Digital Twins of Cancer Patients: A New Perspective to Support Clinical Decisions

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Yale SCHOOL OF MEDICINE

Disclosures

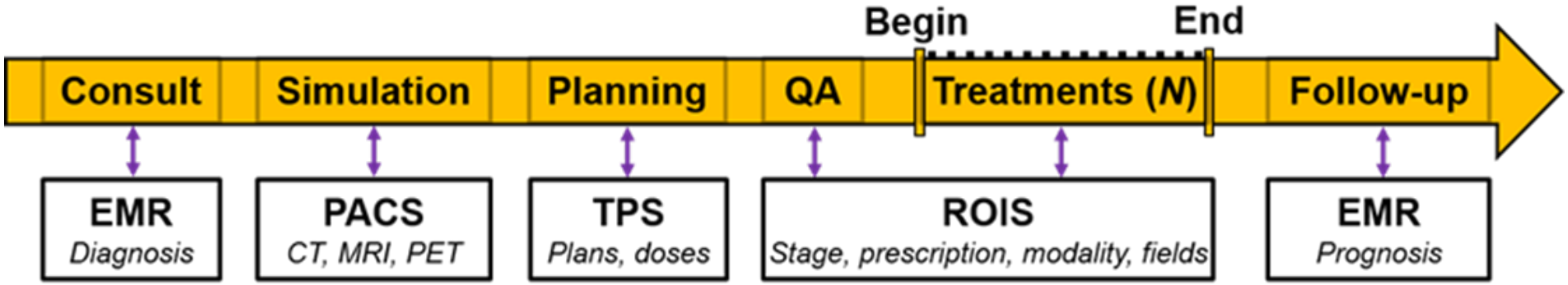
No conflicts of interest

Learning Objectives

- Identify the challenges and opportunities of AI applications in clinical decision support

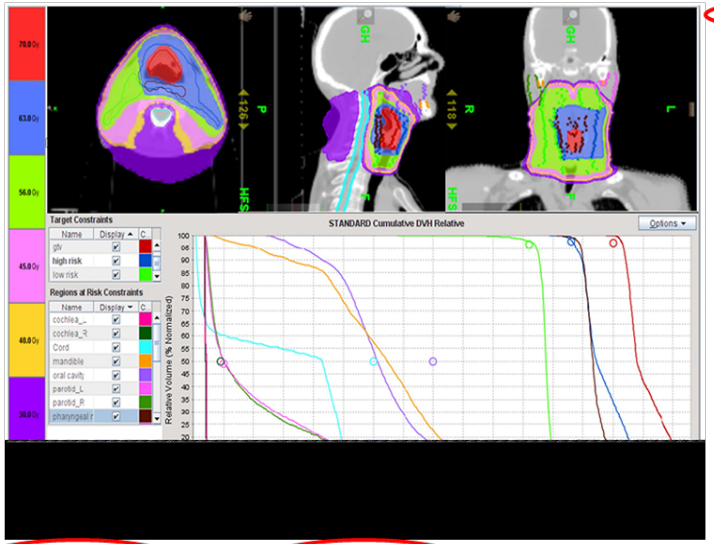
- Understand a digital twin-based clinical decision support tool for radiation oncology

Radiation Therapy Clinical Workflow



Data type	Format	Accumulation rate	Typical size	Storage
Clinical data	Text	Add 1 MB per week	10 MB	EMR
Radiotherapy data	DICOM-RT	Add 10 MB per day	500 MB	TPS/ROIS
Image data	DICOM	Per clinical need	500 MB	PACS

Multimodality data at spatial-temporal scales



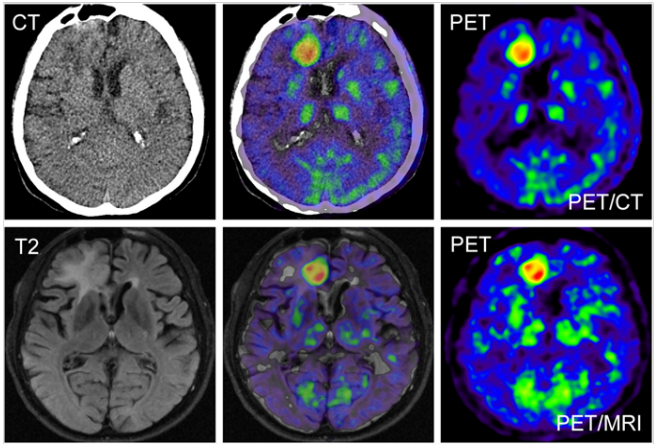
Diagnosis: C79.31 Secondary malignant neoplasm of brain C34.01 Malignant neoplasm of right main bronchus Z51.5 Encounter for palliative care
C34.90 Malignant neoplasm of unspecified part of unspecified bronchus or lung

As indicated in the patient's history of present illness, the patient presented for consideration of radiation therapy and was considered a candidate.
Although a final determination of the treatment regimen cannot be made until the planning process is completed and an acceptable plan is approved, the following considerations are made at this time. If 3D or IMRT is used the level of planning will be developed based on a GTV and PTV following the contouring of critical and sensitive structures.

Brief History: **small cell lung cancer, brain metastases**
Diagnosis and Pathology: **as above**
Stage: extensive stage
ECOG Performance Status: 1
Goal: The goal of this course is: Palliative Comment: .

Proposed Plan of Care
Frequency: A course of treatment using daily fractionation schedule will be prescribed.
Comment:

Modality: The following modalities are currently being considered for the patient.



FAMILY HISTORY:
Family History
Problem
- Heart disease
  Irregular heartbeat
- Atrial fibrillation
- Lung cancer

SOCIAL HISTORY:
Social History
Substance Use Topics
- Smoking status: Never Smoker
- Smokeless tobacco: Never Used
- Alcohol use: No

Lives in New Haven, CT
Retired

PAST MEDICAL HISTORY:
Past Medical History
Allergy
Comment: Seasonal
Anxiety
Bereavement reaction
Depression
GERD (gastroesophageal ref
Hyperlipidemia
IRON DEFICIENCY
Obesity
Prostatism

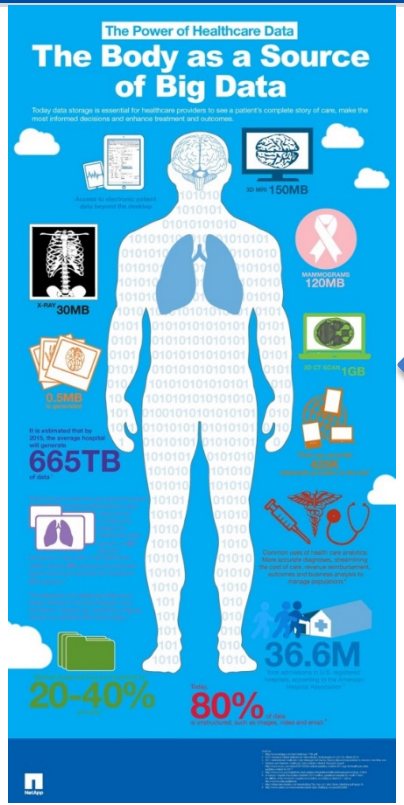
PHYSICAL EXAM:
ECOG performance status: 0
BP (l) 147/77 Pulse (l) 104 Temp 98.3 °F (36.8 °C) Resp 18 Ht 5' 8" (1.727 m) Wt 98.9 kg SpO2 97% BMI 33.15 kg/m2
General: well-appearing male in no apparent distress, appropriate affect.
Cardiovascular: regular rhythm, no m/r/g
Chest: lungs CTAB, no w/r/r
Abdomen: soft, NT, ND, NABS, no r/g, no hepatosplenomegaly, no palpable masses
Extremities: WWP, no c/c/e
Neurologic: A&O to person/place/time, CN II-XII intact, strength 5/5 in upper and lower extremities and symmetric, sensation to light touch intact in upper and lower extremities and symmetric

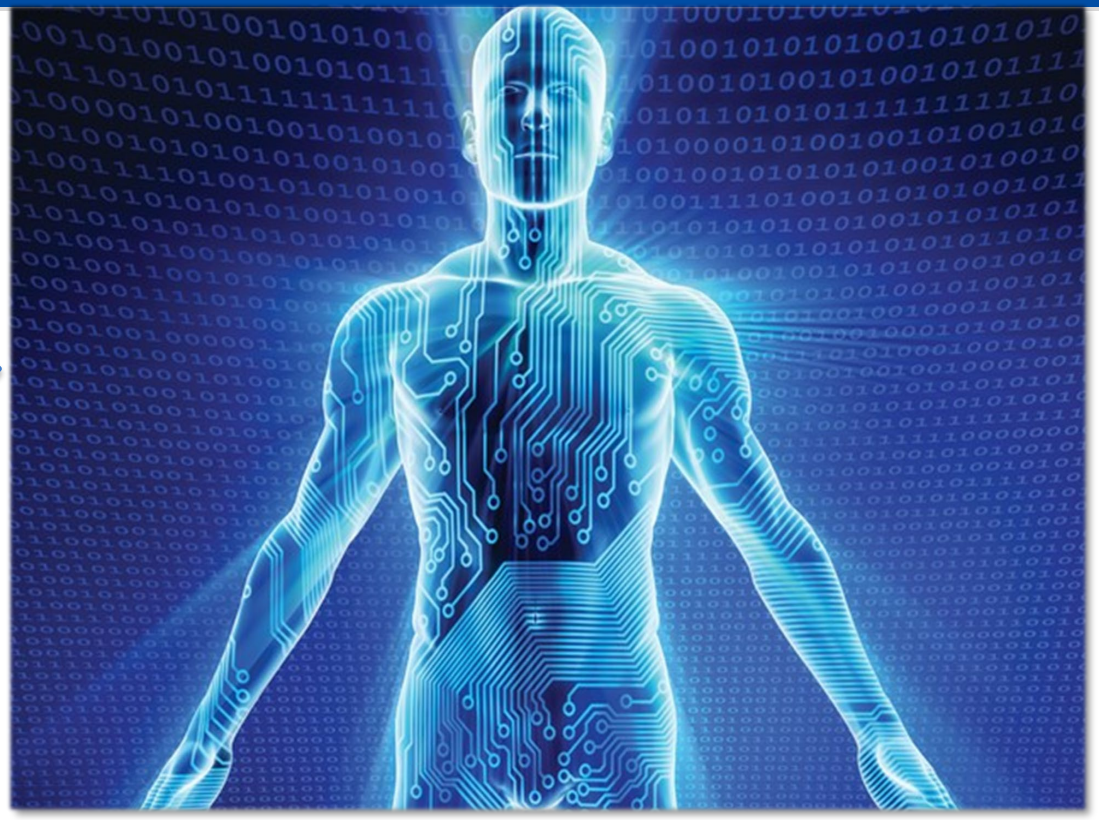
- Clinical: EHR, lab results, diagnoses, procedures, pathology/histology data, radiology images, and microbiology data
- Mobile health: wearable devices, fitness trackers, sensors, and apps
- Molecular profiling: genomic and genetic testing data, and multi-omics data
- Social media
- Environmental
- Lifestyle
- Dietary
- Family history
- Medication

Challenges

- **Data challenges**: generating and acquiring high-volume, high-quality, multiscale data
- **Modeling and integration challenges**: seamlessly integrating data-driven and mechanistic modeling
- **Ethical and community challenges**: ethical biases, privacy concerns, and patient engagement

A Digital Twin for Each Cancer Patient





What is a Digital Twin?

- A digital twin is a ***synchronized digital replica*** of a physical system, which is used to ***monitor, model, and fine-tune performance*** of processes, people, places, systems and devices

- Digital twins can be used for ***in silico*** simulations:
  - *What if* the engine runs 50% hotter?
  - *What if* the wind speed is 10 times faster?

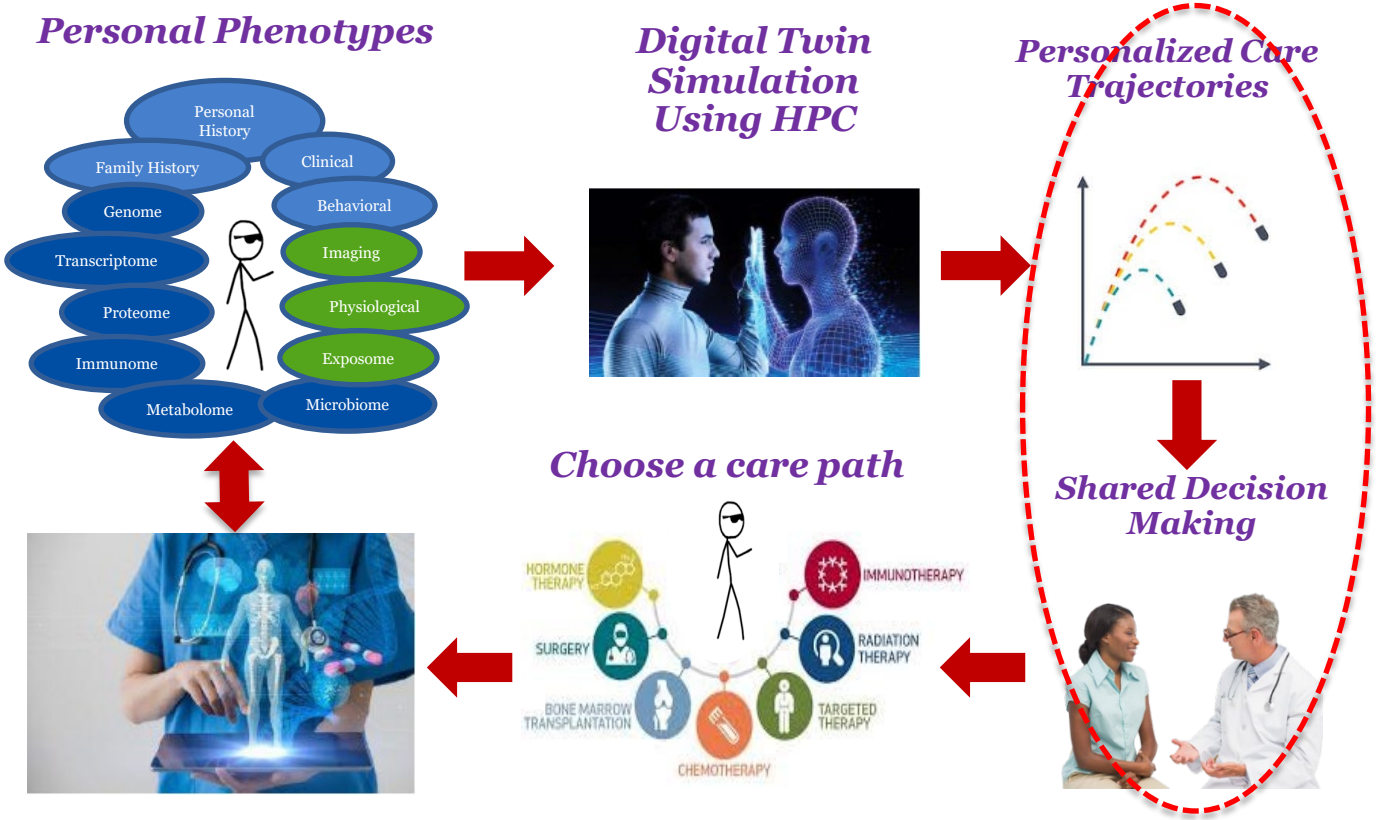
- Proposed by Michael Grieves in 2002, defined by John Vickers of NASA in 2010 to improve physical model simulation of spacecraft (https://en.wikipedia.org/wiki/Digital_twin)

- Aerospace engineering, manufacturing, construction, automotive, healthcare

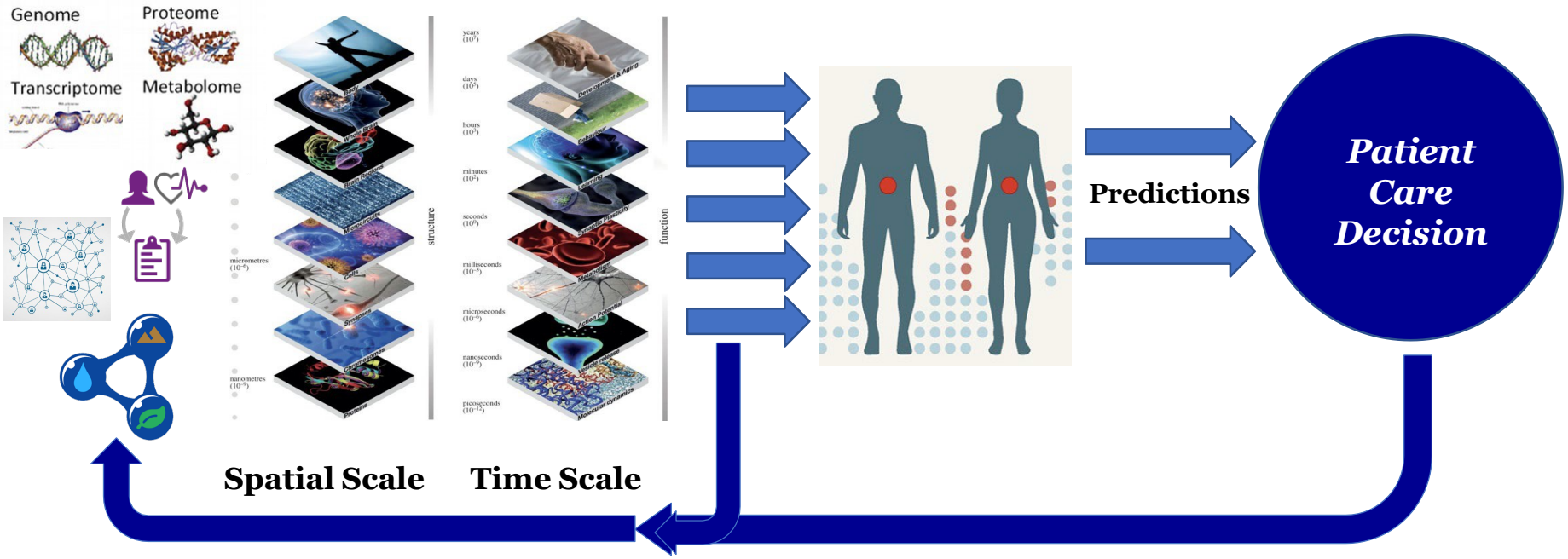
Why Digital Twins in Radiation Oncology?

- A ***patient-tailored model*** that incorporates genetic, molecular, clinical, environmental, and social factors to ***predict individual patient's status*** for
  - Adaptive radiation therapy based on multimodal real-time data
  - Predictive modeling of treatment response short-term and long-term
  - Early intervention based on precise monitoring of adverse effects
  - Virtual clinical trials

The Big Picture

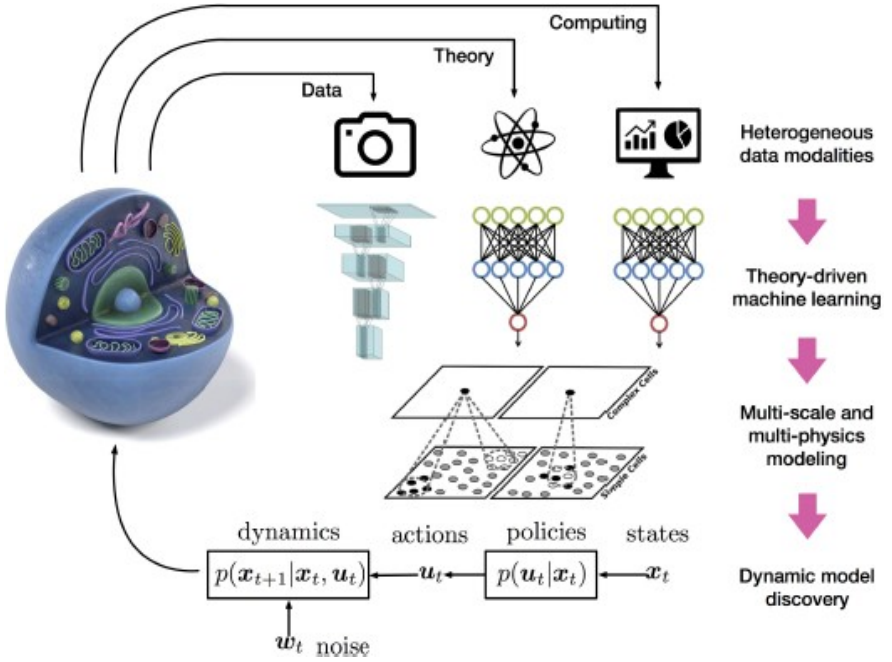


Significance



Innovation

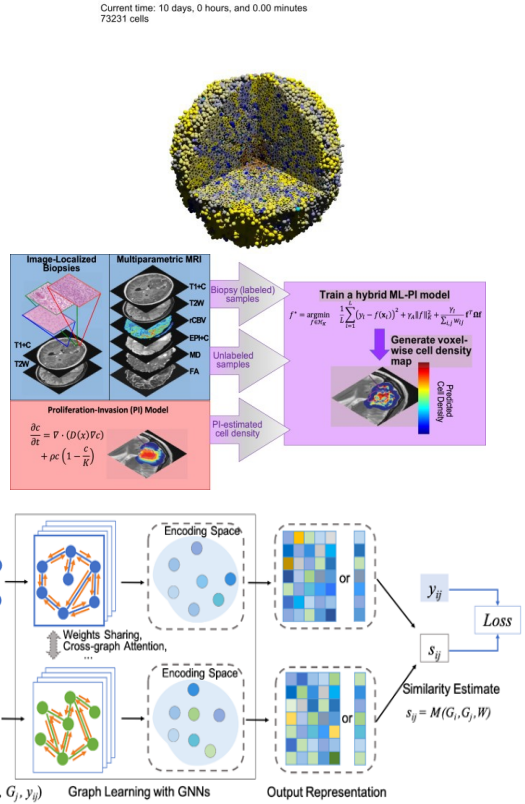
- Connected multiscale multimodality data
- New knowledge of healthy and disease states at spatial-temporal scales
- Computational and mathematical models for dynamic multiscale systems in biology
- Computational learning frameworks



Peng et al., Archives of Comp Methods Eng, 2020

Multiscale Modeling

- Development of multiscale representations
  - PK-PD model of drug-tumor interactions to predict tumor evolution
  - Physics-informed ML on clinical and imaging data to develop dynamical systems
  - Deep graph similarity learning to identify similar patients

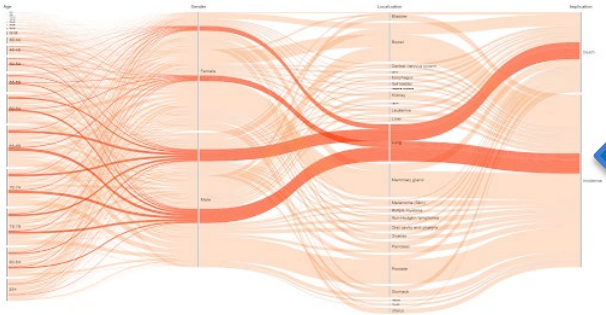


Ghaffarizadeh et al. (2018)
DOI: 10.1371/journal.pcbi.1005991

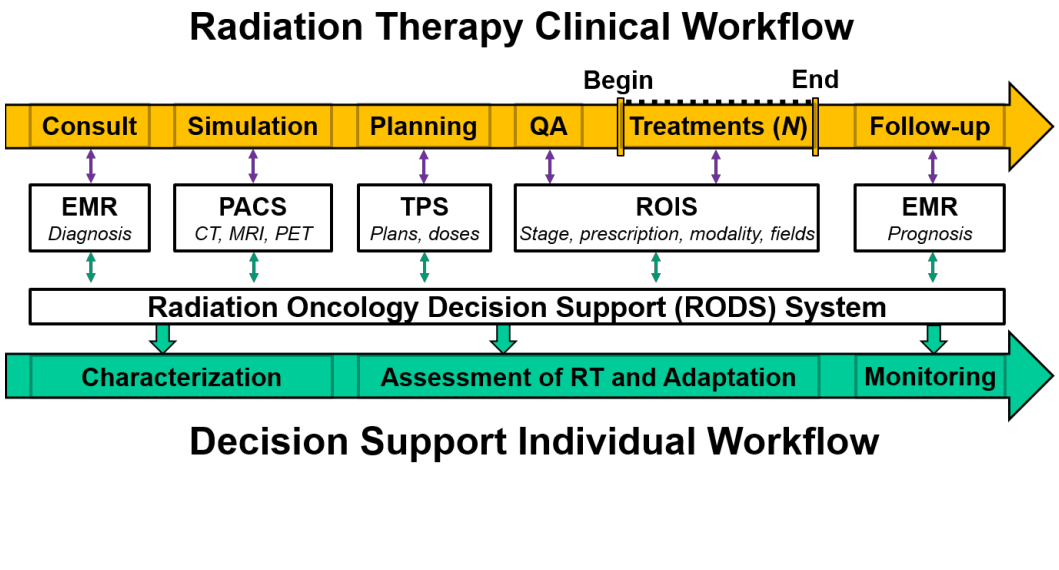
Guy et al. (2019)
DOI: 10.1038/s41598-019-46296-4

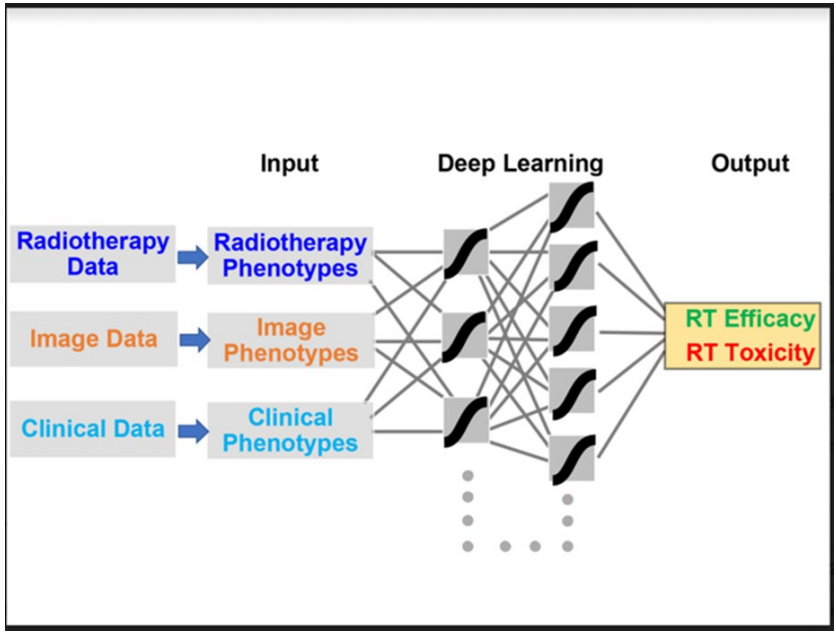
Personalized Decision Support

- User-in-the-loop deep learning for personalized clinical decision support
- Leveraging knowledge graph and HPC for optimal treatment pathways



RT Efficacy vs Toxicity





Conclusions

- Digital twins will enable predictive oncology for cancer patients
- Understanding cancer biology and patient care trajectory is the key
- Modeling of multiscale multimodality data is challenging

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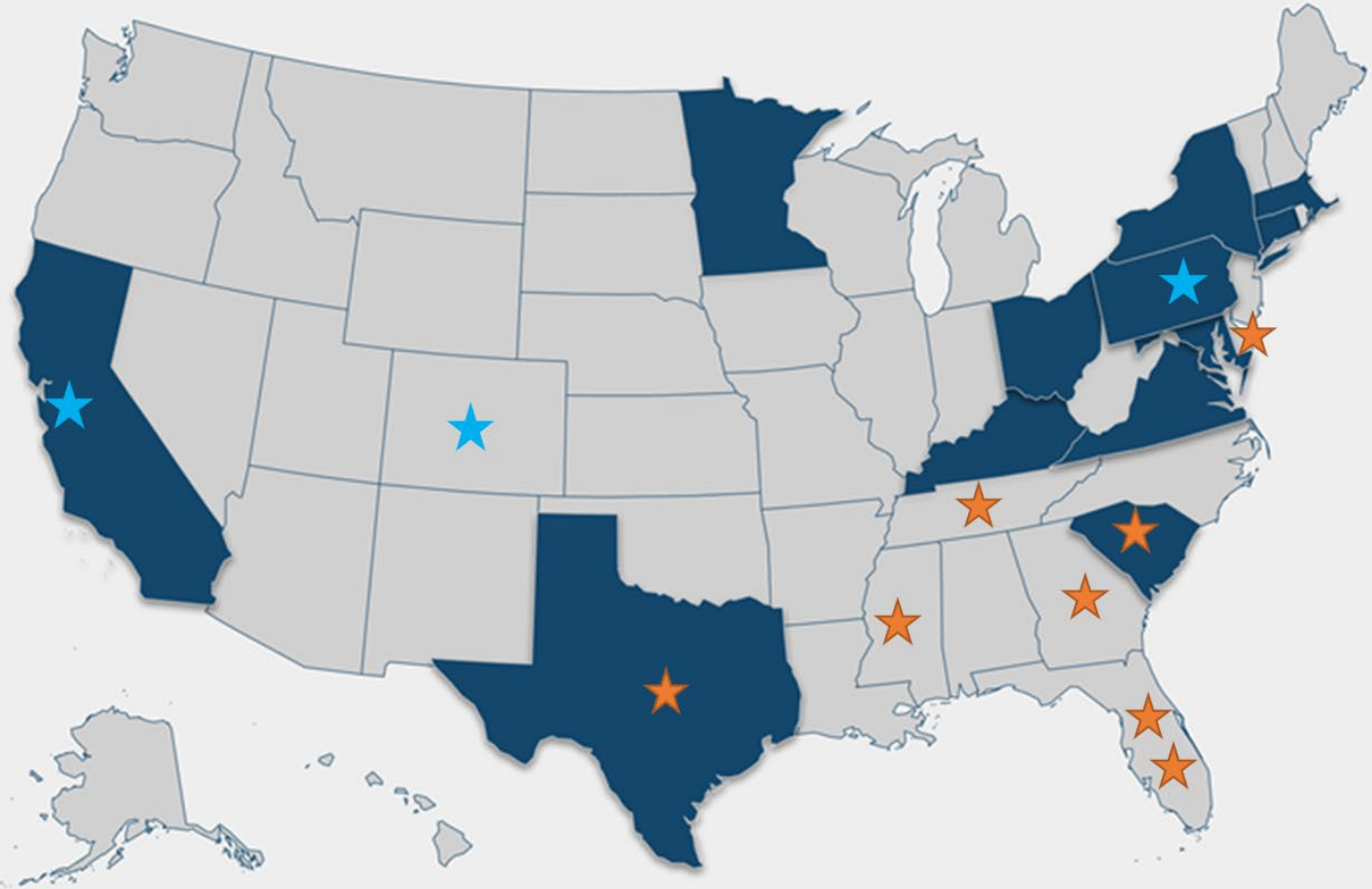

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