Myocardial Blood Flow Quantification in Dynamic PET: An Ensemble ICA Approach

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Abstract. Linear models such as factor analysis, independent component analysis (ICA), and nonnegative matrix factorization (NMF) were successfully applied to dynamic myocardial $H_2^{15}O$ PET image data, showing that meaningful factor images and appropriate time activity curves were estimated for the quantification of myocardial blood flow. In this paper we apply the ensemble ICA to dynamic myocardial $H_2^{15}O$ PET image data. The benefit of the ensemble ICA (or Bayesian ICA) in such a task is to decompose the image data into a linear sum of independent components as in ICA, with imposing the nonnegativity constraints on basis vectors as well as encoding variables, through the rectified Gaussian prior. We show that major cardiac components are separated successfully by the ensemble ICA method and blood flow could be estimated in 15 patients. Mean myocardial blood flow was 1.2 ± 0.40 ml/min/g in rest, 1.85 ± 1.12 ml/min/g in stress state. Blood flow values obtained by an operator in two different occasion were highly correlated (r=0.99). In myocardium component images, the image contrast between left ventricle and myocardium was 1:2.7 in average.

1 Introduction

Linear model-based methods, including factor analysis, independent component analysis (ICA), nonnegative matrix factorization (NMF), were shown to useful in analyzing dynamic positron emission tomography (PET) image data, demonstrating that meaningful factor images and appropriate time activity curves could be extracted [1,2,3]. In the application of such linear models to PET, a main focus was to extract left ventricle input function [1,2], which is an essential part for the calculation of myocardial blood flow (MBF) in the tracer kinetics model of dynamic $H_2^{15}O$ cardiac PET. However, the extraction of the input function is a difficult task, because of the partial volume effect resulting from the limitation of system resolution and the spill-over of left ventricle, right ventricle, and myocardium by the motion of heart. Consequently, a new method

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for the input function extraction is required to estimate the blood flow more accurately. $H_2^{15}O$ dynamic cardiac PET has been used for the quantification of MBF as an ideal blood flow tracer [4,5,6]. The half life of $H_2^{15}O$ is about 2 minutes, which makes repetitive and short interval estimation of MBF possible. In this paper, we apply the ensemble ICA [7] to $H_2^{15}O$ dynamic cardiac PET image data. In the ensemble learning [8], the inference is carried out by averaging over the posterior distribution of the parameters. The main benefit of the ensemble ICA over the conventional ICA or NMF, is to decompose the image data into a linear sum of independent components as in ICA, with imposing the nonnegativity constraints on basis vectors as well as encoding variables, through the rectified Gaussian prior. We evaluate the ensemble ICA for the quantification of regional myocardial blood flow (rMBF) after segmentation of left ventricle, right ventricle, and myocardium images.

2 PET Image Acquisition and Processing

PET images were acquired from ECAT EXACT47 (Siemense-CTI, Knoxville, USA) in Seoul National University Hospital. Totally 24 frames 47 transaxial images were acquired; 12 frames for 5 seconds, 9 frames for 10 seconds, and 3 frames for 30 seconds. After bolus injection of $H_2^{15}O$ (555-740 MBq), adenosine stress was carried out during 7 minutes. $H_2^{15}O$ was injected after 3 minutes during stress, and then dynamic PET images were acquired during 4 minutes continuously. Images were reconstructed using FBP (image matrix = 128 128, magnification factor = 1.5). Twenty patients were investigated using $H_2^{15}O$ dynamic myocardial PET. Patients were underwent gated 99mTc-MIBI myocardial perfusion SPECT for the suspicious coronary artery disease. Rest image and adenosine stress images were acquired. All frame data was reoriented to short axis and two plans were summed in order to extract myocardium component automatically using ensemble ICA. Nine region of interest (ROI) were drown on left ventricle and myocardium (1 apex, 4 middle wall, 4 basal wall) to take out the time-activity curve of dynamic PET image. Using input function and time-activity curve of each region, rMBF was calculated. The values of rMBF were compared with angiography and gated myocardial perfusion SPECT. Regional perfusion was relocated to 9 regions used in dynamic PET analysis.

3 Factor Image Extraction Using Ensemble ICA

$H_2^{15}O$ PET images are converted to vector sequences $\mathcal{D} = \{x_t \in \mathbb{R}^m\}$. ICA assumes that data vectors x_t are generated by

$$x_t = As_t + \epsilon_t, \tag{1}$$

where $s_t \in \mathbb{R}^n$ correspond to factor images (independent components), column vectors of the matrix $A \in \mathbb{R}^{m \times n}$ represent time activity curves, and $\epsilon_t \in \mathbb{R}^m$ reflect the model uncertainty which is assumed to be Gaussian.

In the context of $H_2^{15}O$ PET images, independent components are expected to images corresponding to left ventricle, right ventricle, myocardium, and background, which reasonable satisfy spatial independence. In such a case, basis vectors (corresponding to the column vectors of A) represent the time activity curves which reflect the time-varying influence in PET images [9]. The standard ICA, including mutual information minimization, maximum likelihood estimation (MLE), output entropy maximization, and so on (see [10] for recent review), incorporates with the prior probability of parameters in a limited way and neglects the uncertainty term in (1). That is, in the standard ICA, parameters were inferred by maximizing the likelihood in the limit of zero noise.

On the other hand, NMF [11] also considers the linear model (1) but infers parameters with constraining both A and s_t to be nonnegative, whereas ICA incorporates with independence conditions for s_t. Inference in NMF can also be illustrated in the framework of maximum likelihood estimation with assuming Poisson distribution for ϵ_t. Application of NMF to dynamic PET can be found in [3].

Here we use the ensemble ICA [7] to extract factor images in $H_2^{15}O$ PET. In the Bayesian framework, the posterior probability of parameters θ, given a set of data points $\mathcal{D}$, is described by

$$P(\theta|\mathcal{D},\mathcal{H}) = \frac{P(\mathcal{D}|\theta,\mathcal{H})P(\theta|\mathcal{H})}{P(\mathcal{D}|\mathcal{H})}, \tag{2}$$

where $\mathcal{H}$ represents a model. In the ensemble learning, the inference is performed by averaging over the posterior distribution, so that the inference is sensitive to regions where the probability mass is large, in contrast to ML or MAP where the inference is sensitive to regions where the probability density is large. In practice, exact inference is often intractable. The ensemble learning approximation finds an approximate a posterior distribution Q for the model parameters by minimizing the Kullback-Leibler divergence between the approximate posterior Q and the true posterior

$$\begin{aligned} KL[Q||P] &= \left\langle \log\left[\frac{Q(\theta)}{P(\theta|\mathcal{D},\mathcal{H})}\right]\right\rangle_Q \\ &= \left\langle \log\left[\frac{Q(\theta)}{P(\mathcal{D},\theta|\mathcal{H})}\right]\right\rangle_Q + \log P(\mathcal{D}|\mathcal{H}). \end{aligned} \tag{3}$$

where $\langle\cdot\rangle_Q$ denotes the statistical expectation under the approximate distribution Q.

The following objective function $\mathcal{J}$ was considered in [7]

$$\begin{aligned} \mathcal{J} &= KL[Q||P] - \log P(\mathcal{D}|\mathcal{H}) \\ &= \left\langle \log\left[\frac{Q(\theta)}{P(\mathcal{D},\theta|\mathcal{H})}\right]\right\rangle_Q \\ &\geq -\log P(\mathcal{D}|\mathcal{H}). \end{aligned} \tag{4}$$

The minimization of the objective function $\mathcal{J}$ in (4) is equivalent to maximizing a bound on the log-evidence $\log P(\mathcal{D}|\mathcal{H})$.

The main benefit of the ensemble ICA is to decompose the PET images as a linear combination of factor images with encoding variables being statistically independent as in ICA, with imposing nonnegativity constraints on A and s_t through rectified Gaussian prior. In other words, the ensemble ICA leads us to incorporate with both independence and nonnegativity constraints in the context of the linear model (1). Empirical results in Sec. 4 demonstrate that the ensemble ICA, indeed, works well in the task of analyzing $H_2^{15}O$ PET image data.

4 Quantification Results of rMBF

The rMBF from $H_2^{15}O$ dynamic myocardial PET were compared with the results of perfusion SPECT. Image contrast between myocardium and left ventricle were estimated in segmented myocardial independent component images (see Fig. 1). Image contrast of myocardium was 1 : 2.97 (LV:myocardium) in the rest image and was 1 : 2.56 in stress image of separated independent component images (see Fig. 2). The number of subjects with the image contrast under 2.0 was 6 and the highest value of image contrast was 4.63. Blood flow obtained from PET was 1.2± 0.40 ml/min/g in rest state, 1.85±1.12 ml/min/g in stress state. Reproducibility of myocardial blood flow of 15 subjects PET image data which were acquired twice for each region was high. ($r = 0.99$, $P < 0.0001$) Myocardial perfusion was quantified by autoQuant program. Uptake value of normal segments group were 67.613.3in stress (reversibility score = 1.9), while that of stenotic group were 71.9±9.8in rest and 69.1±12.8There was no significant difference between normal group and stenotic group in terms of reversibility score. The rMBF of reversible segments were 0.98 ± 0.30 ml/min/g in rest, 1.78 ± 0.76 ml/min/g in stress, and blood flow reserve was 0.80 ± 0.69 ml/min/g. The rMBF of persistent segments in myocardial perfusion SPECT was 1.10 ± 0.40 ml/min/g in rest, 2.06 ± 1.35 ml/min/g in stress, and the blood flow reserve was 0.95 ± 1.32 ml/min/g (see Fig. 3).

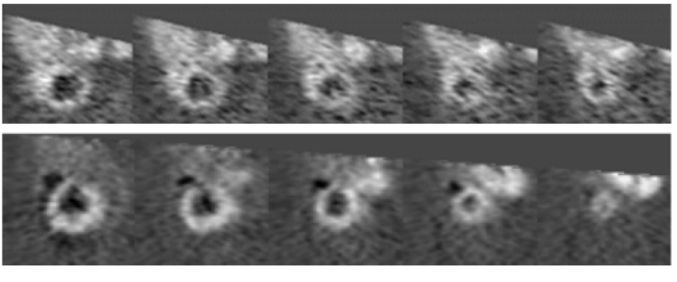
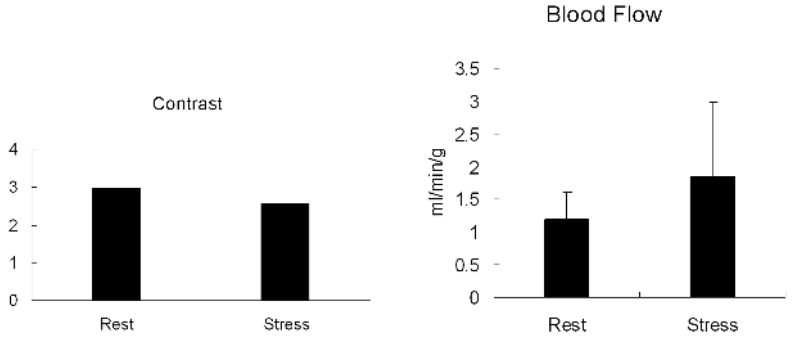


Fig. 1. Segmented component images using the ensemble ICA method



(a) (b)

Fig. 2. (a) Image contrast of myocardium was improved in rest image than stress image; (b) Estimated myocardial blood flow values using $H_2^{15}O$ PET

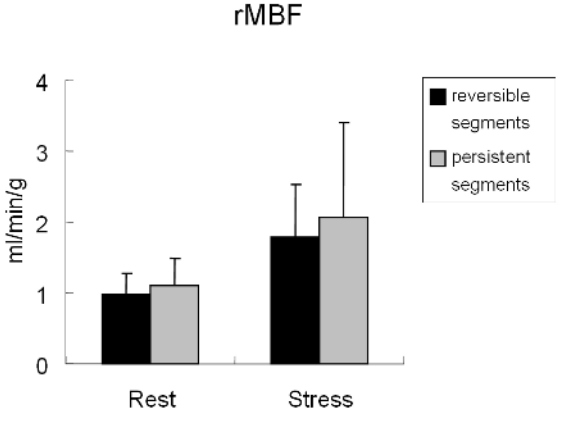


Fig. 3. Regional myocardial blood flow of reversible segments and persistent segments in perfusion SPECT

5 Discussions

The standard ICA had difficulty in extracting appropriate factor images in our clinical data, because of the difference of injection dose according to weight and low sensitivity of hardware system. Recently, left ventricle and myocardium image were visualized through the NMF method in clinical study, and the MBF of patient could be estimated using the NMF [12] The nonnegativity is a natural constraint in medical imaging such as PET. The ensemble ICA is a technique which incorporates with both independence and nonnegativity constraints. In our study, we have observed that the ensemble ICA had a a merit of improved image contrast and quality for ROI processing, compared to the NMF method. The rMBF was estimated using the ensemble ICA in $H_2^{15}O$ dynamic myocardial PET. Reproducibility of measurement and image contrast were good enough to

segment myocardium. We expect that dynamic myocardial PET analysis using the ensemble ICA can be used to assess the absolute myocardial blood flow in clinical situations.

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