Lawrence Berkeley National Laboratory

Recent Work

Title

Strategies for Extraction of Quantitative Data From Volumetric Dynamic Cardiac Positron Emission Tomography Data

Permalink

<https://escholarship.org/uc/item/0h42f06r>

Journal

Cardiology, 88(1)

Author

Huesman, R.H.

Publication Date

1995-09-18

Lawrence Berkeley Laboratory

UNIVERSITY OF CALIFORNIA

Submitted to Cardiology

Strategies for Extraction of Quantitative Data from Volumetric Dynamic Cardiac PET Data

R.H. Huesman, G.J. Klein, B.W. Reutter, P.G. Coxson,
E.H. Botvinick, and T.F. Budinger

September 1995

Donner Laboratory

Biology & Medicine Division

REFERENCE COPY
Does Not
Circulate
Bldg. 50 Library.

LBL-37775

DISCLAIMER

This document was prepared as an account of work sponsored by the United States Government. While this document is believed to contain correct information, neither the United States Government nor any agency thereof, nor the Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or the Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof or the Regents of the University of California.

LBL-37775
UC-408

Strategies for Extraction of Quantitative Data from Volumetric Dynamic Cardiac PET Data

Ronald H. Huesman, Gregory J. Klein, Bryan W. Reutter, Pamela G. Coxson, Elias H.
Botvinick, and Thomas F. Budinger

Center for Functional Imaging
Life Sciences Division
Lawrence Berkeley National Laboratory
University of California
Berkeley, CA 94020

September 1995

This work was supported by the Director, Office of Energy Research, Office of Basic Energy Sciences, Medical Applications and Biophysical Research Division, of the U.S. Department of Energy under Contract No. DE-AC03-76SF00098, and by National Heart, Lung and Blood Institute of the U.S. Department of Health and Human Services under grant HL25840-12A1.

**Strategies for Extraction of Quantitative Data
from Volumetric Dynamic Cardiac PET Data**

Ronald H. Huesman, Gregory J. Klein, Bryan W. Reutter, Pamela G. Coxson, Elias H. Botvinick*, Thomas F. Budinger

Lawrence Berkeley Laboratory, Center for Functional Imaging, Life Sciences Division, Berkeley, CA.

*University of California San Francisco, Medical Center, San Francisco, CA

Short Title: Quantitative Volumetric Dynamic Cardiac PET Data

Key Words: PET, kinetic modeling and analysis, volume of interest (VOI), 82-Rubidium, dynamic emission data, 2D and 3D reconstruction

Mailing Address: Ronald H. Huesman
Lawrence Berkeley National Laboratory
1 Cyclotron Rd. Mailstop 55-121
Berkeley, CA. 94720

Phone: (510) 486-4062

Fax (510) 486-4768

Strategies for Extraction of Quantitative Data from Volumetric Dynamic Cardiac PET Data

ABSTRACT

The ability of PET to serve as a useful myocardial perfusion indicator is well established. We describe a methodology for obtaining reliable quantitative kinetic parameters from dynamic cardiac PET data.

Reconstructed images of the myocardium are subdivided into 3D volumes of interest and are used to obtain quantitative measures of myocardial perfusion over physiologically meaningful anatomical regions. The quantitation technique rigorously models the uncertainty of estimated parameters while compensating for effects such as patient motion and partial volumes to arrive at model parameters with well-defined confidence intervals.

INTRODUCTION

The capabilities of PET and SPECT to acquire reliable and statistically acceptable dynamic data useful for kinetic analyses of flow and metabolic rates have now been well established [1-4].

A critical problem in kinetic analysis is declaration of volumes of interest (VOI) from data sets with as many as 47-levels representing transverse sections through the thorax (Figure 1). The effective size of the VOIs is a tradeoff between spatial sampling of a kinetic parameter and available statistics. Whereas the VOIs comprising an entire myocardial wall or septum vs lateral muscle mass for a single level of 5-10 mm thickness gives statistically acceptable kinetic parameters, the coarseness of sampling might not be clinically useful. However, small contiguous VOIs such as the chain of circles in Figure 2b have too sparse data for reliable kinetic analyses. Thus, there is a need to segment VOIs from these large data sets with minimum bias from the activity seen on the images and with maximum statistics consistent with requirements for spatial resolution of kinetic parameters. This paper presents the methods we developed to reduce the multidynamic data sets to N volumes of interest. N can be whatever is consistent with available statistics.

In addition, patient motion between or during emission and transmission studies must be compensated, as this misregistration between emission and transmission can cause substantial errors in attenuation correction. Though the methods of segmentation of the left ventricle from the thorax still require substantial human contouring other aspects of analyses have been automated and are detailed below.

METHODS

Data Acquisition

Dynamic emission data were acquired on a Siemens / CTI ECAT EXACT HR scanner designed with a 3.6 mm in-plane spatial resolution [5]. The scanner simultaneously acquires 47 image planes over a 15 cm axial field of view, and can image activity concentrations as high as 6 $\mu\text{Ci/cc}$ in the field of view. A 56 cm gantry aperture accommodates normal patient chest and shoulders for a routine cardiac examination.

Rb-82 was used to collect two separate dynamic emission datasets: first demonstrating the patient condition at rest and then under pharmacologically induced stress. The protocol for each emission acquisition consisted of a bolus injection of 35 mCi of Rb-82 followed by six minutes of dynamic acquisition: 18 x 5 sec, 6 x 10 sec, 7 x 30 sec frames. Between the rest and stress scans, a 25-minute transmission scan was acquired. The transmission scan was used for attenuation correction of the emission data. The stress study was performed after 4 min of dipyridamole infusion (approximately 0.142 mg/min/kg was infused for 4 minutes (total 0.56 mg/kg)). Typically, there was no more than 5-10 minutes between the emission and transmission scans, resulting in a total study time for a patient of about one hour.

In order to obtain image datasets for VOI definition, emission data were summed over the final thirteen frames (4.5 minutes) (Figure. 3b). By this time, injected activity had substantially cleared the blood so that the myocardium was more clearly delineated. Each study resulted in three 47-plane reconstructed volume datasets: a rest emission, a stress emission, and a transmission image dataset. Each cardiac study done on the ECAT scanner results in two 191 Mbyte emission sinogram files, one 6 Mbyte transmission file and 18 Mbyte of calibration data. These raw data are reconstructed into three 128x128x47 voxel image

datasets.

The first part of the data reduction is to segment the entire left ventricular myocardium and specify physiologically meaningful VOIs over this portion of the dataset. Though many have proposed automated techniques to achieve this purpose [6-9], we have found that the most reliable method of specifying these regions combines reslicing the image data into the short axis orientation and manually drawing a set of 2D regions (Figure 3c,d). These regions are subsequently tiled together to form a 3D surface model (Figure 3e) which can then be manipulated into the final VOI configuration. The second part of the analysis is to combine the set of VOIs with the raw sinogram data (Figure 3f) and accurately quantify the activity values and their uncertainty, compensating for the effects of patient motion and other factors while doing so. Results of the VOI quantitation (Figure 3g) are then used in a kinetic compartmental modeling program to produce physiological flow parameters and create diagrams showing changes in flow before and after stress (Figure 3h). Availability of time activity curve uncertainties enables confidence measures to be applied to the resulting model parameters.

The important details of the steps shown in Figure 3 are explained below.

Image Reslicing

Direct plane images reconstructed on the ECAT scanner are constrained by the tomograph geometry to an orientation perpendicular to the bed axis. Rather than working directly with these transverse planes, we reorient the myocardium to allow evaluation of short axis slices of the myocardium. In this orientation, the original 47 transverse images are resliced into another set of parallel image planes so that the somewhat cylindrical walls of the left ventricle appear as a stack of concentric rings. Consequently, the myocardial geometry is not only more intuitive to visualize, but the short axis slice orientation simplifies the task of drawing a set of 2D regions delineating the epicardial and endocardial boundaries.

A modified version of the VIDA oblique reslicing module [10] is used to obtain these short axis slices. The reslicing module allows a user to quickly rotate a slicing plane and systematically obtain a standard short axis orientation (Figure 4). When this orientation is found in the reslicing module, a resliced image volume is saved to disk and a description of the reslicing parameters is recorded for later use. VIDA's reslicing module employs a trilinear interpolation scheme to produce output slices that appear smooth regardless of the slicing orientation. Although this interpolation scheme induces a low pass filtering of the image dataset, the filtering does not appear to impair the visual detection of object boundaries.

Volume-of-Interest Generation

Once a preferred oblique slicing direction is selected, 3D VOIs may be defined. For compartmental analysis of the heart, we choose to divide the cardiac dataset into 17 subregions or volumes of interest. The myocardium is split into eight wedges which are then split again in half, resulting in 16 myocardial regions. A single region is also drawn inside the left ventricle towards the base of the heart. This region is used for the activity in the blood pool tracer input function. By subdividing the time-varying heart in this manner, we arrive at a set of regions large enough for statistical significance with a spatial orientation such that they can be easily related to the physiology. Specification of the complete VOI set involves the following steps: drawing a set of 2D epicardial and endocardial contours on a stack of parallel image planes, tiling together the contours to form a triangular mesh surface, and finally subdividing and further manipulating the surface model in 3D to define the final set of 17 VOIs. Freehand spline-based regions are drawn on the epicardial and endocardial boundaries of the short-axis myocardial display (Figure 5). Typically, these 2D regions are drawn on every slice comprising the myocardium (though the tiling software does not require a region on every slice). To aid in 3D visualization of the data while drawing, auxiliary images show the perpendicular long-axis views and the projection of the drawing cursor position on these planes. The user can also display the intersection of the set of regions with the long axis views (Figure 5c).

After a set of 2D regions have been drawn, they are saved to disk. The 2D regions are then tiled together to form a 3D closed surface model. For the relatively simple geometry of the short-axis myocardium, an optimized version of Fuchs' graph searching algorithm [11, 12] was used.

A surface boundary representation known as the winged-edge data structure is used to organize the list of tiled triangular faces of the surface model into a format describing the adjacency information of the models vertices, faces and edges [13]. This data structure facilitates manipulation of the model into the final set of VOIs by allowing searches of adjacent features in linear time. Generally, three classes of manipulations used to obtain this final set include subdivision, deletion, and coordinate transformations.

Users can specify any number of dividing planes to subdivide a VOI. Because of the winged-edge data description of the model, operations like these can be performed quickly. Once divided, the new set of VOIs can be individually selected and further manipulated. Other manipulations which do not induce a topology change of the VOI are also possible, such as interactive scaling, rotation and translation. An interface has been developed for this purpose based upon the Open Inventor 3D Tool kit (Figure 6) [14].

VOI Transformation into Tomograph Coordinates

Coordinate transformations are required to transform a set of VOIs from one slicing orientation to another. Each time a volume is resliced the reference frame changes so a coordinate transformation is required. We record enough information after each reslicing to calculate a 4x4 transformation matrix describing the transformation in homogeneous coordinates. Multiplication of each VOI coordinate by a single 4x4 matrix is all that is required to transform the VOI, regardless of the number of reslicing transformations that the matrix represents. Similarly, when VOIs are obtained by drawing on images from a different modality, a 4x4 transformation matrix describing the registration between the two volumes is all that is required to appropriately transform the VOI.

Another operation which can be quickly calculated as a result of the winged edge representation is the 2D intersection that a VOI makes with any arbitrary set of parallel slicing planes. In this process, VOI edges

are successively checked for intersections with each slicing plane. When an intersection is found, the adjacency relationships of the winged edge structure are used to follow the intersections of that plane from face to face until the intersections loop back to the original edge. The resulting list of points is a 2D contour outlining the VOI boundary in that slicing plane. This function is essential for projecting the VOIs back onto the original transverse tomograph planes during the quantitation step.

Correction for Patient Motion

Misregistrations due to patient motion are often present between emission and transmission scans in a cardiac PET study. Though perhaps acceptable in qualitative analysis of the data, the misalignment cannot be ignored if quantitative results are desired. Using in-house software modeled after the MPM package (Multi-Purpose Match), [15], we measured and corrected the misregistration between the three image datasets in each study. Transaxial images were reformatted in coronal and sagittal planes, and the three sets of views were used to manually align the data. Registration utilized only three translation degrees of freedom (x,y,z) and one rotational degree of freedom about the long axis of the tomograph.

Two observers independently registered transmission data with the summed emission datasets in 16 dynamic Rb-82 cardiac PET studies. As a check of consistency, the summed emission data were also registered with one another. The transmission images contained a full field-of-view, while the field-of-view of the emission images focused just on the heart. The emission data were corrected for attenuation using the registered measured transmission data. Between rest and transmission scans, the two observers found average translational motion of 9.0 ± 3.4 and 10.4 ± 3.3 mm, primarily in the superior/inferior and left/right directions along the tomograph bed. Between transmission and stress scans the average motion was 8.2 ± 5.3 and 8.9 ± 3.9 mm.

Registration parameters are stored as a transformation matrix after each alignment was performed. These parameters are later used to correct for the misalignment while quantifying dynamic emission data in a VOI analysis. The constraint to four of the six possible degrees of freedom in the registration enabled a very efficient implementation of computing a corrected VOI analysis directly from the emission and transmission sinograms.

Extraction of Time-activity Functions

After a set of VOIs has been appropriately defined in the coordinate system of the tomograph, they are used for quantitation. The usual method is integrating over each region on each reconstructed slice and thereafter summing the regions belonging to a particular volume at each time point. There are a number of disadvantages to this approach. First, summing voxel values requires that each time frame must be separately reconstructed into its own image volume dataset, a process that requires considerable computer processing time and disk space. Second, a decision must be made on how to deal with fractional voxels, i.e. those voxels straddling a region boundary, a factor which complicates the VOI calculation. Finally, the primary disadvantage of the voxel based approach is that it makes it impossible to obtain the uncertainty of each VOI value and its correlation with other VOI values. The method used here is to determine the activity in each volume for each time point by projecting each VOI into the tomograph's sinogram space. There, the uncertainty values of each projection bin can be accurately modeled and propagated through the entire VOI activity calculation. The sequence of steps is shown below (Figure 7).

One other advantage of this quantitation method for each VOI is that its coordinate description is no longer tied to the concept of a pixel or a voxel. Since the summing of activity occurs in the projection space, voxel discretation is not a problem. Additionally, even if data were acquired three dimensionally on the scanner (as opposed to the 2D slice-oriented acquisition), the quantitation of the VOI would proceed as before. The only difference is that the projection of each VOI would have to be obtained for all projection angles, instead of those oriented in just the direct transverse planes of the tomograph.

Kinetic Modeling and Determination of Model Parameters

The time activity curves for the myocardial regions and the blood obtained after the VOI quantitation step (Figure 3g) are used to derive meaningful physiologic parameters drawn from a compartment model. Figure 8 shows a three-compartment physiological model representing the behavior of Rb-82 transport in each myocardial VOI. The input function, $u(t)$ consists of plasma concentration of Rb-82. This input

function is obtained from the blood pool VOI time activity curve. Transfer rates between compartments are expressed in terms of blood flow (F), permeability surface products (PS) for two physiological barriers, volumes (V_i) of the interstitial and capillary spaces, and the apparent volume of distribution (V_3) of Rb-82 in the intracellular space. Unfortunately, because PET data are subject to numerous sources of noise, (e.g. tomograph count rate limitations, scattered emissions and positron range), it is not always feasible to estimate all of the parameters of this model. For this reason, a simplified model is often used which lumps the parameters into a simpler subset. For example, a one-compartment model combines all the parameters into two, the uptake rate and the washout rate, and is judged suitable for our analysis [11].

RESULTS

The major results of this work are the development of methods described above. These methods were applied to a clinical evaluation of 22 patients most of whom had coronary artery disease. Each patient had 16 volumes of interest evaluated for perfusion before and during dipyridamole infusion. A plot of the fitted values of Rb-82 uptake for the rest and stress conditions over eight contiguous regions in the myocardium for one patient is shown in Figure 3g. The graphs of flow for rest and stress are shown in Figure 3h. Comparing the rest and stress conditions in this manner gives one a clearer indication of the myocardial regions which lack reserve capacity than can be obtained by viewing the reconstructed static images alone. The comparison of angiographic data to the flow change data will be reported elsewhere.

CONCLUDING REMARKS

The implementation of volume of interest analysis methods commencing from the completion of endo and epicardial contouring (segmentation) (Figure 3d), has been fully automated to the point of parameter presentation as in Figure 3h. Practical segmentation remains one important issue and vigorous activity to develop convenient methods is underway. Whereas some human involvement in the segmentation process is expected to be required, new methods have promise of reducing the requirement of placing 3 contours on 15 short axis images to one of editing automatically placed contours using a combination of transmission and blood pool information. These methods developed for PET are applicable to SPECT and MRI.

Acknowledgment

We thank Dr. Kathleen M. Brennan for aid in illustrations and manuscript preparation. This work was supported in part by the National Heart, Lung and Blood Institute of the U.S. Department of Health and Human Services under grant HL25840-12A1 and in part by the Director, Office of Energy Research, Office of Health and Environmental Research, Medical Applications and Biophysical Research Division of the U.S. Department of Energy under Contract no. DE-AC03-76SF00098.

REFERENCES

- [1] Budinger TF, Greenberg WL, Derenzo SE, Gullberg GT and Huesman RH. Quantitative Potentials of Dynamic Emission Computed Tomography. *J Nucl Med* 1978; 19: 309-315.
- [2] Hutchins GD, Carache JM and Raylman RR. A region of interest strategy for minimizing resolution distortions in quantitative myocardial PET studies. *J Nucl Med* 1992; 33: 1243-50.
- [3] Gewirtz H, Fischman AJ, Abraham S, Gilson M, Strauss HW and Alpert NM. Positron emission tomographic measurements of absolute regional myocardial blood flow permits identification of nonviable myocardium in patients with chronic myocardial infarction. *J Amer Coll Cardiol* 1994; 23: 851-9.
- [4] Gullberg GT, Zeng GL, Datz FL, Christian PE, Tung CH and Morgan HT. Review of convergent beam tomography in single photon emission computed tomography. *Phys Med Biol* 1992; 37: 507-34.
- [5] Wienhard K, Dahlborn M, Eriksson L, et al. The ECAT EXACT HR: performance of a new high resolution positron scanner. *Journal of Computer Assisted Tomography* 1994; 18: 110-118.
- [6] Manhaeghe C, Lemahieu I, Vogelaers D and Colardyn F. Automated initial estimation of the left ventricular myocardial midwall in emission tomograms using kohonen maps. *IEEE Transactions on Pattern Analysis and Machine Intelligence* 1994; 16: 259-265.
- [7] Nuyts J, Suetens P, Oosterlinck A, De Roo M and Mortelmans L. Delineation of ECT images using global constraints and dynamic programming. *IEEE Transactions on Medical Imaging* 1991; 10: 489-498.
- [8] Muzik O, Beanlands R, Wolfe E, Hutchins G and Schwaiger M. Automated region definition for cardiac nitrogen-13-ammonia PET imaging. *The Journal of Nuclear Medicine* 1992; 34: 336-344.
- [9] Davis M, Rezaic B and Weiland F. Assessment of left ventricular ejection fraction from technetium-99m-methoxy isobutyl isonitrile multiple-gated radionuclide angiocardiology. *IEEE Transactions on Medical Imaging* 1993; 12: 189-199.
- [10] Hoffman E, Gnanaprakasam D, Gupta K, Hoford J, Kugelmass S and Kulwiec R. VIDA: an environment for multidimensional image display and analysis. *SPIE Proceedings* 1992; 1660: 694-711.

- [11] Coxson PG, Huesman RH, Sim S, Klein GJ, Reutter BW, and Budinger TF. Comparison of kinetic models for data from a positron emission tomograph Proceedings of The Medical Imaging 1995: Physiology and Function from Multidimensional Images, 224-234, [Edited by E. A. Hoffman], San Diego, CA, 1995.
- [12] Fuchs H, Kedem ZM and Uselton SP. Optimal surface reconstruction from planar contours. *Communications of the ACM* 1977; 20: 693-702.
- [13] Baumgart B. Winged-edge polyhedron representation. Stanford Artificial Intelligence Report No. CS-230, 1972, Pages.
- [14] Wernecke J. The Inventor Mentor: Programming Object-Oriented 3D Graphics with Open Inventor, release 2. Reading, Mass.: Addison-Wesley, 1994.
- [15] Pietrzyk U. A rapid three-dimensional visualisation technique to evaluate function in relation to anatomy of the human cortex. Proceedings of The Nuclear Science Symposium and Medical Imaging Conference, 1810-1812, 1993.

Figure Captions

Figure 1. Cardiac PET Images. Twenty of 47 transverse slices through the thorax are simultaneously acquired as dynamic emission data on a Siemens/CTI ECAT EXACT HR scanner.

Figure 2. Region of Interest Strategies. Three methods of defining regions of interest in the left myocardium are illustrated. A single-slice approach (2a,b) provides insufficient statistics for kinetic modeling. An objective method to obtain larger, yet physiologically valid 3D regions (2c) is needed.

Figure 3. Quantitation Summary. Dynamic emission PET data are acquired (2a), summed and reconstruction into a 47-slice image volume (2b). Transverse images are resliced (2c,2d) into the short axis orientation where a set of 3D VOIs are manually specified (2e). Quantitative time activity curves (2g) are obtained by projecting the VOIs into the raw sinogram space of the tomograph and combining them with the dynamic emission sinograms (2f). Compartmental models are applied to obtain physiological parameters which can be plotted in an intuitive manner (2h).

Figure 4. Short Axis Reslicing. Summed emission images are resliced from the original transverse orientation (4a) into the short axis orientation (4b). A cube schematically showing the orientation of a central slicing plane guides the user as they manually obtain the standard short axis orientation.

Figure 5. Region Drawing Environment. Regions are manually drawn on short axis slices (5a) indicating the endo and epicardial boundaries as well as the region used for the input function in the blood pool. To guide the user through the 3D dataset, auxiliary views of long axis projections (5b,5c) are used which show the 3D cursor position and the intersection of other slice regions with that projection(5c)

Figure 6. VOI 3D Manipulation. A segmented surface representing the myocardial boundary is manipulated into the final VOI set using interactive subdivision and other surface transformations.

Figure 7. VOI quantitation. Activity from a VOI slice is evaluated by projecting the uniformly weighted region at each angle. The projected region is convolved, and a vector inner product is formed with the raw tomographic data set. Activity from all slices of the VOI are summed to obtain the composite activity at a single time point for that volume.

Figure 8. Physiological Three-Compartmental Model of Rb-82 in the Myocardium. Model parameters are PS_{cap} and PS_{cell} , permeability surface products for the capillary and cell walls, fractional volumes (V_i) of the spatial compartments, and specific volume blood flow (F).

Figure 1

a)

Human Judgment

b)

Chain of Circular Regions

c)

Barrel Slats

Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

XBL838-3969

Figure 7

Figure 8

LAWRENCE BERKELEY LABORATORY
UNIVERSITY OF CALIFORNIA
TECHNICAL INFORMATION DEPARTMENT
BERKELEY, CALIFORNIA 94720