Interstitial Space Properties of ^{18}F-fluorodeoxyglucose in Nonalcoholic Fatty Liver Disease

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Objective: Interstitial space is the fluid space surrounding tissue cells. Transport and uptake properties of the radiotracer ^{18}F-fluorodeoxyglucose (FDG) in this space may be distinct in health and disease. Conventional dynamic PET imaging cannot decode this space due to the limited temporal resolution (10-20s/frame). Here we demonstrate the use of high-temporal resolution (2s/frame) dynamic imaging and advanced tracer kinetic modeling enabled on the EXPLORER total-body PET system to explicitly characterize the hepatic interstitial space in nonalcoholic fatty liver disease (NAFLD) and healthy subjects.

Method: Fourteen healthy subjects and ten NAFLD patients were included in this study. Both conventional two-tissue (2T) model, which combines the interstitial space and intracellular space into a free-state space compartment, and the proposed three-tissue (3T) model, which separately models the interstitial space, are used to fit liver time activity curves (TACs). To account for the dual blood supply in the liver, an optimization-derived dual-blood input function (DBIF) approach was utilized. Fitting quality of the 2T-DBIF and 3T-DBIF models was compared by the Akaike information criteria (AIC). The kinetic parameter $K_{1,i}$ (rate of FDG transport from plasma to the interstitial space) and V_i (distribution volume of FDG in the interstitial space) were evaluated for detecting nonalcoholic steatohepatitis (NASH), a more severe form of NAFLD that is determined in NAFLD by biopsy using the total NALFD activity score (NAS) greater than 4.

Result: The 3T-DBIF model provided a better fit quality than the conventional 2T-DIBF model (Fig. 1A), as further demonstrated by the negative AIC difference between the two models in both healthy subjects and NAFLD patients (Fig. 1B). The parameter $K_{1,i}$ (Fig. 1C) and V_i (Fig. 1D) differentiated NASH (NAS > 4) from non-NASH subjects (NAFLD with NAS ≤ 4 and healthy subjects).

Conclusion: This study indicates that FDG characterization of the interstitial space has the strong potential to derive multiparametric PET imaging biomarkers to assess NASH in NAFLD.

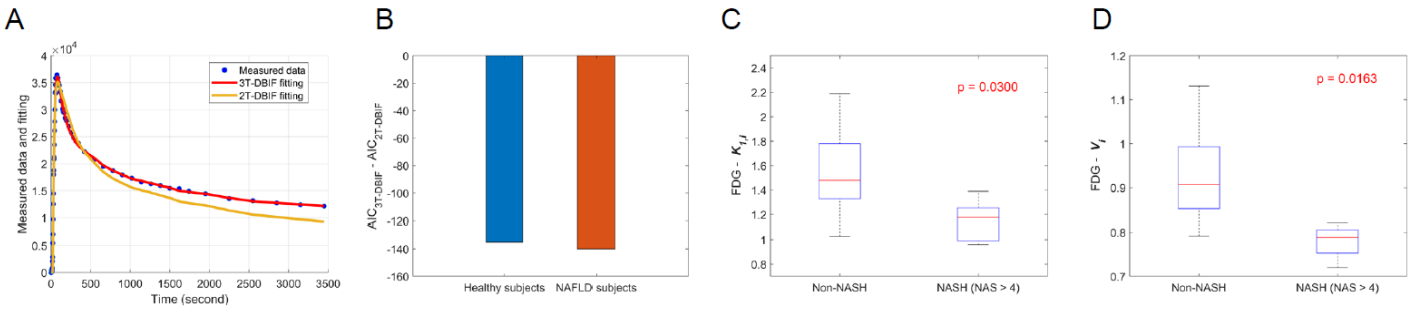

Figure 1. Comparison of 2T-DBIF and 3T-DBIF for fitting liver TACs in NAFLD patients (A). Mean of AIC differences of the two models for all healthy and NAFLD subjects (B). (C-D) NASH subjects (NAS > 4) were associated with lower FDG $K_{1,i}$ (C) and lower V_i (D).