95% CIs** calculated via DeLong's method (2000 bootstrap samples).

Methods- Virtual Cohort

Starting with patient CT scans, we use XCAT-3 to generate virtual human twins through segmentation, quality control, and 3D voxelization. Clinically informed lesions are then simulated and inserted, creating anatomically accurate models for advanced virtual trials.

Health System

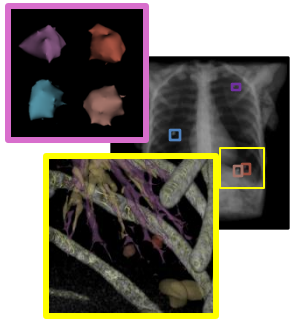
XCAT-3 tool-kit

- Segmentation
- Quality Control
- 3D Representation

Virtual human twins

Lesion tool-kit

- Simulate Lesion
- Lesion Insertion



Digital twins + Simulated Lesion

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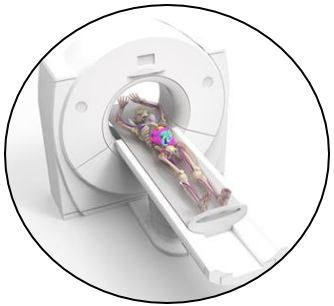
Tushar, *arXiv:2404.11221*(2024); Dahal *arXiv:2405.11133*(2024)

Methods- Virtual Scanner

Cohort of virtual human twins with and without nodules was virtually imaged using validated imaging simulation tool (**DukeSim**)

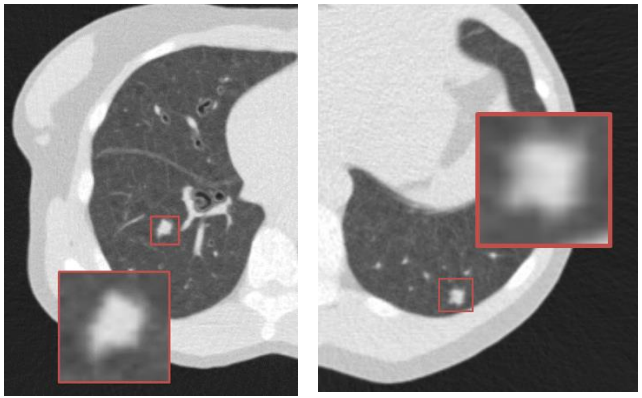


Virtual Scanner

DukeSim

Legacy Scanners

Modern Scanners



Simulated chest CT replicating NLST-era imaging with highlighted nodules.

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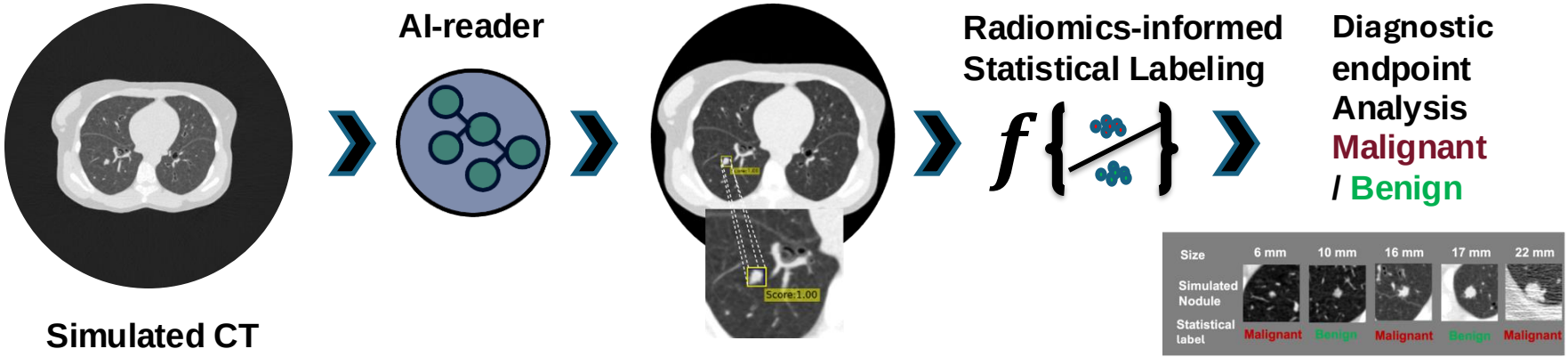
Tushar, *arXiv:2404.11221*(2024); Abadi, *TMI*(2019)

Methods- Virtual Reader

Given simulated CT images from virtual twins, the AI-reader identified potential nodule locations and their probabilities. These nodules were then labeled as benign or malignant based on radiomics features-informed statistical modeling.



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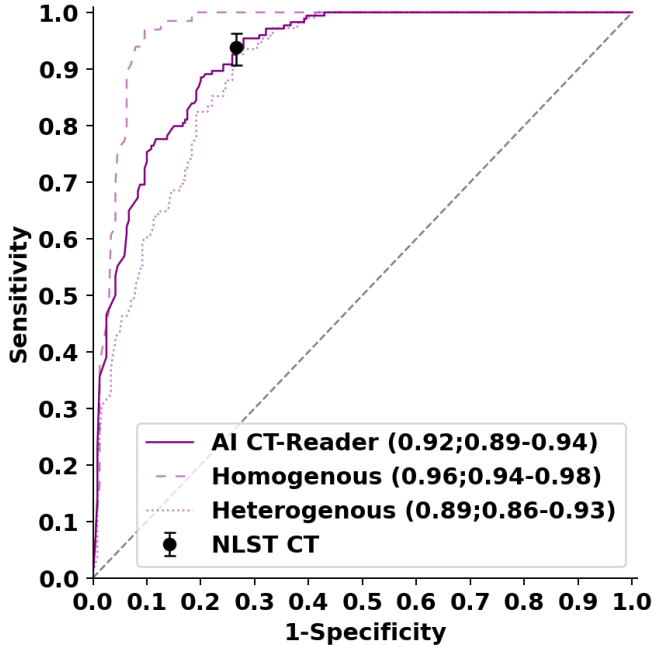
Tushar, *arXiv:2404.11221* (2024), *VITM* (2024)

Key Results

- **Virtual Cohort:** 294 subjects (174 with nodules, 139 without).
  Mean age 59 years, 55.7% male
  Lesion sizes 4-34 mm (median 9 mm)
- **Simulation Efficiency**: 1,764 scans in 49 hours (36 scans/hour).
- **Performance Metrics**: ***In silico*** trial mirrored **NLST: 94% sensitivity, 73% specificity for CT**.
- **Lesion Type**: CT detected homogeneous lesions better (AUC **0.97** vs. **0.89**).



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Clinical Relevance & Future Directions

- **Impact:** In silico trials and Virtual Imaging Trials (VITs) replicate real-world studies, offering a faster, safer, and cost-effective alternative for optimizing diagnostic technologies.
- **Advantages:** They enable personalized, efficient lung health screening by reducing risks and trial costs.
- **Future Directions:** Expand virtual cohorts, incorporate diverse lesion types and demographic data, and explore long-term outcomes like disease progression and survival.

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