Portable brain imaging using Positron Emission Tomography (PET)

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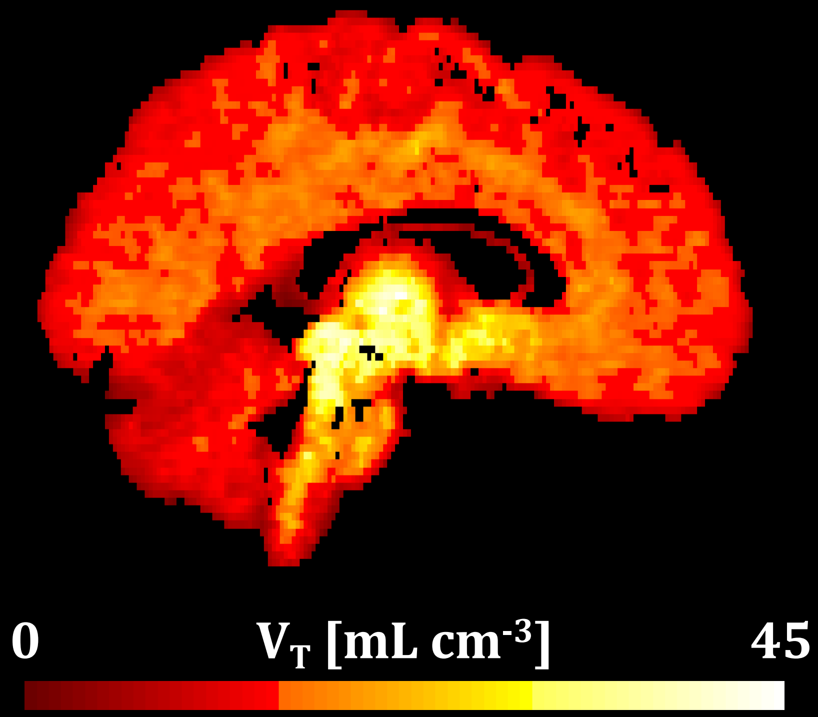
PET is a unique tool to interrogate the human brain

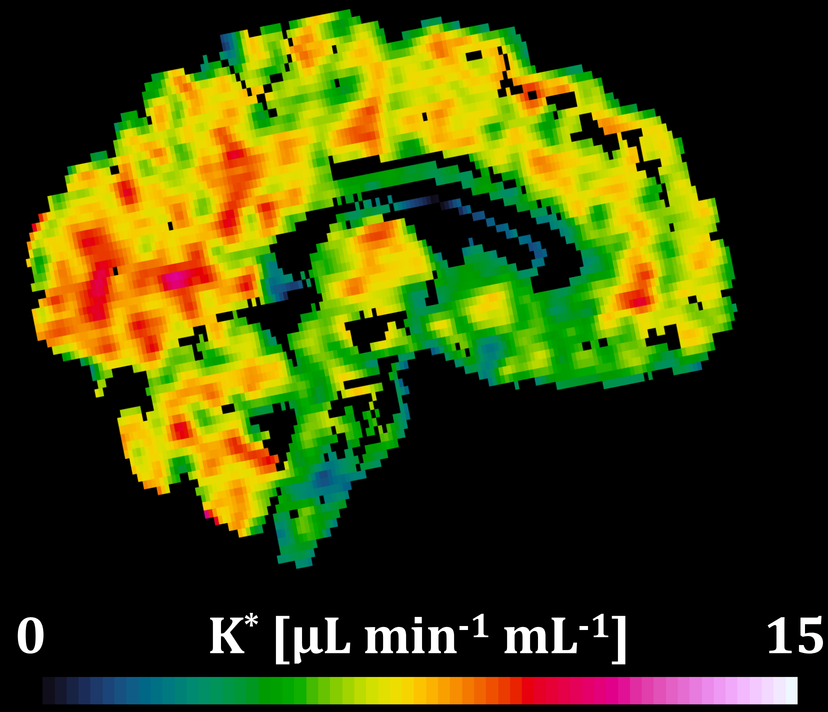
PET can quantify *in vivo* specific components of metabolic and neurochemical processes

density of serotonin transporter



Zanderigo F et al.
Empirical Bayesian estimation in graphical analysis: a voxel-based approach for the determination of the volume of distribution in PET studies
Nuclear Medicine and Biology 2010; 37: 443-451

incorporation of arachidonic acid



Zanderigo F et al.
[^{11}C]arachidonic acid incorporation measurement in human brain: optimization for clinical use
Synapse 2018; 72(2), e22018

What hinders PET feasibility & translation?

https://usa.healthcare.siemens.com/molecular-imaging/pet-ct/biograph-mct

COST

SIZE

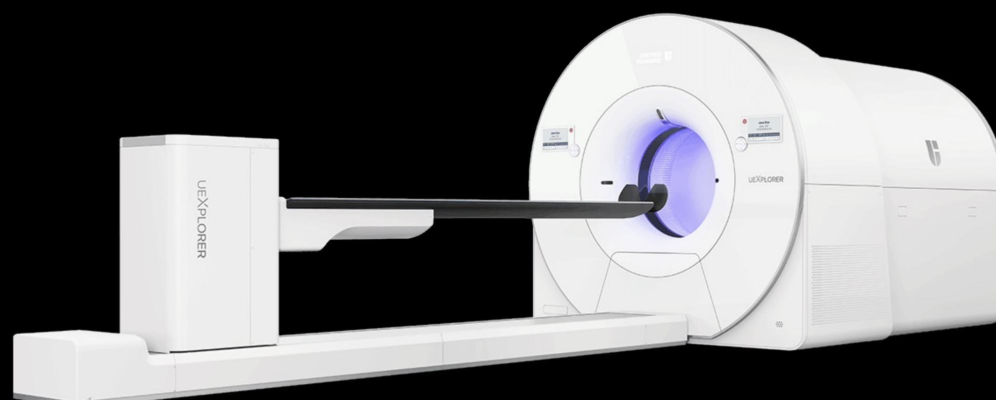
STATIONARY

SUPINE POSITION

INJECTED DOSE

BLOOD SAMPLING

https://pet.ubc.ca/facilities/siemens-hrrt-pet-scanner/

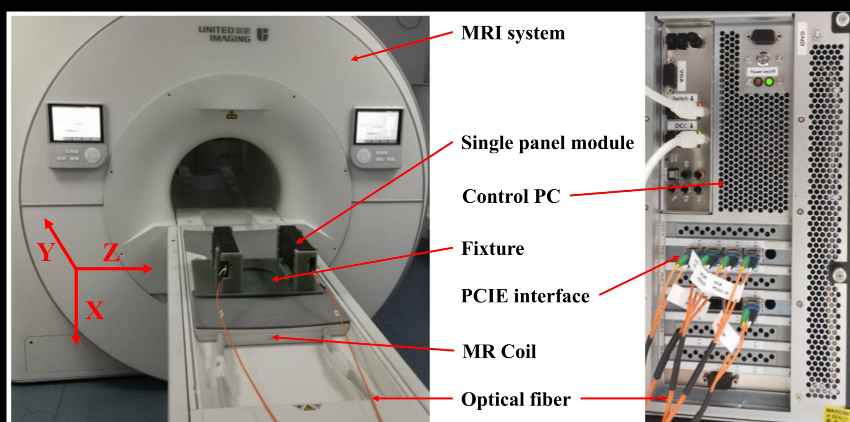


https://usa.united-imaging.com/products/molecular-imaging/uexplorer/

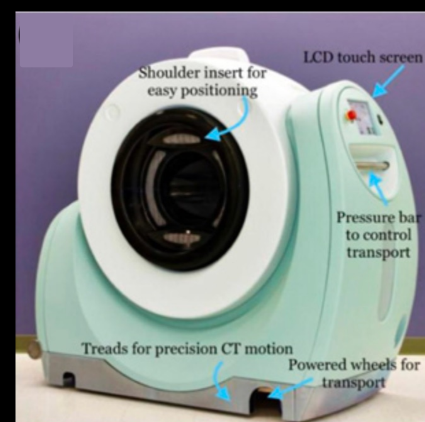
Toward cost-effective and portable dedicated PET scanners

AMPET (West Virginia University)
Kinahan P et al. J Nucl Med 2015; 56: 1540

CerePET (Brain Biosciences)
Bartlett EA et al. Biol Psychiatry 2022; 91 (9): S220



DP-PET (United Imaging Healthcare)
Zeng T et al. EJNMMI physics 2021; 8: 1-16



NeuroPET (Photo Diagnostic Systems)
Grogg KS et al. J Nucl Med 2016; 57: 646-652

Catana C. *Development of Dedicated Brain PET Imaging Devices* J Nucl Med 2019; 60(8), 1044-1052

Portable scanners have the potential to dramatically expand the applications of PET imaging

Imaging in seated/standing configurations while subjects are engaged in tasks and interact with their environment naturalistically

Potential for imaging:

- ✓ proximal to real-world events (sports venues, intensive care units, war zones)
- ✓ in rural areas
- ✓ at outpatient drug abuse treatment centers
- ✓ in underserved populations (homebound patients, bedridden subjects, prison inmates)

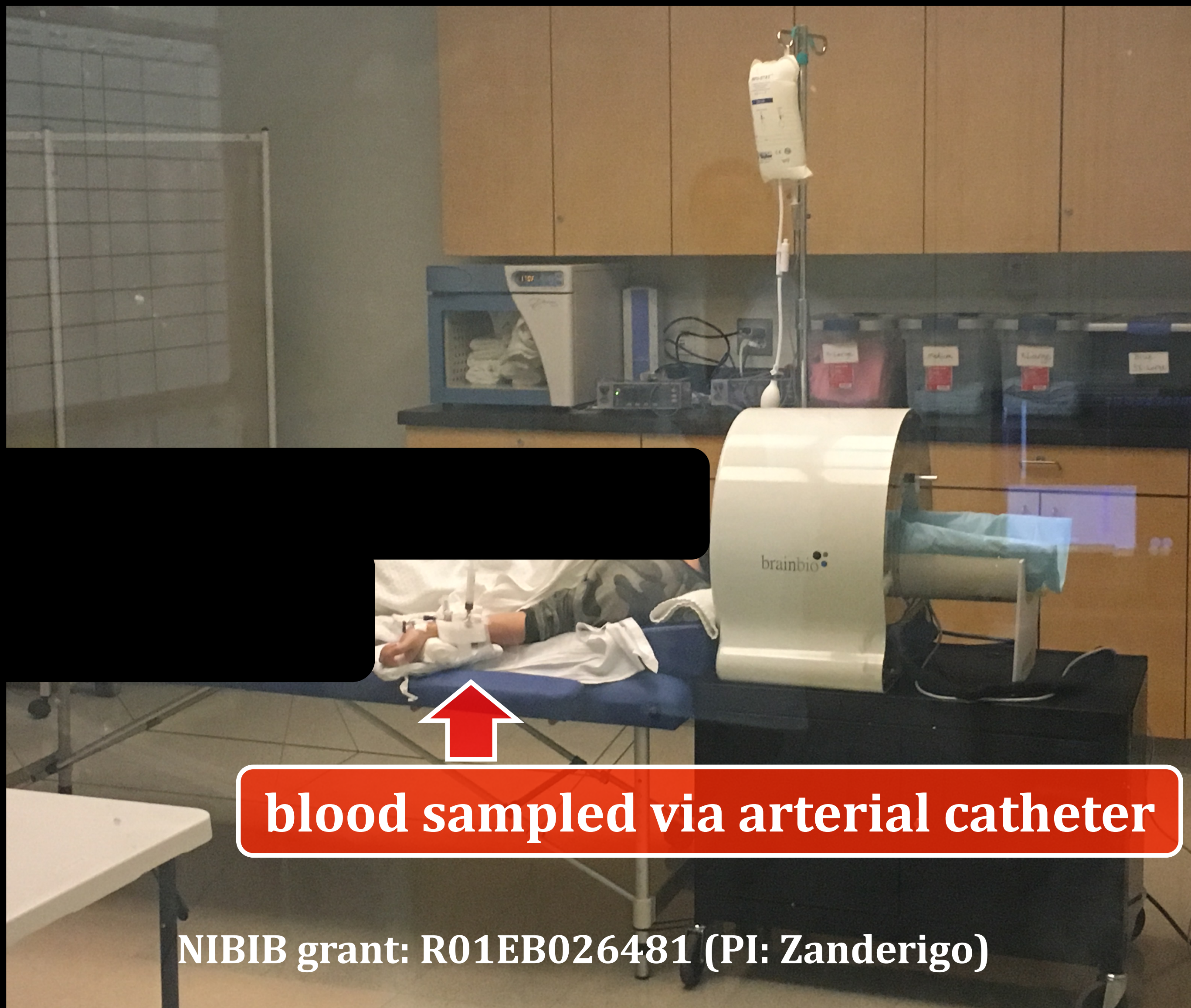
Wald LL et al. *Low-Cost and Portable MRI* J Magn Reson Imaging 2020; 52: 686–696

Challenges for portable brain PET imaging

Developing hardware and software solutions in order to:

1. **REDUCE** the required **INJECTED DOSE** of radiotracer and the **WEIGHT** of the scanner
   Chen KT et al. EJNMMI 2021; 48, 2416-2425
2. Obtain **REAL-TIME DATA RECON** and **PROCESSING** (for certain applications)
   Whiteley W et al. IEEE TRPMS 2021; 5(1), 65-77
3. **ELIMINATE** the need for **CONCURRENT BLOOD SAMPLING** to simplify the acquisition of brain PET imaging data while maintaining their full quantification
   Van der Weijden CWJ et al. EJNMMI 2023; https://doi.org/10.1007/s00259-022-06057-4

Eliminating the need for concurrent blood sampling to facilitate quantitative PET imaging



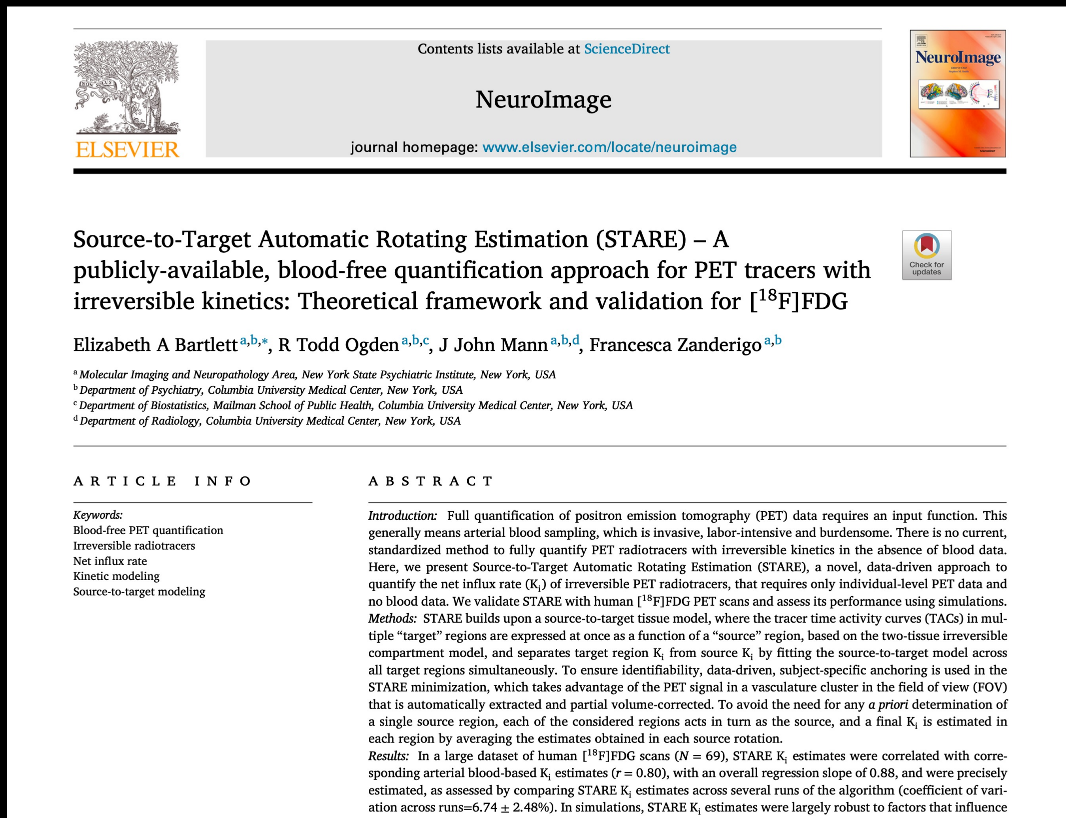
NIBIB R01EB026481: Noninvasive Quantification of Brain Glucose Metabolism Using a Portable Positron Emission Tomography Camera

1. **DEVELOP** a BLOOD-FREE method to quantify the net influx rate (K_i) into the brain tissue of PET irreversible tracers

2. **VALIDATE** the method in new ^{18}F-FDG data collected in 20 healthy controls using both a current PET scanner (Siemens Biograph mCT) and the portable CerePET device

3. **DISSEMINATE** a library of software routines that implement the validated method

STARE: Source-to-Target Automatic Rotating Estimation


Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Source-to-Target Automatic Rotating Estimation (STARE) – A publicly-available, blood-free quantification approach for PET tracers with irreversible kinetics: Theoretical framework and validation for $[^{18}F]FDG$

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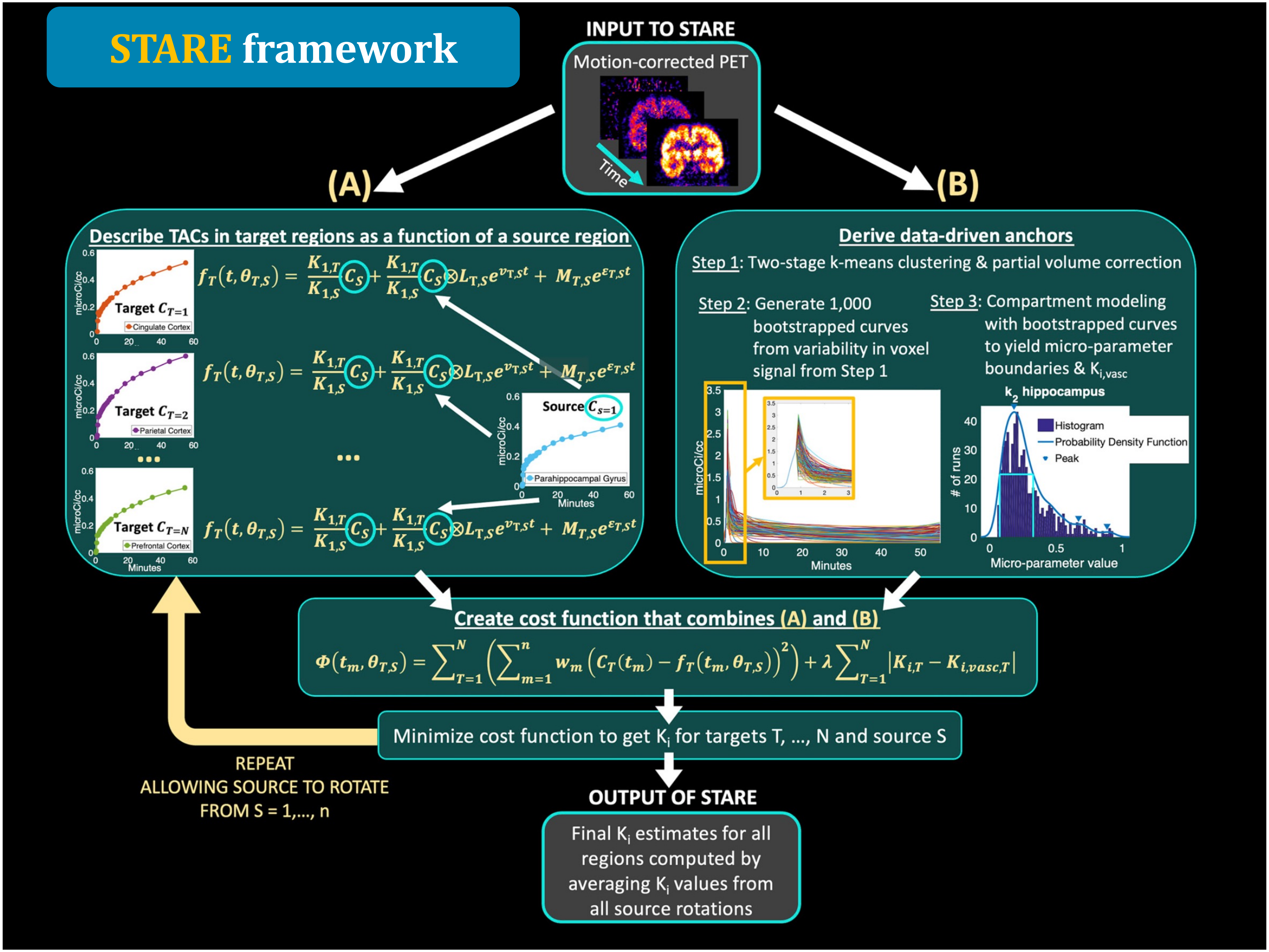
Irreversible radiotracers
Net influx rate
Kinetic modeling
Source-to-target modeling

ABSTRACT

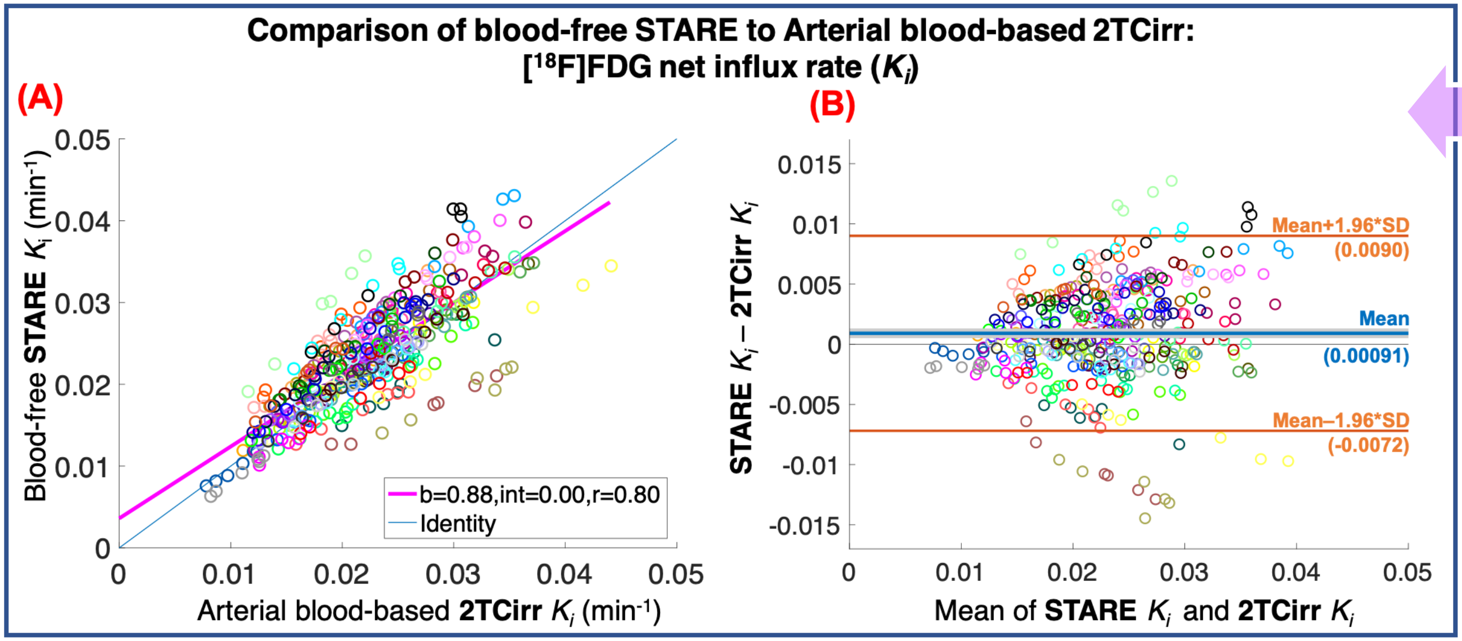
Introduction: Full quantification of positron emission tomography (PET) data requires an input function. This generally means arterial blood sampling, which is invasive, labor-intensive and burdensome. There is no current, standardized method to fully quantify PET radiotracers with irreversible kinetics in the absence of blood data. Here, we present Source-to-Target Automatic Rotating Estimation (STARE), a novel, data-driven approach to quantify the net influx rate (K_i) of irreversible PET radiotracers, that requires only individual-level PET data and no blood data. We validate STARE with human $[^{18}F]FDG$ PET scans and assess its performance using simulations.
Methods: STARE builds upon a source-to-target tissue model, where the tracer time activity curves (TACs) in multiple "target" regions are expressed at once as a function of a "source" region, based on the two-tissue irreversible compartment model, and separates target region K_i from source K_i by fitting the source-to-target model across all target regions simultaneously. To ensure identifiability, data-driven, subject-specific anchoring is used in the STARE minimization, which takes advantage of the PET signal in a vasculature cluster in the field of view (FOV) that is automatically extracted and partial volume-corrected. To avoid the need for any *a priori* determination of a single source region, each of the considered regions acts in turn as the source, and a final K_i is estimated in each region by averaging the estimates obtained in each source rotation.
Results: In a large dataset of human $[^{18}F]FDG$ scans ($N = 69$), STARE K_i estimates were correlated with corresponding arterial blood-based K_i estimates ($r = 0.80$), with an overall regression slope of 0.88, and were precisely estimated, as assessed by comparing STARE K_i estimates across several runs of the algorithm (coefficient of variation across runs=6.74 ± 2.48%). In simulations, STARE K_i estimates were largely robust to factors that influence

BETSY BARTLETT, PhD

- ✓ **Migration of code to Python; Matlab code already available at https://github.com/elizabeth-bartlett/STARE**
- ✓ **Extension to quantification of images with shorter PET acquisition time (to facilitate use in clinical settings)**

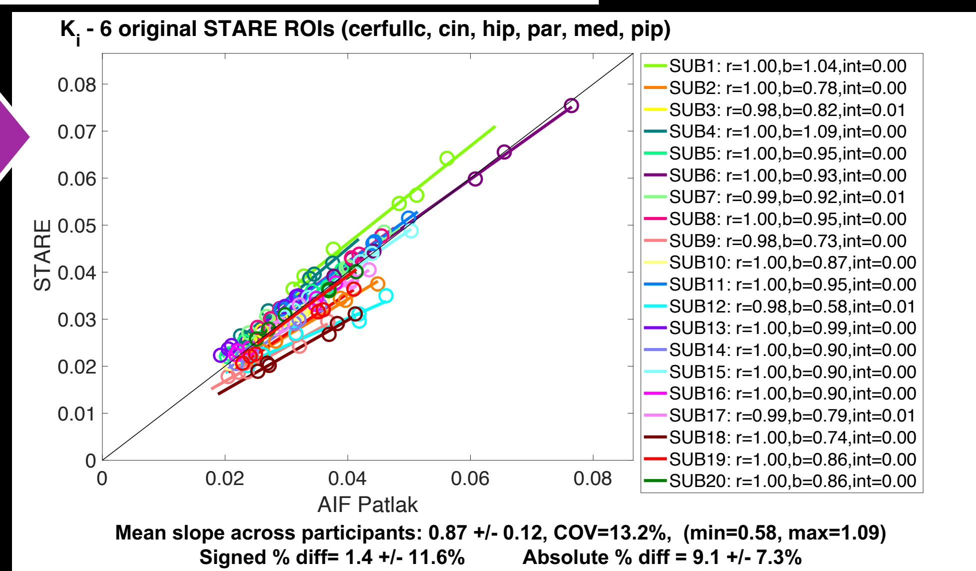

STARE framework
INPUT TO STARE
Motion-corrected PET
Time
(A)
(B)
Describe TACs in target regions as a function of a source region
Target $C_{T=1}$
Cingulate Cortex
Target $C_{T=2}$
Parietal Cortex
Target $C_{T=N}$
Prefrontal Cortex
microCi/cc
Minutes
$f_T(t,\theta_{T,S}) = \frac{K_{1,T}}{K_{1,S}} C_S + \frac{K_{1,T}}{K_{1,S}} C_S \otimes L_{T,S} e^{\nu_{T,S} t} + M_{T,S} e^{\varepsilon_{T,S} t}$
Source $C_{s=1}$
Parahippocampal Gyrus
Derive data-driven anchors
Step 1: Two-stage k-means clustering & partial volume correction
Step 2: Generate 1,000 bootstrapped curves from variability in voxel signal from Step 1
Step 3: Compartment modeling with bootstrapped curves to yield micro-parameter boundaries & $K_{i,vasc}$
k_2 hippocampus
Histogram
Probability Density Function
Peak
# of runs
Micro-parameter value
Create cost function that combines (A) and (B)
$\Phi(t_m,\theta_{T,S}) = \sum_{T=1}^{N}\left(\sum_{m=1}^{n} w_m \left(C_T(t_m) - f_T(t_m,\theta_{T,S})\right)^2\right) + \lambda \sum_{T=1}^{N} |K_{i,T} - K_{i,vasc,T}|$
Minimize cost function to get K_i for targets T, ..., N and source S
REPEAT
ALLOWING SOURCE TO ROTATE
FROM S = 1,..., n
OUTPUT OF STARE
Final K_i estimates for all regions computed by averaging K_i values from all source rotations

STARE vs. arterial blood-based

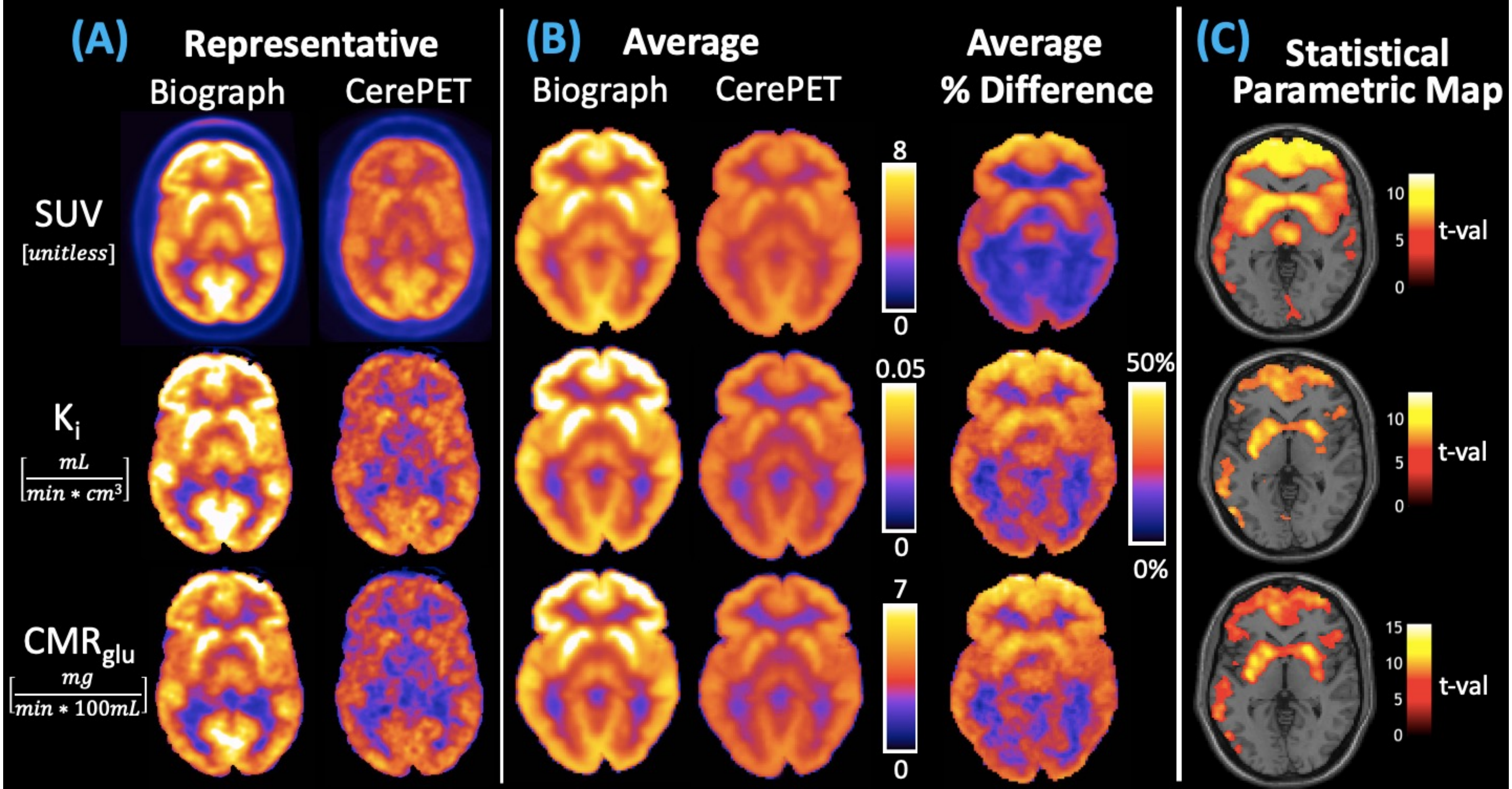


STARE on DATA from ECAT EXACT HR+ (Siemens/CTI)

STARE on DATA from Biograph mCT (Siemens) (preliminary)



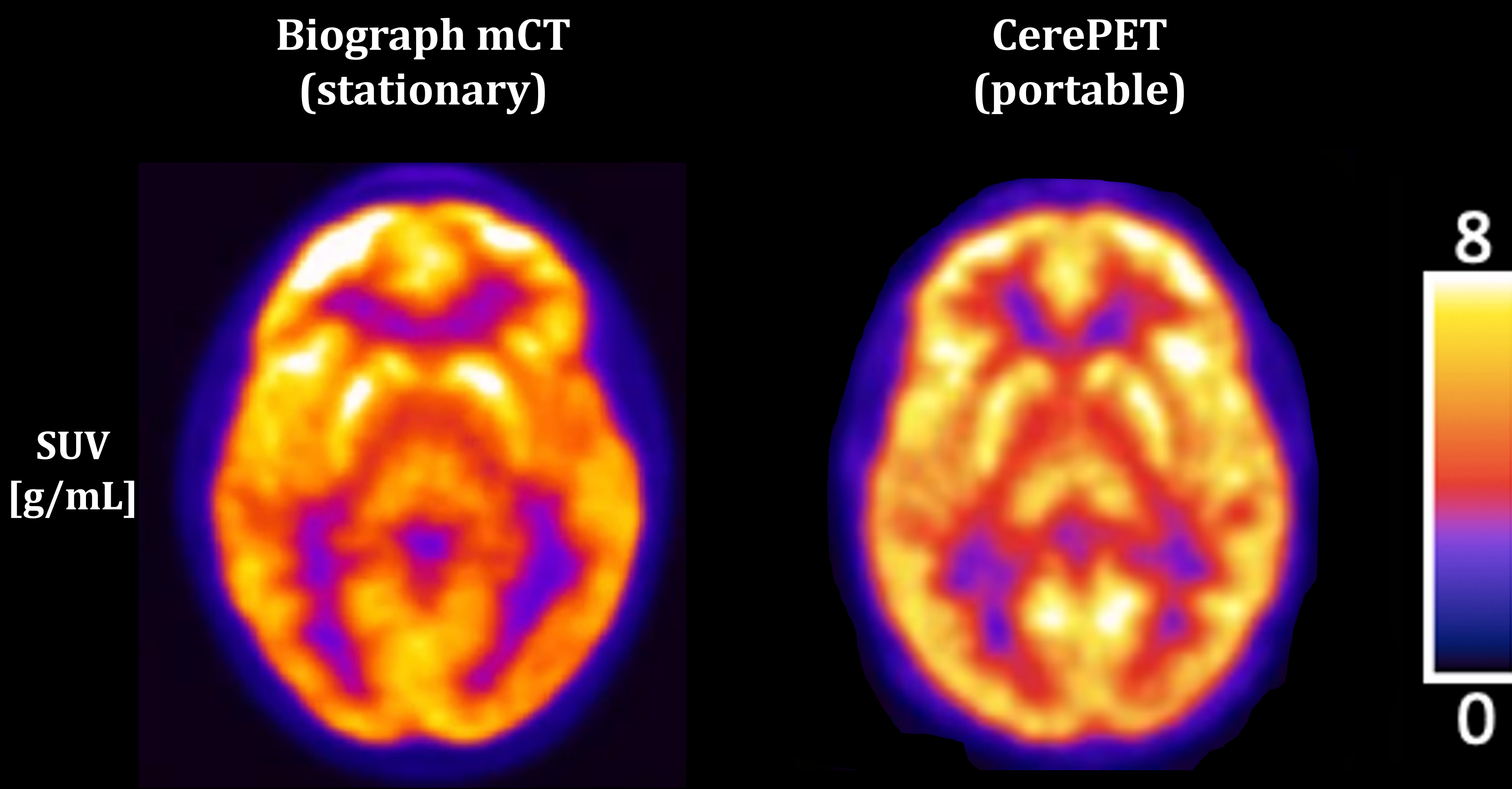
Portable vs. stationary PET brain imaging



Bartlett EA, Lesanpezeshki M, Anishchenko S, Ogden RT, Mann JJ, Beylin D, Miller JM, Zanderigo F
Comparison of the portable CerePET positron emission tomography (PET) scanner with the Siemens Biograph mCT
Proceedings of BRAIN & BRAIN PET 2022, Glasgow, Scotland, May-June 2022; J Cereb Blood Flow Metab 42 (1_SUPPL), 26-26

Portable vs. stationary PET brain imaging: improved scatter correction and cross-calibration

Representative subject (imaged 2 months apart)



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