

Challenges in Improving Sensitivity for Quantification of PET Data in Alzheimer's Disease Studies: Image Restoration and Registration



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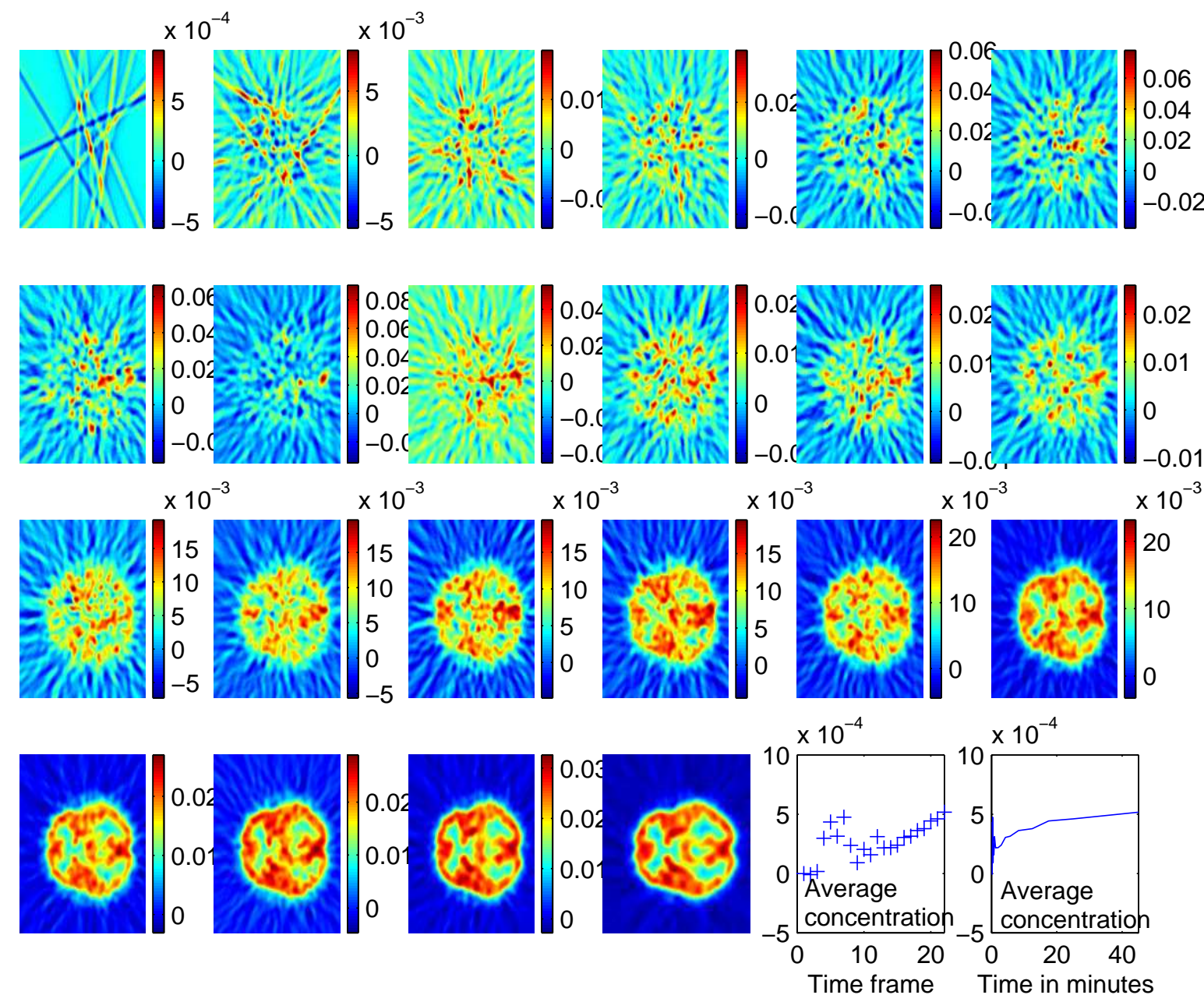
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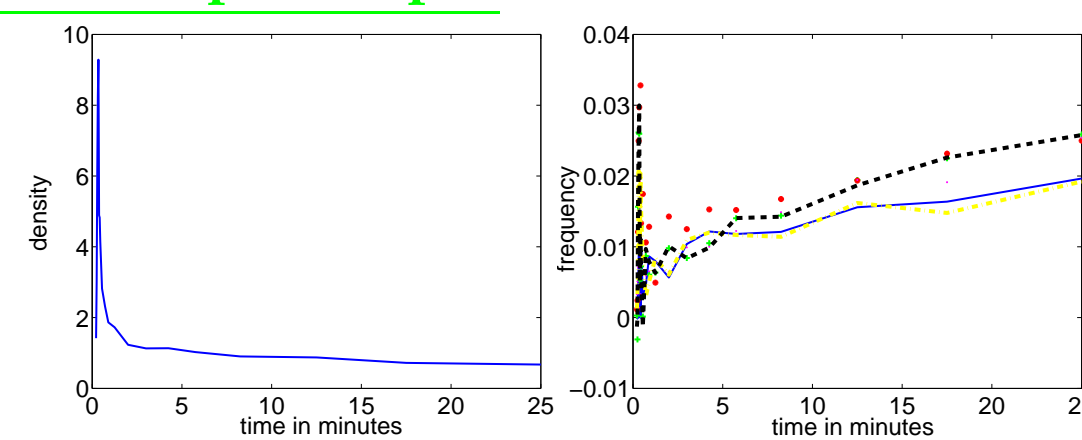
ABSTRACT

With the increase in life expectancy of the general population, the incidence of Alzheimer's Disease is growing rapidly and impacts the lives of those with the disease and their care givers, as well as the entire medical infrastructure. Research associated with AD focuses on early diagnosis, and effective treatment and prevention strategies using neuroimaging biomarkers which have demonstrated high sensitivity and specificity, [8, 6]. Many studies [9, 11, 12, 10, 1] use PET data to measure differences in cerebral metabolic rates for glucose before onset of the disease in the carriers of APOE $\epsilon 4$. Researchers hope to rapidly evaluate various preventive strategies on healthy subjects which requires refining and extending technologies for reliable detection of small scale features indicating functional or structural change. Appropriate computational techniques must be developed and validated. The PET working group of the National Institute of Aging, [8], recently published recommendations for studies on aging that utilize imaging data, acknowledging prior limitations of PET studies, while providing guidelines and protocols for future neuroimaging research. We present initial results of restoration and registration techniques for quantifying functional PET images.

Introduction: Functional Data for One Slice



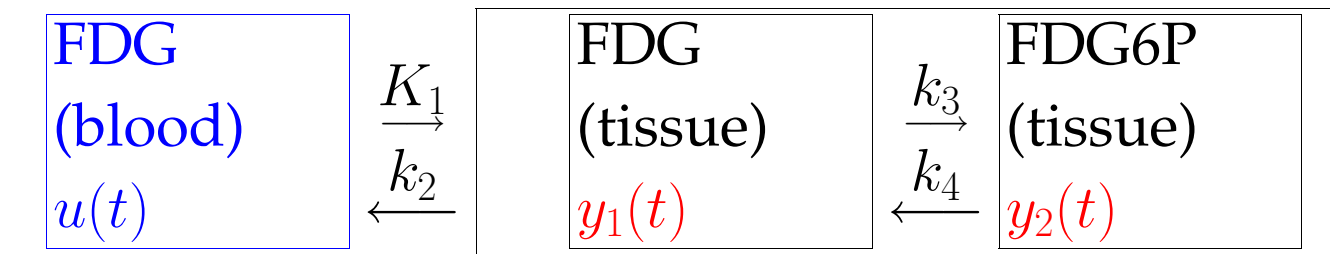
Representative input/output



Input Function $u(t)$ and Output $y(t)$ for 6 pixels
Data only illustrated through time $t_{21} = 25m$.
Functions change little over last scanning duration, $\Delta t_{22} = 30m$.
Input functions vary significantly, are measured from blood, estimated or analytically approximated.

The FDG Tracer Model

Input $u(t)$ - FDG in blood-measured blood samples;
Output $y(t) = y_1(t) + y_2(t)$, FDG and FDG6P in tissue-from PET images.



$$\begin{aligned} \dot{y}_1 &= K_1 u(t) - (k_2 + k_3) y_1(t) + k_4 y_2(t) \\ \dot{y}_2 &= k_3 y_1(t) - k_4 y_2(t). \end{aligned} \quad (1)$$

- K_1, k_2 -FDG transport rates
- k_3, k_4 phosphorylation, dephosphorylation rate.
- LCMRglc: $\frac{K_1 k_3 C_p}{k_2 + k_3 LC} = K \frac{C_p}{LC}$, neuroimaging marker AD.
- Given $u(t)$ and $y(t)$, estimate K_1, k_2, k_3, k_4 and K .

Solution of the FDG Tracer Model

Denote $\mathcal{K} = (K_1, k_2, k_3, k_4)$, \otimes for convolution:

$$y(t) = u(t) \otimes (c_1(\mathcal{K})e^{-\lambda_1(\mathcal{K})t} + c_2(\mathcal{K})e^{-\lambda_2(\mathcal{K})t}).$$

Generally, parameter k_4 is set to 0, because it is relatively very small and the scanning time, 60 minutes, may not be long enough to provide a reliable estimate of k_4 .

$$y(t) = u(t) \otimes \left(\frac{K_1 k_3}{k_2 + k_3} + \frac{K_1 k_2}{k_2 + k_3} e^{-(k_2 + k_3)t} \right). \quad (2)$$

It is easy to solve the problem to find the parameters given the input function $u(t)$ and the output function $y(t)$, when the data are clean and equally spaced!

Issues with parameter estimation problem?

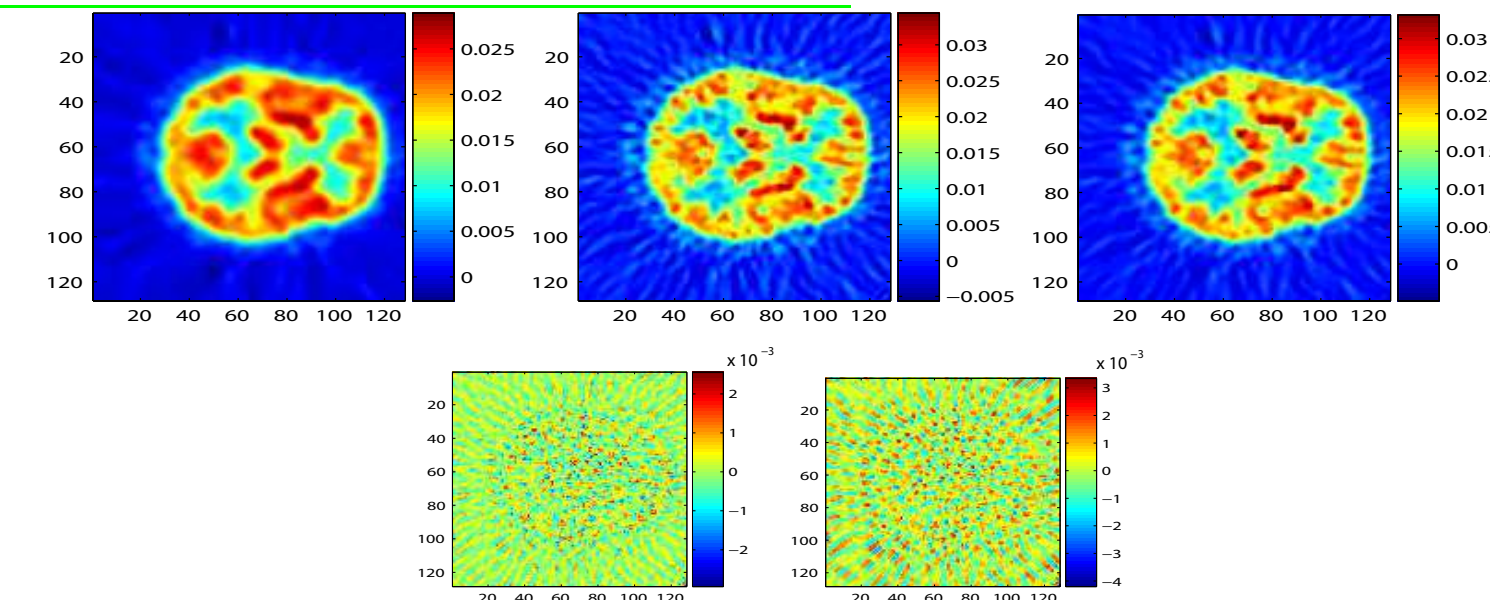
- How do find the input? **Simultaneously**
- Noise in the output is correlated
- Cost: Volumetric data analysis is expensive. Region of Interest Studies **Cluster analysis**
- Utilizing Results: **longitudinal, comparative studies**
- Studies collect images, not original sinogram data
- Statistics: **Limited Available Data**

Examples of Image Restoration and Registration

Wavelet Noise Reduction: $u + v$ decomposition

- Find different scales: multi scale wavelet decompositions, [3].
- Decompose PET image into cartoon u , (piecewise constant) and texture (v , noise), [13].
- Take $u \in BV$, [7]. Expensive. $u \in B_1^{1,1}$ [2], efficiency comparable to FFT.
- $J(u, v) = \|g - (u + v)\|_2^2 + \gamma \|u\|_{B_1^{1,1}} + \alpha \|v\|_{H^{-\beta}}$, [4].

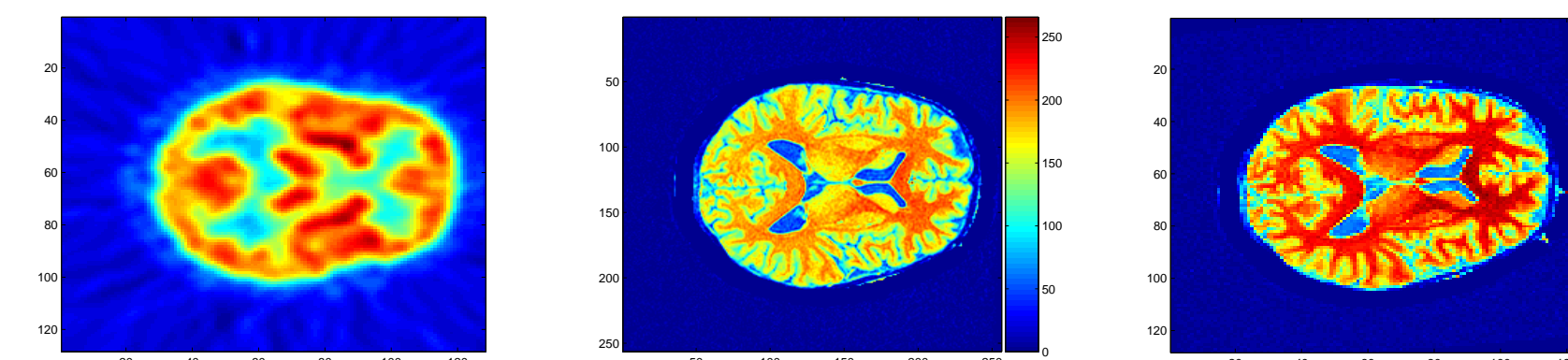
Example Restoration by Wavelets



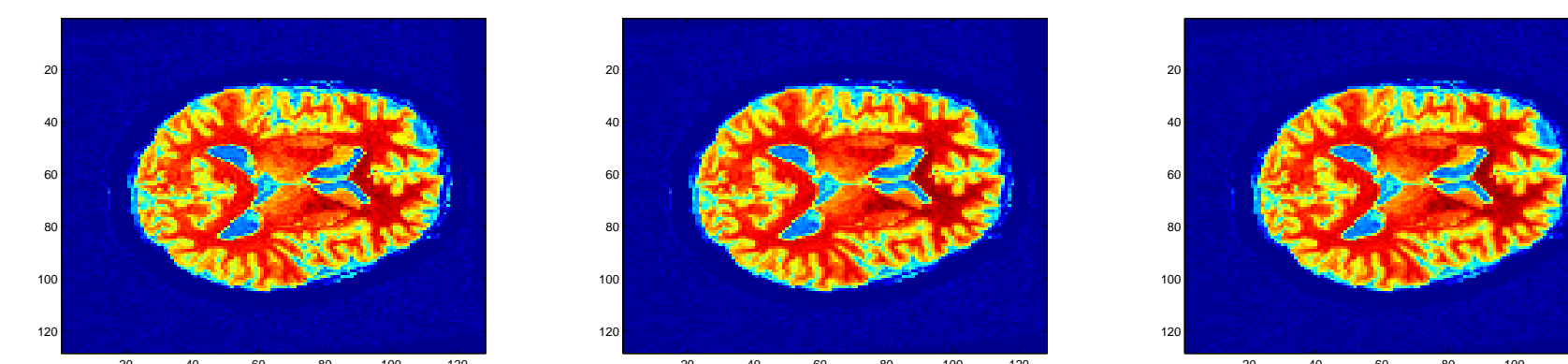
TV and $u + v$ decomposition real PET image (a).
(b) is (a) deblurred by TV. (c) (d) (e) are from $u + v$
(c) is $u \in B_1^{1,1}$ (d) $v \in H^{-1}$, (e) is $v \in H^{-0.01}$.

Elastic Registration: Maximize Mutual Information

- Multimodal registration uses normalized mutual information (NMI) maximization MR-PET [5, 14]
- Longitudinal, intensities change, use NMI
- Hierarchy, histogram equalization reduce cost

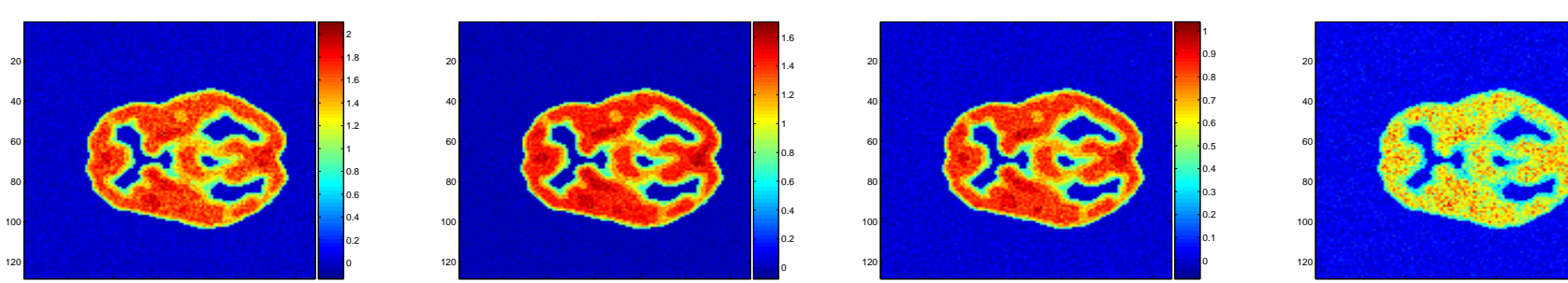


Reference (PET), Target (scalp peeled T1-MR), SPM Map.

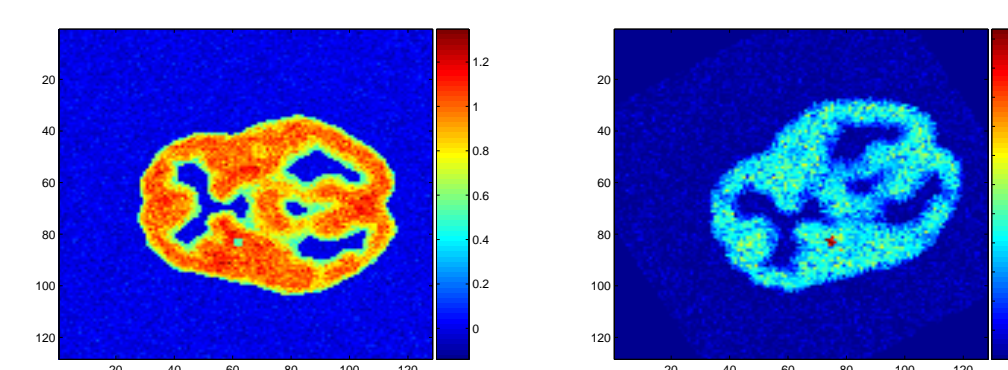


Affine, Elastic, Coarse grained elastic.

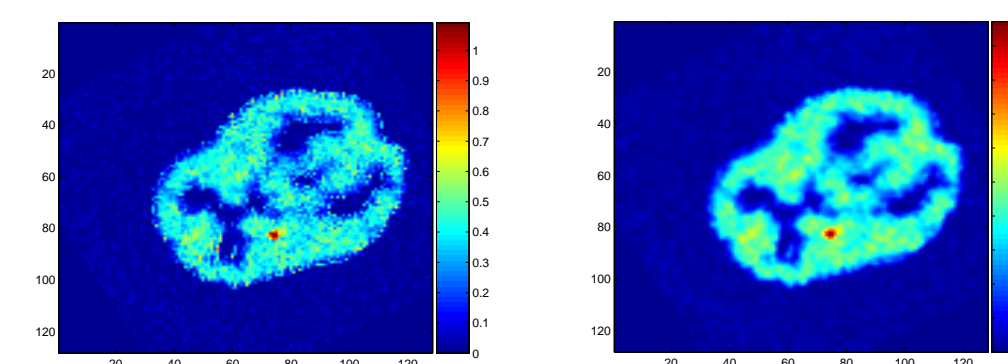
Impact of Input Function on the Observed Image



Identifying Small Change in PET: Register and Restore

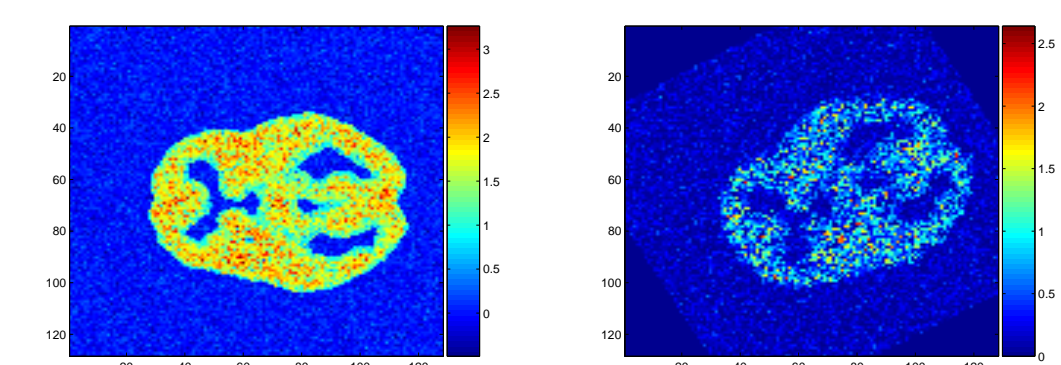


Modified Input, Exact Subtraction Image

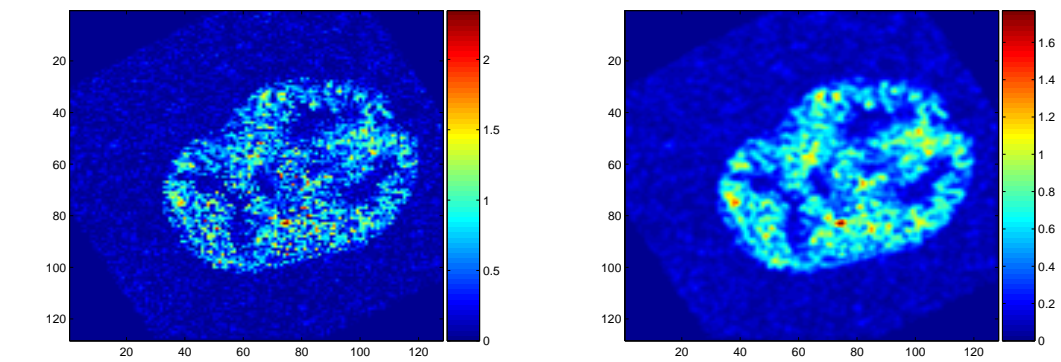


Estimated Subtraction Image, Enhanced Subtraction u .

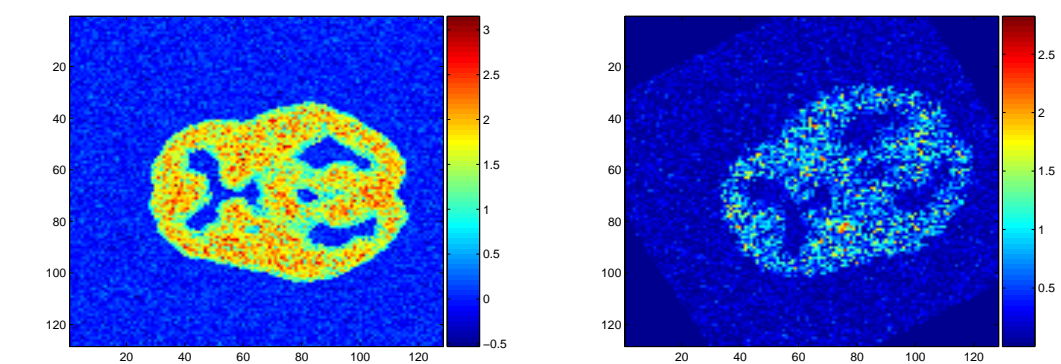
Identifying Small Change in PET: Harder Case



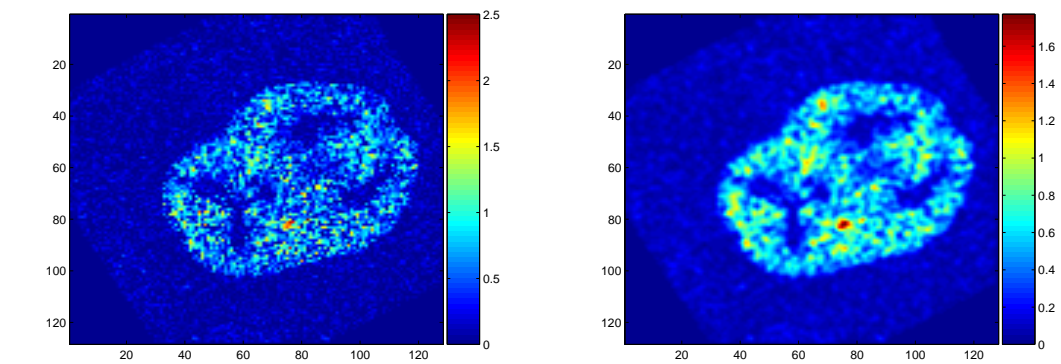
Modified Input, Exact Subtraction Image



Estimated Subtraction Image, Enhanced Subtraction u .



Modified Input, Exact Subtraction Image



Larger abnormality

Research Challenges for Improving Sensitivity

- Simultaneous Estimation of Input with Output from Sinogram
- Restoration of data at Sinogram Level
- Image reconstruction
- Robust Registration
- Reduce Model Simplification

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