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

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Introduction

- 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).
- In this study 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.

Design

- 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.

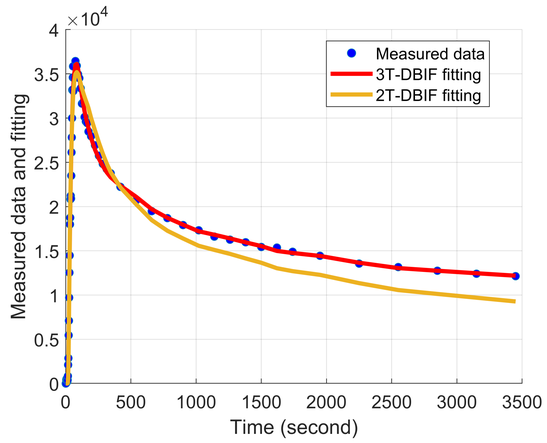
Analysis

- 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.

Results

- 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. 2A) and V_i (Fig. 2B) differentiated NASH (NAS > 4) from non-NASH subjects (NAFLD with NAS <= 4 and healthy subjects).

A



B

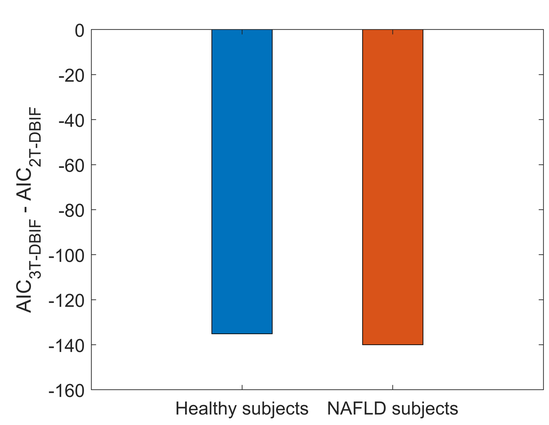
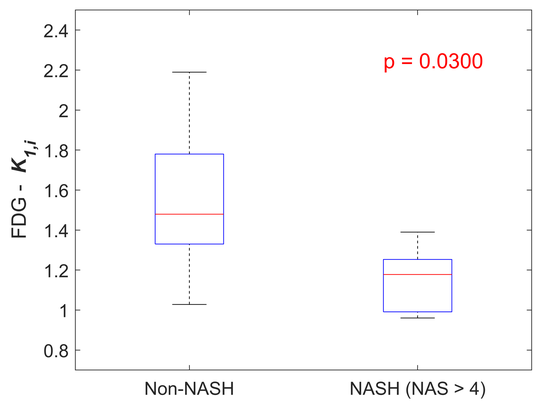


Figure 1: Comparison of 2T-DBIF and 3T-DBIF for fitting liver TACs in NAFLD patients (A). Mean of AIC differences of the two models for all healthy and NAFLD subjects (B).

A



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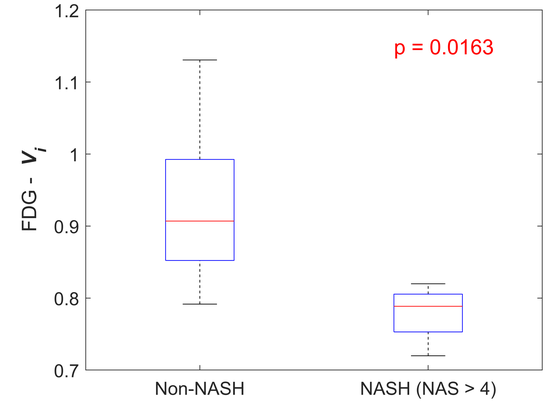

Figure 2: NASH subjects (NAS > 4) were associated with lower FDG $K_{1,i}$ (A) and lower V_i (B).

Summary

- The kinetic modeling of interstitial space (i.e., the three-tissue (3T) compartment model) with dual blood input function in the human liver has been investigated by using high-temporal resolution dynamic FDG-PET imaging available on EXPLORER total-body PET system.
- The 3T model enables the calculation of the distribution volume of the interstitial space V_i that may be distinct in NASH versus non-NASH patients. Furthermore, the 3T model provides an interstitial space-specific transport rate $K_{1,i}$ which can be used as a new biomarker.

Conclusions

- This study explored explicit kinetic modeling of interstitial space in the human liver by using high-temporal resolution dynamic FDG-PET imaging.
- The modeling is better suited as the temporal resolution improves.
- The results indicate that the FDG kinetic characterization of the interstitial space has the strong potential to derive multiparametric PET imaging biomarkers to assess both liver inflammation and liver steatosis in NAFLD.

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