A Simple Evaluation of the Benefit of Combined Kinetic Analysis of Multiple Injection Dynamic PET Scans

Fengyun Gu, Finbarr O'Sullivan, Mark Muzi and David A. Mankoff

***Abstract*—The multiple injection dynamic Positron Emission Tomography (PET) scanning is used in the clinical management of certain groups of cancer patients and in medical research. The analysis of such studies can be approached in one of two ways: analyze individual injections separately to recover tracer kinetic information, or concatenate data from separate injections and carry out a combined analysis. Separate analysis offers some simplicity but may not be as efficient statistically. The mixture technique is readily implemented in a separated or combined analysis mode. We evaluate these approaches in a 1-D simulation setting matched to the mathematical complexity of PET. These simulations are largely guided by experience with breast cancer flow-metabolism mismatch studies using ^{15}O-Water (H2O) and ^{18}F-Fluorodeoxyglucose (FDG). An efficient implementation in the R (an open-source environment) is used to implement simulations. The simulations evaluate mean square error (MSE) characteristics, for separate and combined analysis, both as a function of dose. The relationship between MSE characteristics of the underlying source distribution is described and the combined analysis is found to reduce MSE by between 18.1% and 33.85%. The quantitative advantages of combined approach have been demonstrated.**

***Index Terms*—Multiple Injections, Combined Kinetic Modelling, Simulation, Mixture analysis**

I. INTRODUCTION

THE multiple injection Positron Emission Tomography (PET) scanning have the ability to image two or more tracers in a single scan. Usually one tracer can just provide one kind of information, like ^{15}O-H2O for measuring blood flow and ^{18}F-FDG for glucose metabolism. Such multitracer PET imaging would provide a wealth of complementary information for tumor grading and prognosis[7]. This technique is used in the clinical management of certain groups of cancer patients and in medical research, for example, ^{18}F-FDG and ^{18}F-FLT for brain tumors, ^{15}O-H2O and ^{18}F-FDG for breast cancer and six different tracers for risk characterization in Sarcoma[5]. Data in these studies can be approached in one of two ways: (i) data from individual injections can be separately analysed to recover kinetic information corresponding to individual tracers, or (ii), studies can be concatenated and a combined analysis of the resulting data carried out. Initial efforts at analysing multiple-tracer PET image were performed in phantoms[6], dual-tracer brain imaging [10, 11] and there are a series reports by group in Uath [9, 16, 2, 7, 8, 17]. But most of work has focused on the first approach by applying the compartmental modelling, which is not as efficient(statistically) as a combined analysis.

Additive mixture models [13, 14, 15] can be implemented in the separate and combined approach and it has been applied to the flow-metabolism mismatch study [3, 4, 12] in a breast cancer patient using ^{15}O-H2O and ^{18}F-FDG. Motivated by experience with mixture model and flow-metabolism mismatch study in breast cancer, this work conducts some numerical analysis matched with this study. Our objective is to measure the quantitative advantages of combined analysis for multiple injections evaluated by analysizing MSE of underlying source distribution as a function of dose.

The basic theory and methodology is developed in section II. Results are presented in Section III. The paper concludes with discussion.

II. METHODOLOGY

We examine the efficiency of the mixture model estimation process for combined analysis in 1D simulation. The focus is on evaluation of MSE calculated in combined and separated analysis. This process, matched to the flow-metabolism studies with ^{15}O-H2O and ^{18}F-FDG[12].

A. Analysis Approaches

In the multiple-injection PET studies, two approaches can be applied and one dual-tracer study example is presented in (Fig. 1).

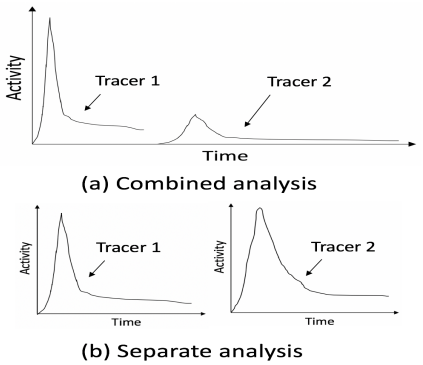

Fig. 1: A dual-tracer study example

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1) Combined analysis: concatenate all of the time courses from multiple injections and analyse them together.

2) Separate analysis: analyse each time course one by one.

B. Mixture Model

In a study involving two tracer injections, the full voxel-level time-course can be approximated by an additive mixture model [13, 14, 15]:

$$z(x,t) \approx z(x,t|\alpha) = \sum_{k=1}^{K} \alpha_k(x)\mu_k(t) \tag{1}$$

where z are the full voxel-level data, $\alpha = (\alpha_1, \alpha_2 .... \alpha_K)$ are positive mixing coefficients and $\mu = (\mu_1, \mu_2 .... \mu_K)$ are underlying time courses (sub-TACs), $t = (t_1, t_2 ... t_T)$.

In the combined analysis, mixing coefficient estimator ($\hat{\alpha_c}$) is calculated by using the full time-course data for both tracers. In the separated analysis, mixing coefficient estimator for H2O ($\hat{\alpha_s}^1$) and FDG ($\hat{\alpha_s}^2$) is from part time-course data separately.

C. 1-D Simulation

In our simulation study (Fig.2), 1-D numerical phantom was conducted to examine and compare the efficiency of combined and separated analysis in multiple injection dynamic PET scans.

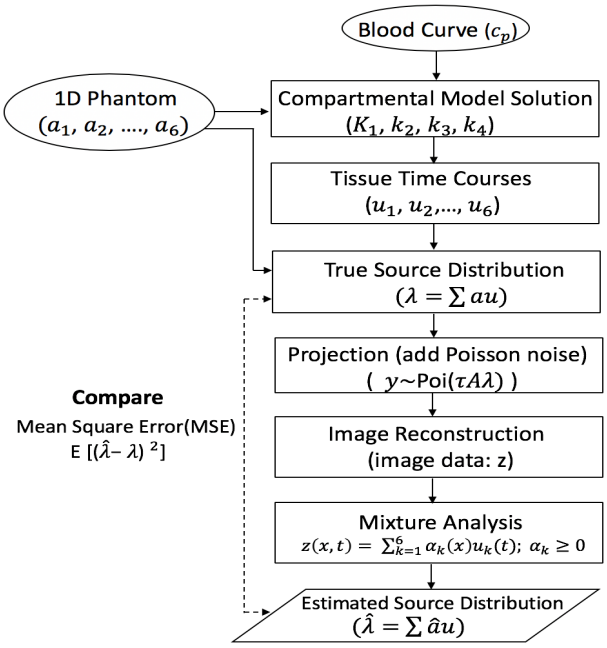

Fig. 2: 1D Simulation Process

1-D mixture model with K known components is employed to recover the mixing coefficients(α) from simulated image data.

$$\lambda(x,t) = \sum_{k=1}^{K} \alpha_k(x)\mu_k(t) \tag{2}$$

where λ is the true tissue source distribution of PET acquisition. Mixing coefficient estimators from combined ($\hat{\alpha_c}$) and separated analysis ($\hat{\alpha_s}^1$;$\hat{\alpha_s}^2$) are recovered as introduced in section II-B. Estimated distributions ($\hat{\lambda}$) in combined and separate analysis are $\hat{\lambda}_c = \hat{\alpha}_c\mu$ and $\hat{\lambda}_s = (\hat{\alpha}_s^1\mu^1, \hat{\alpha}_s^2\mu^2)$

MSE can be calculated as below:

$$\begin{cases} MSE1 = E[(\hat{\lambda}_s - \lambda)^2] \\ MSE2 = E[(\hat{\lambda}_c - \lambda)^2] \end{cases} \tag{3}$$

III. RESULTS

The MSE of the source distribution estimation as the function of the dose levels from combined and separated approach in 1-D simulation are presented in Fig.3. It illustrates errors from combined and separated analysis decrease with the dose. It is demonstrated that combined analysis is more efficient than the separate analysis and the magnitude of the improvements ranges from 18.10% to 33.85% for two injections with different dose levels. These results show combined analysis has quantitative advantages and it also validates the efficiency of mixture model approach for multiple injections.

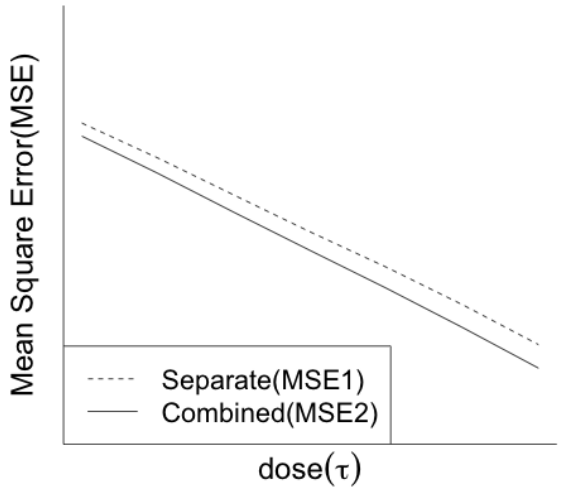

Fig. 3: MSE Comparison in 1D Simulation Study

TABLE I: Improvements at different dose levels

dose levels	dose1	dose2	dose3	dose4	dose5	dose6	dose7
improvements(%)	18.10	21.78	24.60	26.56	30.16	32.67	33.85

IV. DISCUSSION

The quantitation of data from multiple-injection PET studies is enhanced by combining information from separate injections. Mixture modelling provides simple mechanism to realise the combined analysis with long time-frames. It has a potential to process large scale dynamic data with the announcement of the next generation of total-body PET scanners[1] for research and clinical practice. More detailed examination of the benefits of combined analysis in different settings would be helpful.

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