

Developing a Digital Twin Framework for Personalized Radiotherapy of NSCLC

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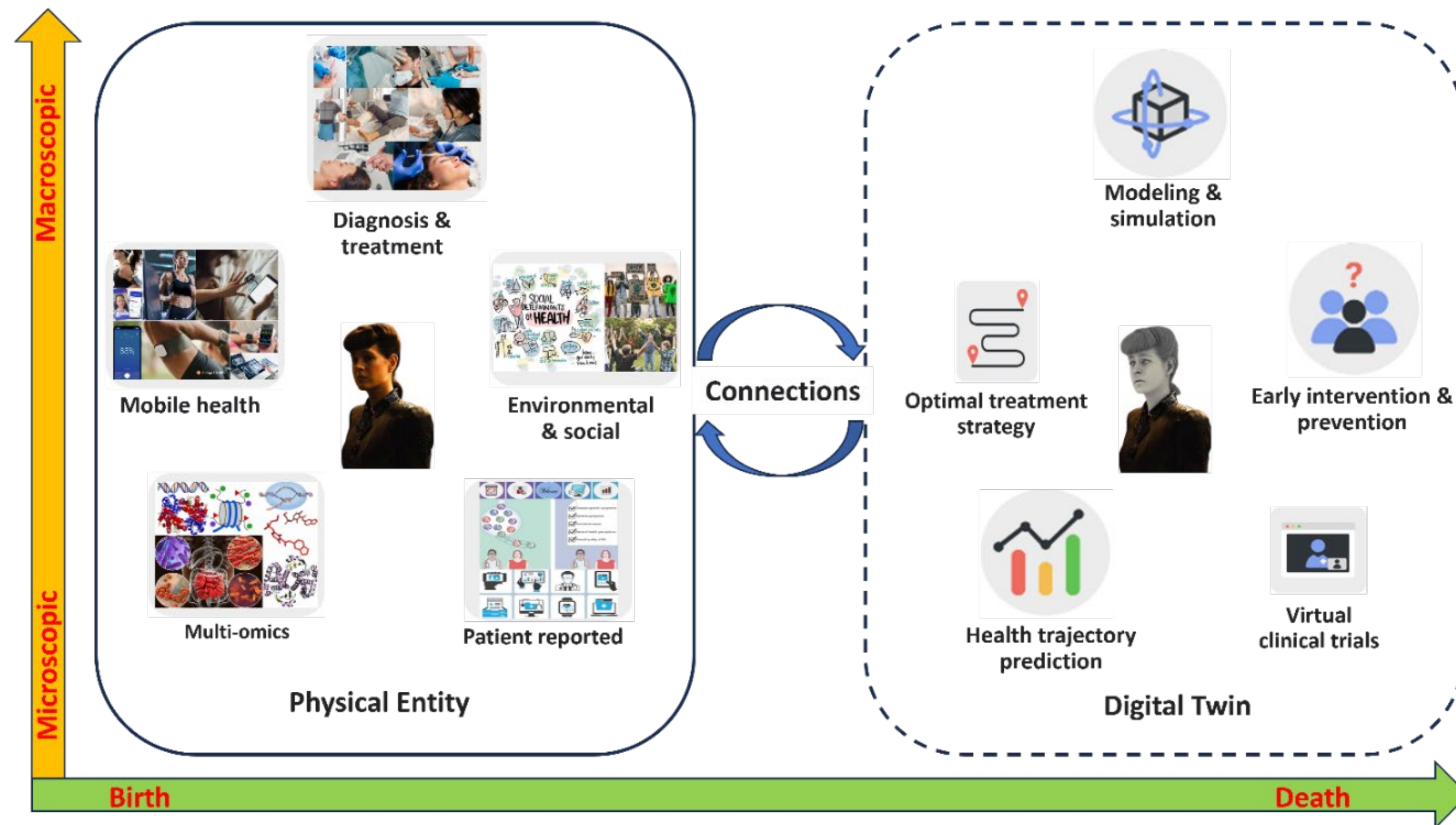
Yale University School of Medicine

Virtual Human Global Summit II, October 23, 2025



A Human Digital Twin

- A dynamic virtual representation of an individual, an organ, or an organ system based on multiscale modeling of multimodal data

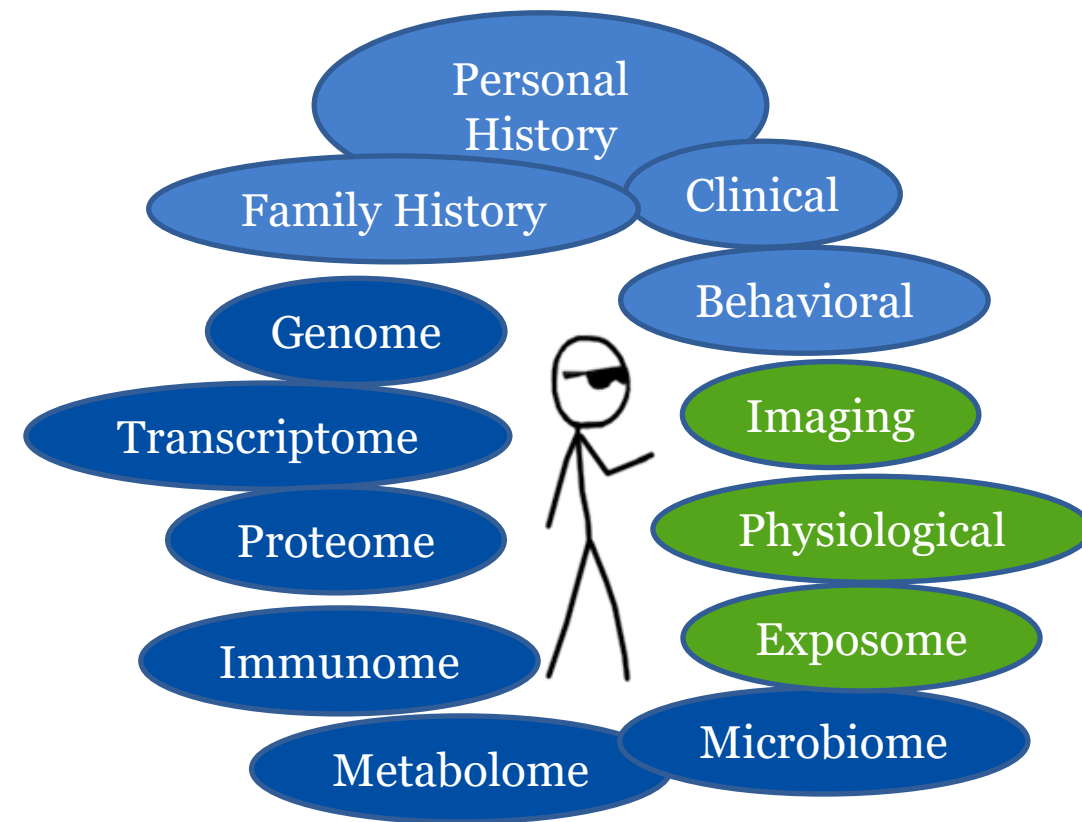


What Would DT Enable?

- Identify optimal treatment strategy by incorporating genetic, molecular, clinical, environmental, and social factors
- Improve quality of life by predicting outcomes and side effects throughout one's health trajectory
- Enable virtual clinical trial and benchmark clinical performance via virtual control
- Early intervention and prevention for individual's health

DT-Enabled Clinical Workflow

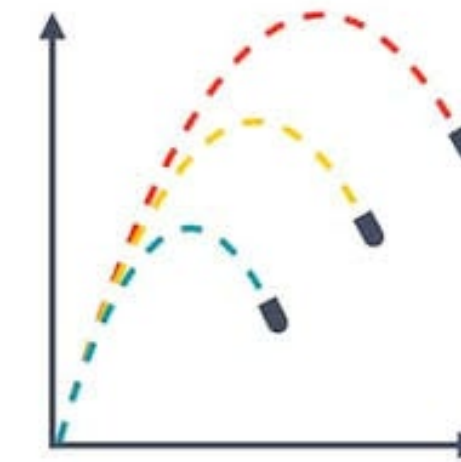
Personal Phenotypes



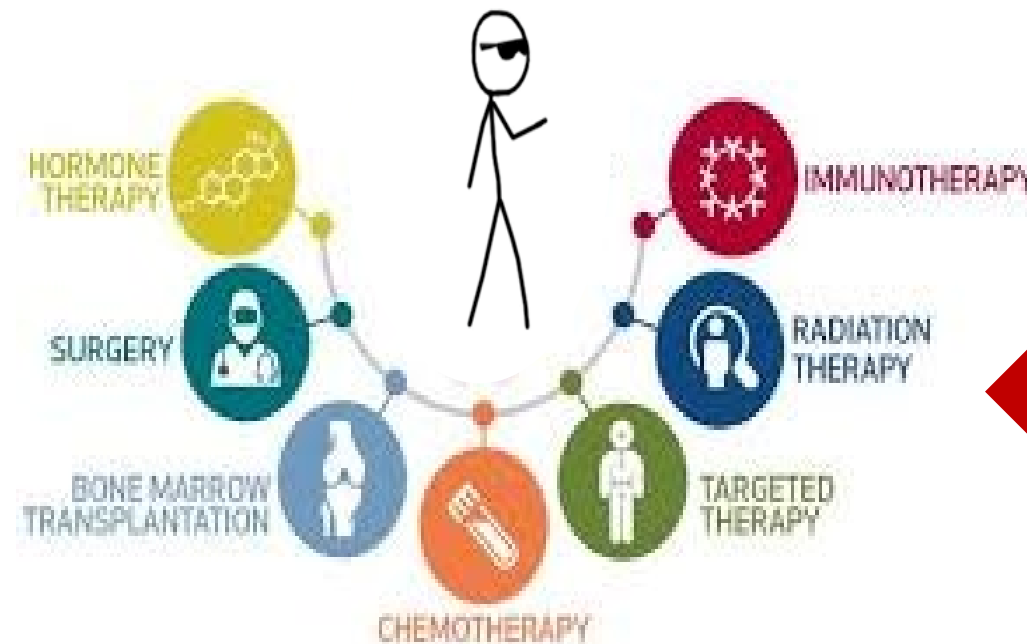
Digital Twin Simulation Using HPC



Personalized Care Trajectories



Choose a care path

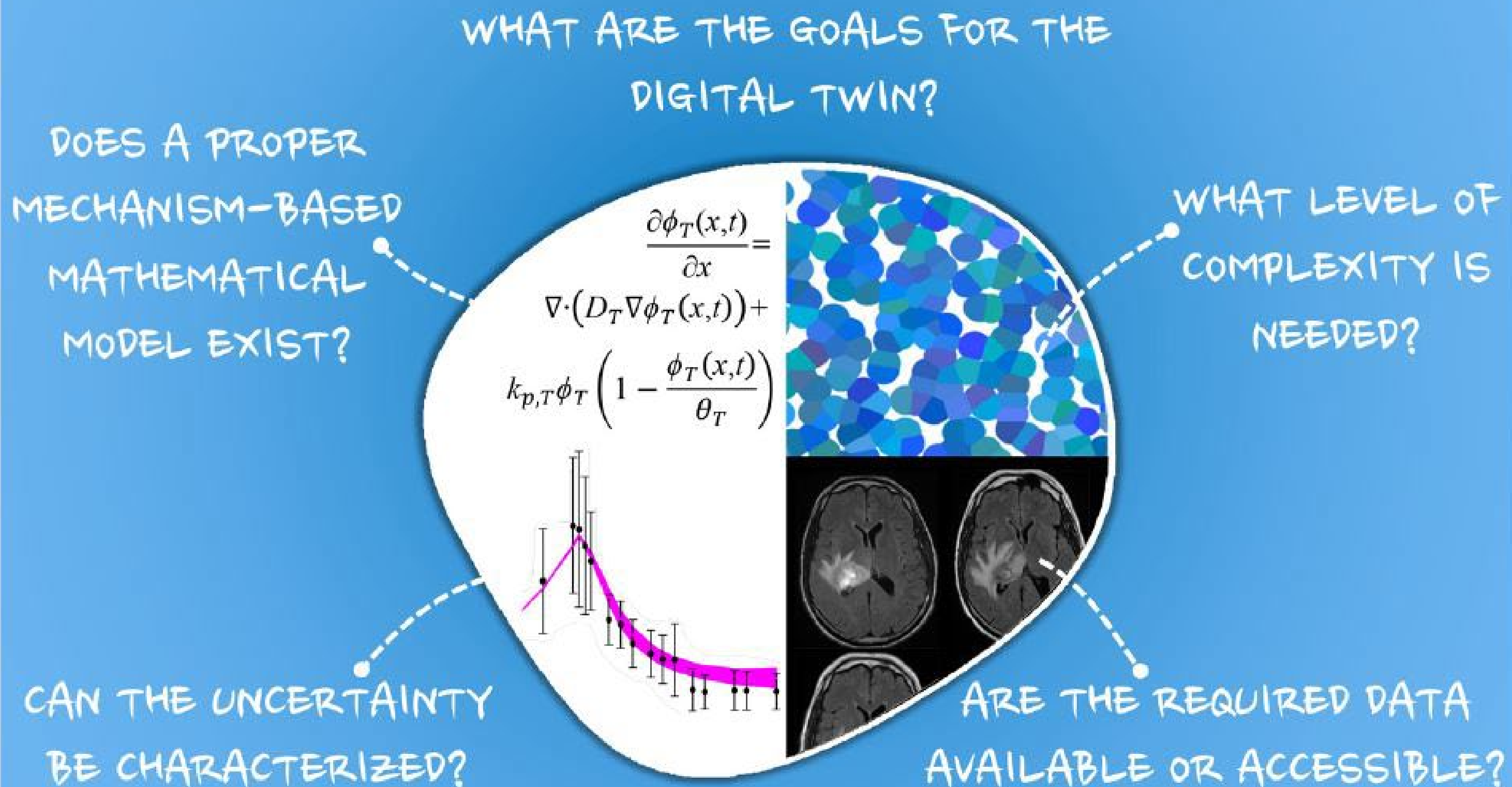


Shared Decision Making



Digital Twin Implementation

Digital Twin Blueprint



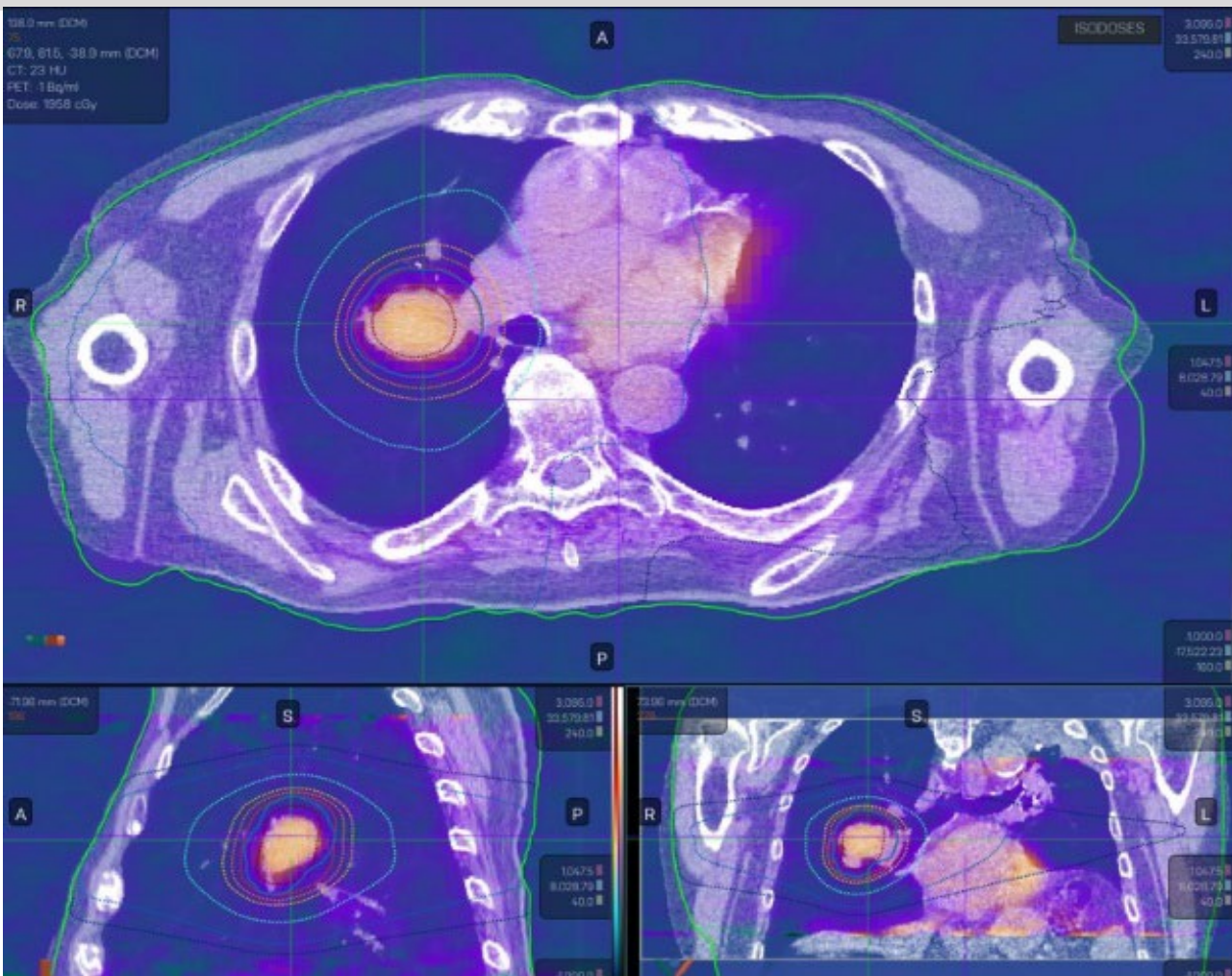
- George Box

“All models are wrong but some are useful”

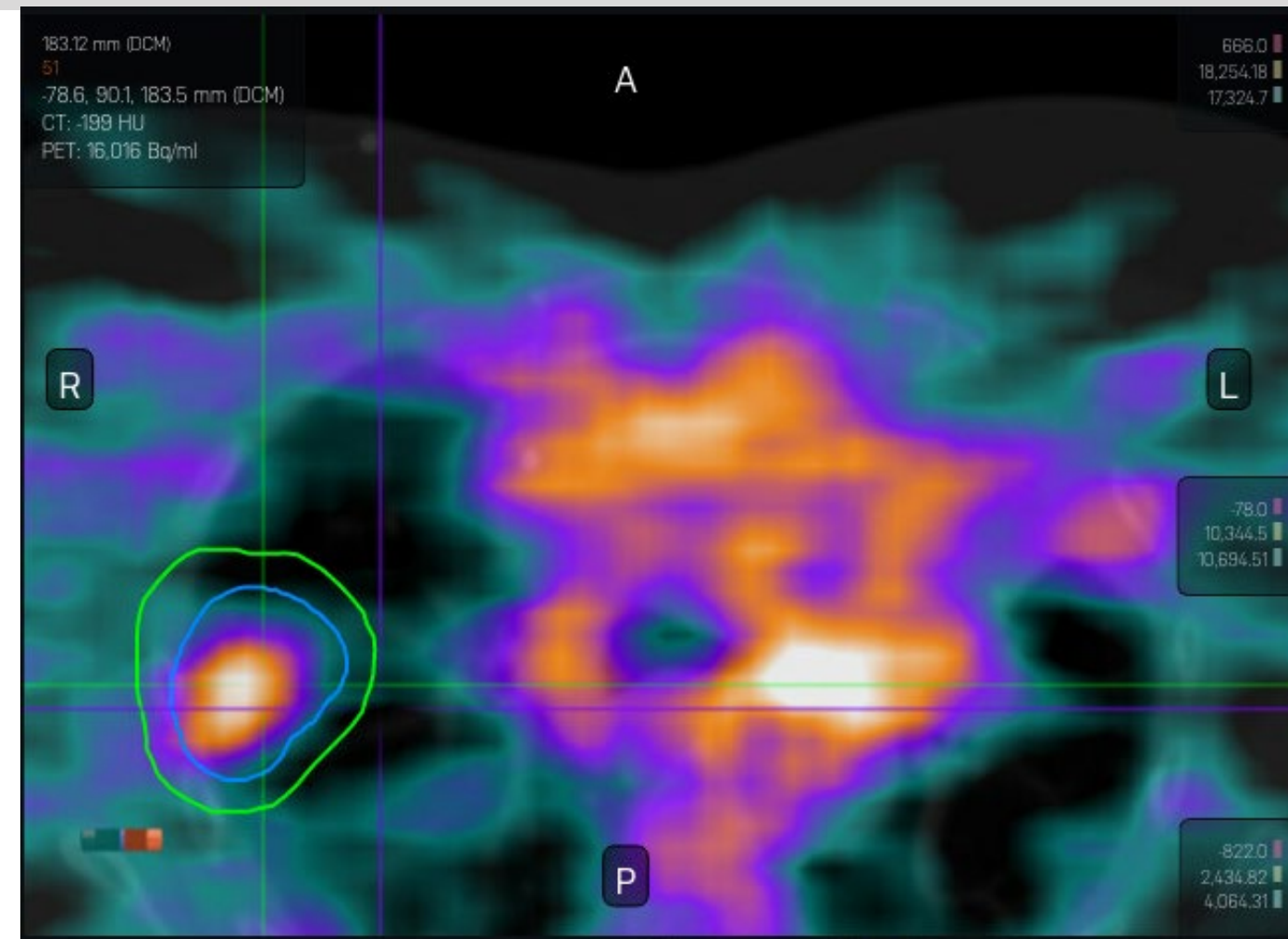
- Albert Einstein

“Everything should be made as simple as possible, but not simpler”

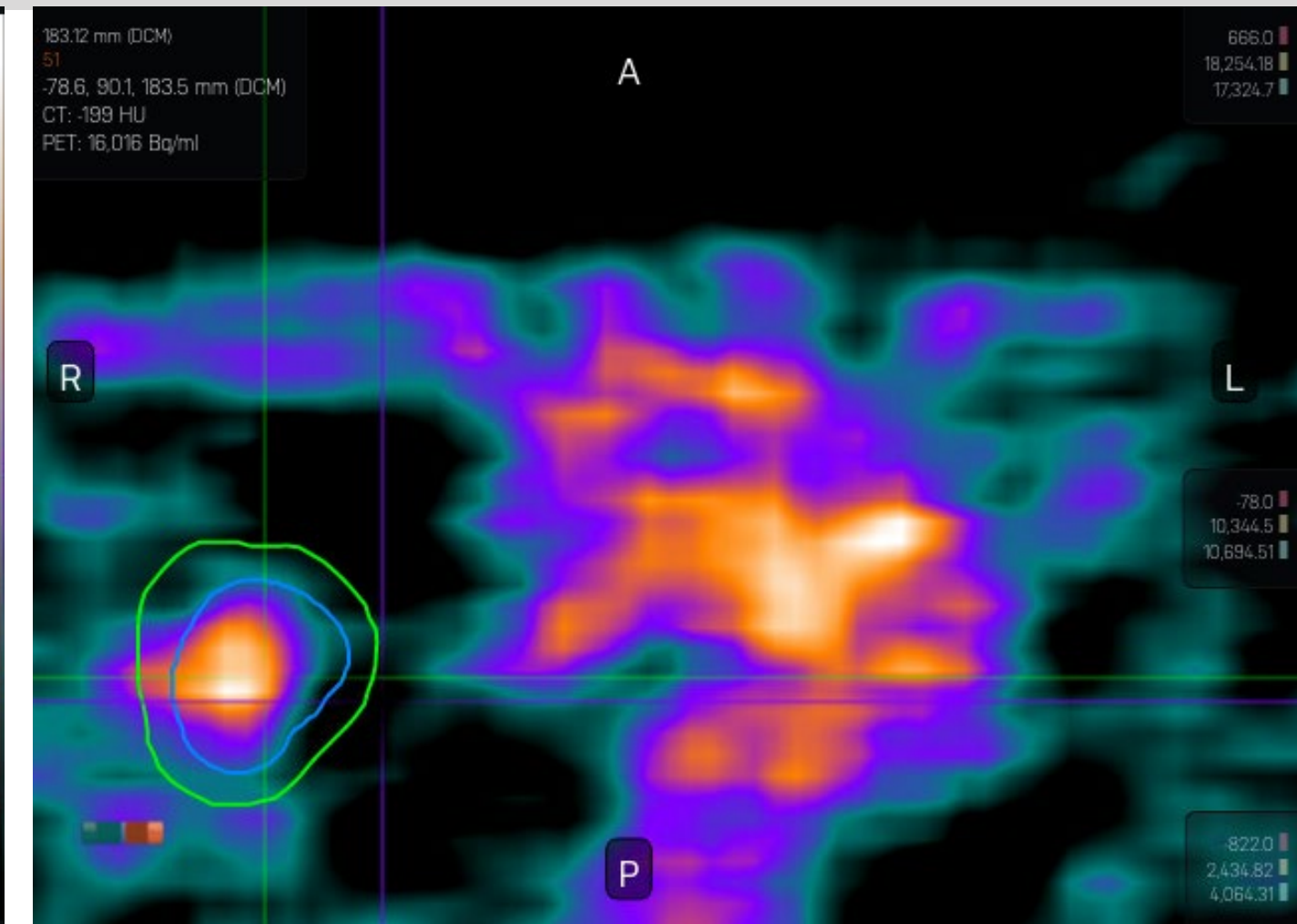
Biology-Guided Radiotherapy



PET/CT merge



PET scan before treatment



PET scan in treatment

**A reaction diffusion model
including RT-induced cell death**

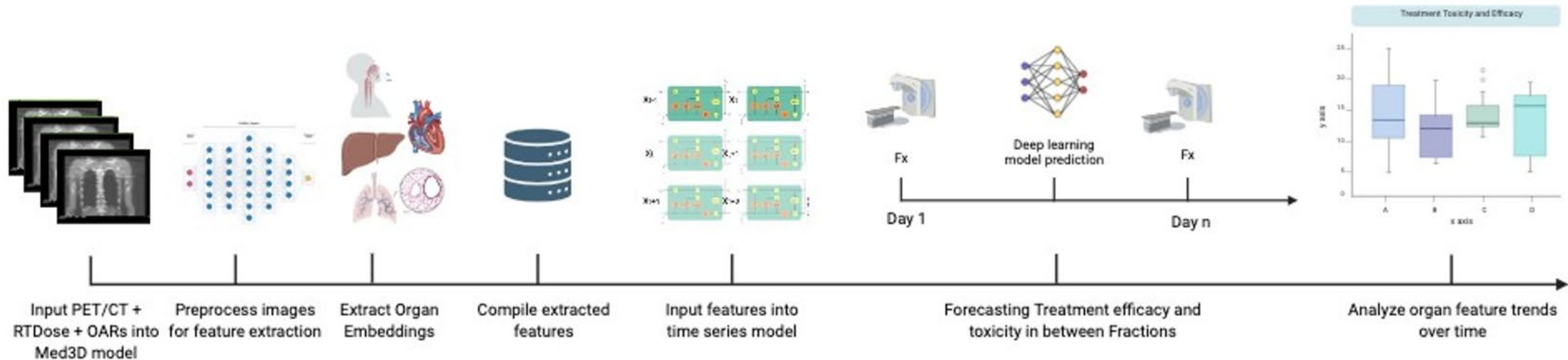
$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c \left(1 - \frac{c}{k}\right) - R(x, t, Dose) c \left(1 - \frac{c}{k}\right)$$

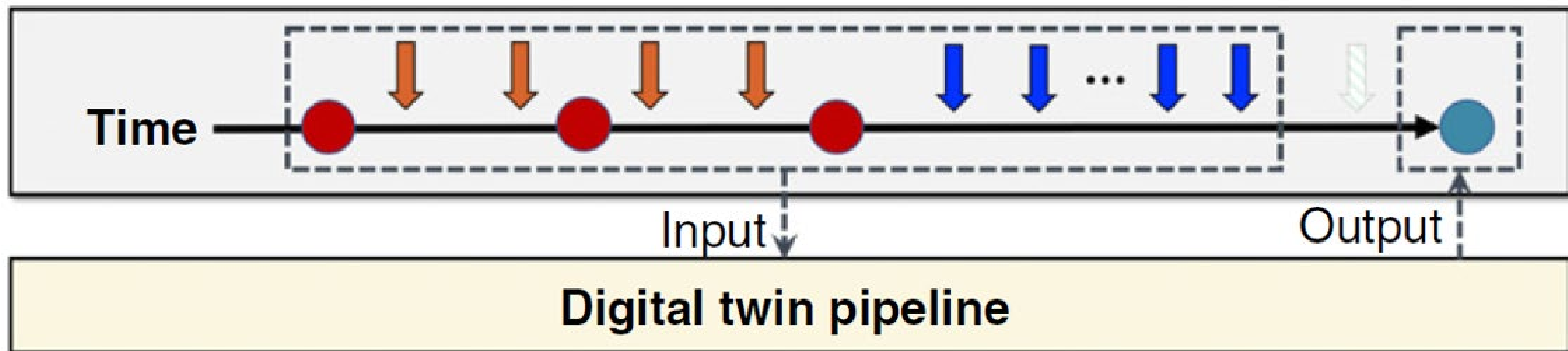
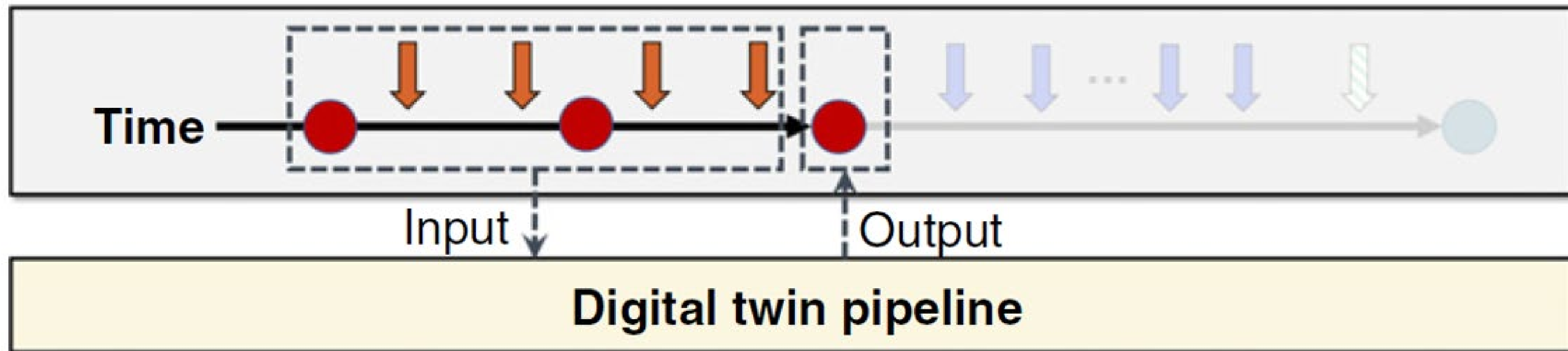
Develop digital twins to predict NSCLC response to RT *via* integrating ***mechanistic modeling*** with ***patient-specific longitudinal PET scans***

BGRT Workflow



Digital Twin Workflow





Select Patient

New Patient

Visit/Procedure

Load Data

John Doe

Male

MRN: 12345678

DOB 2025-10-07

Biopsy

RT/PET

RT/PET

RT/PET

Follow-up

2024-12-8

2025-1-9

2025-1-14

2025-1-17

2025-3-11

+

Outcome Prediction: Complete Response after SBRT of NSCLC

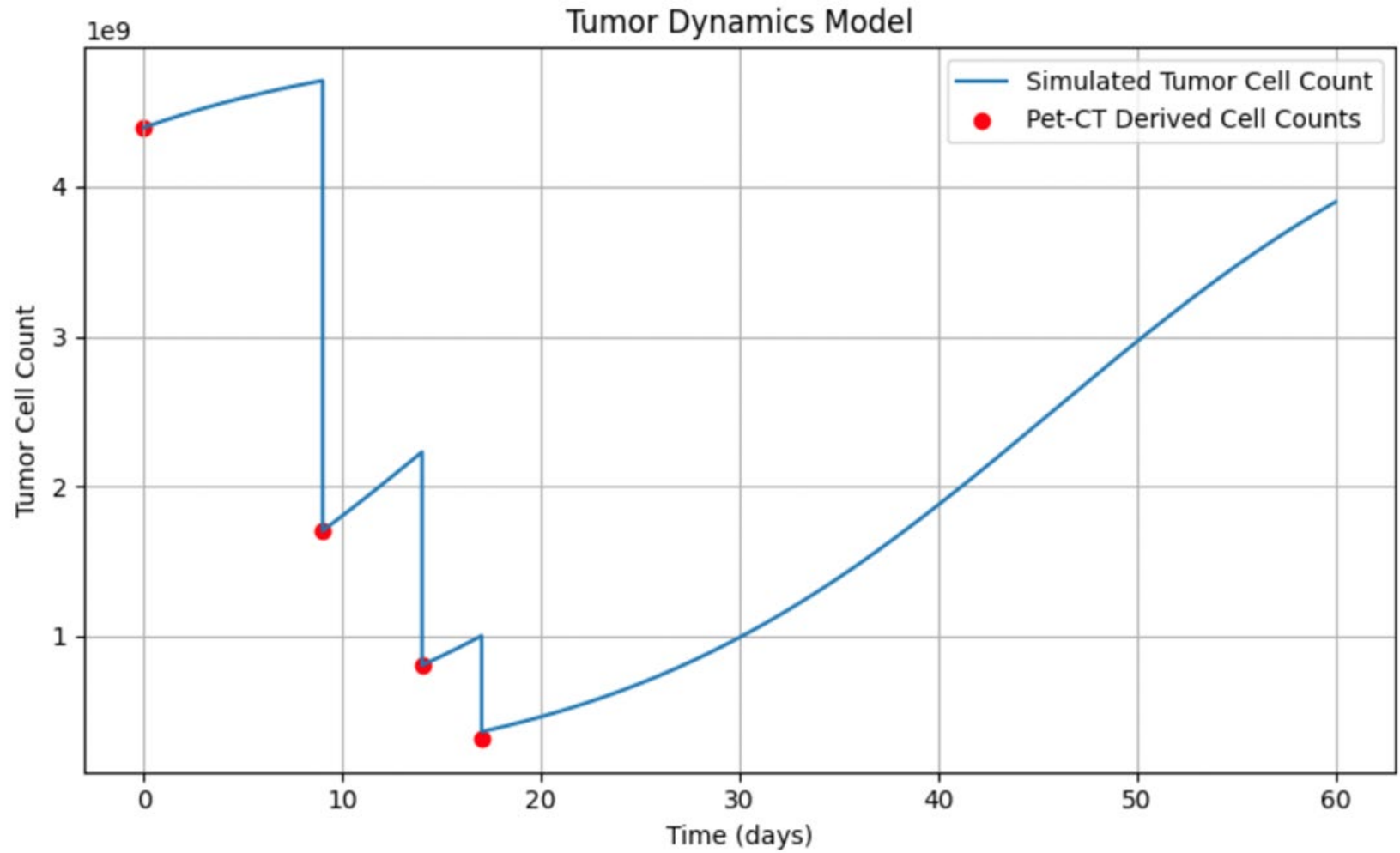
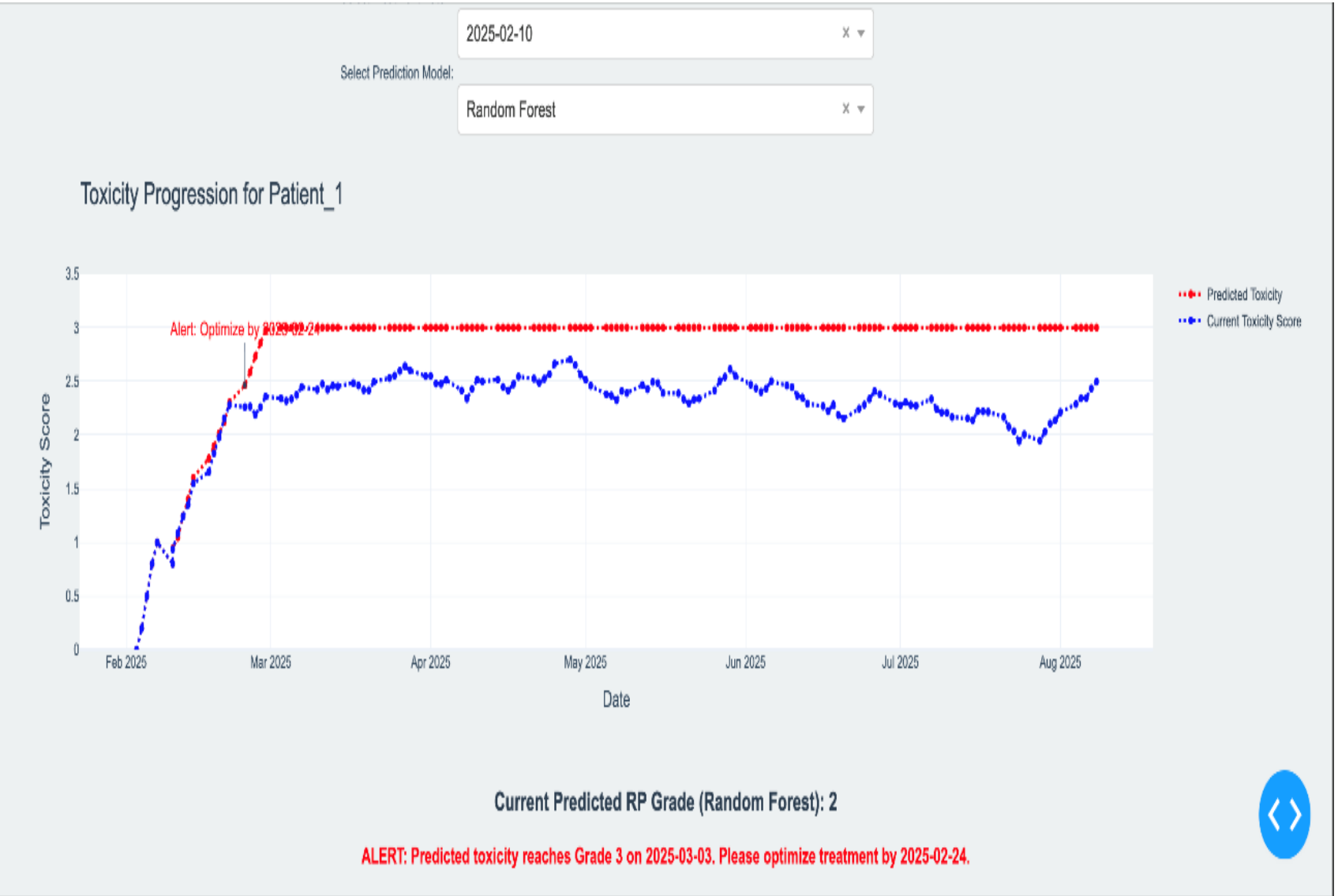
Tumor Control	Esophagus Toxicity	Lung Toxicity	Heart Toxicity	Spinal Cord Toxicity	Liver Toxicity
95%	15%	28%	5%	3%	9%

Treatment Option Comparison (may use radar plot like Figure 4 in Greg's statistical biopsy paper)

OAR toxicity tracking

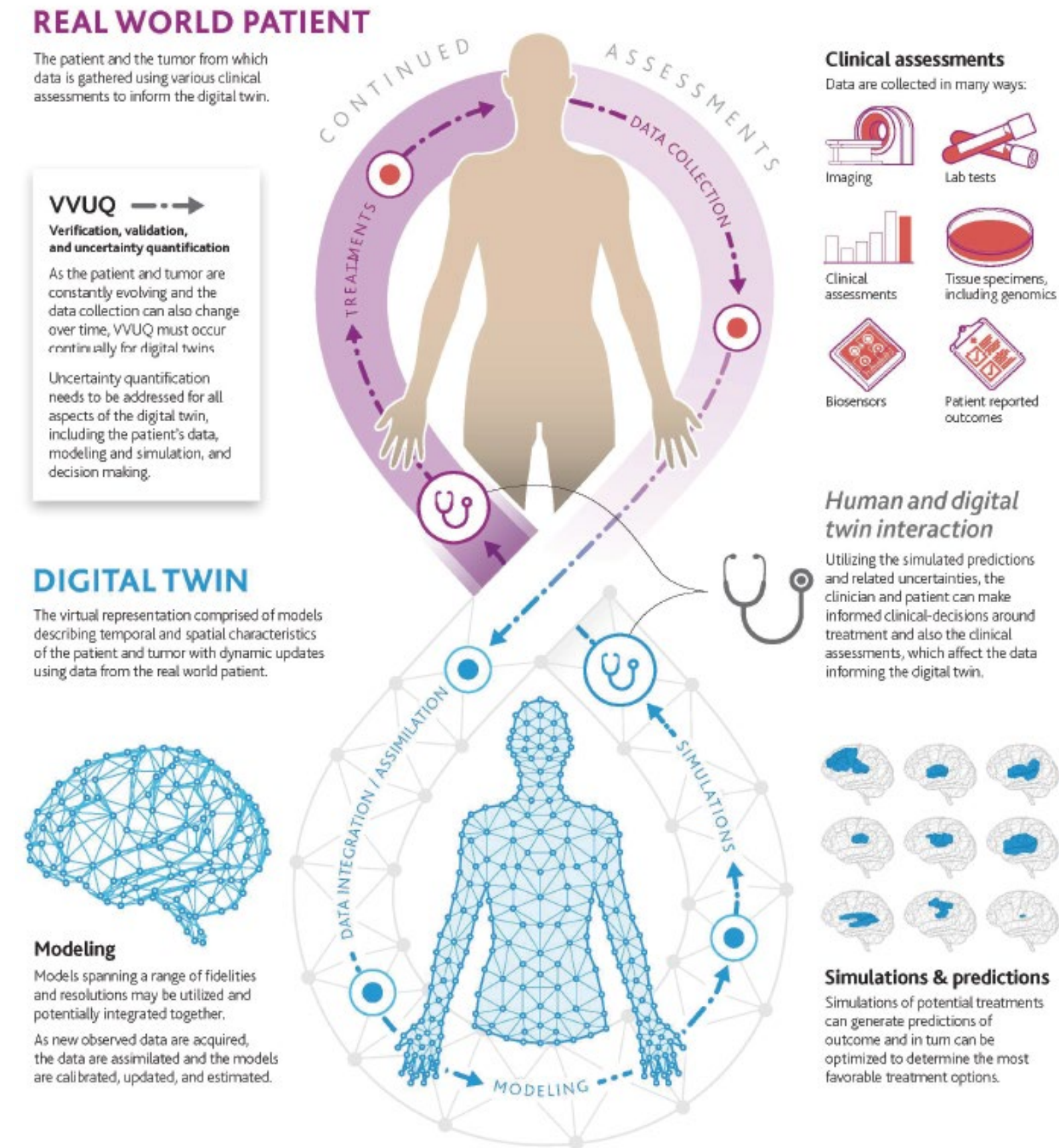
Tumor volume tracking

3D voxel risk heatmap



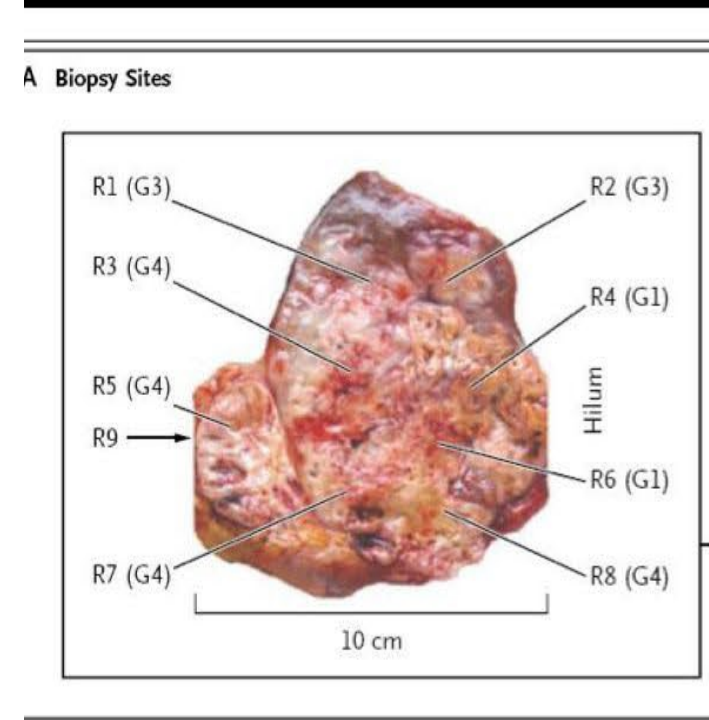
Cancer Patient Digital Twin

- Patient health prediction
- Treatment outcome trajectory
- Shared decision-making involving patients
- Whole body all organ tracking and monitoring
- In silico simulation of 'what if' scenarios

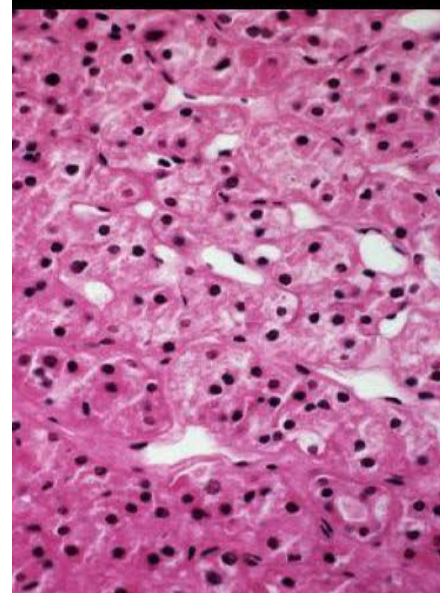


Multimodal Data Fusion

- Functional and molecular imaging
- Radiomics
- Liquid biopsies
- Digital pathology
- Genomic profiling
- Single-cell profiling
- Patient-derived cell cultures
- Intravital imaging
- Wearable devices
- Implantable sensors



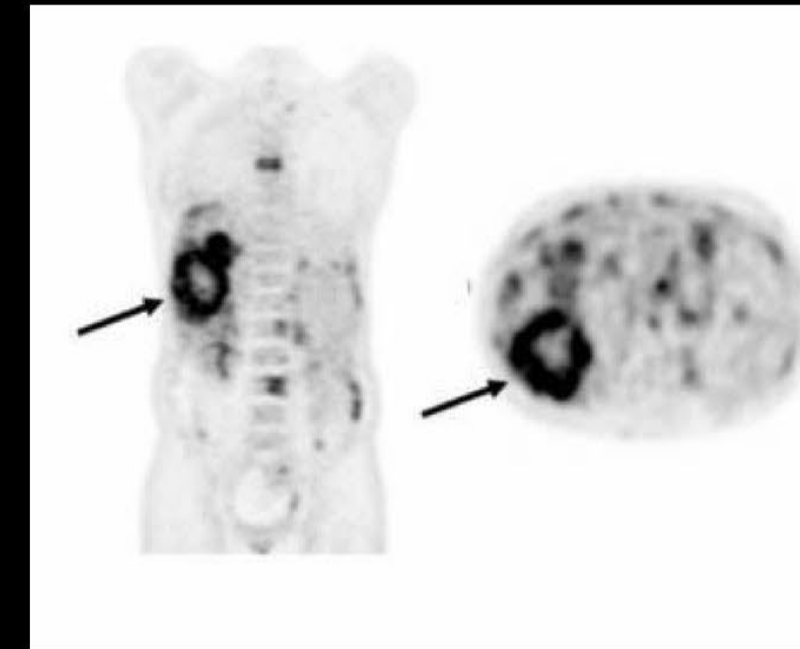
Kidney Cancer tumor camera imaging



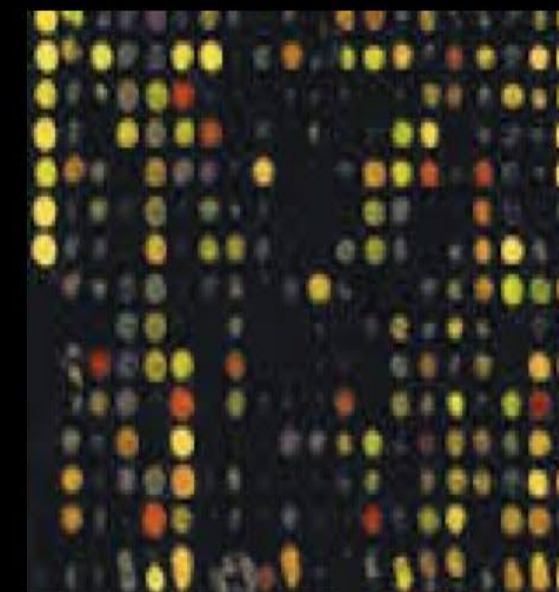
Pathology imaging



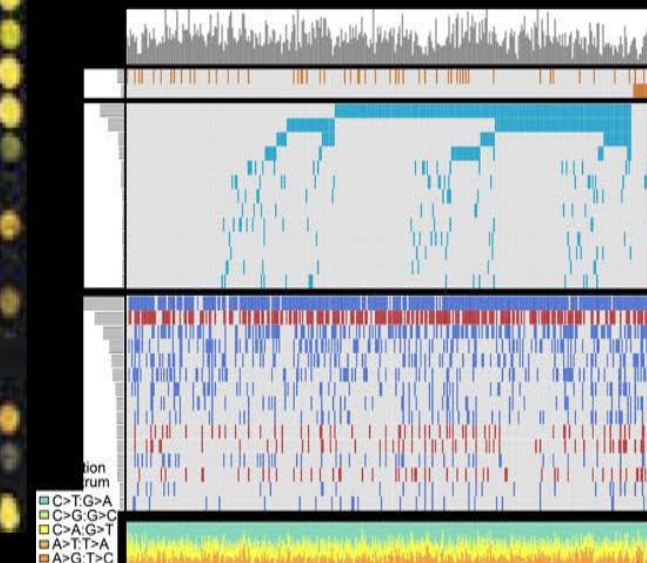
medical imaging CT



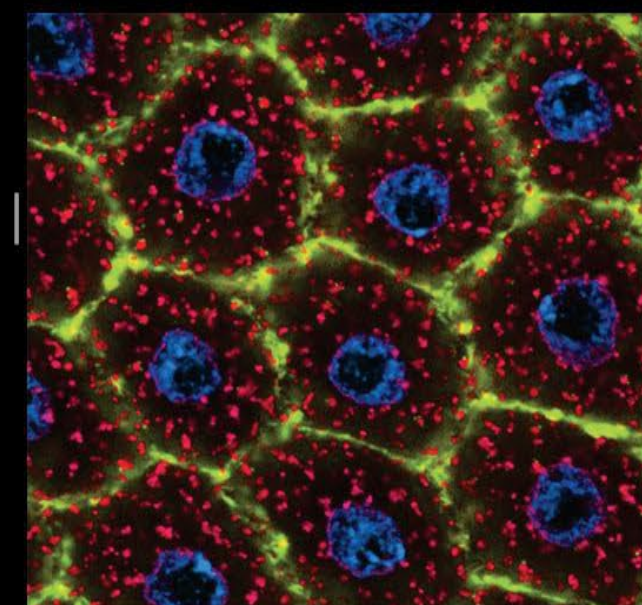
medical imaging PET



genomic imaging



genomic profiling

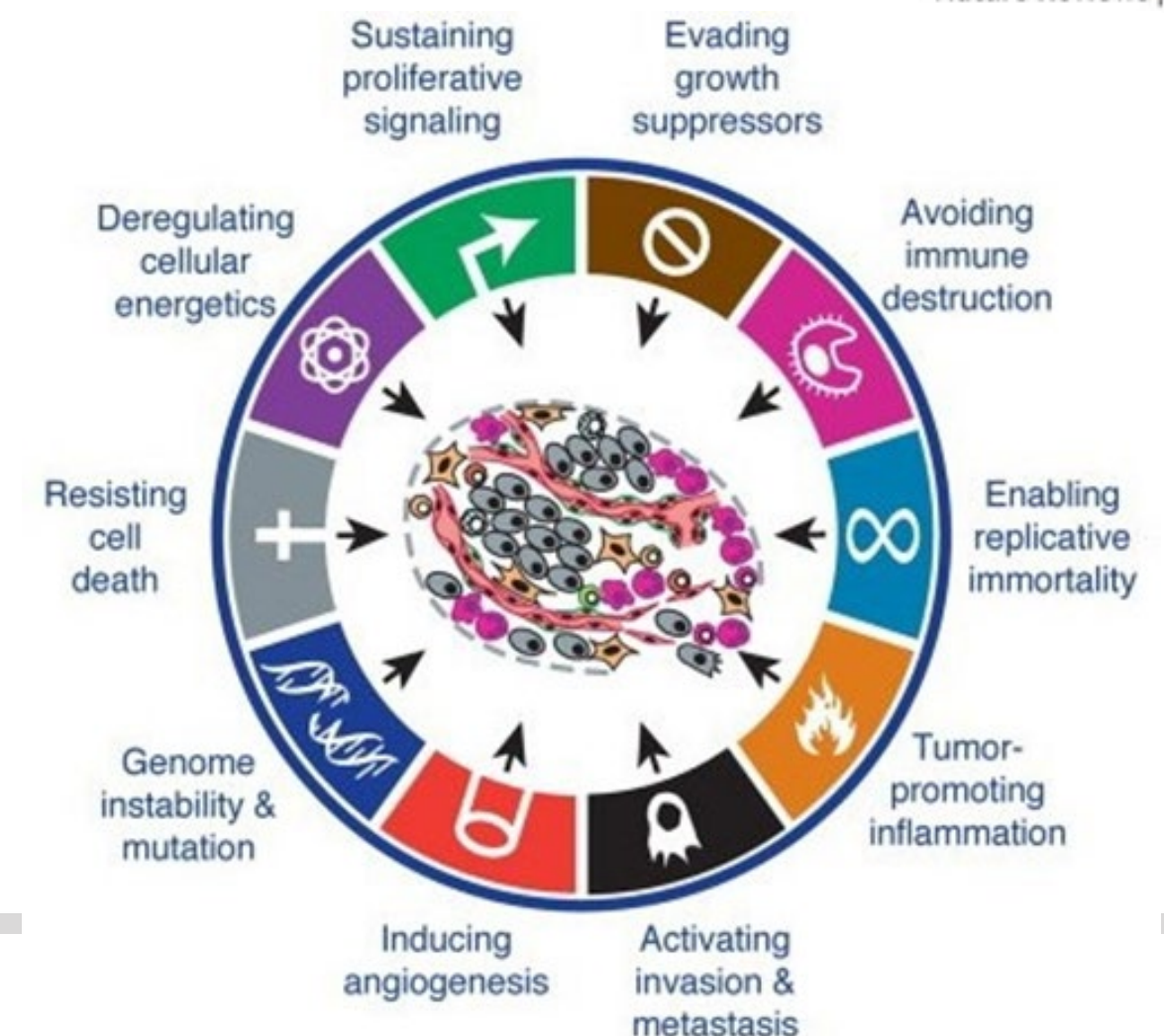
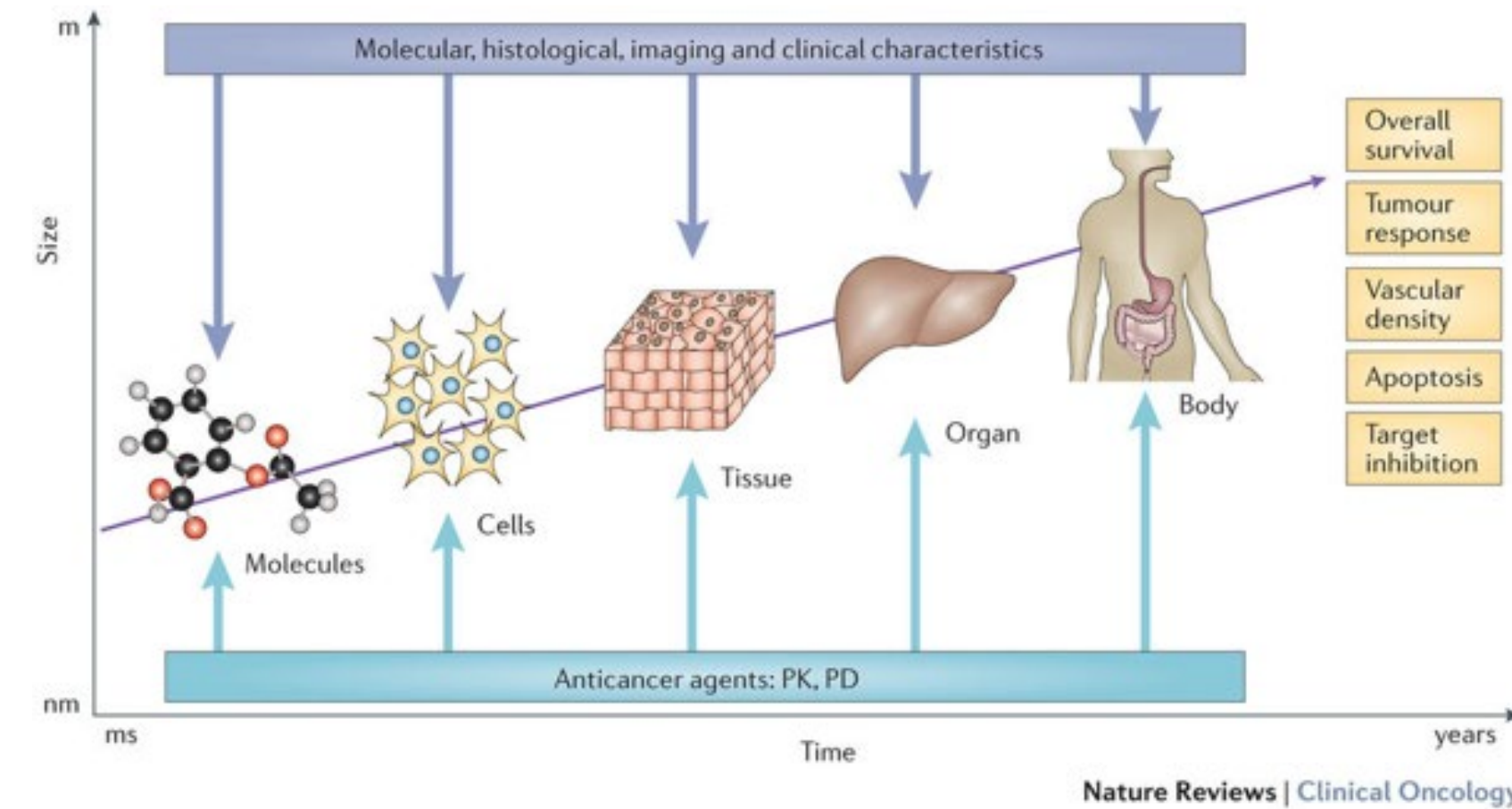


cellular imaging

From Gerlinger et al *NEJM* 366:2012

Complex Human Body

- Individual cell processes and dynamics
- Interactions between heterogeneous cells
- Physical constraints (e.g., oxygen diffusion, mechanical barriers)
- Procedures can cause toxicity, resistance, and long-term adverse effects
- Constant interactions with environment
- Social determinants influence one's health and wellbeing across life course
- Many factors involved (e.g., lifestyle, dietary, family history, medication)



Take Home Messages

- AI and digital twins have great potential in precision oncology
- Deep understanding of human biology is the key
- Multimodal data integration and multiscale modeling are challenging
- VVUQ and responsible AI must be ensured in DT implementation
- Cross-disciplinary collaborations are essential



Digital Twins for Health Society



DIGITAL TWIN FOR HEALTH SOCIETY



WHO WE ARE

DT4HS is a global interdisciplinary network of scientists, engineers, clinicians, and innovators committed to advancing digital twin technologies for transformative health solutions.

DT4HS.ORG

Inaugural Annual Meeting of Digital Twins for Health Society

UTHealth Houston

1825 Pressler Street
Houston, Texas 77030

SAVE *the* DATE

JAN. | 19-20 | 2026

Join the brightest minds and boldest innovators in healthcare, artificial intelligence, public health, and systems biology for the flagship event of the Digital Twins for Health Society.



Scan Me for More Information!

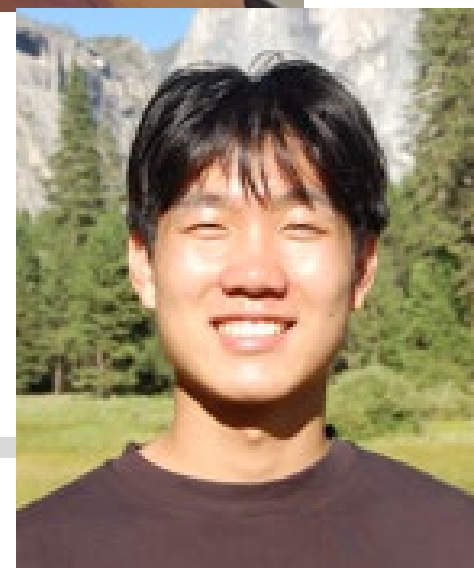


DIGITAL TWINS FOR HEALTH SOCIETY

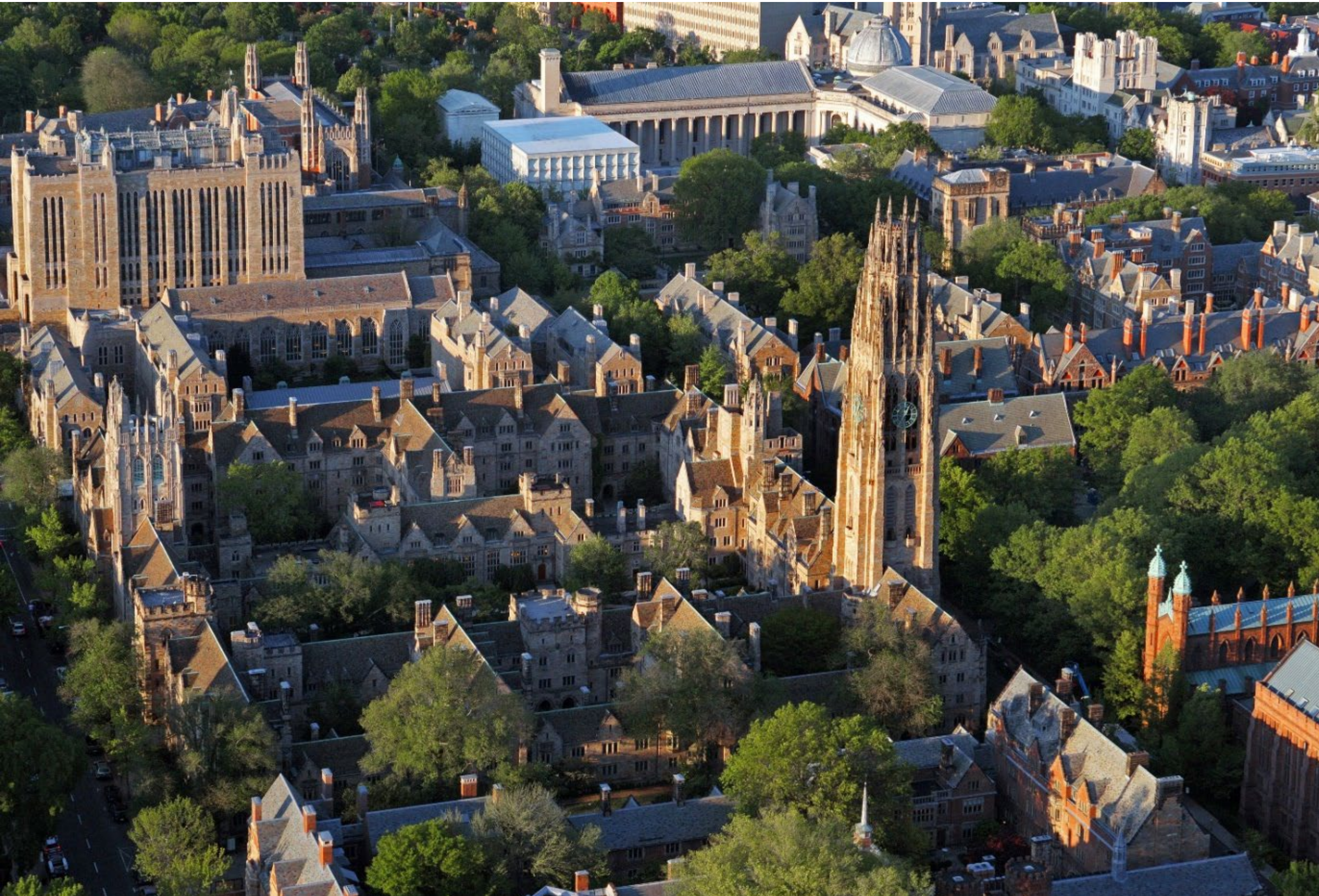
Yale Smart Medicine Lab



Gregory Hart
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Anvi Sud
Angie Huang
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Ghazal Mirzazadeh
Vito Scutari
Kevin Tanious
Youssuf Hussein Khanafer



Thank You



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