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A NEW TECHNIQUE FOR RECONSTRUCTING POSITRON EMISSION TOMOGRAPHY DATASETS FROM ROTATING SCANNERS

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Introduction: The positron emission tomography (PET) image reconstruction can be formulated as an equation system where each element of a system response matrix (SRM) represents the probability of detecting in every line of response (LOR) an annihilation event emitted from every voxel of the image volume. In the case of scanners based on pairs of opposite detectors fixed in a rotating gantry this SRM can be decomposed into a projection and rotating components. In this work we propose a new strategy to invert the SRM. Material and Methods: The reconstruction strategy is based on separating the process into two steps: 1) the projection part is solved using the pseudo-inverse of the projection component and then 2) this estimated image is rotated and added to the final image. This strategy reduces the computation requirements to invert the complete SRM, maintaining 3-D information. This new reconstruction was tested with real data from a hot Derenzo-like phantom and data from a mouse study (20-40 g), acquired in list mode during continuous rotation of the gantry. The data were organized as a histogram of LORs' with an angular binning of 1º, covering 180º. Results: Our reconstruction achieved results visually indistinguishable from those obtained by 3-D-OSEM, while reducing by a factor of two the computation time. Moreover, the pseudo-inverse strategy permits a finer control of the noise level in the final reconstructed image. Conclusion: Our method represents an intermediate solution between the speed of analytical algorithms and the quality of standard iterative reconstruction applied to rotating PET scanners.

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TEMPORAL ASPECTS OF KINETIC PARAMETER ESTIMATION USING LIST-MODE AND HISTOGRAM DATA

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Background: This work is concerned with dynamic positron emission tomography (PET) reconstruction along the lines proposed by Nichols (TMI,2002) and Kamasak (TMI,2005). In the former case, spatial time activity curves are characterised by B-spline coefficients estimated directly from list-mode data. In the latter, histogram (hist-mode) data are used to reconstruct compartment model rate constants. Methods: We propose an alternative approach in which rate constants are directly reconstructed from either list-mode or hist-mode data, based on the observation that emissions originating from each contributing exponential-mode in the compartment model are independent and identically distributed samples drawn from an inhomogeneous Poisson distribution, as suggested by Snyder (TMI,1984). Specifically, we concentrate on the temporal aspects of the problem by making the simplifying assumption that photon pairs are detected directly and study the bias and covariance properties of the resulting estimator. We have developed an approximation formula for the covariance of the fitted parameters for 1- and 2-compartment models under the assumption of an unbiased estimator for both hist- and list-mode and compared the results to multiple realizations of simulated data. Results: Experimental data were simulated using count levels ranging from 100 to 2,200 counts, and rate constants typical of metastatic colorectal cancer and brain glioma 2-deoxy-2-[F-18]fluoro-D-glucose human PET uptake. Comparison of covariance between hist- and list-mode implementations indicates a small loss of information through temporal binning, whilst variance and count level were seen to be correlated. Conclusions: Estimation of kinetic parameters from list-mode data is theoretically achievable and covariance in parameter estimates can be usefully predicted.

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COMPARISON OF BOOTSTRAP METHODS APPLIED TO POSITRON EMISSION TOMOGRAPHY DATA FOR IMAGE NOISE ESTIMATION

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Overview: Assessing the reliability of data measurement is an important challenge in quantitative data analysis. A number of bootstrap re-sampling methods have been proposed for estimating regional noise in reconstructed images from a single measurement. This study compares four methods to assess the accuracy with which they predict noise properties of the data. Theory: A natural approach to applying the bootstrap method to positron emission tomography (PET) data consists of forming multiple realizations by drawing random events from a list-mode data-set (method-A). This is theoretically grounded but often inconvenient. An alternative approach consists of temporally dividing the sinogram into sub-sinograms and drawing rows from this population (method-B). We have extended it to the cases where entire sub-sinograms and where single pixels are drawn (methods-C, D). Methods: A uniform cylinder filled with Germanium[68] was imaged for five minutes on a microPET-R4. 500 list-mode replicates were generated (method-A), then histogrammed using 3-D-binning. The original list-mode data were binned and re-sampled into 500 sinograms, according to each of methods B, C and D. All four methods were compared in sinogram space according to various figures of merit including comparison of covariance, and chi^2 tests to assess goodness of fit to different distributions. Results: All methods produced Poisson distributed bins. Sinogram-based methods were found to yield significantly lower mean values than the list-mode approach. Moreover, method B introduced artificial correlations in the sinogram. These discrepancies in the estimation of noise properties indicate that sinogram-based methods should be used with caution, and list-mode methods used when practical.

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A NOVEL PLASMID VECTOR FOR POSITRON EMISSION TOMOGRAPHY IMAGING OF THE BALANCED REPORTER-THEREPEUTIC LINKED *EX VIVO* CARIDAC TRAANSGENE EXPRESSION IN LARGE ANIMAL HEARTS

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Previously we have shown the feasibility of noninvasively monitoring *ex vivo* delivered therapeutic cardiac transgene expression in the whole heart of large animals by positron emission tomography (PET) imaging a co-transfected reporter gene that were contained in two separate plasmids. To achieve more balanced reporter and therapeutic transgene expression, recently, we constructed two new plasmid vectors. Plasmid I (PI) contains a herpes simplex virus type 1 mutant thymidine kinase (sr39tk) as the reporter gene and a recombinant human interleukin-10 (hIL-10), an immunosuppressive cytokine as the therapeutic gene driven by two identical CMV promoters. Plasmid II (PII) contains a CMV promoter-driven reporter gene and a SV40 promoter-driven therapeutic gene. Twenty-three rabbits underwent heterotopic functional cervical heart transplantation. Plasmids were complexed with liposome, then *ex vivo* intracoronarally delivered into the donor hearts before implantation. In donor hearts treated with PI, the gene transfer efficiency was similar for reporter and therapeutic genes (15±2% vs. 15±2%). However, the efficiency for reporter gene was significantly higher than therapeutic gene (15±2% vs. 12±2%, $p<0.05$) In PII group. A significant correlation was observed between the expression of sr39tk gene and the total myocardial [F-18]-FHBG accumulation quantified in percent of intravenously injected [F-18]-FHBG dose in both groups ($p<0.001$). In PI group, the correlations between hIL-10 and sr39tk gene expression, and hIL-10 expression and activity of [F-18]-FHBG were significantly higher than that in PII group. We concluded that two identical promoters driven reporter and therapeutic