Enhanced Parameter Estimation From Noisy PET Data:

Part I—Methodology[1]

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Rationale and Objectives. The reliability of positron emission tomographic (PET) images depends on the number of annihilation events that are detected. Short image durations are required to capture rapid tracer dynamics, and the resultant images are noisy. Consequently, direct parameter estimation from time-activity curves at high resolution often is unreliable. If adjacent voxels are combined into larger regions of interest the reliability of parameter estimation may be improved, but at the expense of decreased spatial resolution. In this report, a method is presented that provides an alternative to degrading image resolution.

Materials and Methods. Following the approach of Kimura et al, voxels are grouped not by spatial proximity, but by the similarity of their kinetics. Parameter estimation is performed on these groups, and derived parameters are assigned to all members of the group. Spatial information thus is preserved, but at the expense of parametric discretization. An improvement to the method of Kimura et al is described, in which data are grouped using principal components derived from artificial data.

Results. The application of the method is demonstrated by analysis of PET images of human lungs obtained by the nitrogen-13 infusion-washout technique. In a comparison of the accuracy of parameter estimates, the enhanced method is shown to outperform the original method at all noise levels, with the difference increasing as the amount of noise increases. The robustness of this parameter estimation method in the presence of noise is described in part II of this report in this issue of Academic Radiology.

Conclusion. A method is described that provides demonstrably robust parameter estimates from noisy PET data, while not compromising image resolution.

Key Words. Position emission tomography; parameter estimation; functional imaging

All forms of tomography intrinsically exhibit a trade-off between spatial-temporal resolution and noise. In positron emission tomography (PET), this is particularly apparent because image analysis frequently requires estimation of multiple functional parameters from a tracer's regional kinetics. Given a maximum level of local radioactivity (determined by radiation dose or isotope production limitations), image noise increases as tracer concentration is measured within smaller and smaller regions of interest (ROIs). The problem is exacerbated if short image acquisition durations are required to capture rapid changes in local tracer concentration. As a result, the accuracy of parameters estimated at high resolution from dynamic PET images are almost always limited by noise.

In PET, the number of annihilation events detected within an ROI can be increased by increasing the number

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of voxels in the ROI (enlarging it) or imaging for a longer duration. As a result, signal-to-noise ratio improves as temporal or spatial resolution is degraded. Hence, one approach to the noise problem is to decrease the effective spatial resolution of the PET images. This can be accomplished by combining adjacent voxels into larger regions, low-pass filtering, or reconstruction at a lower resolution. However, unless the aggregated regions have homogeneous tracer kinetics, results of subsequent parameter estimation may not be valid.

Kimura et al (1,2) proposed an alternative strategy: instead of collecting voxels into groups based on their spatial proximity (as in low-pass filtering or other degradation of spatial resolution), voxels are grouped by the similarity of their kinetics. Parameter estimation then is performed on the mean kinetics of each group, and the resulting parameters are assigned to all voxels within the group. If we divide the voxels within an image into n groups, each parameter must take one of n discrete values estimated for each group. Thus, spatial information is preserved at the expense of parametric discretization. However, if n is sufficiently large, the reduction in precision due to discretization is not physiologically relevant.

In this report, refinements to the approach of Kimura et al (1,2) are presented, and the viability of the improved method is shown by analysis of nitrogen-13 washout kinetics of a bronchoconstricted patient with asthma. In part II of this report (4), the robustness to noise of the enhanced method is investigated.

METHODS

Nitrogen 13 Infusion-Washout Technique

Nitrogen-13 is a short-lived (half-life ~10 minutes) positron-emitting radioisotope of nitrogen. Its uncombined molecular form (^{13}N-^{13}N or ^{13}N-^{14}N) is biologically inert and weakly soluble in water. The radioisotope is generated in a cyclotron, purified, and dissolved in saline solution under pressure. In the infusion-washout technique, the study subject is instructed to hold his or her breath (for 20–40 seconds) while a bolus of tracer solution is infused into a peripheral vein. Because of its low solubility, when the tracer reaches the pulmonary capillaries, it evolves out of solution and redistributes into the alveolar airspaces in proportion to local perfusion ($\dot{Q}$). When breathing is resumed, the tracer is washed out of the lungs at a rate proportional to local specific ventilation ($s\dot{V}$). Thus, by analysis of a series of short PET images obtained during the arrival, plateau, and washout of the tracer, a three-dimensional high-resolution image of $\dot{Q}$ and $s\dot{V}$ can be generated. These are the principal physiological parameters describing gas exchange in the lung.

In a normal lung, regional ventilation is fairly uniform, and the tracer is washed out from the alveoli with kinetics that approximate a simple exponential decay. However, in asthma (3) or other lung diseases, ventilation can be highly heterogeneous at length scales less than the effective resolution of the PET scanner (~5 mm). As a result, even single voxels may show multicompartmental washout behavior (5). In such cases, the tracer concentration during washout is described best with a two-compartment model (as the sum of two exponential decays):

$$\hat{C}(t) = A_f e^{-\alpha_f t} + A_s e^{-\alpha_s t} \quad (1)$$

Here, the amplitude parameters A_f and A_s are proportional to the perfusion to fast and slow compartments, and the washout rates α_f, α_s describe the specific ventilation of the corresponding compartments.

Application of Principal Component Analysis

The objective of this analysis is to estimate multiple physiological parameters in a voxel-by-voxel manner from a dynamic PET data set describing regional tracer concentration. In the example used here, these parameters are the four washout parameters described, A_f, A_s, α_f, and α_s.

The first step in the method is to select groups of voxels that show similar kinetics. A typical data set will comprise approximately 20,000 voxels with 17 washout frames (acquisitions). Considering the kinetics of each voxel as a point in 17-dimensional space, the data set can be visualized as a cloud of 20,000 points in this high-dimensional space.

The dimensionality of the problem can be decreased by using principal component analysis (PCA). In this technique, the data set is transformed to a different orthogonal coordinate system in which the basis vectors are defined and ordered by their contributions to the total variance of the data. The first basis vector defines the direction in which data show maximal variance, the second basis vector defines the orthogonal direction to the first basis vector that accounts for the next highest residual variance once the first component has been removed, and so on. These basis vectors are termed the *principal components* of the data set. Because they are ordered ac-