Non-invasive Estimation of Metabolic Uptake Rate of Glucose using F18-FDG PET and Linear Transformation of Outputs

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Abstract: For quantitative analysis and kinetic modeling of dynamic PET-data an input function is needed. Normally this is obtained by arterial blood sampling, potentially an unpleasant experience for the patient and laborious for the staff. Aim: To validate methods for determination of the metabolic uptake rate (Km) of glucose from dynamic FDG-PET scans using Image Derived Input Functions (IDIF) without blood sampling. Method: We performed 24 dynamic FDG-PET scans of the thigh of 14 healthy young male volunteers during a hyperinsulinemic isoglycemic clamp. Ten of the subjects were scanned twice 11 weeks apart and all with concurrent Arterial Blood Sampling (ABS). We proceeded to evaluate different earlier proposed methods as well as several new ones based on Archetypal Analysis for generating IDIFs. Comparison of the methods was based on the sets of Km-values generated for each scan from Patlak plots based on one common tissue curve against all the IDIFs. When compared to ABS Km values, an underestimation was found for all methods. Using ordinary least squares estimation on the ABS Km values vs. the IDIF Km a calibration factor and term was identified for each method and used for transformation. The Mean Squared Error (MSE) was determined for the different methods before transformation, and estimated by N-fold cross validation and .632+ bootstrapping after transformation. Further, since ordinary least squares is an unbiased estimator we could use the estimated MSE to determine the standard deviation of the different unbiased methods after transformation using the relation MSE(θ) = variance(θ)+bias(θ)^2. Results: All methods performed poorly before transformation, except one described by Backes et al.. After transformation all methods yields unbiased Km based on the IDIF alone but have different standard deviations with the best method-Parker and Feng- at 0.0030 i. e. around 10 %. Conclusion: Based on this study, we can estimate the metabolic uptake rate of glucose with good accuracy and precision in similar future studies without blood sampling. Given the high variance of the femoral artery diameter in the material, the method should also be applicable to women and people of other ages, but used with caution in the elderly due to variance in intramuscular adipose distribution. If only Km and no other kinetic parameters are needed, the described method with transformation of the results based on ordinary least squares, gives unbiased low variance results without arterial blood sampling and it has the potential for use in other regions of the body.