Statistical Methods for Reconstruction of Parametric Images from Dynamic PET Data

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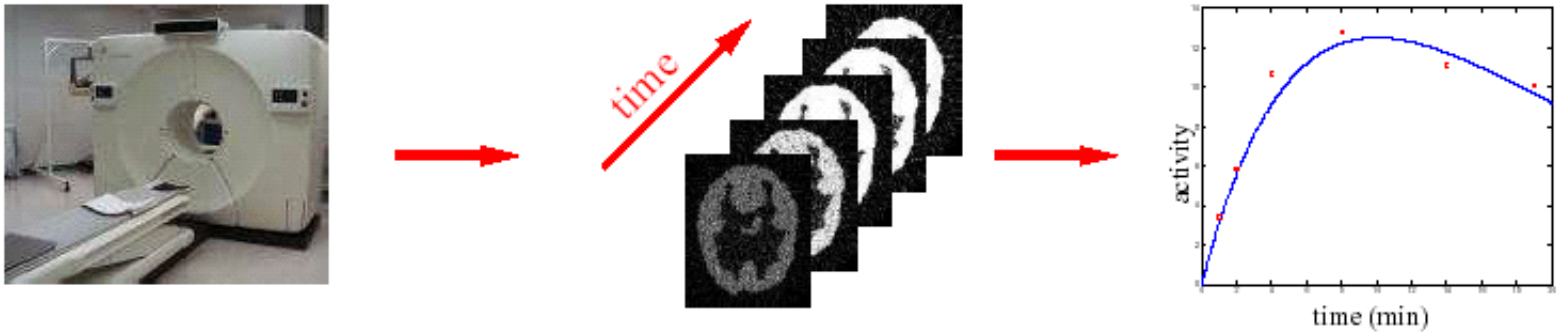
March 25, 2005

Outline

- Introduction and Problem Statement
- Two-tissue Compartment Model
- Image Domain Parameter Estimation Methods
- Direct Parameter Estimation
- Simulations
- HR+ Monkey Data
- Future Work and Conclusions

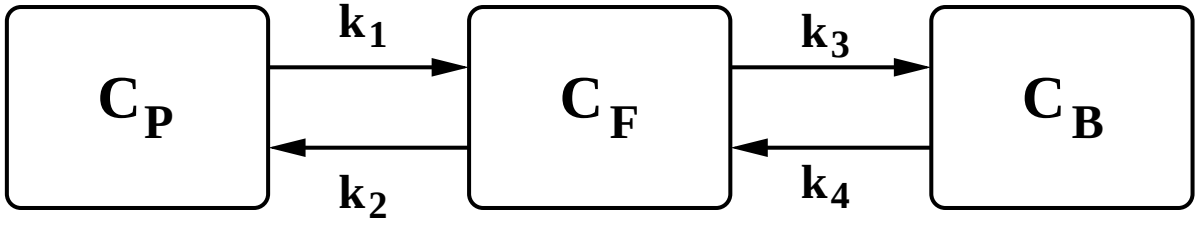
Dynamic PET



- PET accumulates/averages the emissions of voxels.
- Time resolution can be achieved by dividing the data into time frames.
- Used in imaging heart perfusion, brain activation, glucose metabolizing rate, receptor availability
- Time response of voxels are governed by ODEs
- Parameters of these ODEs are physiologically relevant

2-tissue Compartment Model

- Used in;
  - Glucose metabolism imaging (FDG)
  - Receptor availability imaging (^{11}C-raclopride,^{18}F-fallypride)



- C_P (nCi/ml): Molar tracer concentration in plasma
- C_F (nCi/ml): Molar concentration of unbound tracer
- C_B (nCi/ml): Molar concentration of metabolized or bound tracer

Physiologically Important Parameters

- For receptor-ligand imaging *binding potential (BP)* and *volume distribution (VD)* are physiologically important parameters.

$$\begin{aligned} \text{BP} &= \frac{k_3}{k_4} \\ \text{VD} &= \frac{k_1}{k_2}\left(1+\frac{k_3}{k_4}\right) \end{aligned}$$

- $BP \rightarrow$ available receptor sites
- $VD \rightarrow$ steady state distribution of tracer between plasma and tissue

2-tissue Compartment Model Equations

- C_P is assumed to be
  - known (arterial sampling, estimation),
  - same for all voxels
- Kinetic parameters vary for each voxel location
- Time variation of molar tracer concentrations at voxel s

$$\begin{aligned} \frac{dC_F(t)}{dt} &= k_{1s}C_P(t) - (k_{2s} + k_{3s})C_F(t) + k_{4s}C_B(t) \\ \frac{dC_B(t)}{dt} &= k_{3s}C_F(t) - k_{4s}C_B(t) \end{aligned}$$

- PET signal at voxel s,

$$f(\varphi_s, t) = (1 - V_B)(C_F(t) + C_B(t))S_A e^{-\lambda t} + V_B C_{WB}(t)$$

Image Domain Dense Parameter Estimation Methods

- Require reconstructed image
- Pixelwise weighted least squares (PWLS):

$$\hat{\varphi}_s = \arg\min_{\varphi_s} \|x_s - f(\varphi_s)\|^2_{W_s}$$

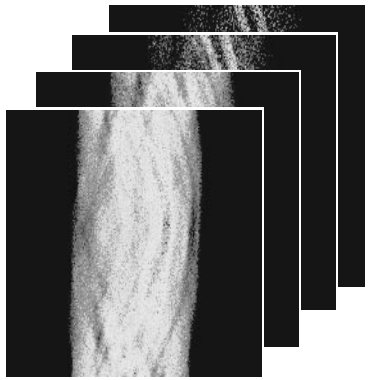
  - no *a priori* information, high spatial variance

- Pixelwise weighted least squares with spatial regularization:

$$\hat{\varphi} = \arg\min_{\varphi} \sum_{s=0}^{N-1} \|x_s - f(\varphi_s)\|^2_{W_s} + S(\varphi)$$

  - PWLSZ - constrain using smoothed PWLS estimates (Zhou *et al.*)
  - PWLSR - GMRF

Our Approach: Direct Parametric Image Reconstruction



PET DATA

t=1 .. K

Parametric Image Reconstruction

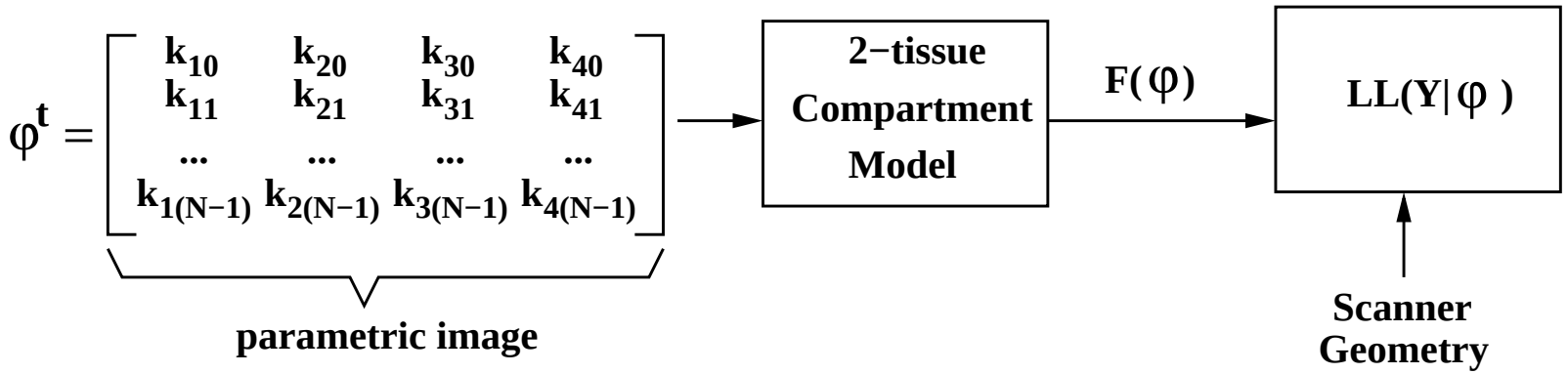
Scanner Geometry

$$\varphi^t = \begin{bmatrix} k_{10} & k_{20} & k_{30} & k_{40} \\ k_{11} & k_{21} & k_{31} & k_{41} \\ \dots & \dots & \dots & \dots \\ k_{1(N-1)} & k_{2(N-1)} & k_{3(N-1)} & k_{4(N-1)} \end{bmatrix}$$

parametric image

- Advantages:
  - Directly reconstructs parameters from sinogram data
  - Dimensionality reduction
  - Improves SNR
  - Produces a single full image of parameter vector

Parametric Reconstruction Model



- φ_s parameter vector of voxel s
- $f(\varphi_s) = \begin{bmatrix} f(t_1, \varphi_s) \\ \vdots \\ f(t_K, \varphi_s) \end{bmatrix}$ time response at voxel s
- $F(\varphi) = [f(\varphi_1),\ f(\varphi_2), \ldots, f(\varphi_N)]$ time response of all voxels
- Y is the sinogram data

MAP Estimate of Parametric Image

$$
\begin{aligned}
C(Y|\varphi) &= -LL(Y|\varphi) + S(\varphi) \\
\hat{\varphi} &= \arg\min_{\varphi} C(Y|\varphi)
\end{aligned}
$$

How do we efficiently compute $\hat{\varphi}$?

Log Likelihood (data) Term

- Y sinogram matrix; Y_{mk} independent Poisson distributed
- A system matrix; A_{ij} detection probability of an event from voxel j by detector pair i

$$E[Y|F(\varphi)] = AF(\varphi) + \mu \; .$$

- Log likelihood

$$\begin{aligned} LL(Y|\varphi) \quad = \quad & \sum_{k=0}^{K-1} \sum_{m=0}^{M-1} Y_{mk} \log(A_{m*}F(\varphi, t_k) + \mu) \\ & -(A_{m*}F(\varphi, t_k) + \mu) - \log(Y_{mk}!) \; . \end{aligned}$$

Stabilizing (regularization/prior) Term

- Model the distribution of parametric image with Markov Random Field (MRF)
- Gibbs distribution

$$p(\varphi) = \frac{1}{z} \exp\{- \sum_{\{s,r\} \in \mathcal{N}} g_{s-r} \|\varphi_s - \varphi_r\|_W^q\}$$

- Negative logarithm of distribution is used as stabilizing function

$$S(\varphi) = \sum_{\{s,r\} \in \mathcal{N}} g_{s-r} \|T(\varphi_s) - T(\varphi_r)\|_W^2 \ .$$

- $T(\cdot)$, let you regularize physiologically relevant parameters.

PICD - Parametric Iterative Coordinate Descent

- Efficient implementation of ICD for reconstruction with kinetic models
- Sequentially update parameter φ_s vector at each voxel

$$\Delta C(\tilde{\varphi}_s, \varphi_s) \approx \Delta f(\tilde{\varphi}_s, \varphi_s)\theta_1 + \frac{1}{2}\left\|\Delta f(\tilde{\varphi}_s, \varphi_s)\right\|_{\theta_2}^2 + \sum_{r \in \partial s} g_{s-r} \|T(\tilde{\varphi}_s) - T(\varphi_r)\|_W^2$$

where

$$\Delta f(\tilde{\varphi}_s, \varphi_s) = [f(\tilde{\varphi}_s, t_0) - f(\varphi_s, t_0), \cdots, f(\tilde{\varphi}_s, t_{K-1}) - f(\varphi_s, t_{K-1})]$$

- Update φ_s

$$\varphi_s \leftarrow \arg\min_{\varphi_s} \Delta C(\tilde{\varphi}_s, \varphi_s)$$

- $-LL(y|\varphi) + S(\varphi)$ will decrease with each PICD iteration

PICD - Update Strategy

- We re-parametrize using $\varphi_s = [a_s,\ b_s,\ c_s,\ d_s]$
- Then the time response is

$$f(t, \varphi_s) = (1 - V_B)[(ae^{-ct} + be^{-dt})u(t) \otimes C_P(t)]S_A e^{-\lambda t} + V_B C_{WB}(t)$$

- Two-stage nested optimization.

$$(c_s, d_s) \leftarrow \arg \min_{\tilde{c}_s \geq \tilde{d}_s \geq 0} \left\{ \arg \min_{\tilde{a}_s, \tilde{b}_s \geq 0} \left\{ \Delta C([\tilde{a}_s, \tilde{b}_s, \tilde{c}_s, \tilde{d}_s], \varphi_s) \right\} \right\} .$$

  - $c_s, d_s \rightarrow$ line search
  - $a_s, b_s \rightarrow$ gradient search

Computational Complexity

- $N \rightarrow$ number of voxels
- $M_0 \rightarrow$ average number of projections per voxel
- $K \rightarrow$ number of time frames
- $K_c \rightarrow$ number of time points in the time-convolution kernel
- $L_{ab} \rightarrow$ number iterations required for each update of $(\tilde{a}, \tilde{b})$
- $L_{cd} \rightarrow$ number iterations required for each update of $(\tilde{c}, \tilde{d})$

Algorithm	Per Iteration Complexity
PICD	$KN(L_{cd}L_{ab} + K_cL_{cd} + M_0)$
PWLS	$KN(L_{cd}L_{ab} + K_cL_{cd})$
PWLSR/PWLSZ	$KN(L_{cd}L_{ab} + K_cL_{cd})$
ICD	$KN(M_0)$

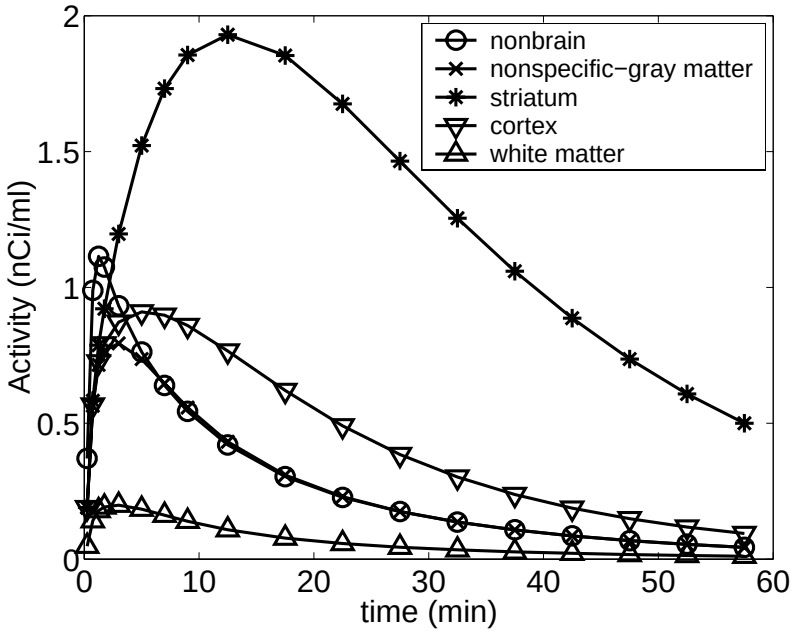
Multiresolution Reconstruction

- Multiresolution reconstruction
  - Coarsest scale initialized to constant value
  - Coarse scale solutions are used to initialize fine scale solutions
  - Used 3 scales (32×32, 64×64 and 128×128)
- Speeds up convergence at low frequency components.

Simulations - Phantom

- Rat phantom with seven separate regions is used to assess the estimation methods

nonbrain
nonspecific−gray matter
striatum
cortex
white matter



- Regions are obtained by segmenting MRI scans of a rat

Simulations - Phantom

- Kinetic parameters of regions are obtained from literature

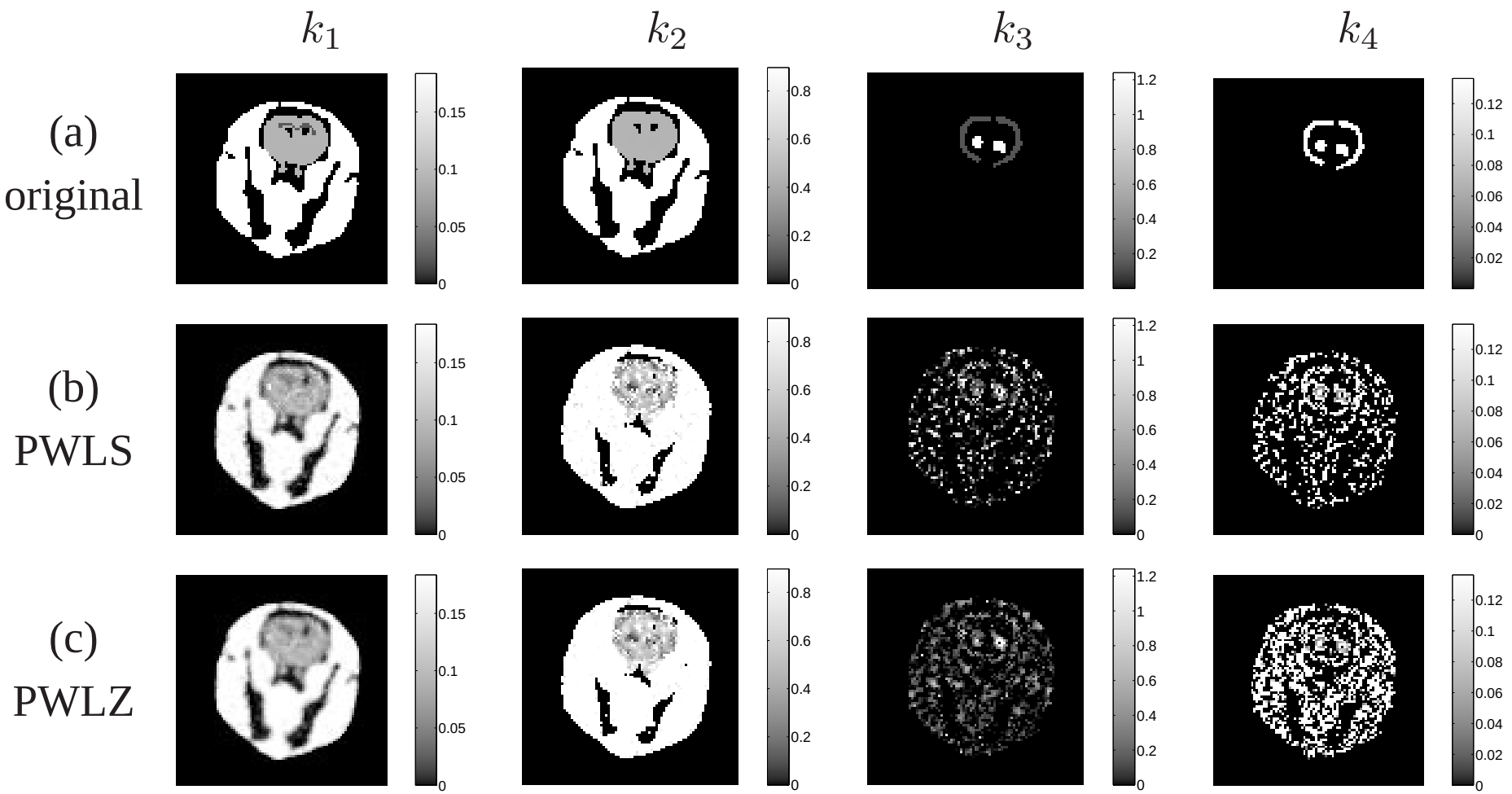
Region	k_1	k_2	k_3	k_4
Background	0	0	0	0
CSF	0	0	0	0
Nonbrain (NB)	.1836	.8968	0	0
Whole brain (WB)	.0918	.4484	0	0
Straitum (STR)	.0918	.4484	1.2408	.1363
Cortex (COR)	.0918	.4484	.141	.1363
White matter (WM)	.02295	.4484	0	0

- Total scan time is 60 min. , divided into 18 time frames: 4×0.5 min, 4×2 min and 10×5min

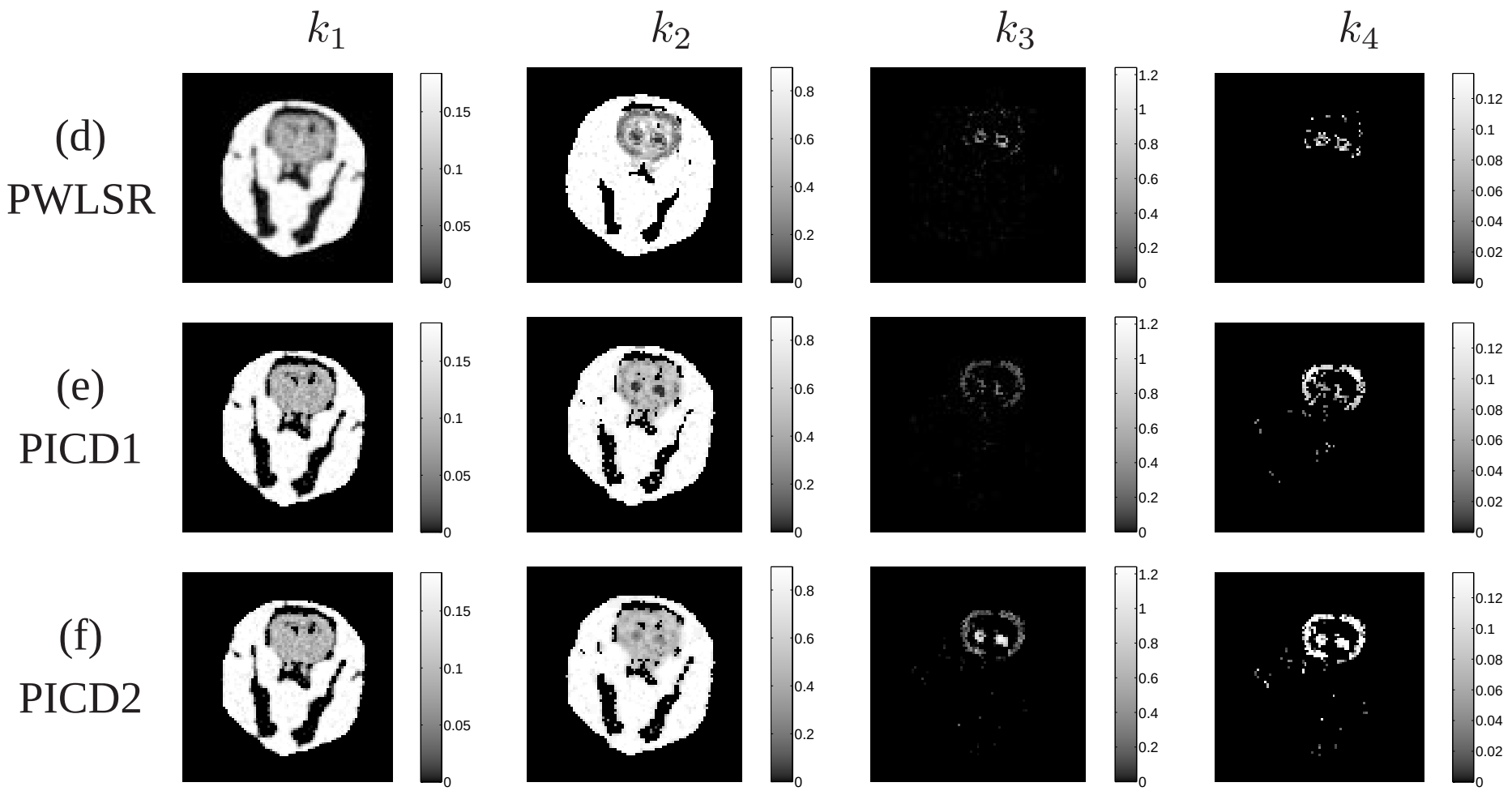
Simulations - Assumptions

- Raclopride with ^{11}C is used as tracer.
- The blood function, $C_P(t)$ was generated as described in [Wong *et. al. 01*]
- Activity scaled to are scaled 10M counts
- 180 projection angles each with 200 projection (0.875 mm spacing)
- Used 4 mm. wide triangular PSF
- Poisson noise model with accidental coincidences
- Image domain methods use MAP reconstruction with a single regularization parameter for all time frames

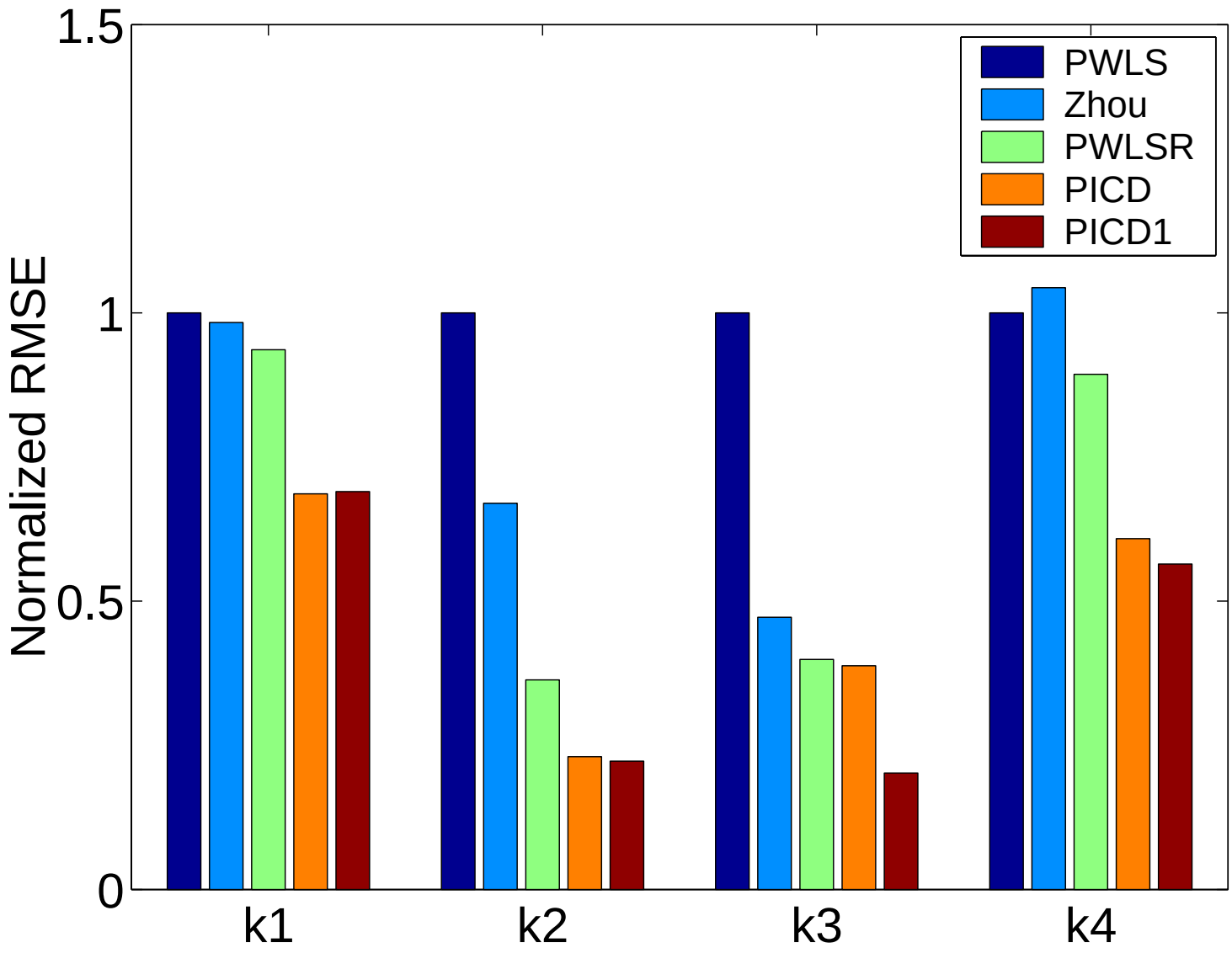
Kinetic Parameter Estimates



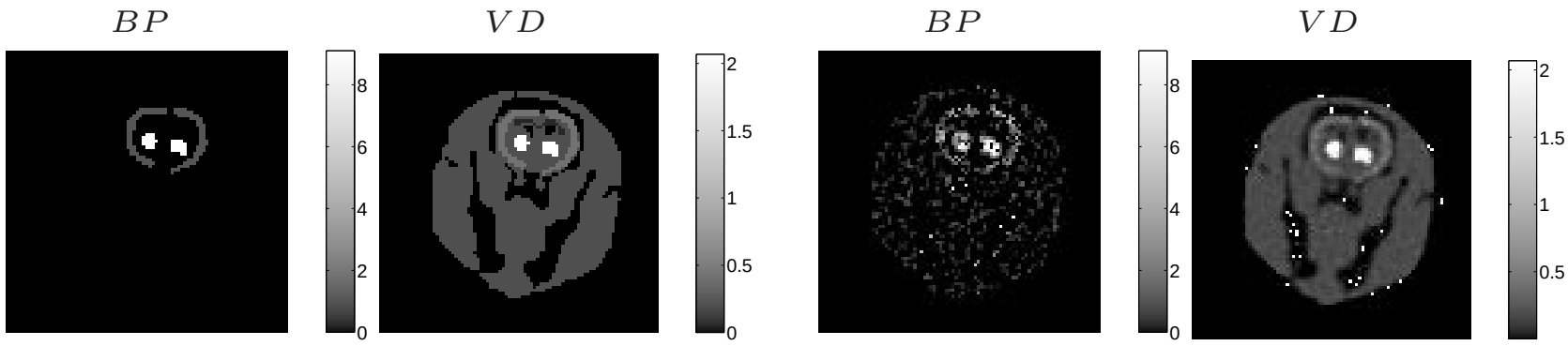
Kinetic Parameter Estimates



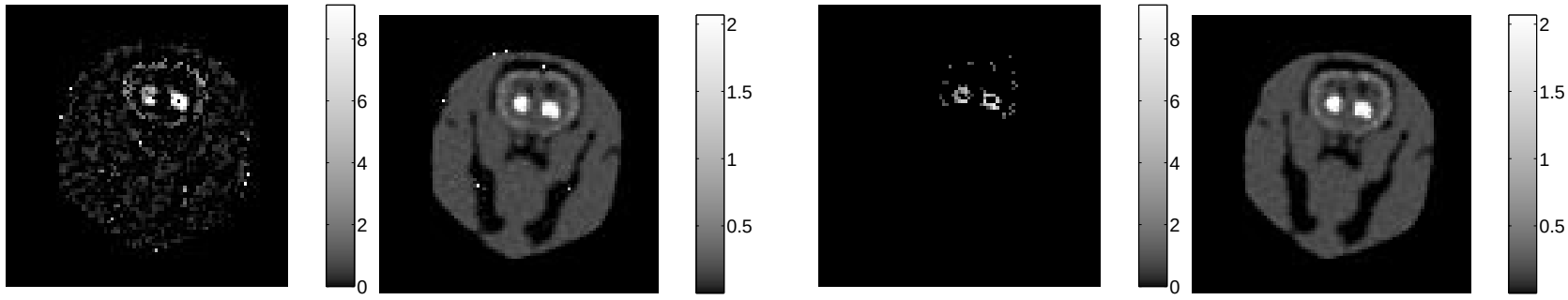
Normalized RMSE of the kinetic parameter estimates



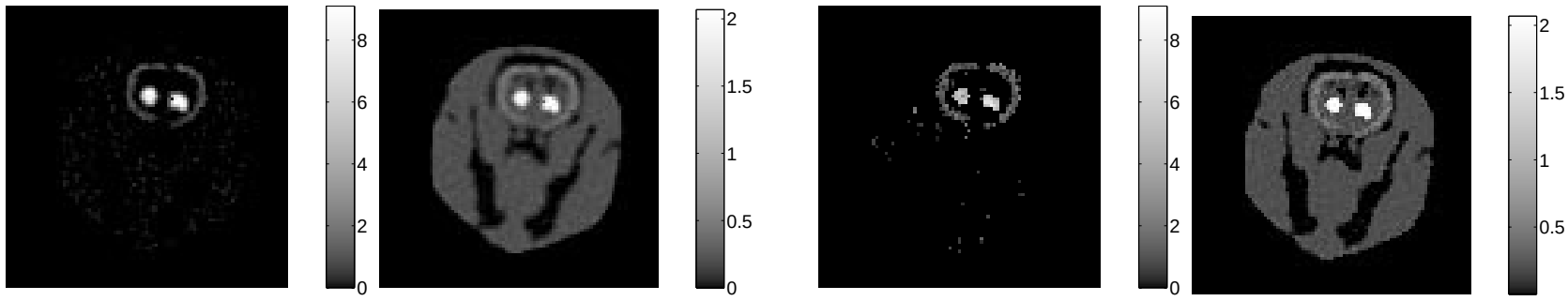
Estimates of Physiologically Important Parameters



(a) Original (b) PWLS

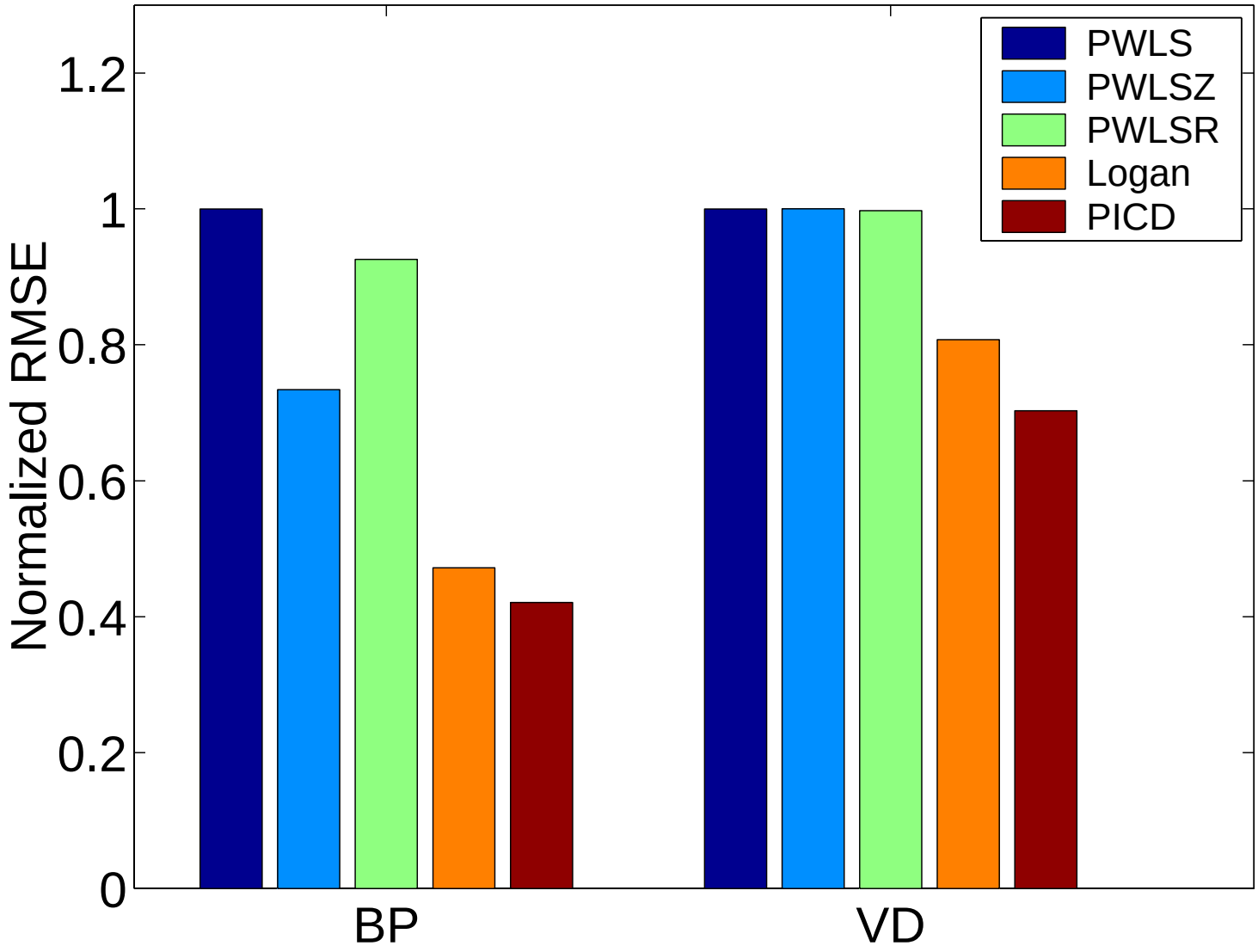


(c) PWLSZ (d) PWLSR



(e) Logan (f) PICD

Normalized RMSE of BP and VD

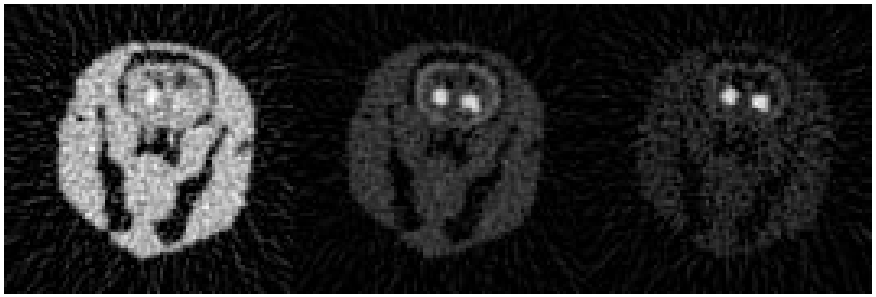


Emission Images

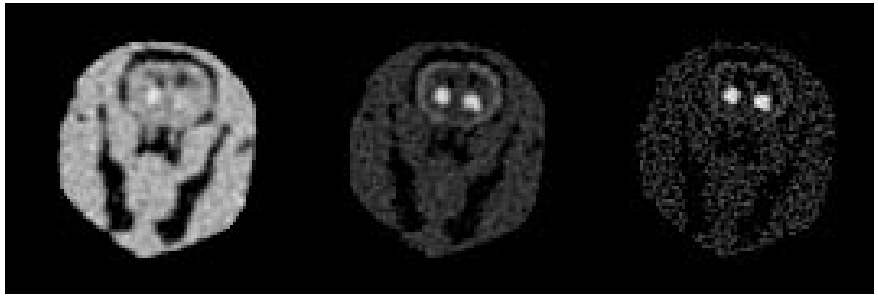
Frame 5 Frame 10 Frame 15

(a) Original

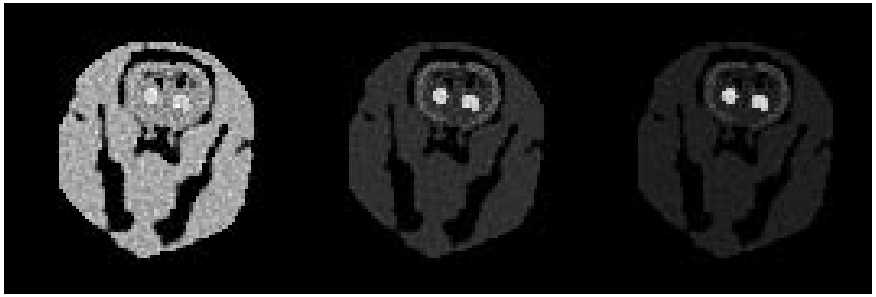
Frame 5 Frame 10 Frame 15



(b) FBP

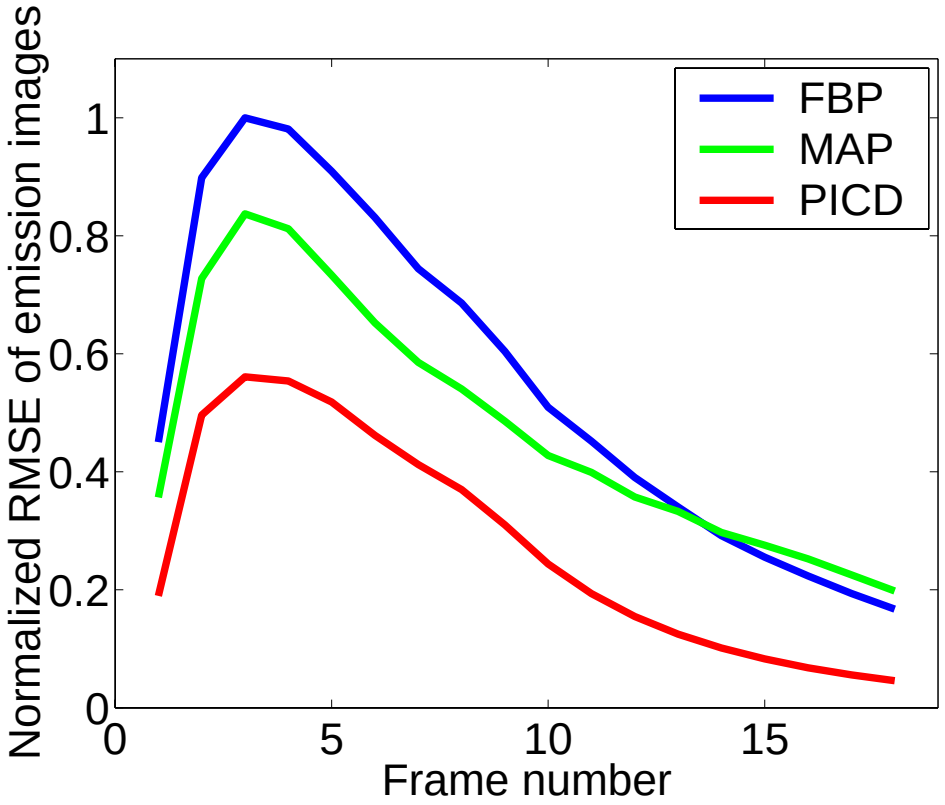


(c) MAP

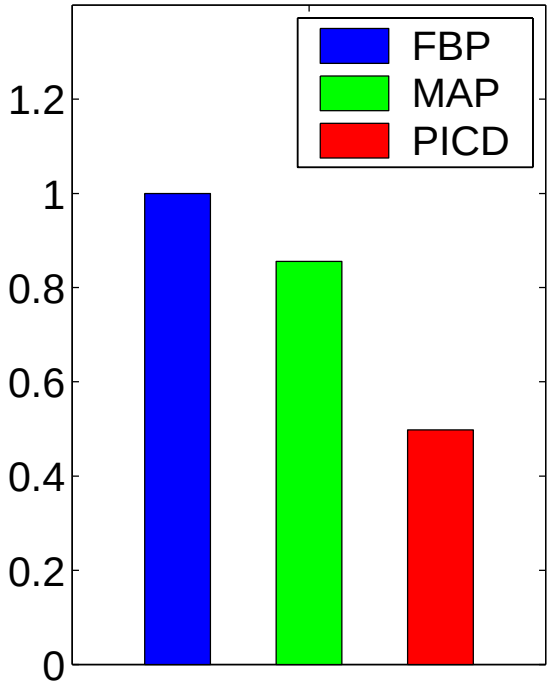


(d) PICD

Normalized RMSE of Emission Images



(a)

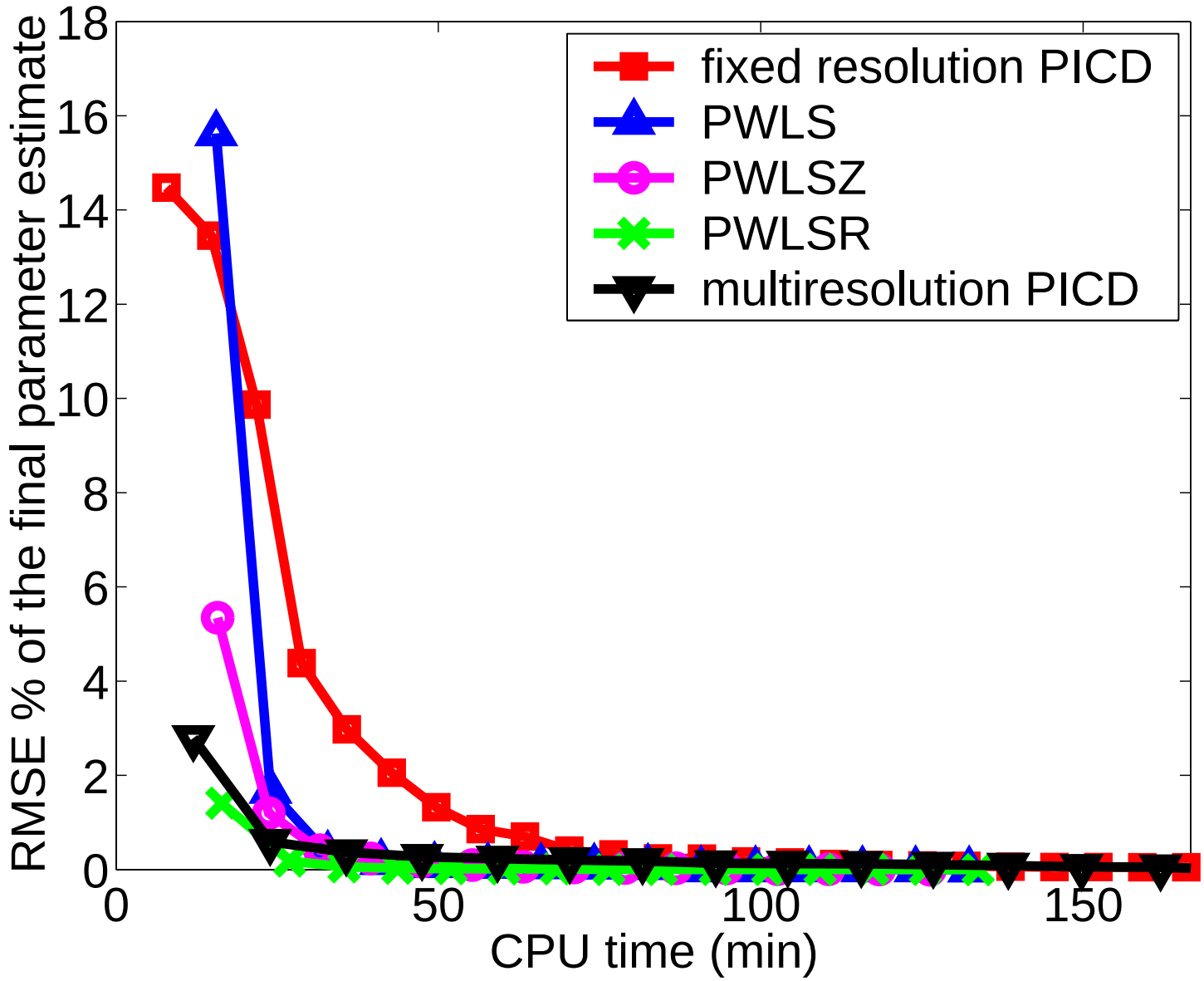


(b)

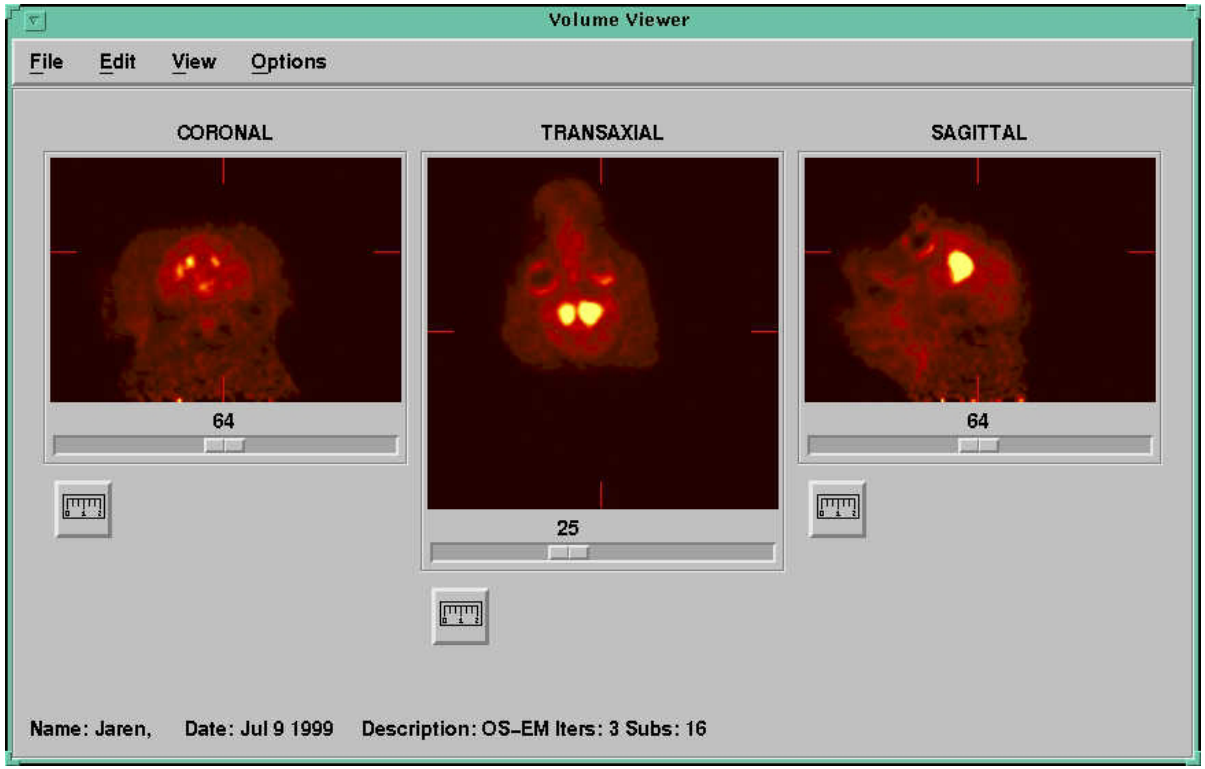
CPU Time per Iteration

Method	time for 1 iteration (sec.)
PWLS	474
PWLSZ	487
PWLSR	526
PICD	594

Convergence



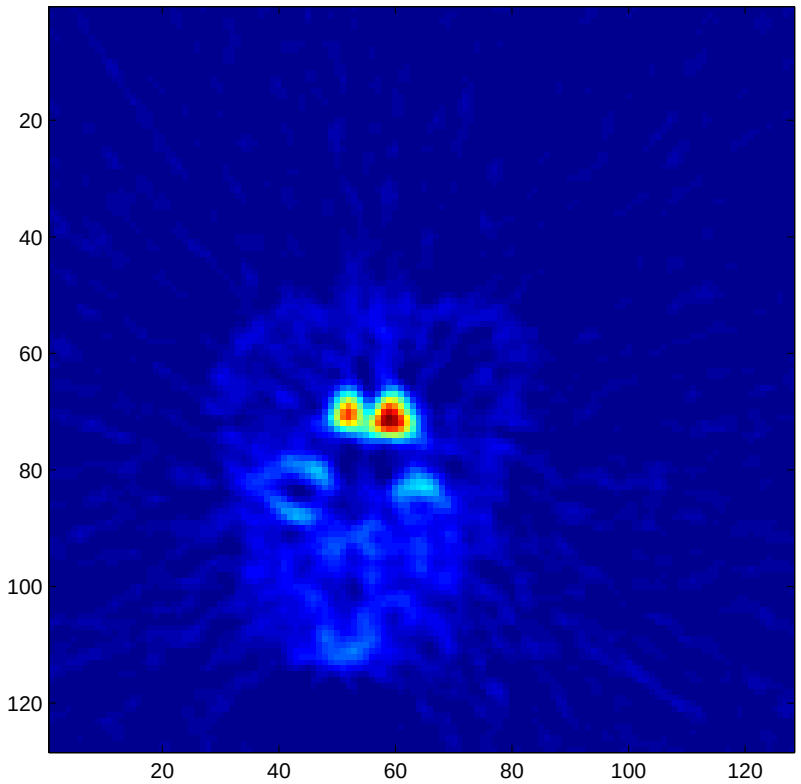
EXACT HR+ Dataset



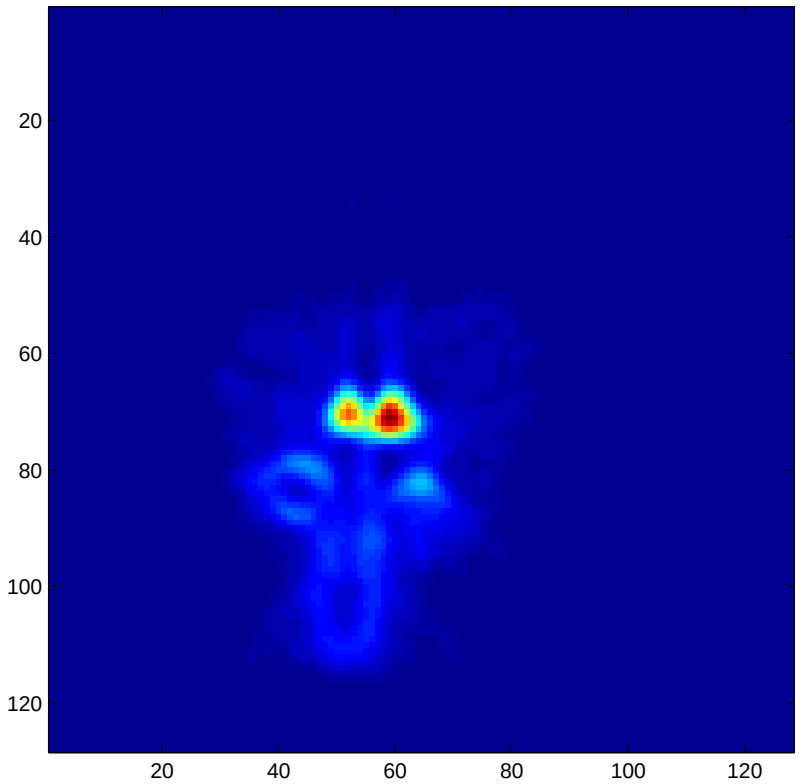
- Monkey head imaged with ^{18}F-fallypride
- scanner: Siemens EXACT HR+
- supplied by Dr. Brad Christian, Kettering Medical Center, OH.

FORE + Corrections for scatter, attenuation, and detector normalization[a]

2D + no corrections

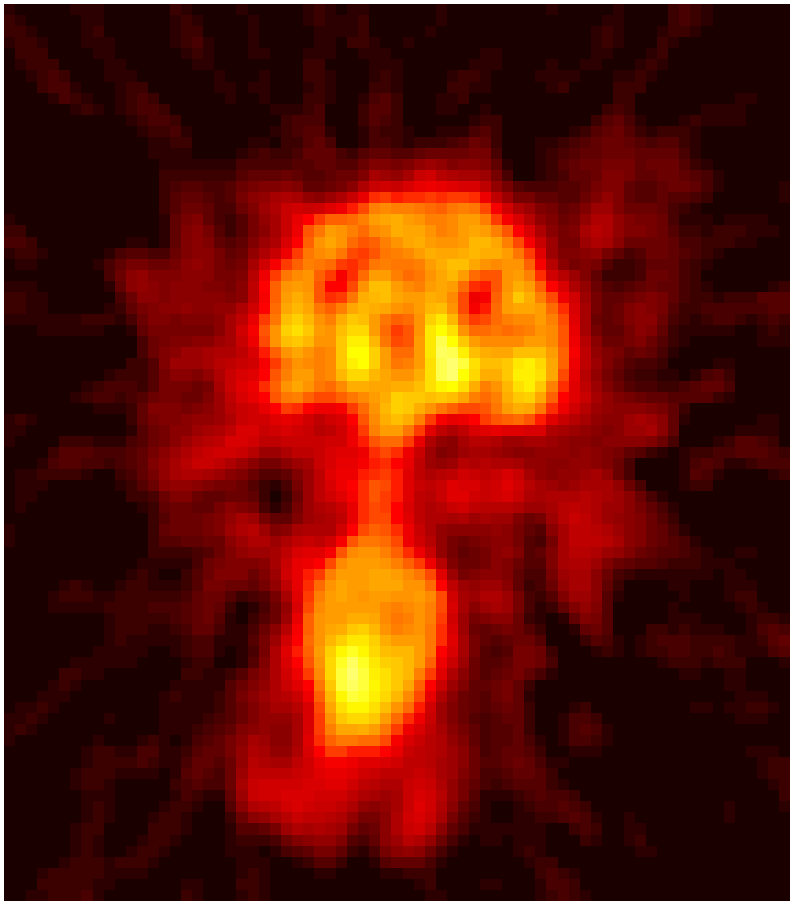


FORE + corrections

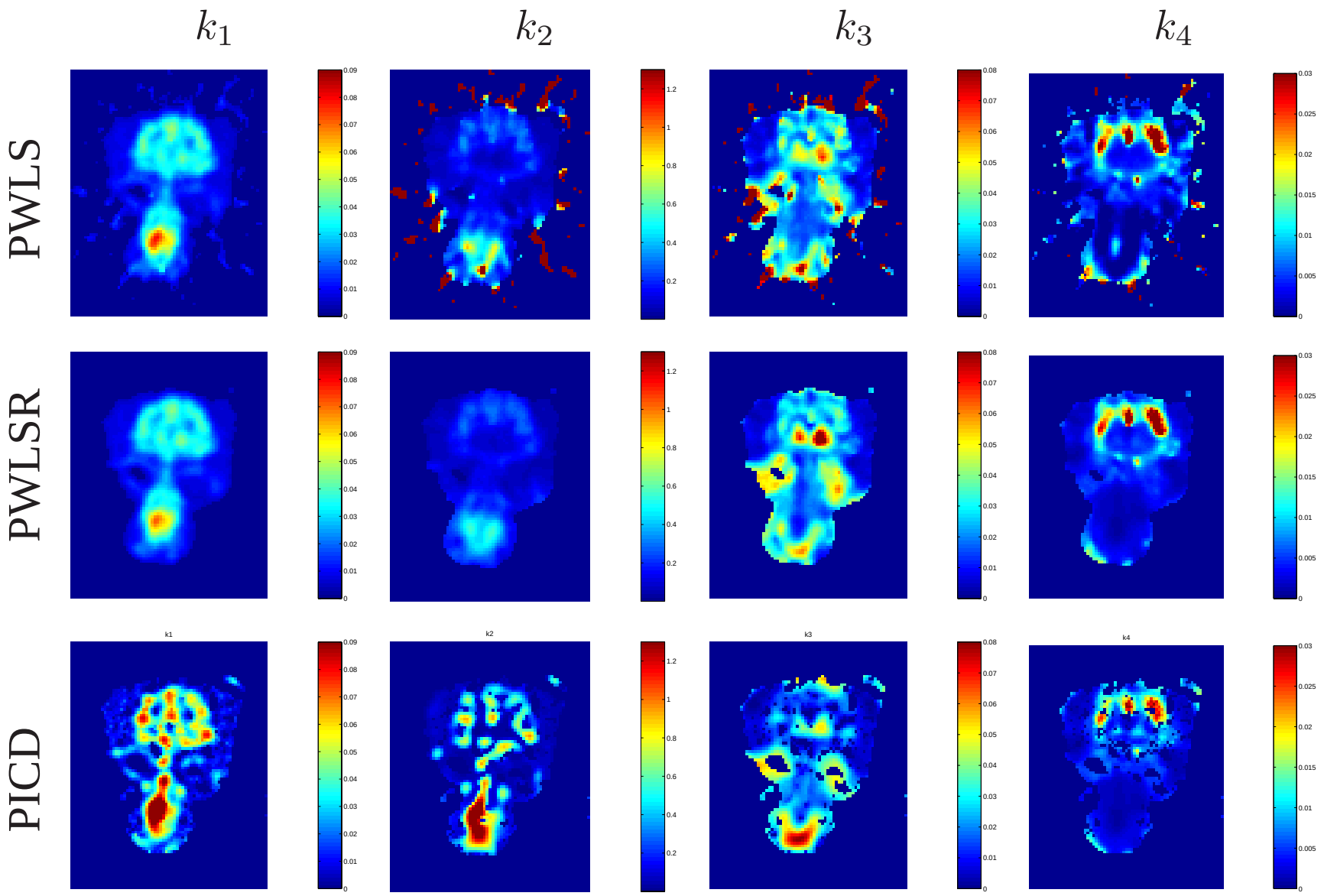


[a]Thanks to Dr. Christian and CTI

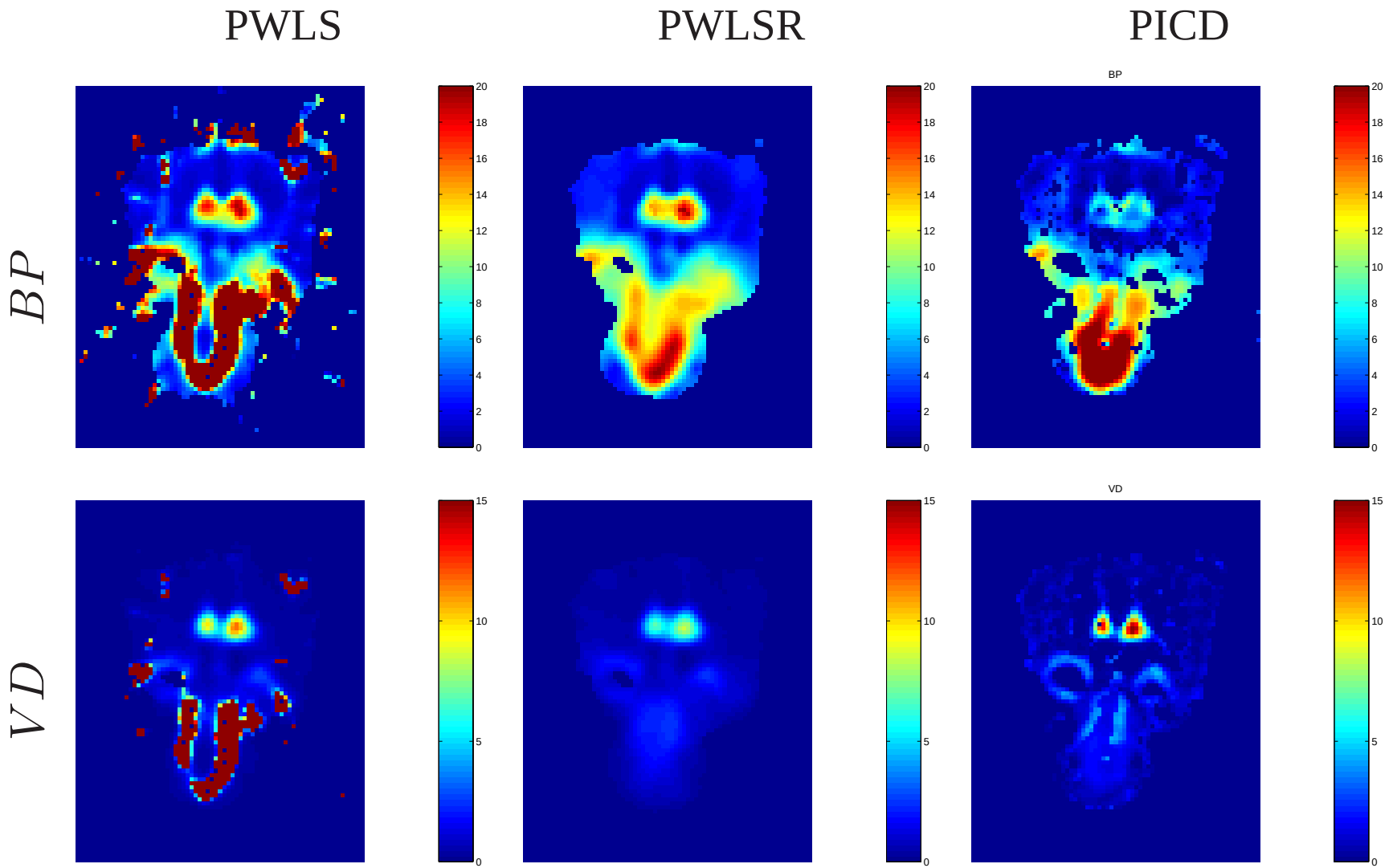
What Does Data Look Like



k_1, k_2, k_3, k_4 Images for Monkey Data

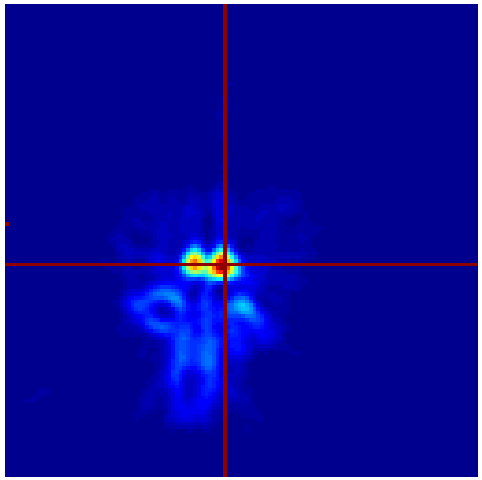


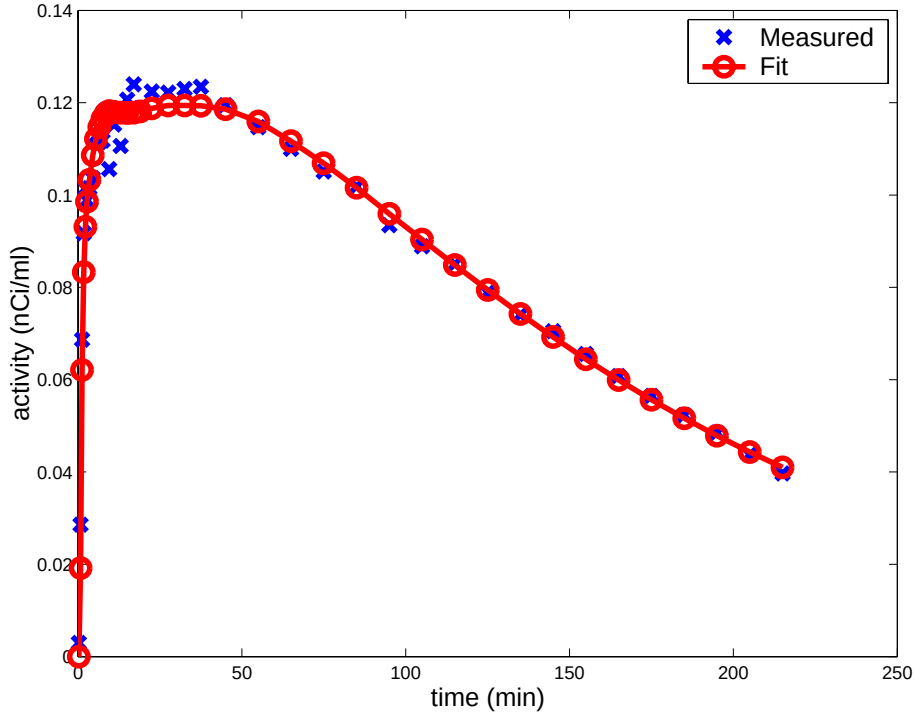
BP and VD Images for Monkey Data

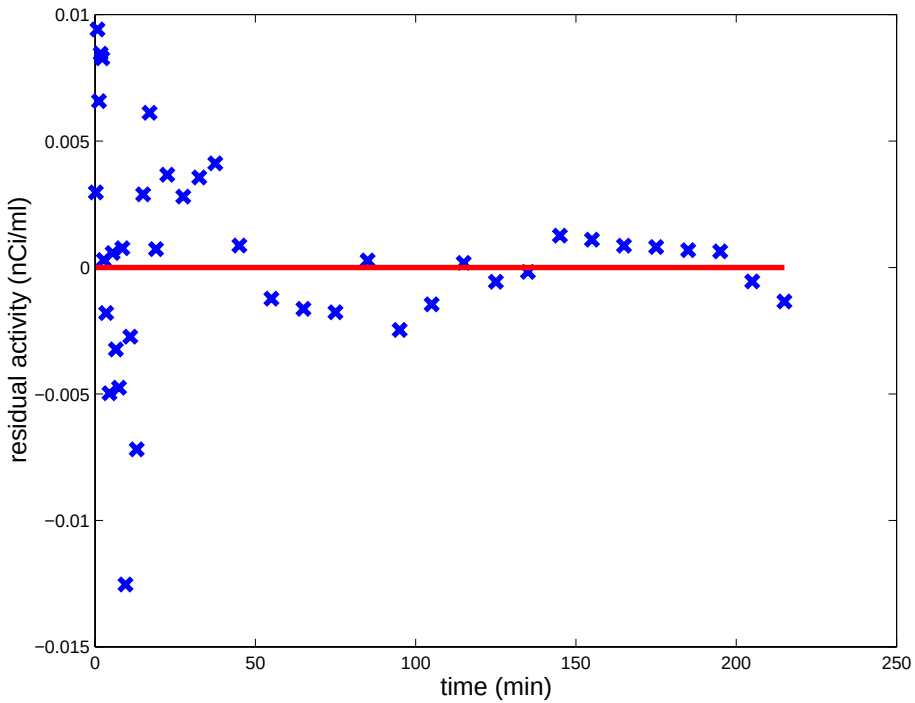


PWLS Fit for voxel (71,60)

$\varphi_{(71,60)} = [0.0422, 0.0794, 0.0697, 0.0037]^T$, BP=18.869, VD=10.558

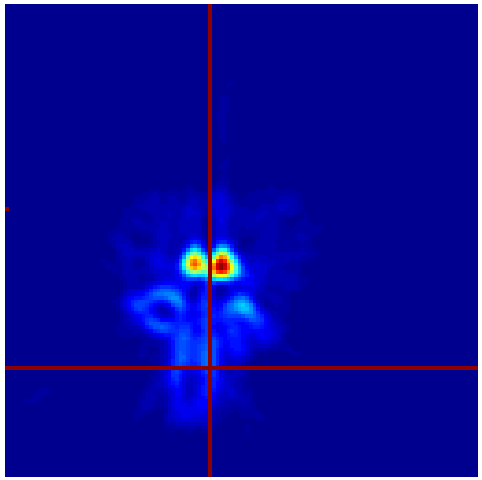


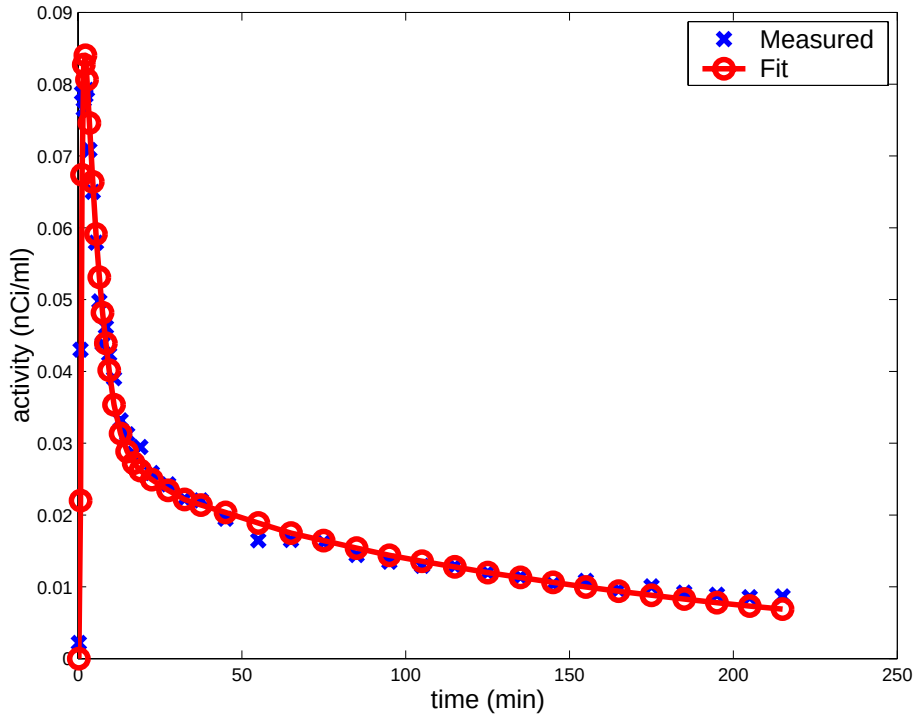


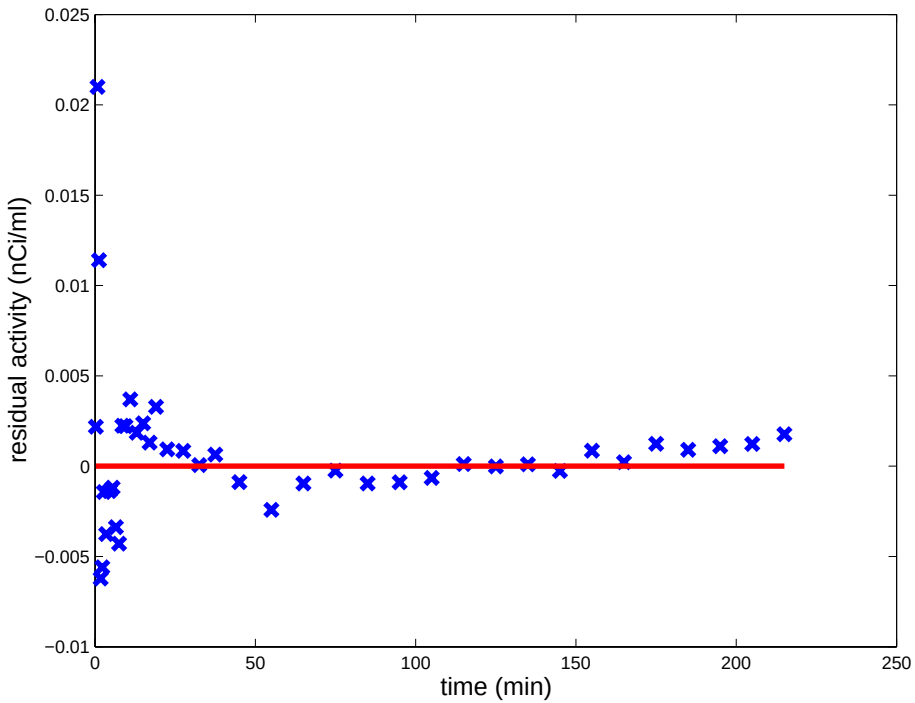


PWLS Fit for voxel (99,56)

$$\varphi_{(99,56)} = [0.0495, 0.353, 0.0178, 0.0]^T, \{BP, VD\} = \infty$$

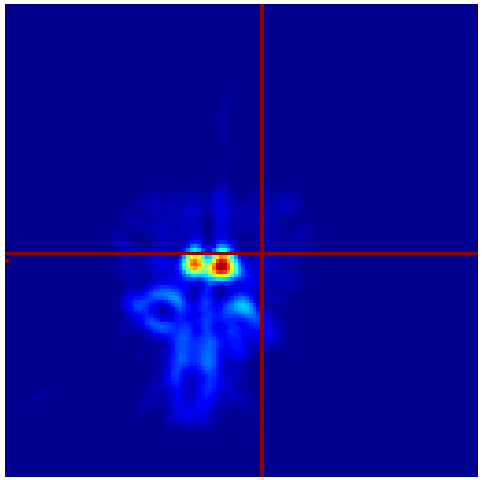


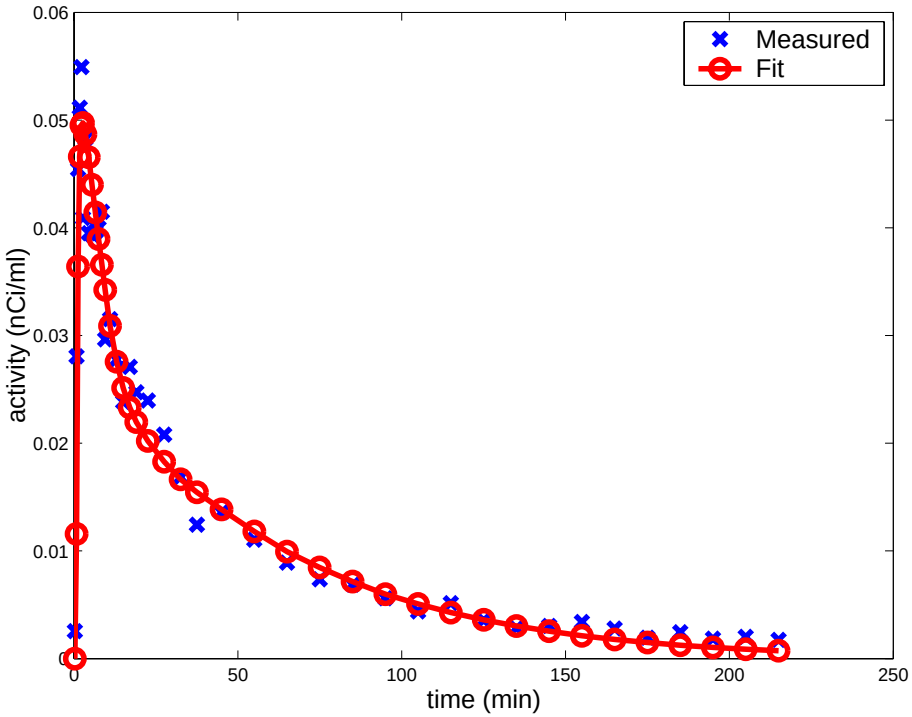


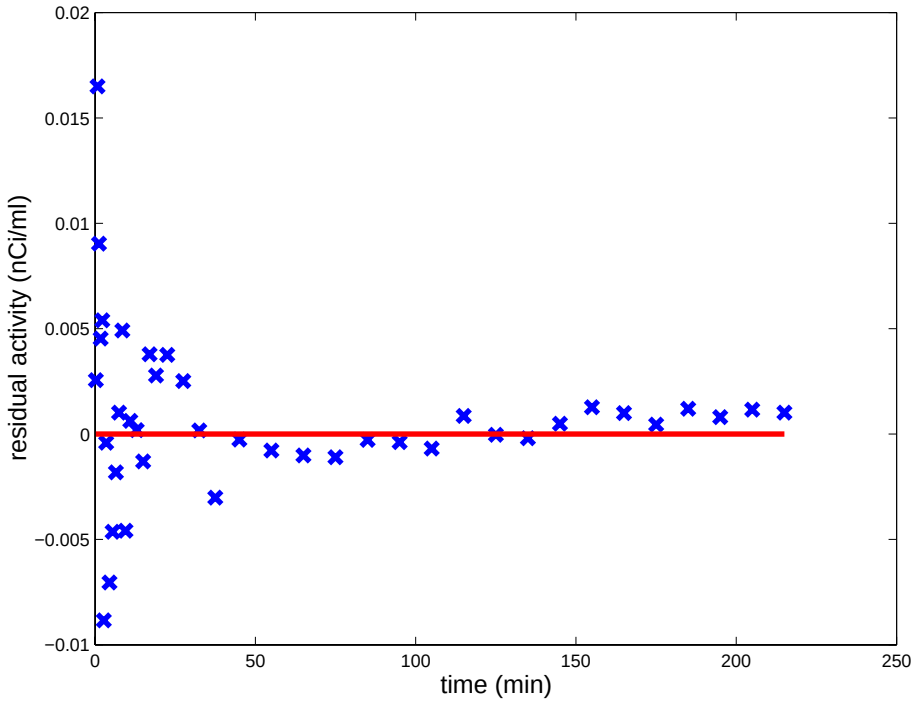


PWLS Fit for voxel (68,70)

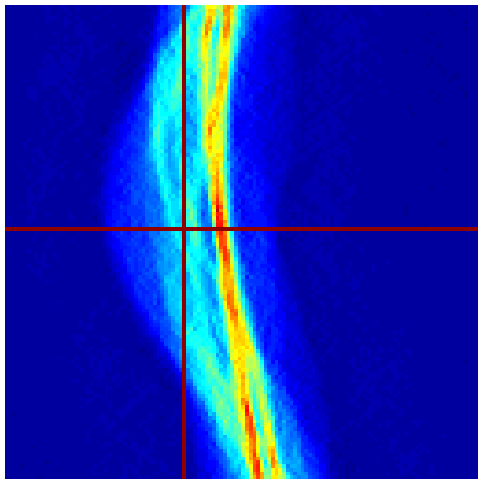
$\varphi_{(68,70)} = [0.0258, 0.220, 0.020, 0.0174]^T$, BP=1.155,VD=0.252

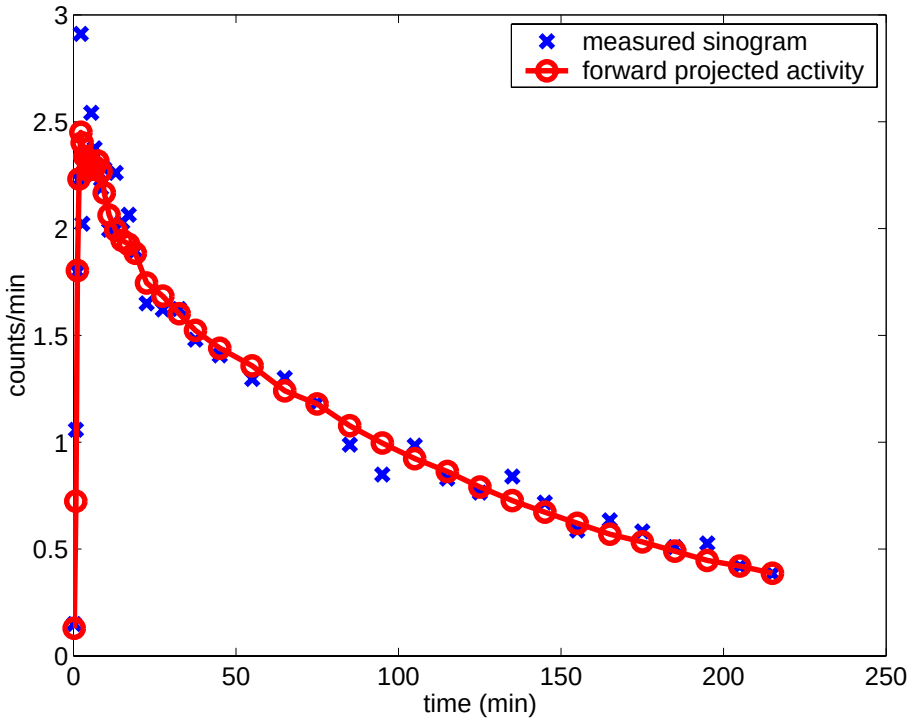


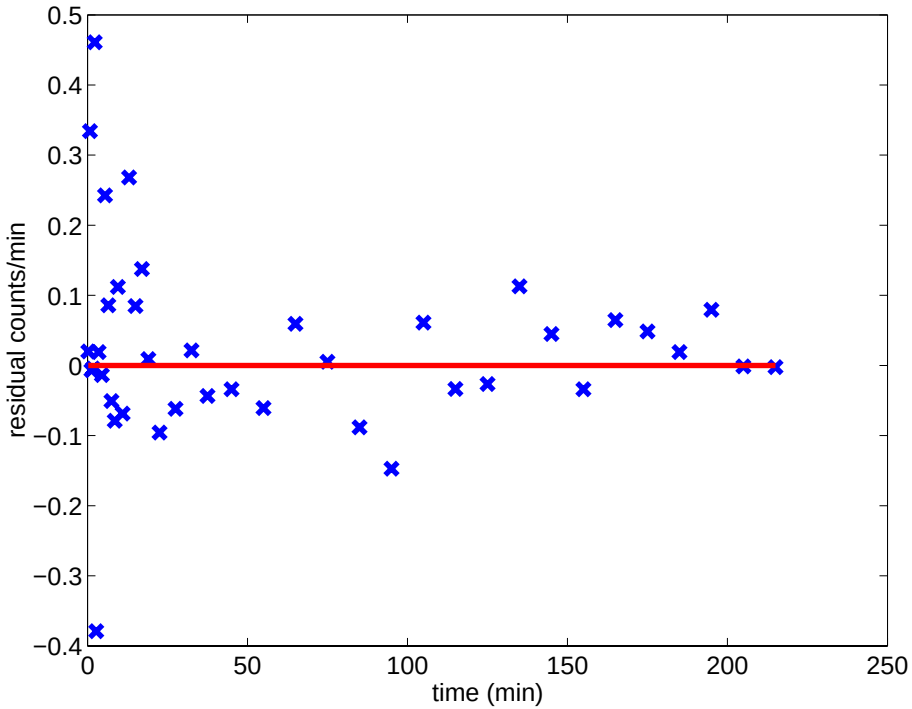




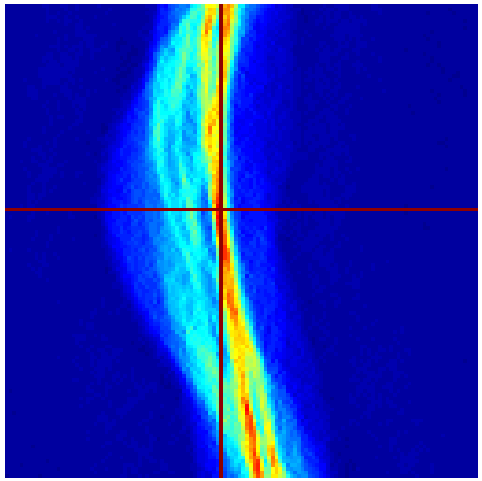
PICD Fit for sinogram voxel (61,49)

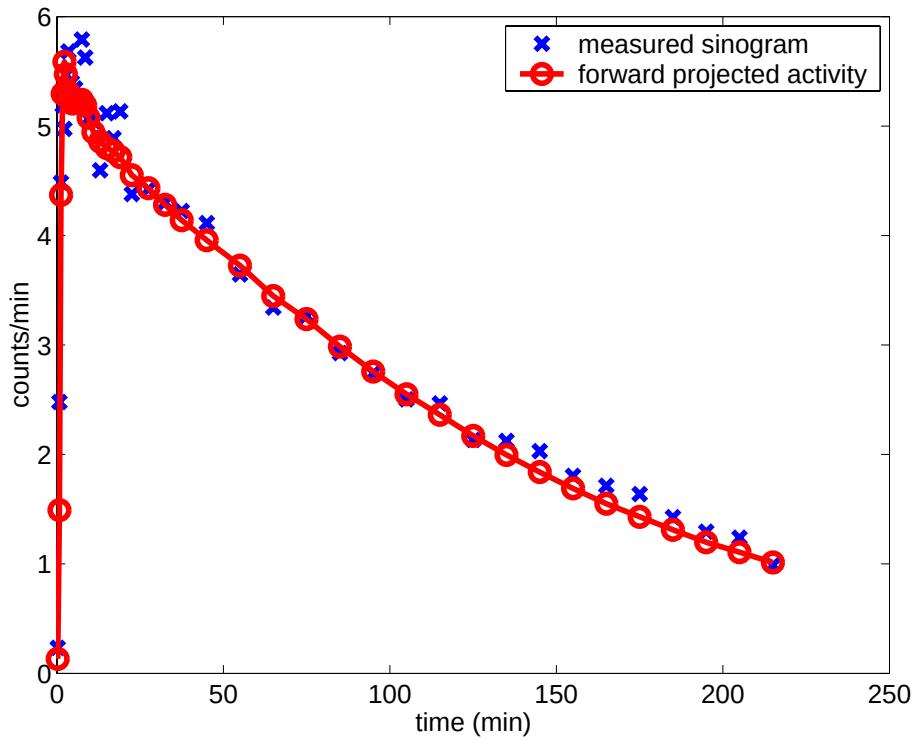


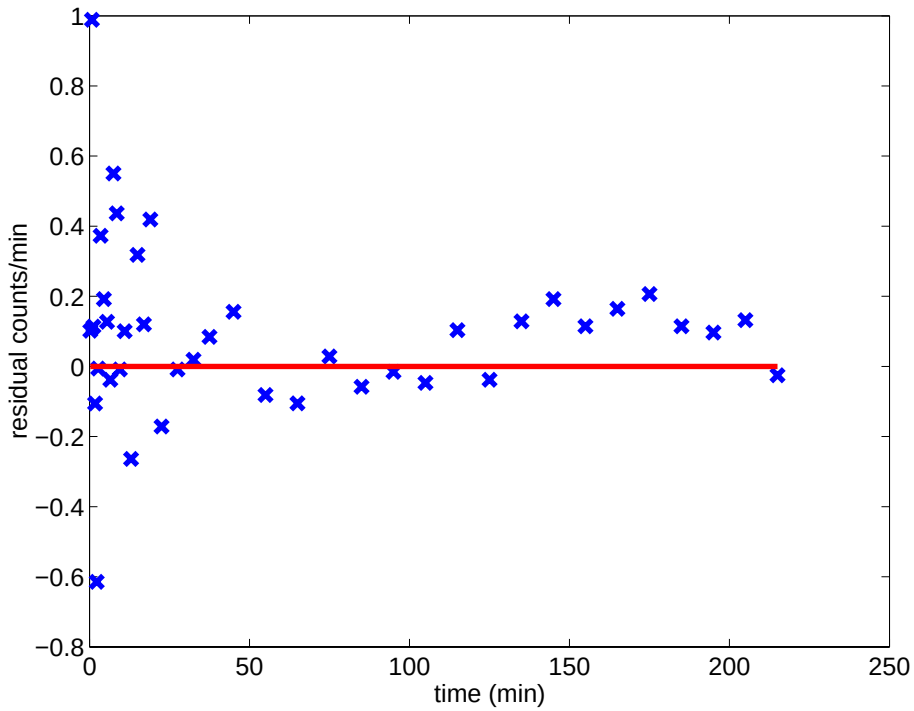




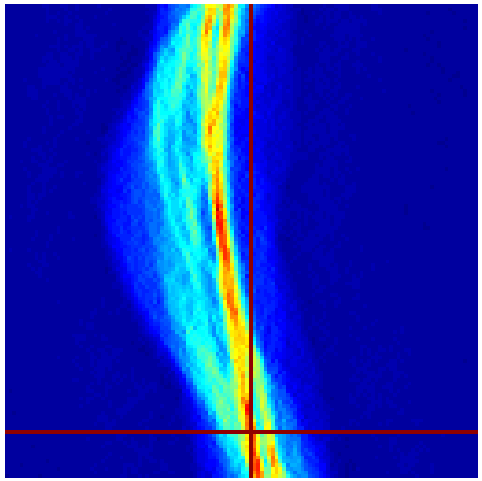
PICD Fit for sinogram voxel (56,59)

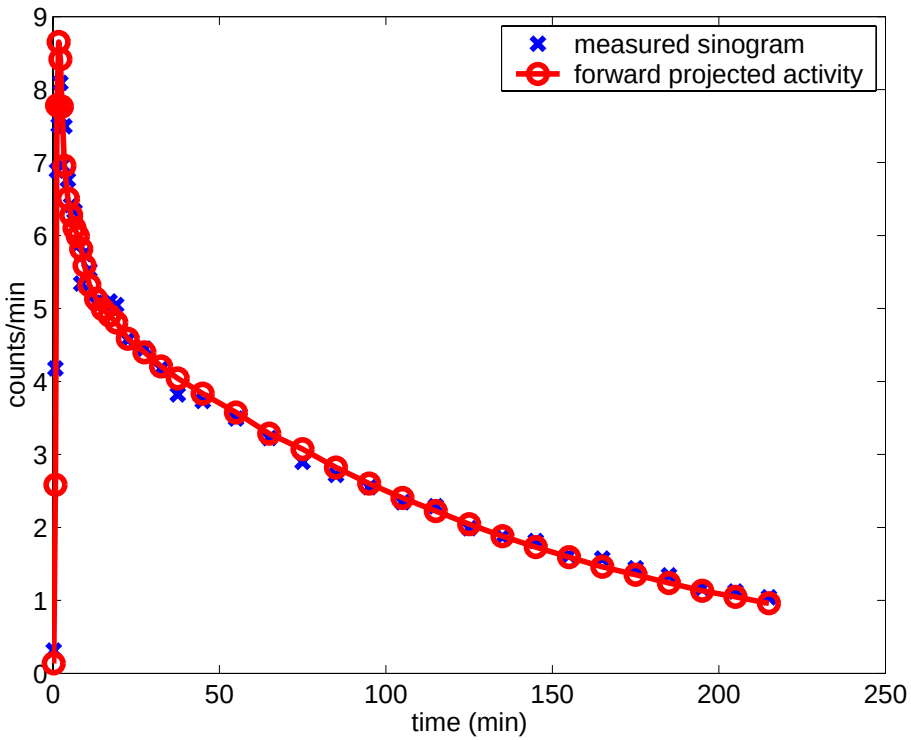


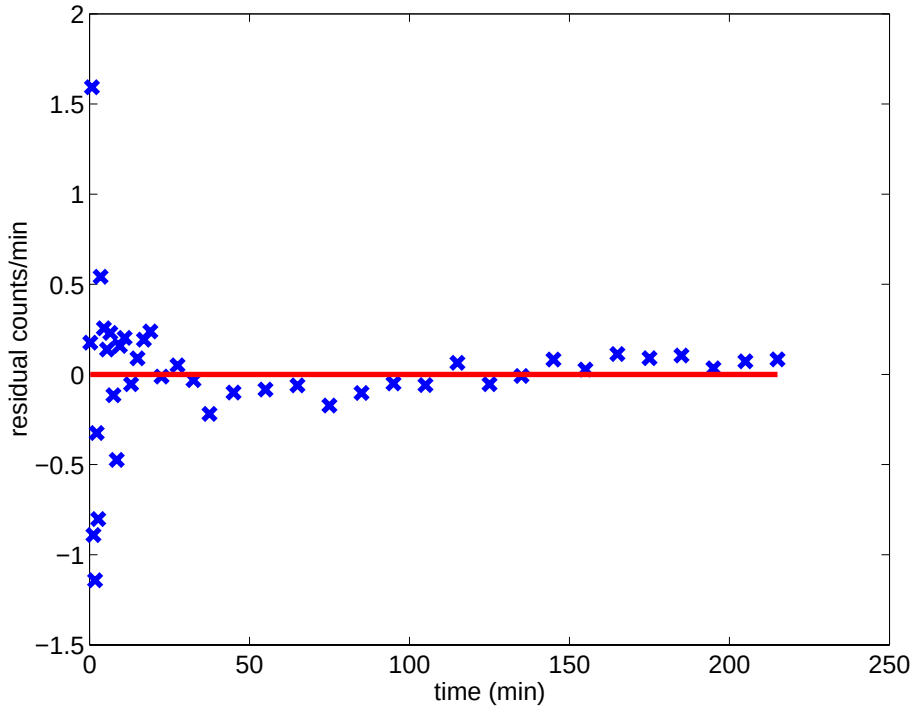




PICD Fit for sinogram voxel (116,67)







Limitations of PICD

- Interframe image registration and motion compensation
- Time response of some voxels do not follow the model
- Goodness-of-fit measure
- Model validation for new tracers

Some of these can be solved → **future work**

Conclusions

- Propose direct reconstruction of parametric image
- Advantages
  - Dimensionality reduction
  - Higher SNR
  - Dense parameter estimates
- Propose computationally efficient optimization algorithm
- Propose regularization on physiologically relevant domain(s)
- Demonstrated improved quality, lower RMSE estimations and fast convergence on realistic simulation data
- Demonstrated increased resolution on real data

Future Work

- More accurate scanner model
- Extension of the work to nonlinear models (with more parameters)
- Goodness-of-fit analysis on sinogram domain
- Model selection
- Parameter estimation reliability

  $\rightarrow$ Requires estimation of

$$\frac{\partial}{\partial \varphi_s} f(\varphi_s, t) = \begin{bmatrix} \frac{\partial}{\partial k_{1s}} f([k_{1s}, k_{2s}, k_{3s}, k_{4s}], t) \\ \frac{\partial}{\partial k_{2s}} f([k_{1s}, k_{2s}, k_{3s}, k_{4s}], t) \\ \frac{\partial}{\partial k_{3s}} f([k_{1s}, k_{2s}, k_{3s}, k_{4s}], t) \\ \frac{\partial}{\partial k_{4s}} f([k_{1s}, k_{2s}, k_{3s}, k_{4s}], t) \end{bmatrix}$$

  for each voxel s.

Even More Future Work

- Parameter identifiability

  $\rightarrow$ Requires estimation of Hessian

$$H = \left[\frac{\partial}{\partial \varphi_s} f(\varphi_s, t)\right] \left[\frac{\partial}{\partial \varphi_s} f(\varphi_s, t)\right]^T$$

  for each voxel s.

- Better optimization algorithms ie. multigrid method
- Motion estimation and compensation
- Higher order spline implementation for list-mode data
- $\ldots$

Acknowledgements

- Prof. Bouman and Prof. Morris
- Prof. Christian and Prof. Sauer
- Prof. Allebach, Prof. Delp, and Prof. Lucier
- EISL colleagues
- Cristian Constantinescu, Chunzhi Wang, Dr. Karmen Yoder, Marc Normandin, and Dr. Ti-Qiang Li
- . . .

Thank You !