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The Power (and Challenges) Of Total-Body PET Dynamic Imaging

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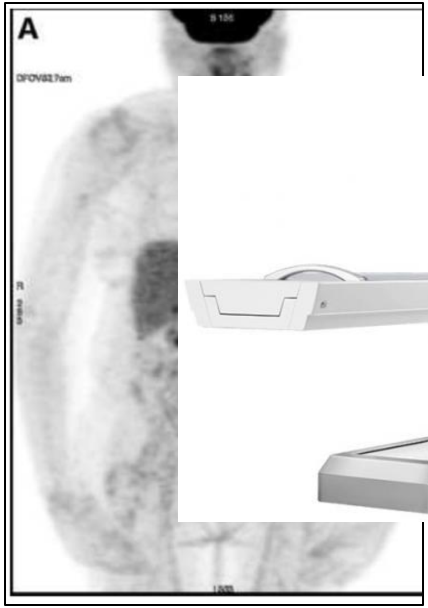
PET – Current Status

- >10 million scans per year
- > 10,000 sites in the world
- Major Applications:
  - Oncology:
    staging, treatment response
  - Cardiology:
    perfusion, viability
  - Neurology:
    amyloid and tau burden

^{18}F-FDG

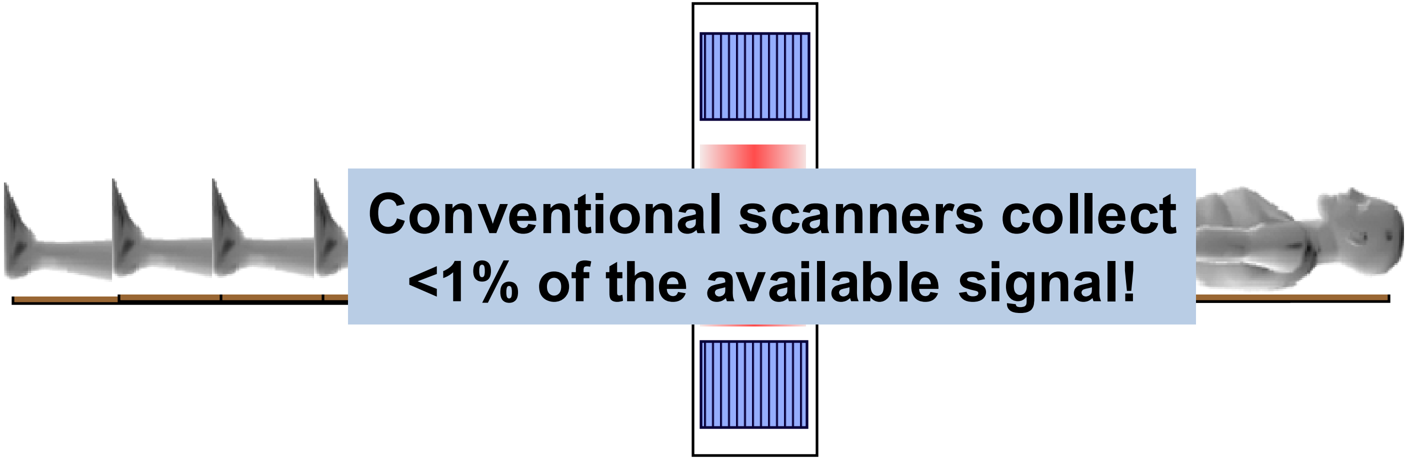


Groheux, *Sem Nucl Med* 52: 508-519, 2022

^{68}Ga-PSMA

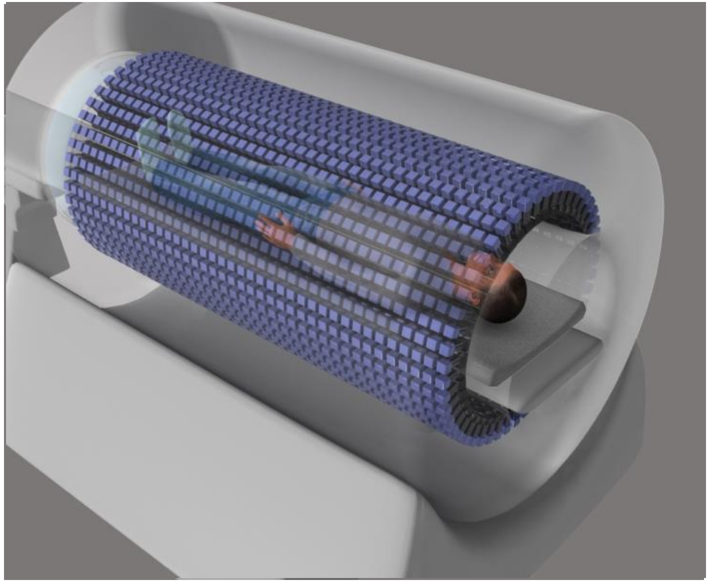
Shagera et al, J Nucl Med 63: 1191-98 (2022)

Signal Collection in PET



- PET provides the most sensitive non-invasive molecular assay of the human body
- All PET studies are limited by low signal

Total-Body PET



Conventional PET/CT scanner

Total-Body PET/CT

Opportunities:

- High geometric collection efficiency leads to ~20-60 fold higher signal for whole-body imaging
- All organs/tissues in field of view

Capabilities of Total-Body PET

High quality imaging

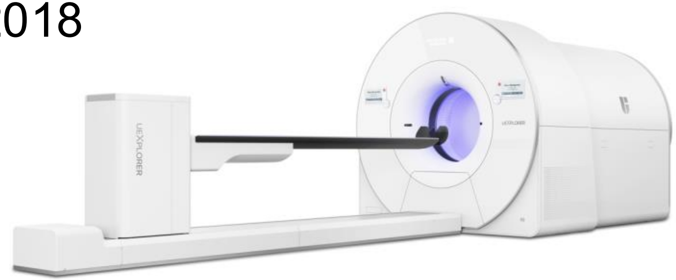
Image quickly: 30 sec scan

Image gently: 18 MBq dose

Delayed Imaging: ^{18}F @12h

Commercial “Total-Body” PET Scanners

2018

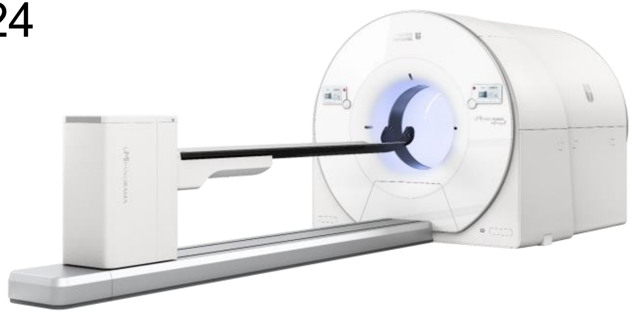


United Imaging uEXPLORER (194 cm)

2020

Siemens Vision Quadra (106 cm)

2024



United Imaging Panorama GS (148 cm)

2025

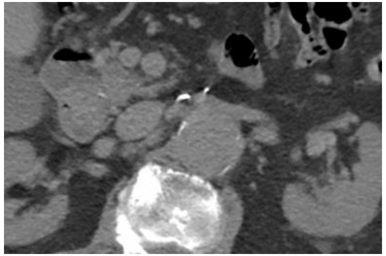
GE Omni (128 cm)

Total-Body ^{18}F-FDG PET

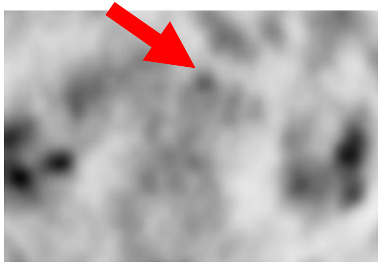
Female, 32y, BMI 21
310 MBq injection
7 min acquisition
Scan at **60 min p.i.**
2.34 mm voxels

Patient Impact

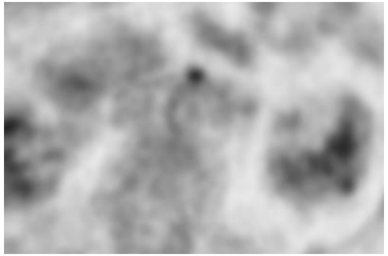
More than 500,000 patients have benefitted globally…



CT



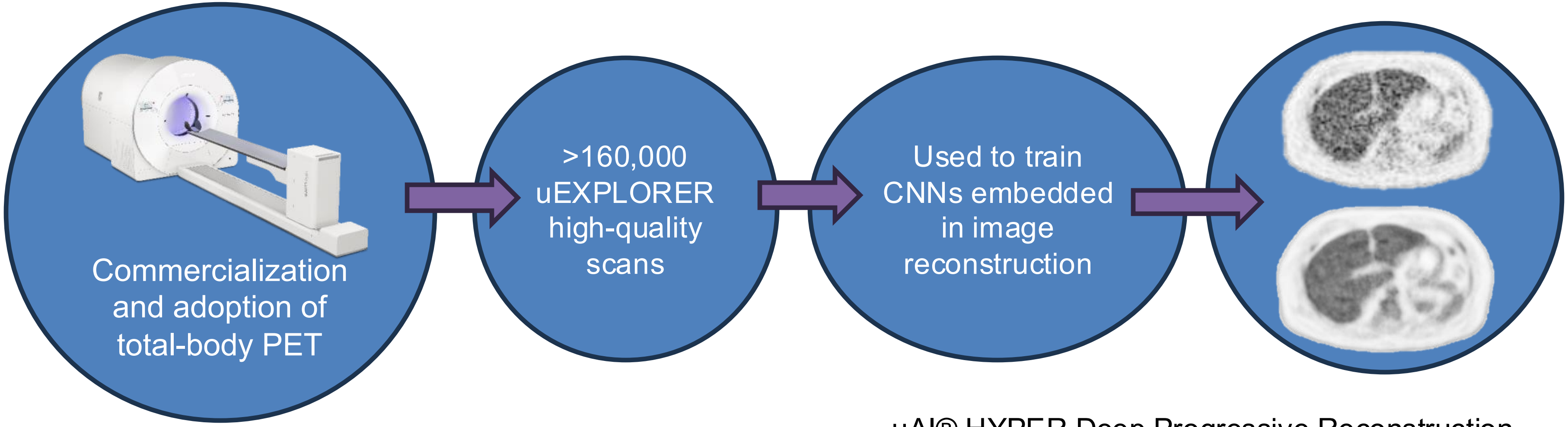
Conventional PET



Total Body PET

Impact on Conventional PET

Total-Body PET development often criticized for cost, and *increasing* rather than *decreasing* barriers to access, but…

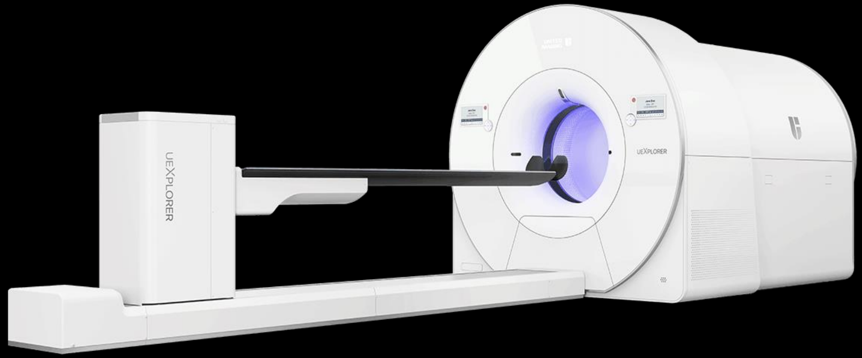


uAI® HYPER Deep Progressive Reconstruction, United Imaging Healthcare, White Paper, 2021

What are total-body PET's unique scientific characteristics?

Total-Body Coverage + **Fast Dynamic Imaging**

Advanced 4D Reconstruction and Modeling AI

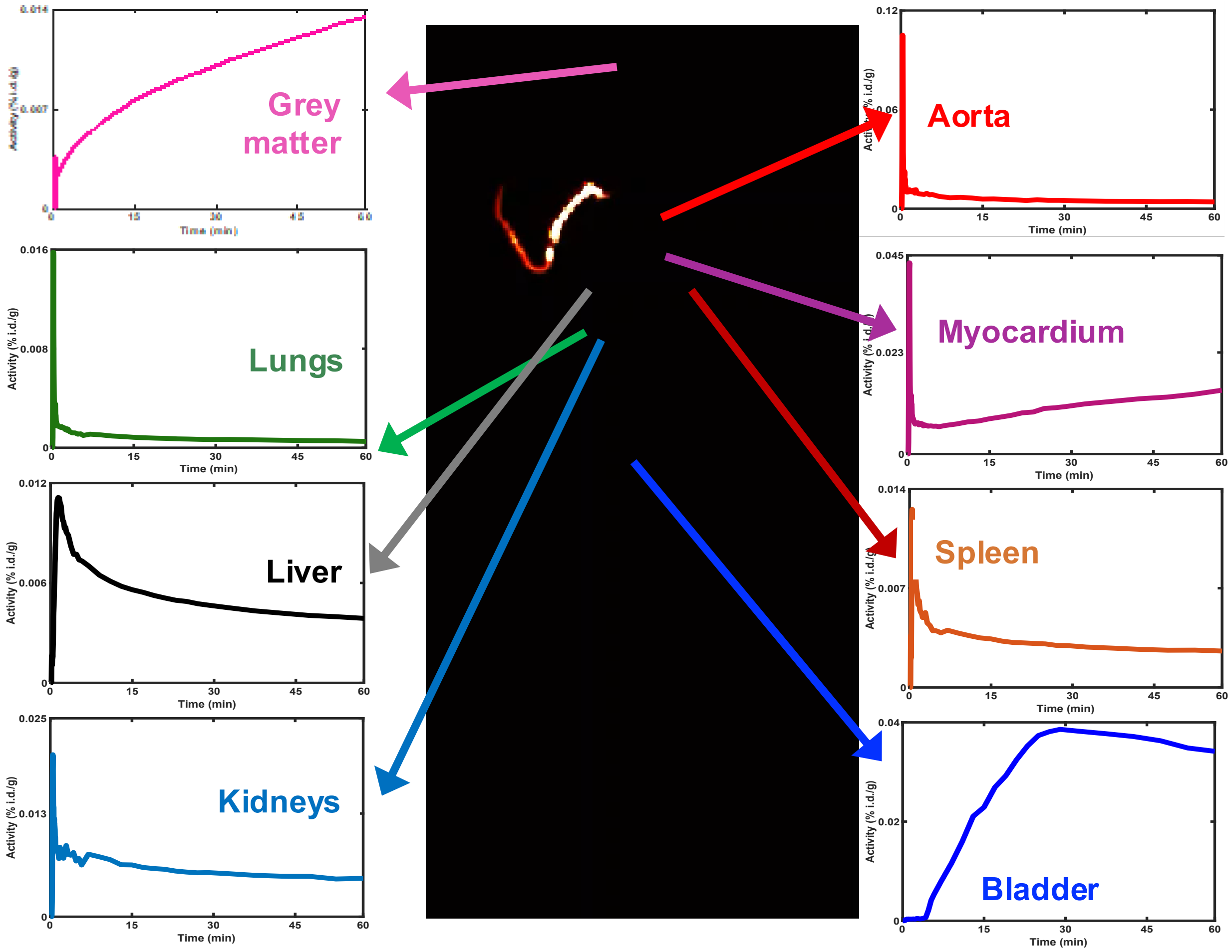


Yiran Wang, UC Davis

Total-Body Dynamic Imaging

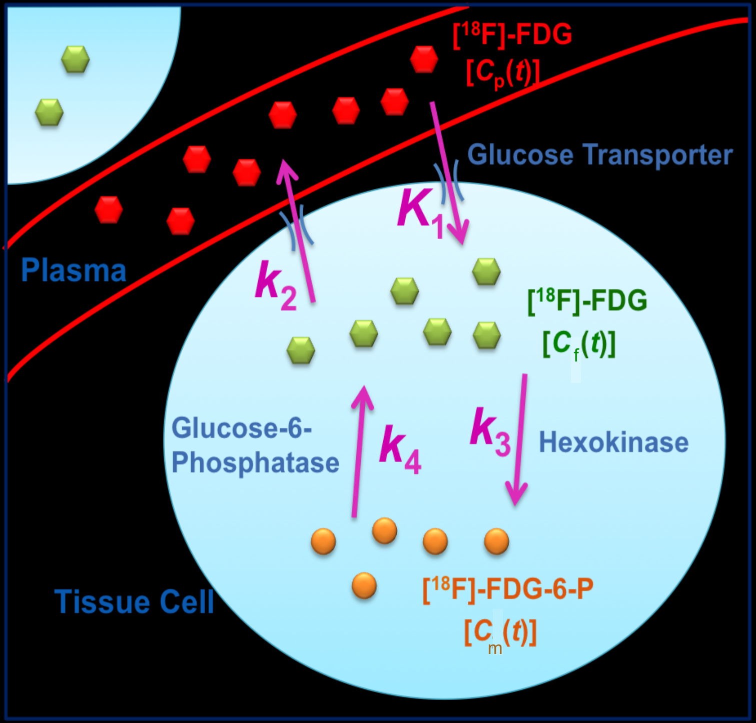
Measuring pharmacokinetics in every tissue and organ of the body

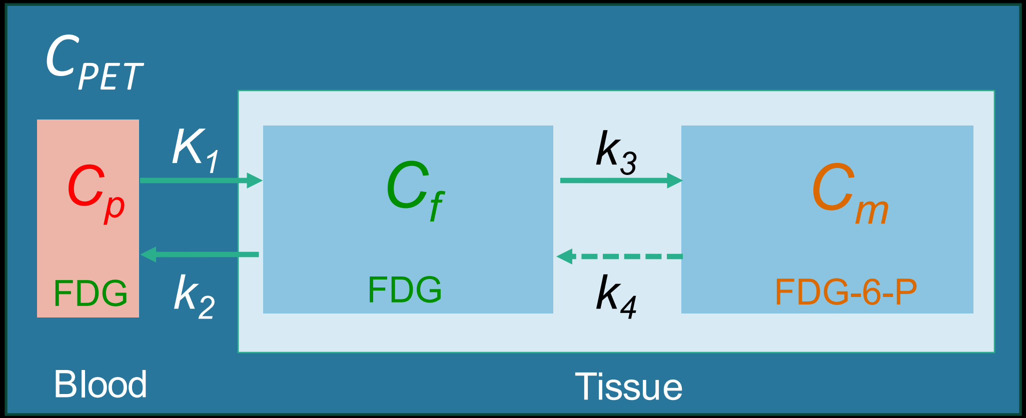
~1,000,0000 measured time-activity curves



Kinetic Modeling

^{18}F-fluorodeoxyglucose





$$\frac{dC_f}{dt} = K_1 C_p - (k_2 + k_3) C_f + k_4 C_m$$

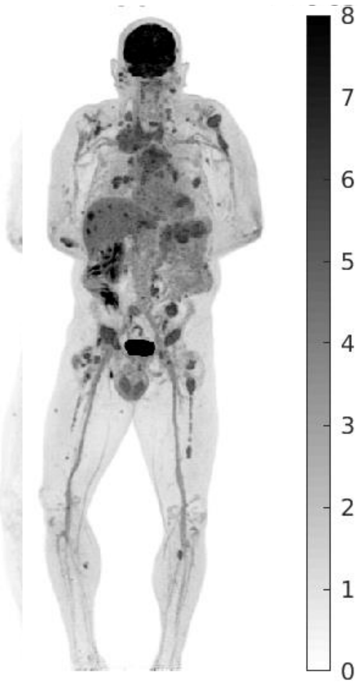
$$\frac{dC_m}{dt} = k_3 C_f - k_4 C_m$$

$$C_{PET}(t) = (1 - v_b)(C_f(t) + C_m(t)) + v_b C_p(t)$$

Guobao Wang, UC Davis

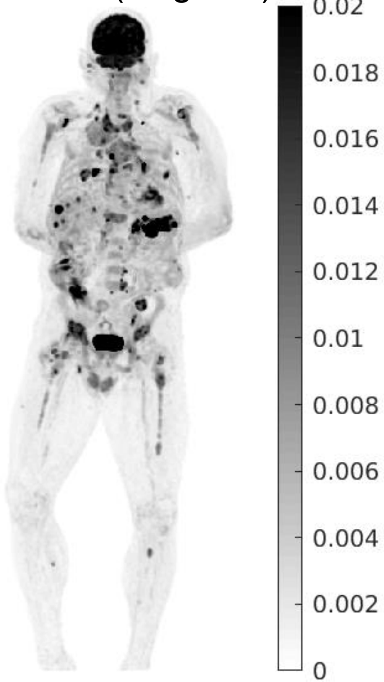
Parametric Imaging with ^{18}F-FDG

SUV (g/ml)



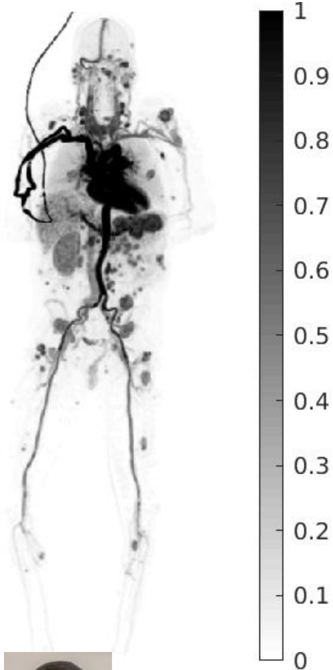
$$SUV = \frac{C_{PET}(kBq/ml)}{A(kBq)/w(g)}$$

K_i: Overall FDG influx rate (ml/g/min)

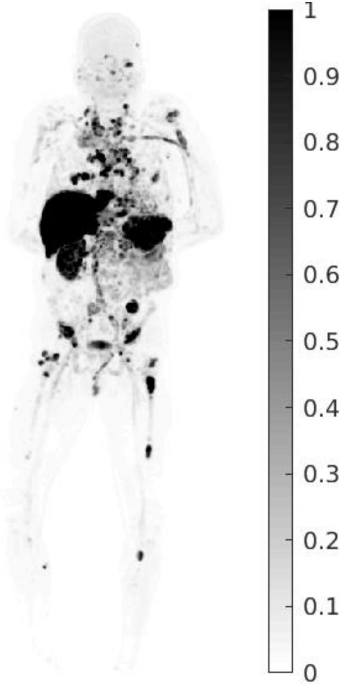


$$K_i = \frac{K_1 k_3}{(k_2 + k_3)}$$

v_b: fractional blood volume



K_1: glucose transport rate (ml/g/min)



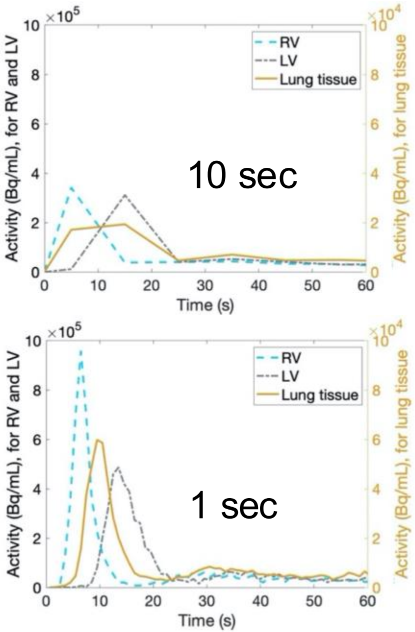
Wang et al, J Nucl Med 63; 1274-81 (2022)

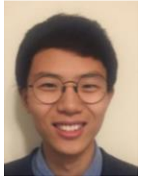
Fast Dynamic Imaging

- Frame times of 1-2 seconds achievable
  (conventionally 5-10 secs)

- Frame times of 0.1 secs possible!

- What can be done with much higher temporal resolution?





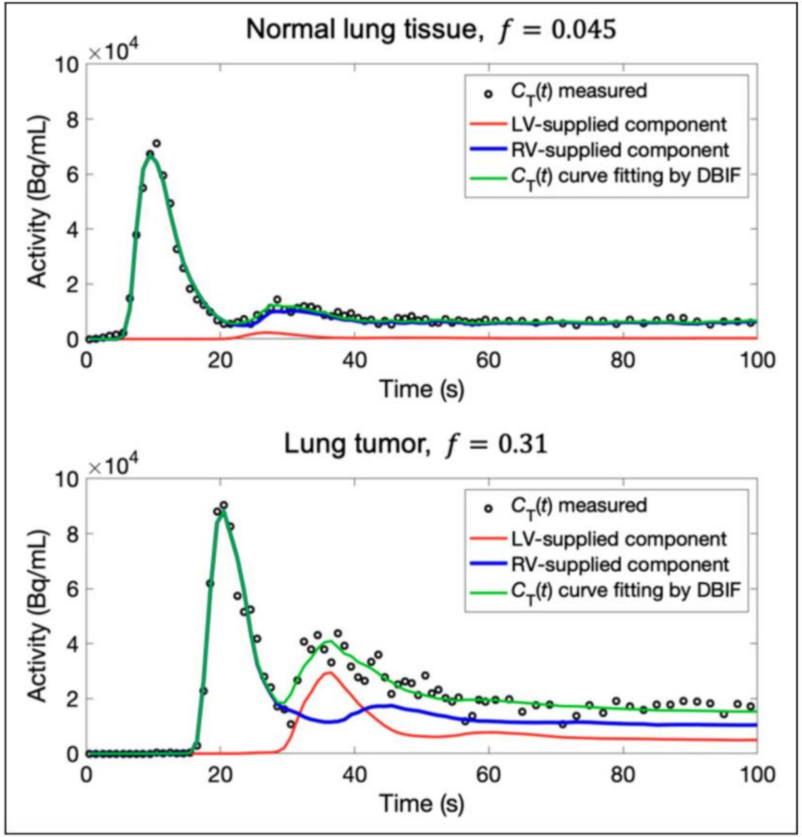
Effect of better temporal resolution

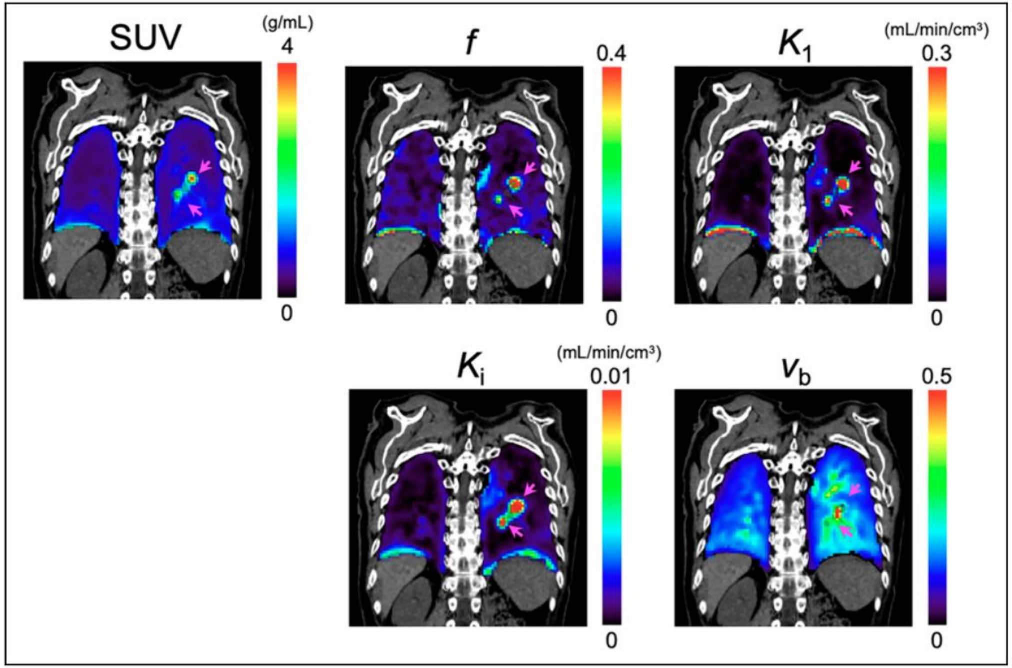
Wang et al,
JNM 2023;64:1154-61

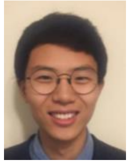
Fast (~100 ms) Dynamic Imaging

Zhang et al,
PNAS 2020;117:2265-2267

Modeling of Lung Tumor Kinetics

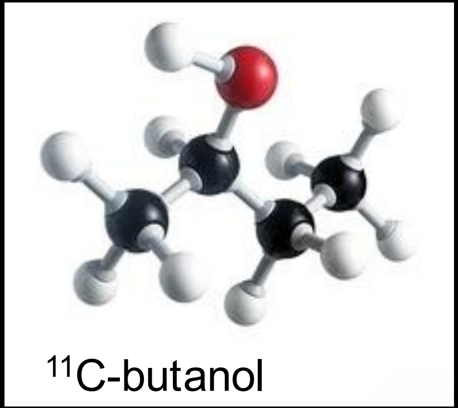


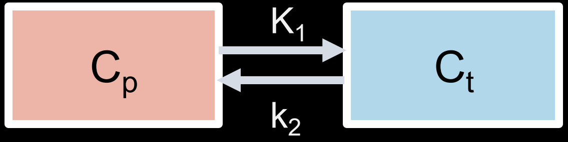


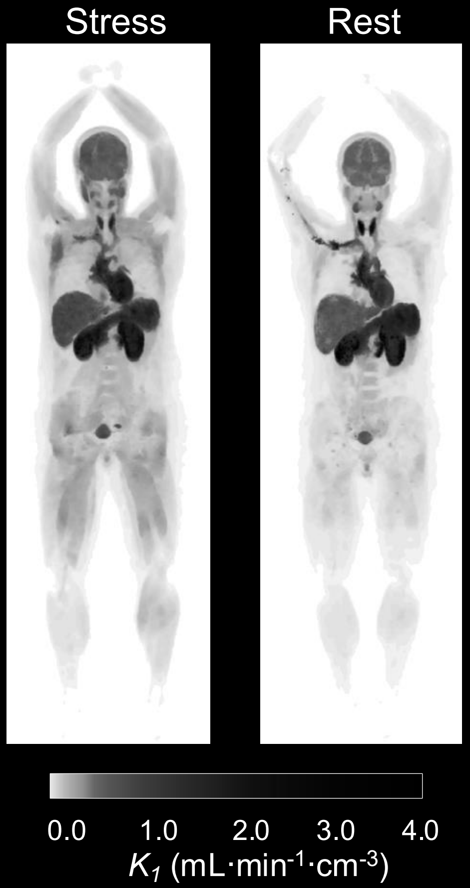


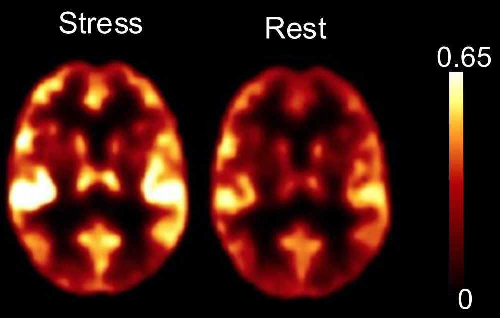
Wang et al, J Nucl Med 64; 1154-61 (2023)

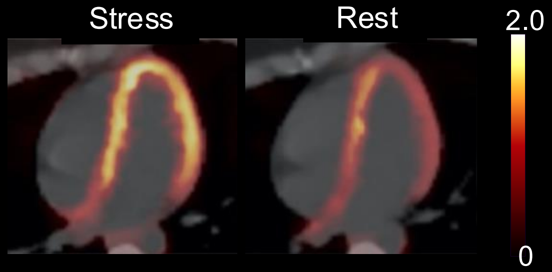
Total-Body Perfusion Imaging

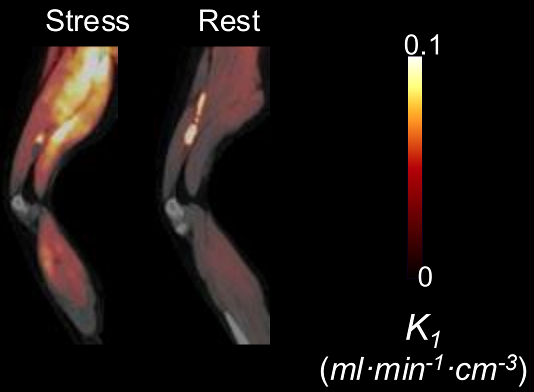






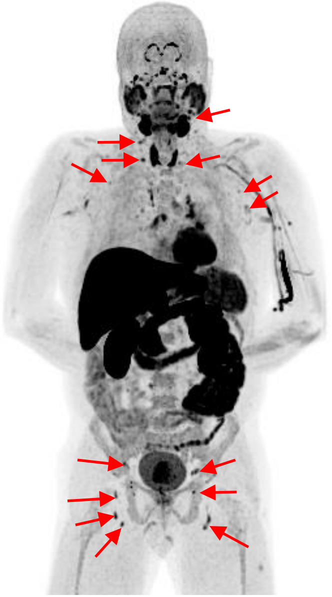


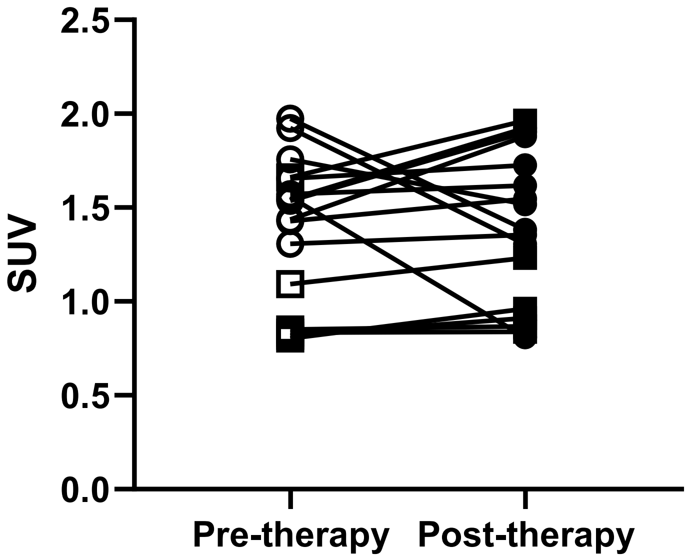


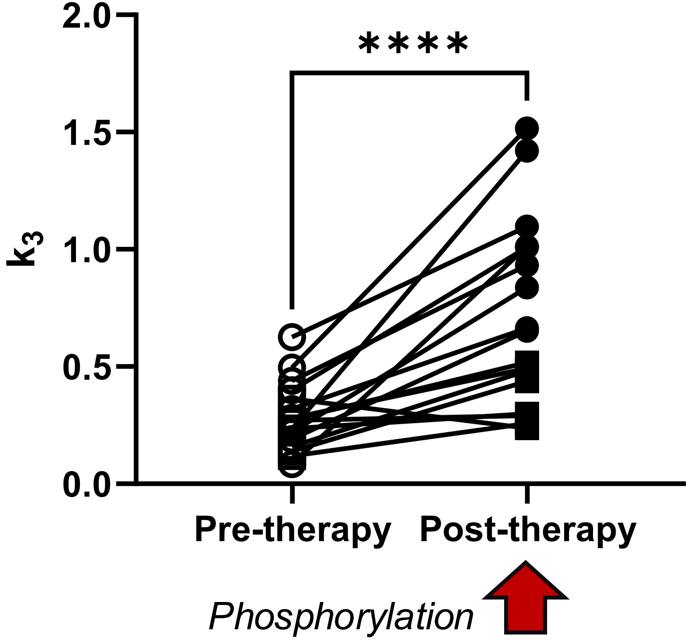


Li et al,
J Nucl Med
64; 1831-8 (2023)

Imaging Activated T Cells with [^{18}F]F-AraG Response to Therapy







Kinetic parameters shed light on **T cell activation in peripheral lymph nodes** after anti-PD-1 immunotherapy

Omidvari et al. *J Nucl Med* 65: 1481-88 (2024)

Opportunities and Challenges Quantification in Dynamic Imaging

- ~400-fold activity range (800 MBq of ^{11}C versus 2 MBq of ^{89}Zr)
- ~6000-fold range in frame duration (10 mins versus 0.1 secs)
- >1000-fold range in count density

- Maximizing accuracy and precision
  - How well are we doing and are we doing as well as we can?

- Advanced computational tools (esp. for low count density frames)
  - Robust and quantitative regularization and/or AI to improve data accuracy/precision?

- Motion correction
  - Methods for robust and comprehensive motion correction

(*Sundar et al, J Nucl Med 2023; 64: 1145-1153*)

Opportunities and Challenges
Modeling of Total-Body Dynamic Data

- Unprecedented high temporal resolution data quality
- Possible areas to explore
  - How to intelligently further reduce noise in TACs
    - temporal similarity
    - (deep) kernel-based methods
    - direct reconstruction of kinetic parameters
    - AI for temporal denoising
  - How to handle metabolites
    - Image-derived correction possible?
  - Different types of models
    - Spectral analysis / Factor analysis
    - Spatiotemporal models (*e.g. Shavandi et al, Sci Rep 2022; 12: 14582*)
    - Networks and connectivity

Opportunities and Challenges
Modeling of Total-Body Dynamic Data

- Computation
  - High temporal resolution → 60-600 frames per minute!
  - Organ level (segmentation) or voxel level (high noise)?
  - Voxel-wise model selection and fitting on ~1,000,000 time-activity curves
  - Delay/dispersion correction
  - AI approaches to reduce computation time

- Activation paradigms
  - Physiologic, pharmacologic, environmental etc…
  - Non-steady state modeling methods (Morris et al, J Nucl Med 2014; 65: 1824-37)

- Multi-tracer studies
  - Optimized delivery protocols (*e.g. Liu et al EJNMI 2023; 50: 2271-81*)
  - Minimize crosstalk

Modeling of Total-Body Dynamic Data

Total-Body PET

$K_{i,}$ K_1, k_2, k_3, v_b… (across all organs)

blood flow, F

tracer permeability, PS

heart rate, respiration rate

Heart: ejection fraction, wall motion

Heart: cardiac output

Blood transit times (peripheral vascular resistance?)

Kidney function

Liver: ratio of hepatic artery/portal vein supply

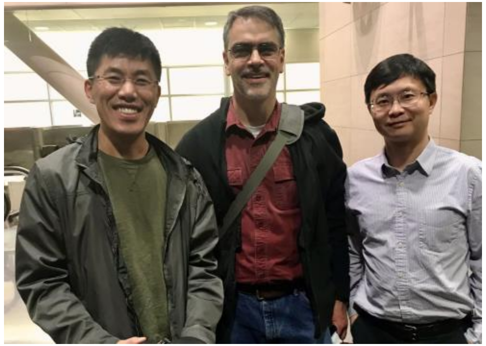
Lung: ratio of bronchial/pulmonary artery supply

…and we didn't even consider CT measures!

Summary

- Advanced total-body PET scanners enable dynamic imaging in the entire human body with very high temporal resolution
- Many opportunities exist to further improve and extract more information from 4-D total-body PET data
- Total-body PET studies offer new opportunities for studying the human body as a system in health and disease

Acknowledgements



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