Model-Based Factor Analysis of Dynamic Sequences of Cardiac Positron Emission Tomography

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***Abstract* – Factor analysis (FA) has been pursued as a means to decompose dynamic cardiac PET images into different tissue types based on their unique physiology. Each tissue is represented by a time-activity profile (factor) and an associated spatial distribution (structure). Decomposition is based on non-negative constraints of both the factors and structures; however, additional constraints are required to achieve a unique solution. In this work we present a novel method that combines physiological models of factor relationships into the decomposition process. Preliminary results are evaluated, suggesting that model-based FA decomposition results in physiologically accurate factors and structures.**

I. Introduction

Factor analysis (FA) techniques have been explored as a means to improve cardiac function quantification. An image series is decomposed into a finite number of temporal factors and their corresponding spatial distribution (structures) which, ideally, should correspond to the physiology of the imaged tissue [1]. The decomposition may be expressed in matrix form as

$$Y = FS+E,$$

Where Y is the dynamic image sequence (the pixels of each time frame in a row), the columns of F contain the time-activity profiles of the factors, the rows of S contain spatial distribution (structure) of the factor, and E is error, or residual signal not accounted for by the factors.

Decomposition is non-unique, requiring constraints that model the physical imaging process. In cardiac PET, these have historically been decomposition into non-negative factors and structures, which is representative of the physics and imaging process. In addition, Poisson statistics have been used to model the imaging process, but these constraints still do not ensure a unique solution.

In 2006 El Fahkri *et al.* [2] introduced an additional constraint that minimizes structure overlap in order to ensure a unique solution. And in 2007 we [3] proposed a constraint that minimizes factor overlap. However, both approaches do not completely agree with our knowledge of the physical model. In this work we propose an alternative approach that couples the factors using models that describe their physiological relationship over time. Specifically, these models relate the three main components of the heart – right cavity blood, left cavity blood, and myocardium.

The right ventricle cavity (RV) blood factor is a free variable with n-1 time points (due to unity area of each factor), where n is the number of frames. The left ventricle cavity (LV) blood is modeled by convolution of the RV blood with a shifted gamma-variate function (having 3 free parameters) that accounts for transport delay and dispersion [4] during transport of blood from the RV to the LV via the lungs. This is expressed as,

$$G(t) = \begin{cases} 0 & t < t_1 \\ (t - t_1)^{\beta} e^{-\beta*(t-t_1)/(t_1-t_p)} & otherwise \end{cases} \quad (1)$$

where t_1 is the time delay to first activity, t_p is time delay to peak activity, and β controls the broadness of dispersion.

The myocardium factor is modeled by convolution of the LV blood factor with a compartmental response function assumed for the specific tracer. In the case of ^{82}Rb we assumed a one compartment model which is defined by a single free parameter k_2 (tracer washout) and shown in eq. 2.

$$M(t) = e^{-k_s t} \quad (2)$$

Once again, since the factors are scaled to unity area, there is no need for scaling factors in either equations (1) or (2). The model parameters are optimized as part of the decomposition process.

II. Methods and Materials

Two sets of data were analyzed:

1. Simulated: Factors were created using an arbitrary RV blood time activity curve, RV to LV transfer model, and a rubidium-one-compartment model. These factors were cross multiplied with respective structures as shown in the top row of figure 1. Each time frame of the simulated image sequence was smoothed with a 12mm FWHM Gaussian and summed with varying degrees (0 and 10%) Gaussian distributed random noise. Two subsets of images were used in order to assess the solution's robustness to tracer uptake characteristics:
    a. Blood activity clearing entirely
    b. Non-zero residual blood activity
2. Canine: A single dog underwent a series of dynamic PET scans with varying ^{82}Rb (150 MBq) infusion durations (15, 30, 60, 120, 240, 240, 120, 60, 30, 15 seconds) with a Siemens ECAT ART scanner. The images were iteratively reconstructed to 12 mm resolution.

These data sets were analyzed using the following steps:

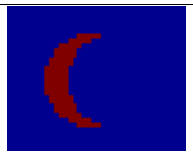
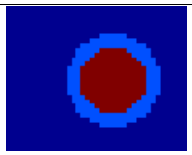
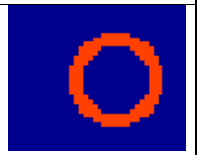
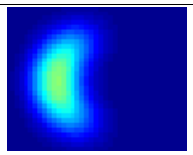
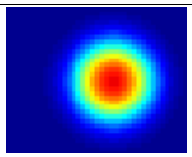
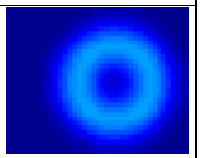
1. Semi-automated cropping of field-of-view to include regions of high signal intensity.
2. Optimization of Model-based factor analysis (automatic determination of number of factors).

III. Results

A. Simulation

The structures and factors of the simulated data were recovered with good accuracy regardless of the noise levels. For all factors the root-mean-squared-error (RMSE) was below 6% with an average of 3.6%. The majority of variation appears in the magnitude of blood factor peaks, which relates to blood peaks that are overly sharp (large β), as seen in figure 1. The resolved structures correlated very well (R^2>0.966 with an average R^2=0.991) with the simulated data (smoothed structures, shown in lower row of table 1).

Table 1 – Short Axis Slices of Simulated Structures Before and After Smoothing

	RV Blood	LV Blood	Myocardium
Unsmoothed Structures			
Smoothed Strucutres			

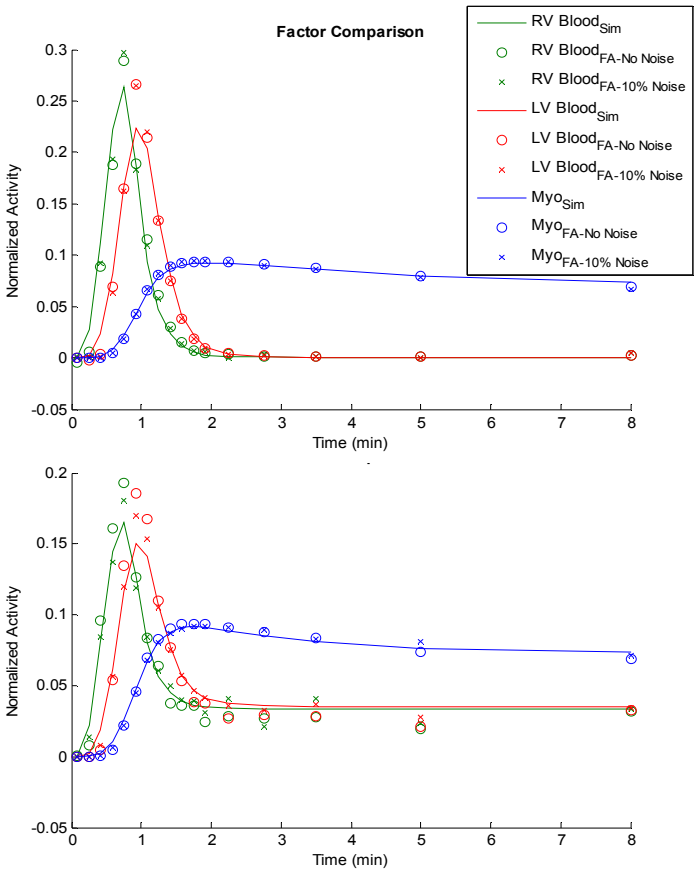


Figure 1 – Comparison of resolved RV blood (green), LV blood (red), and myocardium (blue) factors without noise (o) and with 10% noise (x) to the original profiles (lines) used in simulating the dynamic image sequence. Top figure represents total blood clearance and bottom figure represents residual blood activity.

B. *Canine Model*

The number of resolved factors varied between 2 for long tracer infusions and 3 for short infusions (30s or less). Where 3 factors were resolved, distinct RV and LV structures were observed as shown in Table 3.

Factors were representative of the infusion duration with blood factors having a more gradual rise with prolonged infusions. Likewise myocardial uptake was more gradual. In all cases, blood activity dropped to near zero values over time (after decay correction), which agrees with observations made in rats using arterial blood sampling, as illustrated in figure 2.

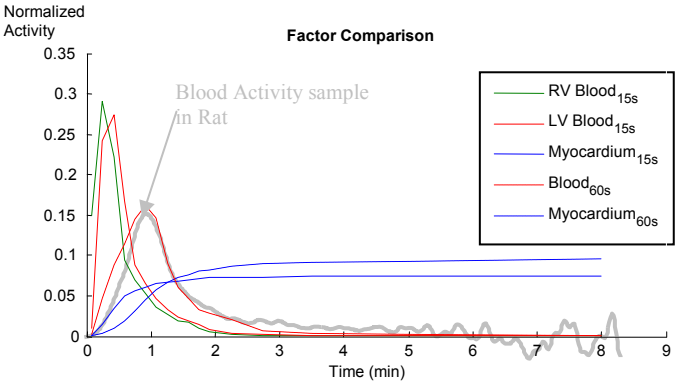
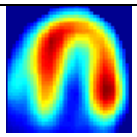
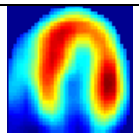
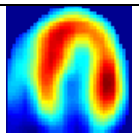
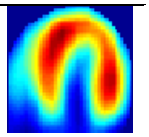
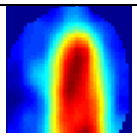
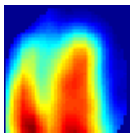
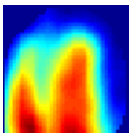
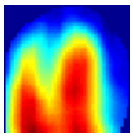
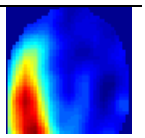


Figure 2 – Example comparison of resolved LV blood (red) and myocardium (blue) factors using model-based FA in a dog with 15 and 60 second constant activity rate ^{82}Rb infusion. The gray line demonstrates decay corrected blood ^{82}Rb concentration measured in a rat using carotid artery sampling (injection interval was 30 seconds).

TABLE 3 – Example of Resolved Structures
(same cases 15s and 60s examples as in figure 2)

Infusion	15s	60s	120s	240s
Myo. Structure				
Blood Structures – LV				
Blood Structures – RV				

Reproducibility of structures was excellent. In all correlation combinations (n=45) R^2-values were >0.866 for myocardium and >0.964 for blood structures with mean values 0.943 and 0.975 respectively.

IV. DISCUSSION

A. *Model Parameters*

Although the factors resolved from the simulated data agreed closely with the original data, the RV-LV model parameters did not. This suggests that the model function is over-determined which may lead to non-unique solutions. Simplification of the model (removal of one or more parameter), may aid in resolving this issue. Likewise, longer tracer infusions may mitigate the need for resolving 3 factors without compromise to quantification of cardiac function, thus simplifying the modeling further.

B. *Computation Complexity*

Model based factor analysis benefits from reduced computational complexity over traditional factor analysis methods due to a reduced number of free variables. In the case of a one compartment model and three factors (RV blood, LV blood, and myocardium) an image with n time frames has (n-1)+3+1 free parameters to optimize as opposed to 3(n-1) for traditional factor analysis. As a result computation times may be shortened, even if the algorithm is more complicated.

V. CONCLUSION

Constraints must be placed on dynamic cardiac PET image decomposition in order to resolve physiologically accurate factors. Model-based FA may be a suitable an alternative that incorporates a-priori information of the physical model. Further investigation is required to assess the effect on cardiac function quantification.

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