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G-ART
Advanced Radiation Therapy

TRANSFORMING NSCLC MULTIDISCIPLINARY CARE WITH A PULMONARY DIGITAL-TWIN: FROM PERSONALIZED SURGERY TO RADIOTHERAPY PLANNING



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PULMONARY DIGITAL-TWIN

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*A **lung digital twin** is a **personalized computational model** of a patient's respiratory system that continuously integrates multimodal patient-specific data (e.g., imaging, pulmonary function tests, clinical variables, and biological information) to **reproduce** the current state of the lung and **predict** its future behavior **under different conditions or interventions.***



Unlike a static 3D reconstruction, a digital twin evolves as new patient data become available, allowing a dynamic representation of the patient's lung status.

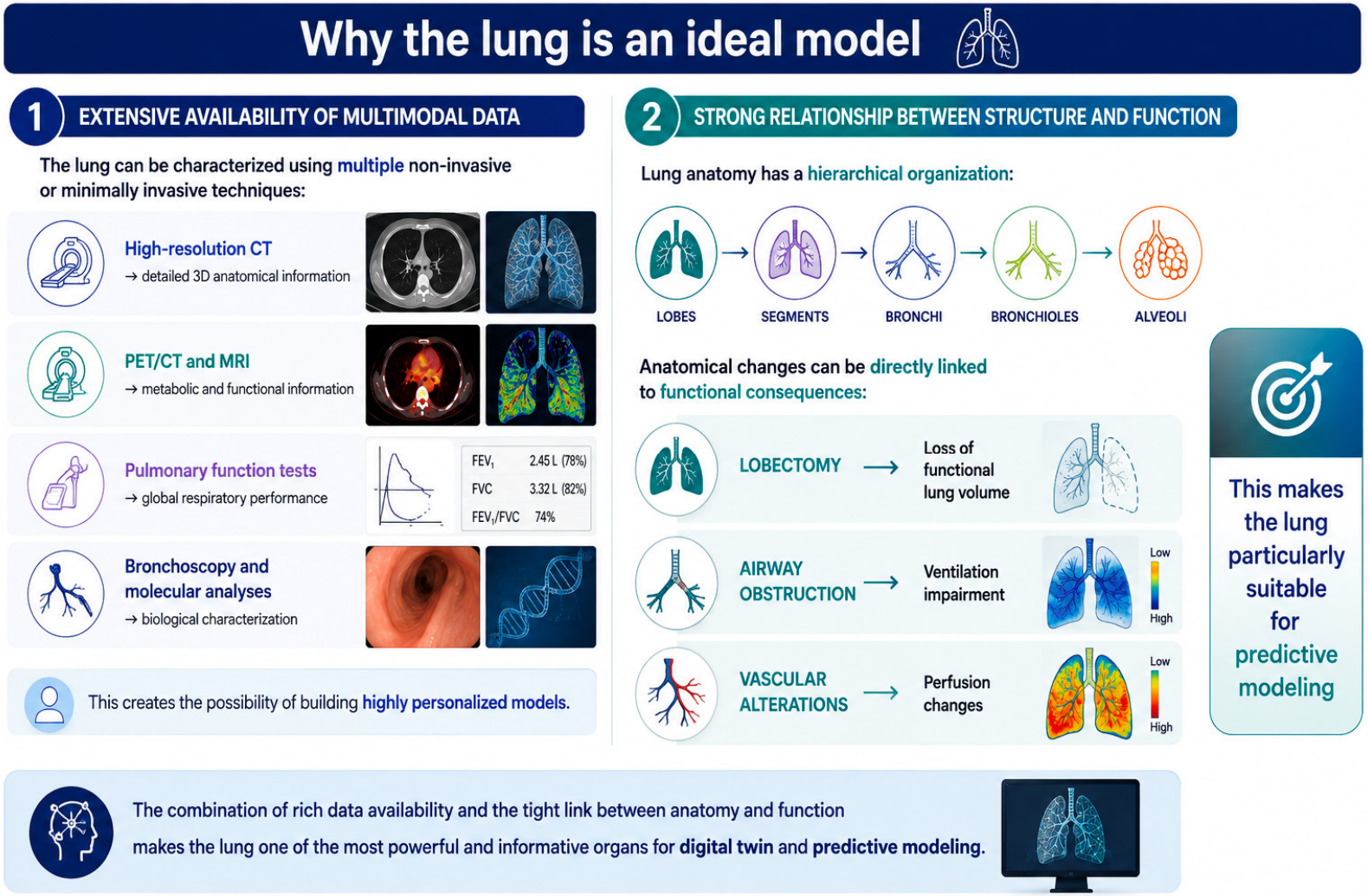
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PULMONARY DIGITAL-TWIN

3D LUNG RECONSTRUCTION		LUNG DIGITAL TWIN
 Anatomical model	→	Anatomical + physiological model 
Mostly static	→	Dynamic and updateable
Describes structure	→	Predicts behavior 
 CT-based	→	Multimodal data integration (imaging data, functional and clinical data..)
 Visualization tool	→	Decision-support system 

FROM ANATOMY TO INTELLIGENCE: from static images to personalized, predictive, and actionable insights

The **lung** represents an **ideal** yet **challenging organ** model for digital twin development because it is directly accessible through advanced imaging technologies and functional measurements, while simultaneously exhibiting complex multiscale interactions between anatomy, biomechanics, ventilation, perfusion, and gas exchange



→ Unlike many organs, lung function can be repeatedly assessed, therefore the digital twin can be continously updated!

WHY THE LUNG IS A COMPLEX MODEL

1 MULTISCALE ORGANIZATION

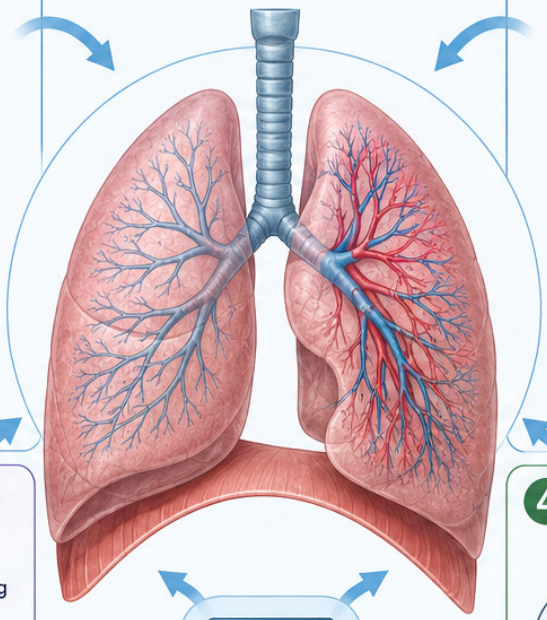
The lung operates across several biological scales:

Macroscopic:
lobes, segments, airways, vessels

Microscopic:
alveoli and capillary networks

Cellular/molecular:
immune response, inflammation, tumor microenvironment

A model must integrate phenomena occurring at very different spatial and temporal scales.



2 COUPLED MECHANICAL AND PHYSIOLOGICAL PROCESSES

Lung function depends on the interaction between:

- airway geometry
- tissue elasticity
- respiratory mechanics
- diaphragm movement
- pleural pressure
- blood flow distribution

→ **Small anatomical changes may produce nonlinear functional effects.**

3 HETEROGENEOUS REGIONAL FUNCTION

The lung is not a uniform organ:



- ventilation varies according to graviity and posture
- perfusion distribution changes dynamically
- emphysema, fibrosis, tumors, and previous surgery create regional differences

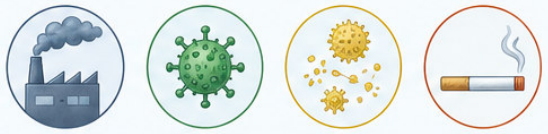
→ Therefore, predicting function requires spatial rather than only global models.



An accurate lung model must integrate structure, function and environment across multiple scales.

4 CONSTANT INTERACTION WITH THE ENVIRONMENT

The lung is continuously exposed to external factors:



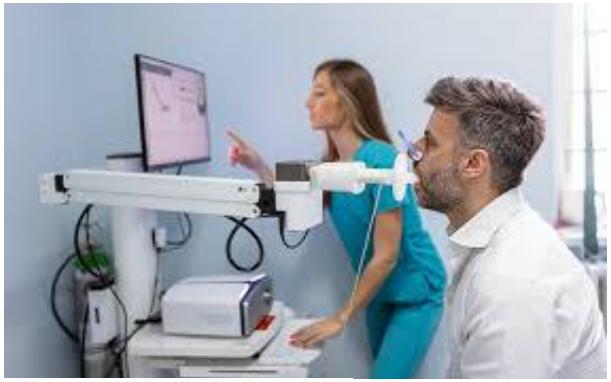
air pollutants · pathogens · allergens · smoking-related injury

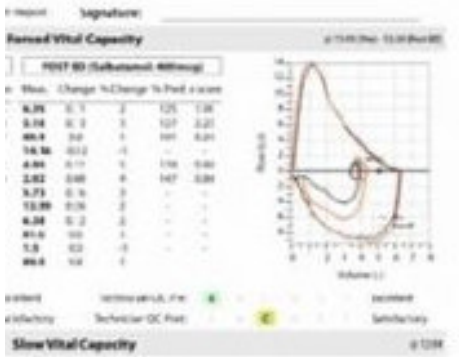
→ These exposures drive inflammation, remodeling and disease progression.

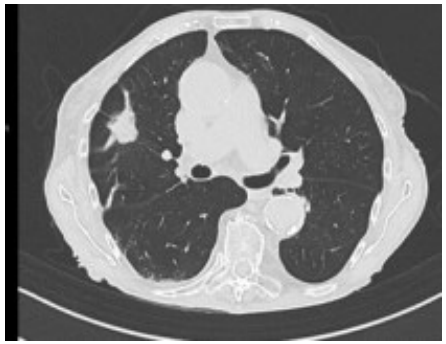
THORACIC SURGERY: State of Art

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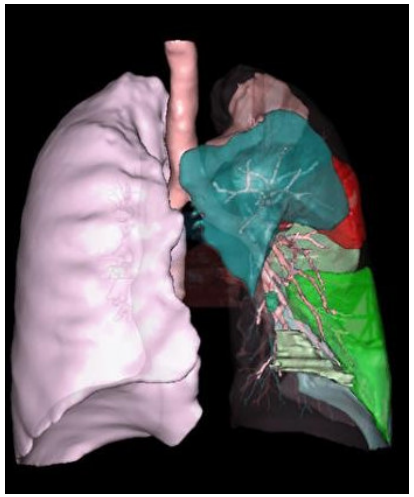
Preoperative functional evaluation

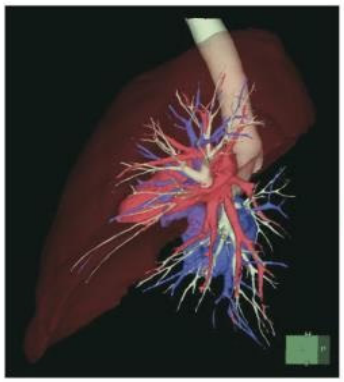




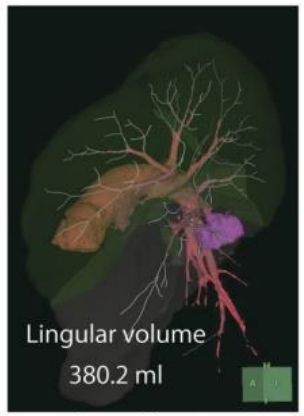


Advanced surgical planning using 3D reconstruction

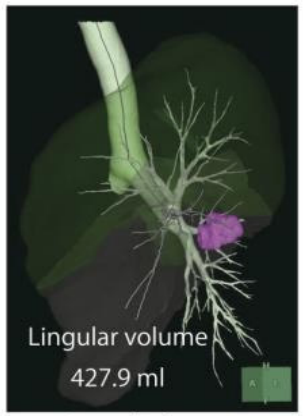




3D image reconstructed from DICOM data



Arterial territory

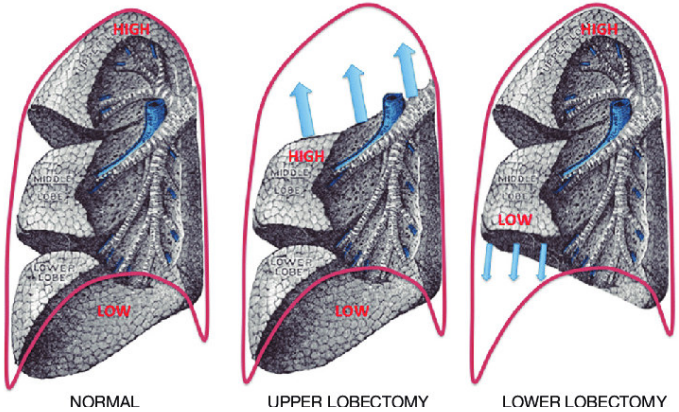


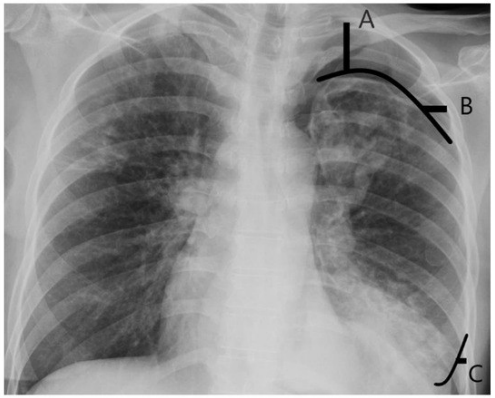
Bronchial territory

THORACIC SURGERY: State of Art

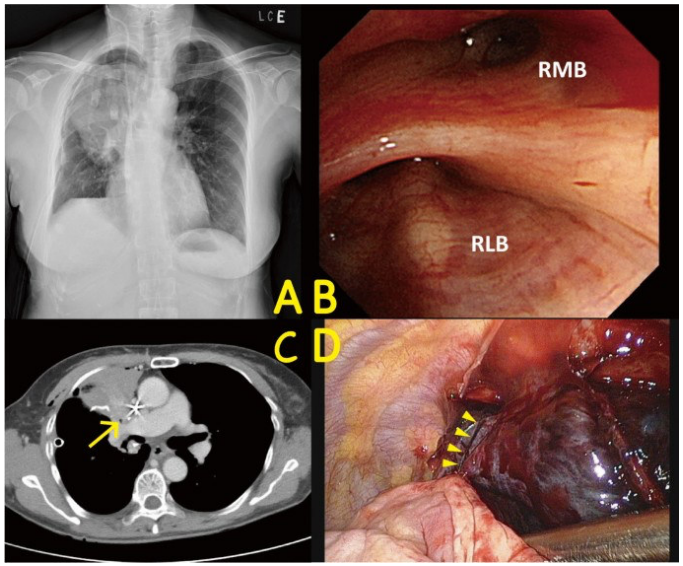


Post-operative respiratory insufficiency





Residual pleural space



Lobar Torsion

“PERSONALIZED” **THORACIC SURGERY**

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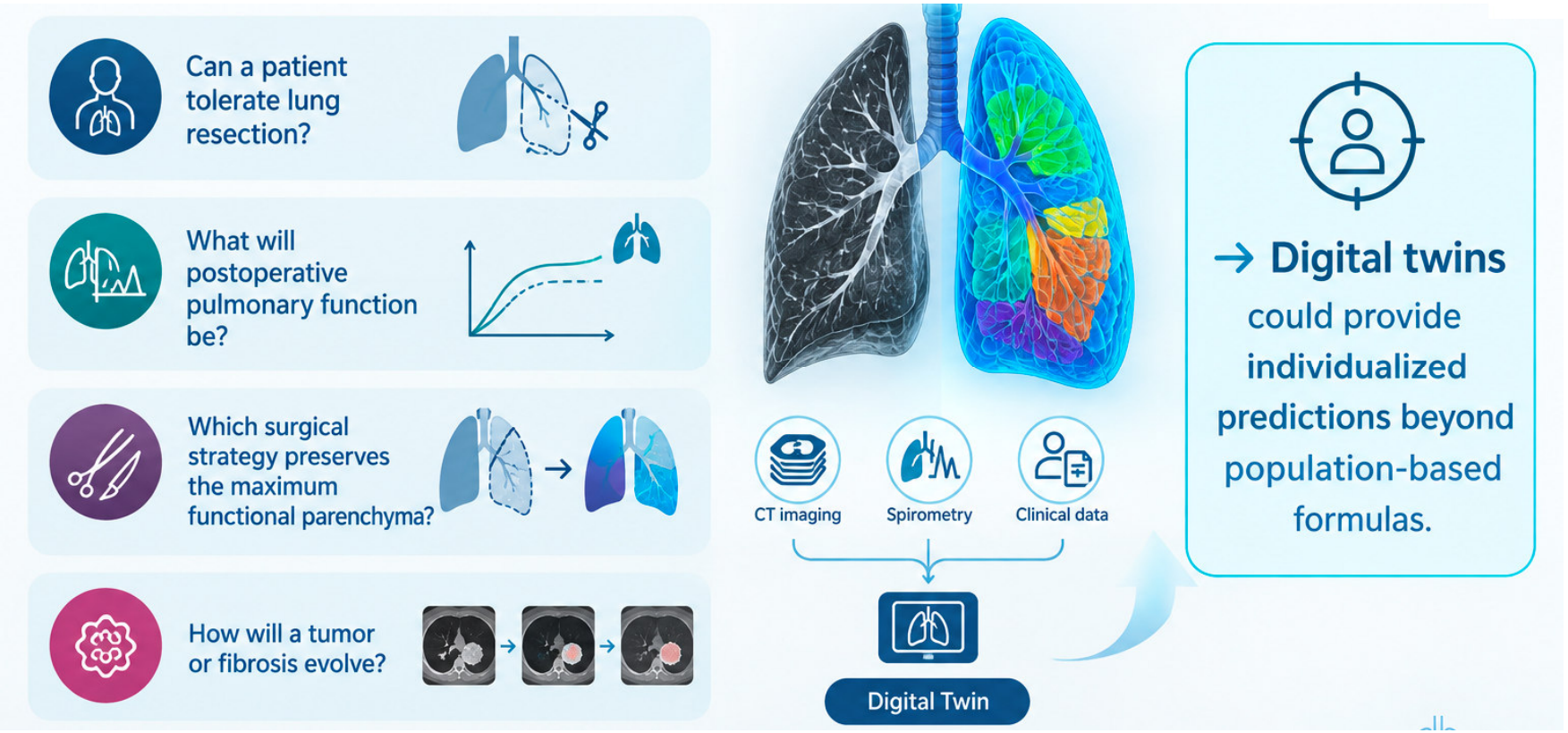
Clinical need for personalized prediction in Thoracic Surgery

Many thoracic decisions depend on ***anticipating future lung behavior****:*

- Can a patient tolerate lung resection?
- What will postoperative pulmonary function be?
- Which surgical strategy preserves the maximum functional parenchyma?
- How will a tumor or fibrosis evolve?

“PERSONALIZED” **THORACIC SURGERY**

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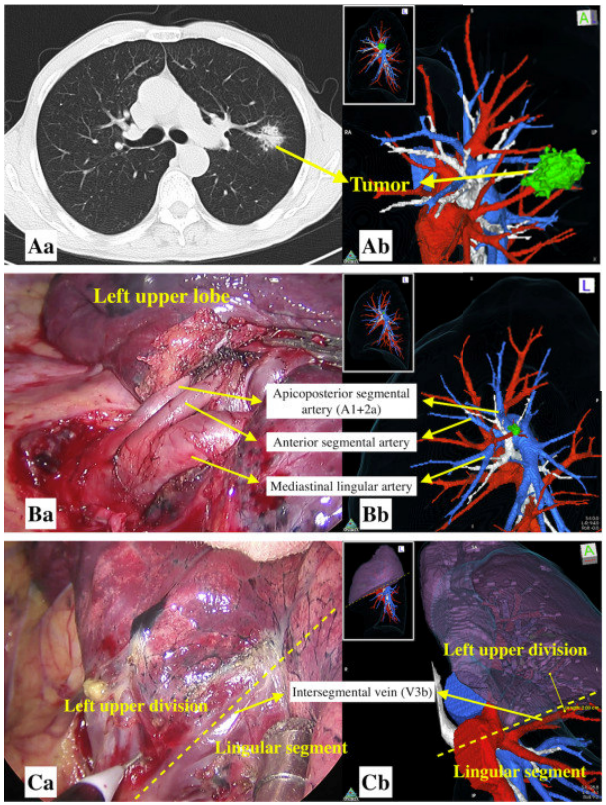
→A **lung Digital Twin** represents the **(R)evolution**, with a patient-specific predictive lung model able to prevent complications after Thoracic Surgery

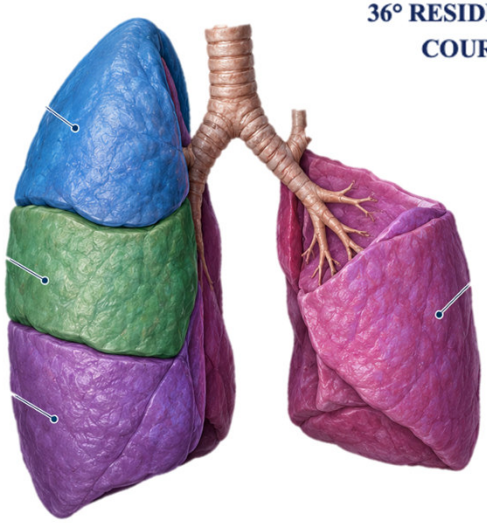
“PERSONALIZED” **THORACIC SURGERY**

A potential intraoperative scenario in the near-future

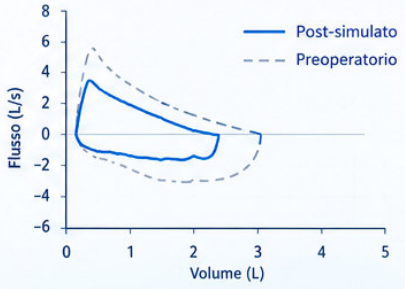


Da Vinci TilePro





FEV_1	1.82 L (58% pred)
FVC	2.87 L (70% pred)
FEV_1/FVC	63%



Simulation of post-operative spirometry and lung re-inflation

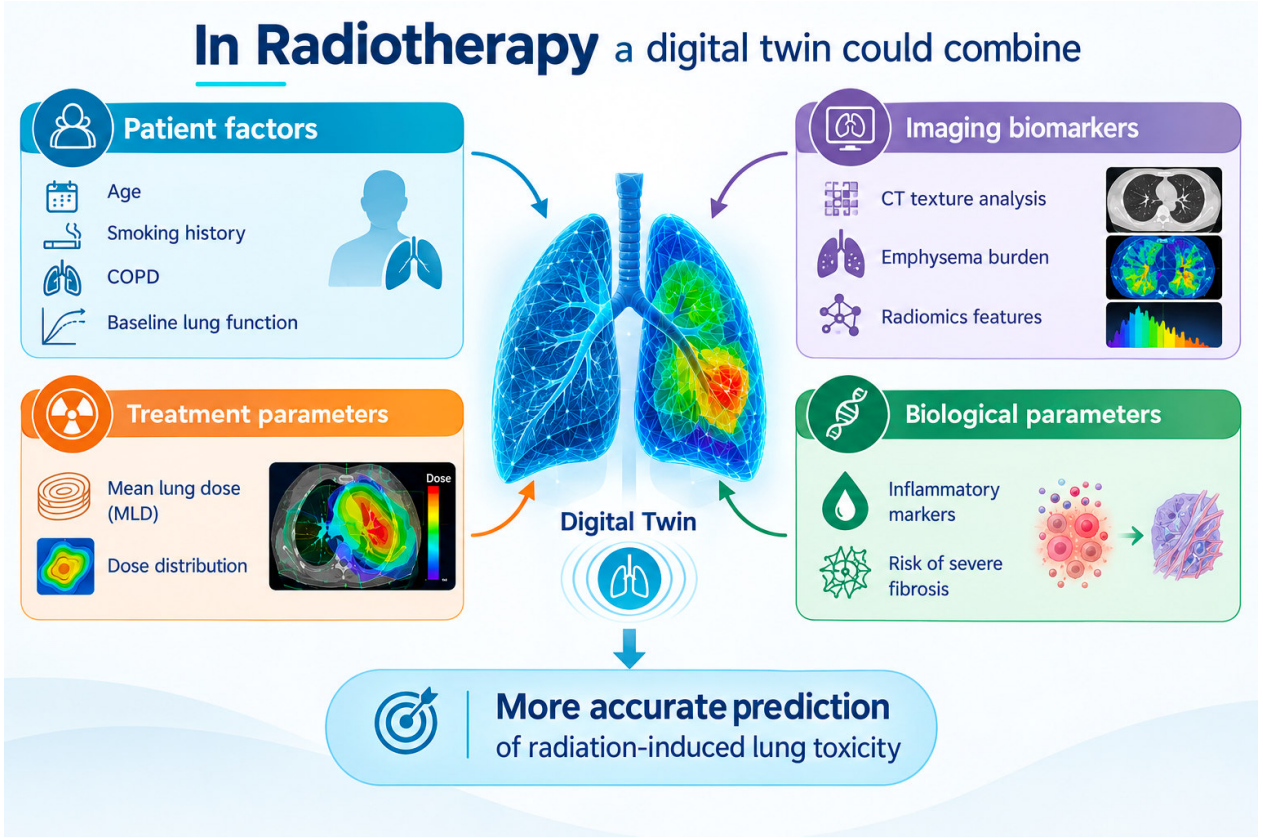
PULMONARY DIGITAL-TWIN in **RADIOTHERAPY**

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In radiotherapy, a lung digital twin represents a dynamic, patient-specific computational model that integrates imaging, functional, biological, and treatment-related data to simulate tumor response and normal/pathological tissue behavior under different radiation scenarios, enabling personalized treatment optimization and toxicity prediction.

Prediction of radiation-induced lung toxicity

Radiation pneumonitis and fibrosis remain major limitations of thoracic radiotherapy.



PULMONARY DIGITAL-TWIN in **RADIOTHERAPY**

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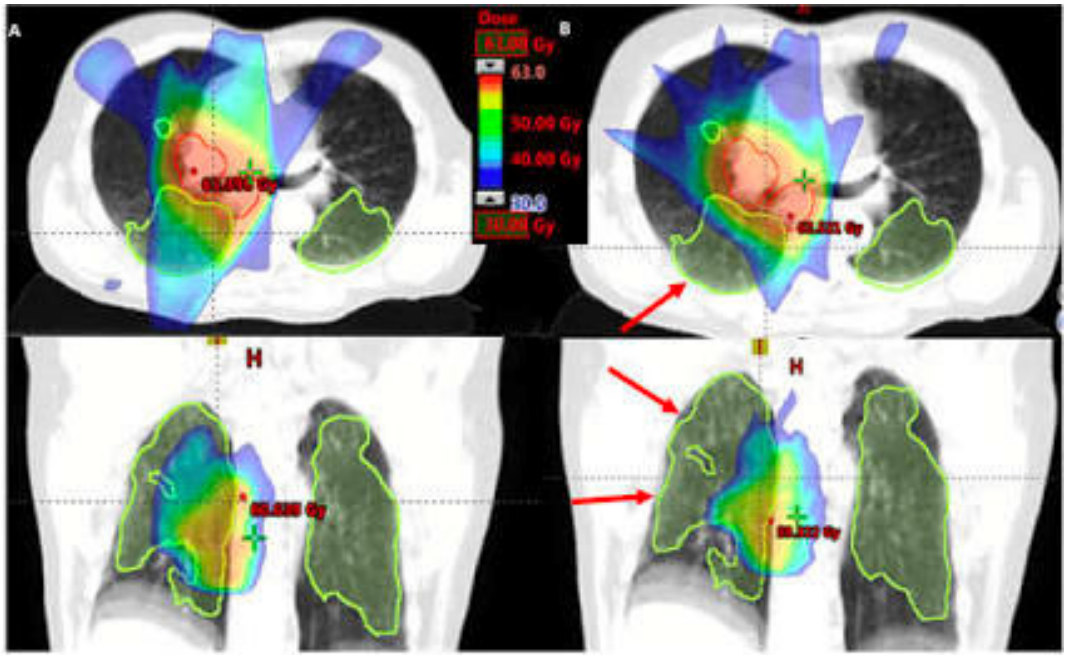
Personalized radiotherapy planning ("virtual treatment simulation")

A digital twin could simulate different radiation plans before treatment delivery:

- Different dose distributions
- Different beam arrangements
- Different fractionation schedules
- Stereotactic body radiotherapy (SBRT) vs conventional radiotherapy

The model could predict:

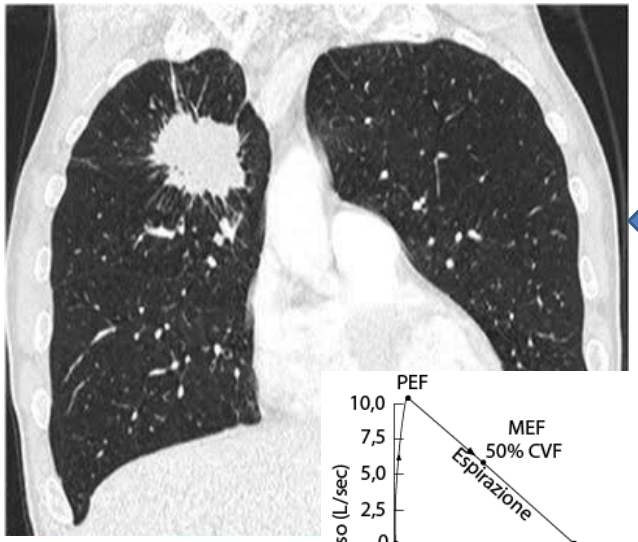
- Tumor dose coverage
- Dose to organs at risk (OARs)
- Functional lung preservation

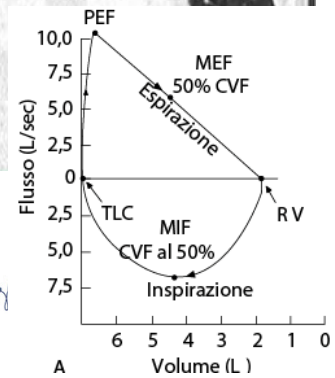


PULMONARY DIGITAL-TWIN in **RADIOTHERAPY**

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Example: Two patients with identical tumor size and location may have very different tolerance because one has normal lung reserve and the other has emphysema. A digital twin could incorporate this difference into treatment planning.

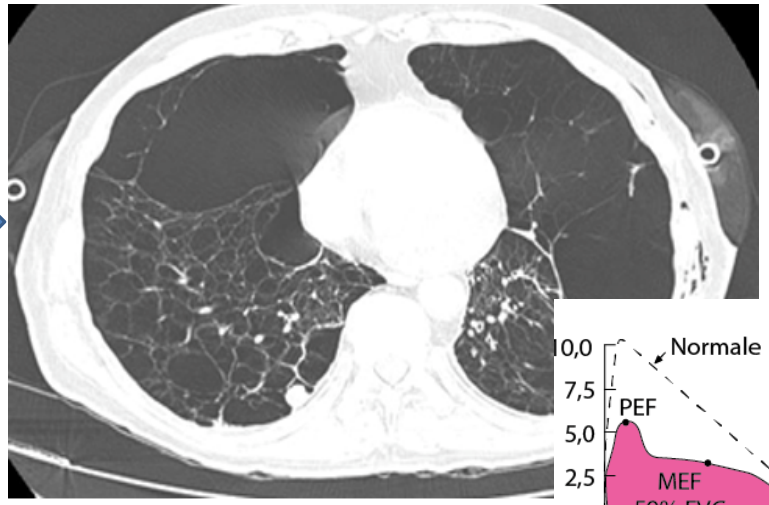


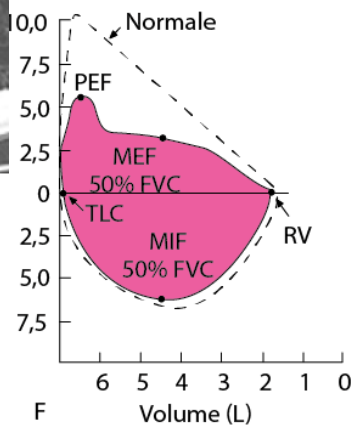




LUNG DIGITAL TWIN

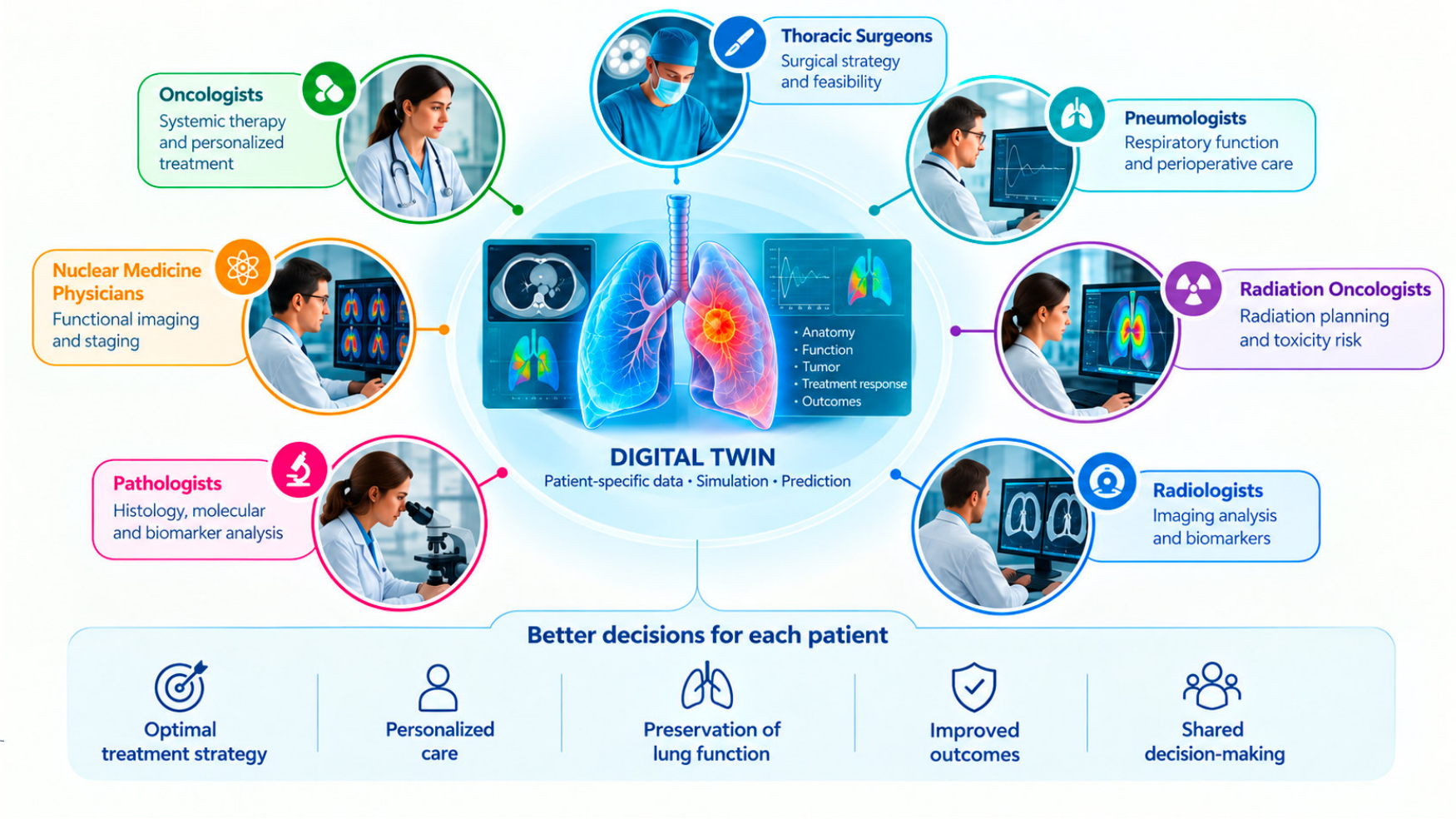
Different treatment planning





Digital twin as a decision-support tool in multidisciplinary decision-making

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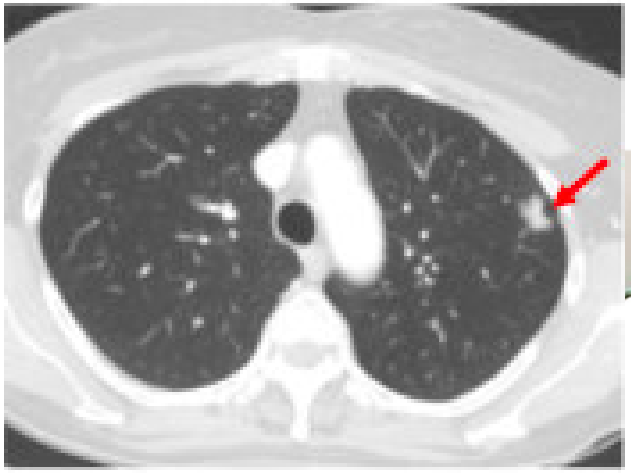
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Case 1

Elderly patient with COPD, and a peripheral lung tumor <2 cm.

Which treatment can be more suitable?

- Surgery: lobectomy?
- Surgery: segmentectomy?
- SBRT?





The Lung Digital-Twin can simulate functional loss and % of complications after surgery and after SBRT→ supporting the right ”personalized” decision

Case 2:

Patient with borderline respiratory function.

The digital twin could help predict:

· Postoperative FEV1;

· Risk of respiratory failure after Surgery or RT;

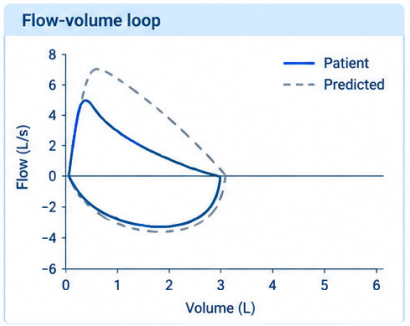
· Radiation-induced toxicity.

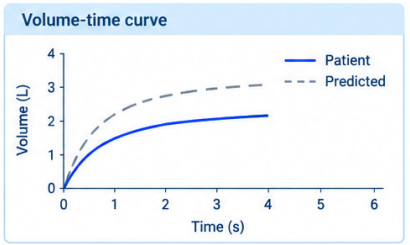
Key message:

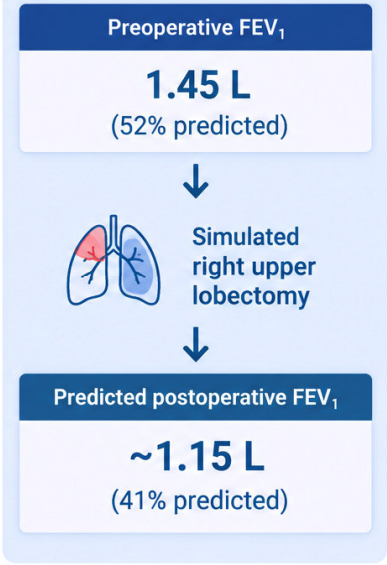
Parameter	Value	% predicted
FVC	2.55 L	72%
FEV_1	1.45 L	52%
FEV_1/FVC	0.57	–
TLC	5.10 L	82%
DLCO	48%	48%

Interpretation

- Moderate obstructive ventilatory defect
- Reduced diffusion capacity
- Functional respiratory reserve potentially limited for major lung resection







It is not intended to replace the MDT, but rather to make its decision-making quantitative

LIMITS

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Availability of high-quality multimodal datasets

A functional lung digital twin requires integration of:

- *High-resolution CT imaging*
- *Quantitative imaging biomarkers*
- *Pulmonary function tests (FEV1, FVC, DLCO)*
- *Ventilation/perfusion data*
- *Surgical details*
- *Radiotherapy dose distributions*
- *Long-term clinical outcomes*

Regulatory issues

- *Certification as medical devices*
- *Data privacy and governance*

Prospective clinical validation

- *Prospective multicenter validation*
- *Comparison with current clinical prediction models*
- *Demonstration of improved clinical decision-making*
- *Evidence of improved patient outcomes*

Integration into clinical workflow

A digital twin must provide information that is:

- *Rapid*
- *Reliable*
- *Clinically interpretable*



Challenges include:

- *Time required for image processing*
- *Integration with PACS and electronic medical records*
- *Training clinicians to interpret outputs*

The model must support—not replace—clinical expertise!

FUTURE PERSPECTIVES

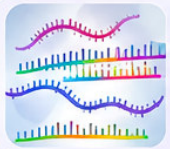
From multi-omics to a multiscale lung digital twin



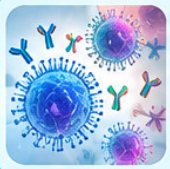
Radiomics
Imaging features from CT and functional imaging



Genomics
Mutations, molecular profiles, biomarkers

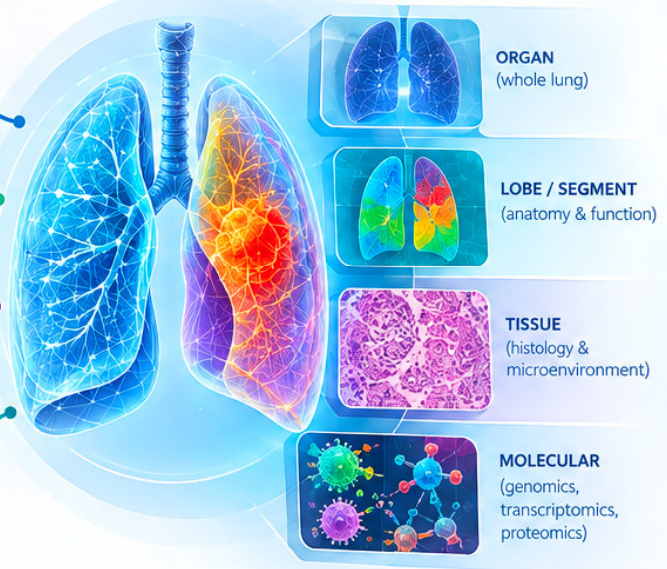


Transcriptomics
Gene expression and cellular pathways



Immunological markers
Immune cell profile, cytokines, checkpoint expression

MULTISCALE LUNG DIGITAL TWIN



Towards more personalized decisions

- **Better treatment selection** (surgery, systemic therapy, radiotherapy)
- **Improved prediction of outcomes** (response, toxicity, survival)
- **Preservation of lung function** (personalized surgical planning)
- **More precise and adaptive follow-up** (early detection, monitoring)

INTEGRATING DATA • UNDERSTANDING THE INDIVIDUAL • IMPROVING CARE

CONCLUSIONS



*The **lung digital twin** is not simply a virtual replica of the lung, but an **individual laboratory** in which the surgeon, radiation oncologist, and pulmonologist can **simulate the patient's future** before selecting the treatment.*

*The future of lung digital twins lies in **transforming** current anatomy-based decision-making **into dynamic, predictive, and personalized models** that **integrate** structure, function, and biology to **optimize** surgical and radiotherapeutic strategies*

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