Principal Component Analysis in Dynamic Positron Emission Tomography

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Abstract

Dynamic Positron Emission Tomography (PET) offers differential diagnostic information and has increasingly been used for diagnosis, therapy management and evaluation. We have applied Principal Component Analysis (PCA) on dynamic PET studies. Its general objectives are data reduction and interpretation. PCA in PET images reduces the dimensionality of dynamic data sets and can be used to identify the structures with different kinetic patterns prior to other types of analysis (e.g. ROI analysis).

1. Introduction

PET stands in the forefront of molecular imaging and allows the quantitative evaluation of the distribution of several pharmaceuticals in a target area *in vivo*. PET is a non-invasive, diagnostic imaging technique for measuring the metabolic activity of cells in the human body. It provides valuable information on the biochemical and biological activity inside a living subject in a non-invasive way, combining techniques applied in nuclear medicine with the precise localisation achieved by computerised image reconstruction. PET is therefore a powerful diagnostic test that is having a major impact on the diagnosis and treatment of disease, as it can detect and stage tumors, often before they are visible through other conventional exams. Furthermore, PET can provide medical doctors with important early information about heart disease or several neurological disorders (Alzheimer's, Parkinson's, epilepsy, dementia).

Dynamic PET studies (sequence of images during the whole radioactivity period) offer differential diagnostic information and are becoming an increasingly important component of PET methodology for disease diagnosis, therapy management and evaluation.

Several methods have been proposed for the analysis of dynamic studies: compartmental models, graphical evaluation, Fourier analysis, multivariate analysis, fractal analysis etc. Principal Component Analysis in PET is optimizing the signals by simultaneously considering the complete set of images in the dynamic sequence and does not include any model-based restrictions since it is independent of any kinetic model [1]. PCA images appear with decreasing signal-to-noise ratio (SNR) and only the first few need to be inspected. However, PCA does not give the physiologic importance of each component and therefore, side information is essential for interpretation of the results, e.g., time activity curves (TAC) or correlative anatomic imaging [2]. Consequently, PCA is a relatively simple method of generating high-contrast images that make feature identification easier [3]. In this work, PCA has been applied to dynamic PET studies as a tool for better understanding of the disease mechanisms in oncology.

2. Materials and Methods

Principal Component Analysis, also known as the Hotelling or the Karhunen-Loève transform, has several applications in nuclear medical imaging [1,2], [4], X-ray Computed Tomography (CT) [3] and other X-ray fields [5,6], Magnetic Resonance Imaging (MRI) [7,8] etc.

PCA is a data driven technique that cannot separate signals from noise. In the presence of large background noise, the resulting PCA images are similar to the original ones [1]. There are several approaches to this problem [4]. Since the background noise has several components and is also locally dependent (e.g., high/low localised tracer accumulation), we have used a global normalisation according to the total number of counts, a general measure that should meet the majority of situations.

Let $\mathbf{X}'=[X_1, X_2, \ldots, X_p]$ have covariance matrix $\mathbf{\Sigma}$, with eigenvalue-eigenvector pairs $(\lambda_1, \mathbf{e_1})$, $(\lambda_2, \mathbf{e_2})$, …, $(\lambda_p, \mathbf{e_p})$ where $\lambda_1 \geq \lambda_2 \geq \ldots \geq \lambda_p \geq 0$. The k_{th} principal component is given by:

$$Y_k = \mathbf{e'_k X} = e_{k1}X_1 + e_{k2}X_2 + \ldots + e_{kp}X_p, \quad k=1,2,\ldots,p$$

with:

$$\mathrm{Var}(Y_k) = \mathbf{e'_k \Sigma e_k} = \lambda_k$$

$$\mathrm{Cov}(Y_k, Y_i) = \mathbf{e'_k \Sigma e_i} = 0, \quad i \neq k$$

The total population variance is given by:

$$\sum_{i=1}^{p} Var(X_i) = \sum_{i=1}^{p} Var(Y_i) = \sum_{i=1}^{p} \lambda_i$$

Consequently, the proportion of total variance due to (explained by) the k_{th} principal component is:

$$\frac{\lambda_k}{\sum_{i=1}^{p}\lambda_i} \qquad k=1, 2, \ldots, p$$

If most (for instance 80 to 90%) of the total variance can be attributed to the first few components, then these components can "replace" the original p variables without much loss of information.

An ECAT EXACT HR+ (CTI/Siemens, Knoxville, TN, USA) tomograph was used for the patient studies at the German Cancer Research Center. The tomograph delivers images in 63 planes (32 direct and 31 cross-planes) and has an axial field-of-view of 15.5 cm. It is constructed using 4 rings of 72 8×8 BGO detector blocks. Each of its 32 rings consists of 576 individual detector crystals, each of dimensions 4.39×4.05×30 mm^3 and images a transaxial FOV of 56.2 cm. During a typical dynamic study at the Medical PET Group in DKFZ, 23 frames are acquired for 60 min following intravenous injection of F-18-deoxyglucose (FDG): 10 frames of 60 sec, 5 frames of 120 sec and 8 frames of 300 sec. All emission acquisitions are preceded by transmission scans (10 min for the dynamic scan, 5-min post-injection for the static scans) for the attenuation correction.

A software tool has been developed for the PCA of dynamic PET images, based on algorithms presented at [9, 10]. The implementation is performed using C/C++ on Pentium (Intel Corp., CA, USA) systems under Windows NT/2000 (Microsoft Corp., WA, USA). The program checks the directory for analysis requests and opens the parameters file. Input parameters are the filename of the dynamic study, the data set characteristics (i.e., number of bytes/pixel, number of pixels/slice, number of slices/frame), as well as the number of slices and frames to be analyzed. After the analysis, the results are stored and the parameters file is moved to the directory with the successfully terminated analysis requests or to the directory with the failed requests.

3. Results

The program was tested on simulated data sets as well as on clinical patient data. Here, Images from a dynamic PET study (F-18 FDG, image size 256×256) of a liver metastasis were used. Results for a central slice are shown in the following figures.

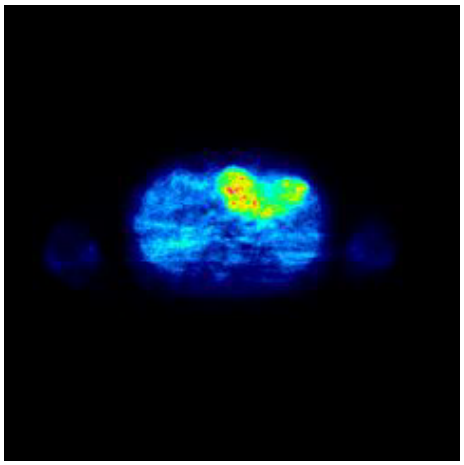

Figure 1. Standardized Uptake Value (SUV) image of slice 10

Principal Component Image (PCI) #13 reflects the FDG metabolism: The metastasis (green/red area in the middle) can be clearly distinguished, while the normal liver parenchyma is nearly black (large area beneath the metastasis, on the left image side). PCI #14 is related to blood volume. Normal liver parenchyma is visible (left in the image), the aorta (circular area in the middle), and the spleen (right in the image), while the metastasis is shown as a black area (middle). PCIs #1-12 contribute to the noise fraction. The injection site (left in the images) is shown in #13-14, due to both blood flow and FDG uptake.

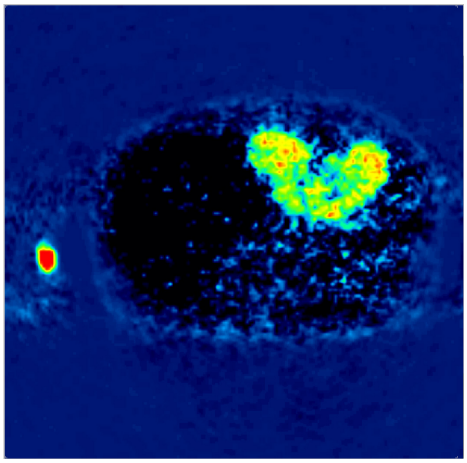

Figure 2. Principal Component Image #13

PCA was also applied to a dynamic FDG study on 5 Parkinson patients and 3 control persons. The study started 3 minutes postinjection and ran for 25 frames of 60 sec. PCA images provide a good visualization of the brain features by removing the noise seen in the slices of each frame. The image quality was not only visually evaluated but also measured: the SNR ratio was calculated and found higher than the SNR of the original images.

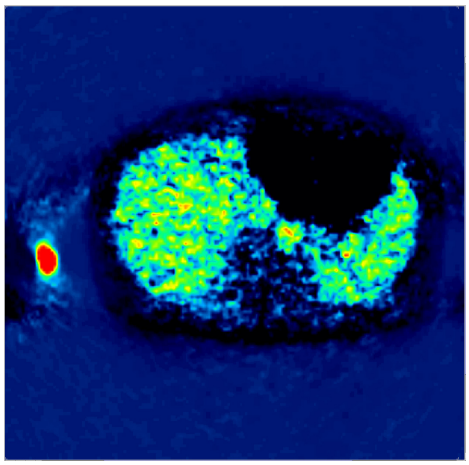

Figure 3. Principal Component Image #14

These preliminary results show that PCA can separately identify different functional fractions of the radiotracer metabolism.

4. Conclusions

Principal Component Analysis in dynamic PET studies is able to separate structures with different kinetic patterns and to generate parametric images with improved signal-to-noise ratio helping both visual interpretation and further analysis. Although generally only the first few PCA images need to be inspected, sometimes, principal component images with small but nonzero variances enhance the subtle contrast between two extremely similar components and help separate them. PCA main limitation stems from the fact that it is a data driven technique and cannot separate signals from noise. Therefore, data normalization prior to PCA improves the quality of the produced images.

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