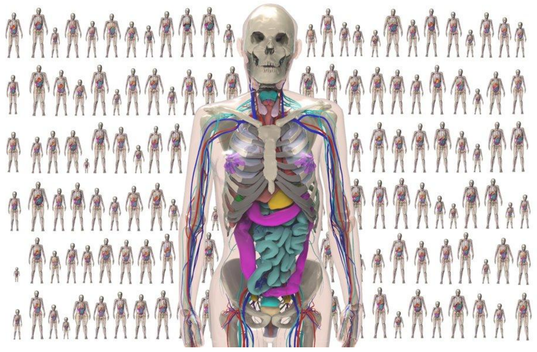
Human Digital Twins and Virtual Clinical Trials as Surrogate Models for Warfighters

Jayasai Rajagopal[1], Zakaria Aboulbanine[1], Greeshma Agasthya[2], Narender Singh[1], Anuj Kapadia[1]
[1]Oak Ridge National Laboratory, Oak Ridge, TN, USA, [2]Georgia Institute of Technology, Atlanta, GA, USA

Human digital twins

Digital twins are **virtual representations of people**

- They behave like humans, not just an average human
- Capture **multiple domains** across **multiple scales**
  - From whole body to organs to cells to DNA
  - From populations to single humans



Virtual clinical trials (VCTs)

Clinical trials answer questions about **health management**

Virtual clinical trials (VCTs) are **computational alternatives**:

- Have applications across CBER scenarios
- Evaluate problems that are challenging in a conventional setting

Challenge	Clinical Trials	VCTs
Ethical considerations with repeated scans	✗	✓
Ground truth of imaged targets	✗	✓
Logistical cost (time, economic)	✗	✓
Ease of scalability	✗	✓

High-performance computing (HPC)

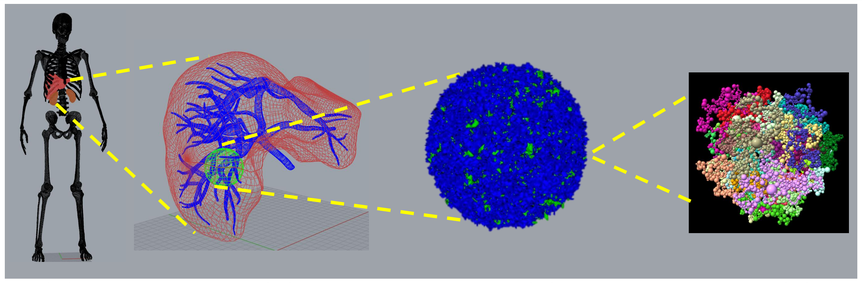
Use of advanced computing resources to solve **complex problems across**

Enable **acceleration** and **scope expansion** for VCTs

Broad scale from compute clusters to **supercomputers**

Image credit to : https://commons.wikimedia.org/wiki/File:Frontier_supercomputer_(8).jpg

Multiscale model framework



(1) (2) (3) (4)

1. **Whole body scale**: Modeling anatomy/physiology
2. **Organ system scale**: Modeling function and pathology (*CFD, Pathology*)
3. **Multi-cellular scale**: Modeling inter/intra-cellular effects (*Molecular simulation, Diffusion kinetics*)
4. **Sub-cellular scale**: Modeling DNA and protein effects (*Radiation transport*)

Demonstrative applications

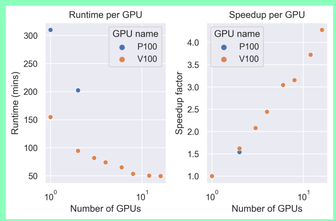
Computed tomography (CT)

Goal: Generate large-scale synthetic dataset of clinical CT images

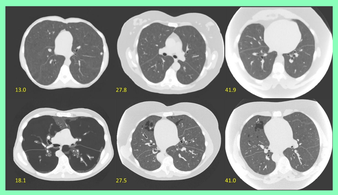
Uses whole body digital twins models with a validated CT simulation platform (DukeSim) to generate data on HPC (Summit)

Evaluated bottlenecks and challenges of using HPC resources to expand the simulation scale and **generated the largest synthetic CT dataset** (10,000+ simulations) to-date

Take home message: HPC-enabled digital twins can generate clinically relevant synthetic CT datasets at scale for imaging research and VCTs



Performance improvement due to additional GPUs in terms of runtime and speedup factor. Colors indicate different servers and device types.



Example of simulated CT scans from virtual patients. BMI indicated in yellow. Top row show patients with lung lesions, bottom row shows patients with COPD.

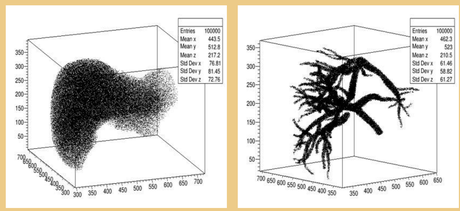
Radiopharmaceutical therapy (RPT)

Goal: Develop a computational pipeline for organ and tumor dose in RPT

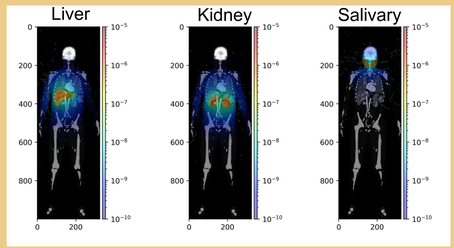
Combine physiological modeling (PBPK), CFD (OpenFOAM), and MC (GEANT4)

Simulated patient specific dosimetry based on patient anatomy, radioisotope specific decay, and drug specific pharmacokinetics

Take home message: Integrated multiscale modeling enables patient-specific prediction of RPT distribution and organ dose



Placement of radiopharmaceutical isotope sources in liver parenchyma (left) and vasculature (right)

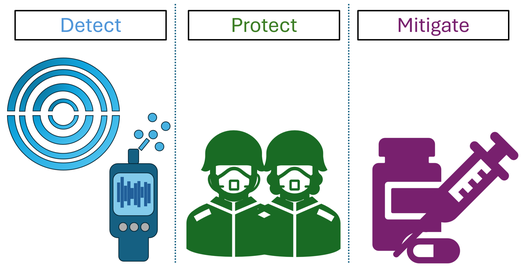


Areal dose maps of Lu-177 radiation sources placed in liver (right), kidneys (middle) or salivary glands (left)

Surrogate models for warfighters

Potential **CBRN** use scenarios:

- **Detection**: Generate synthetic datasets for rare scenarios where human data is limited
- **Mitigation**: Compare timing and effectiveness of response options across different parameters and doses
- **Population variability**: Representation of differences in sex, age, anatomy, and operational stress
- **Planning and preparedness**: Support what-if scenario analysis, triage, and response planning for rare events



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