Introduction

Spectral Analysis Iterative Filter (SAIF) is an input/output model based on a modification of the original Spectral Analysis (SA) method. SAIF was developed for quantifying rates of cerebral protein synthesis (rCPS) at both ROI and voxel levels in L-[1-13C]Leucine PET studies [1-2]. SAIF implements a filtering procedure that optimizes estimation of irreversible uptake of tracer in tissue (Ki, ml/g/min), transport of tracer from plasma to tissue (Kj, ml/min/g), apparent distribution volume of tracer (Vtr, ml/cm³). As with other SA techniques, SAIF provides useful information about tracer kinetics without assuming a specific compartmental model.

Aim of the study

In this work we examined the applicability of SAIF for voxel-wise quantification of several PET tracers with irreversible uptake by comparing its results with those provided by gold standard quantification methods.

Materials and methods

Spectral Analysis for PET quantification

With SA the total concentration of tracer in the field of view of the PET camera is modeled as:

\[ C_S(t) = (1-v_b) \left[ a_0 \frac{d}{dt} C_P(t) + \sum_{i=1}^{n} a_i \frac{d}{dt} C_P(t) e^{-\beta_i (t-t_i)} \right] + v_b C_P(t) \]

\[ \text{Legend:} \quad C_S(t) = \text{total measured activity} \quad C_P(t) = \text{parent plasma time activity curve} \quad C_P(t) = \text{whole blood time activity curve} \quad v_b = \text{blood volume fraction} \]

VARIABLES OF THE MODEL: v_b, v_s, estimated by non-negative linear least squares.

Characteristics
- Data Driven Quantification Method
- Based on single-input single-output model
- Quantification performed using weighted non negative least squares
- Applicable to homogeneous as well as to the heterogeneous tissues without any a priori assumptions

Limitations
- Sensitive to the presence of noise in data (unfeasible for analysis at the voxel level)
- Required a grid of components defined a priori

Settings
- Number of component: 100; Beta_min 0.001 min⁻¹; Beta_max 1 min⁻¹

Spectral Analysis with Iterative Filter

Characteristics
- Same model as standard SA;
- Based on a passband filter which iteratively corrects the SA estimated spectrum;
- Number of iterations driven by weighted residual sum of squares (WRSS);
- Optimized for the estimation of trapping (Ki) and the weighted average influx rate (Kj) constants in irreversible tracer.

Limitations
- Passband interval defined a priori

Settings
- Number of component: 100; Beta_min 0.001 min⁻¹; Beta_max 1 min⁻¹
- Passband for L-[1-13C]Leucine: [0.03; 0.3] min⁻¹
- Passband for [11C]CH442416: [0.1; 1] min⁻¹
- Passband for [18F]FDG: [0.02; 0.5] min⁻¹

Dataset

Three datasets were analyzed: L-[1-13C]Leucine [2] (6 subjects), [11C]CH442416 [3] (5 subjects) and [18F]FDG [4] (1 subject). Voxel-wise analysis was performed with SAIF and unfiltered SA, and results compared to other voxel-wise methods: a Basis-Function-Method (BFM) that assumes a homogenous tissue kinetic model for L-[1-13C]Leucine, and Patlak analysis applied to a two tissue compartment model for [11C]CH442416, and a Patlak plot for [18F]FDG. Relative differences between methods of voxel estimates were evaluated for the principal parameters of interest: rCPS (L-[1-13C]Leucine), Vm (L-[11C]CH442416), and K (18F)FDG.

Results

Discussion

Analysis of L-[1-13C]Leucine data showed very good agreement between SAIF and BFM: relative differences in rCPS voxel estimates in a representative subject were 5%-24% (mean=SD). Means of all voxels within a ROI determined with SAIF and BFM were highly correlated. Unfiltered SA estimates were not in the physiological range and excluded from further analysis. With [11C]CH442416, high correlation and limited relative differences in Vm across ROIs (+2%-4%) were detected between WNLLS and SAIF. Unfiltered SA did not provide reliable estimates (Vm, mean±SD 6.6±1.2%). For all tracers SAIF provided high quality parametric maps consistent with those of their respective reference methods.

Conclusions

For all our analysis SAIF results were in good agreement with reference voxel analytic methods and better than results based on unfiltered SA. SAIF was shown to be adaptable for analysis of different irreversibly trapped tracers without requiring a specific compartmental model. Unlike Patlak analysis, SAIF provides a complete description of both reversible and irreversible tracer kinetic components. SAIF, therefore, represents a robust and valid alternative for voxel analysis of PET tracers with irreversible uptake. Note that the choices for the beta grid as well as for the passband are fundamental for a correct and reliable data quantification.

References


Contact information:
Mattia Veronese PhD Student
via Gradennig 6/B Padova Italy
mattiaveronese@gmail.com
Phone: +39 049 827 7640