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Application note 016

# Mitochondrial Dysfunction as Assessed by an ABCA2 Breath Test and its Relationship to Liver Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease

Liver fibrosis is caused by non-alcoholic fatty liver disease (NAFLD); the usual way of assessing such damage is via a liver biopsy, which is invasive and an uncomfortable procedure for patients. Mitochondrial dysfunction plays a role in liver fibrosis, so an alternative approach to assessing liver damage is the use of an isotopic breath test with a Sercon ABCA2.

The $^{13}$C-ketoisocaproate ($^{13}$C-KICA) breath test evaluates hepatic mitochondrial function. The aim of this study was to determine associations between the $^{13}$C-KICA breath test and measurement of liver fibrosis.


## Method

52 patients with NAFLD were studied in order to assess their hepatic mitochondrial function using the $^{13}$C-KICA breath test. $\delta^{13}C$ in $CO_2$ in breath was determined by continuous-flow isotope ratio mass spectrometry (CF-IRMS) with a Sercon ABCA2. The mass of C produced was determined by indirect calorimetry. The severity of liver fibrosis was assessed by measuring liver stiffness using transient elastography (FibroScan®).

Breath samples were collected for 1hr during the $^{13}$C-KICA breath test after consuming an oral dose of 1mg/kg [$^{13}$C]-ketoisocaproate ($^{13}$C-KICA). The recovery of $^{13}$C on breath was calculated as the cumulative excretion over the duration of the $^{13}$C-KICA breath test and expressed as percent of $^{13}$C-KICA dose given (cPDR over 1hr).

**Results**

NAFLD patients with significant fibrosis were less able to metabolise $^{13}$C-KICA than those without significant fibrosis (median, range for cumulative PDR over 1hr: 14, 5.3-21% versus 11, 8-20%; p <0.0001 Mann-Whitney test) - **Figure 1**.

Liver stiffness measured by the FibroScan® correlated inversely with $^{13}$C-KICA breath test. NAFLD patients with more severe liver fibrosis (liver stiffness scores >7kPa).

In a regression model that included BMI, MRS % liver fat, ALT, $^{13}$C-KICA breath test and diabetes as explanatory variables, and liver stiffness as the outcome, only the 13C-KICA breath test and ALT were associated with liver stiffness.

Hepatic mitochondrial function is reduced in patients with NAFLD particularly in those with low liver stiffness scores and without significant fibrosis.

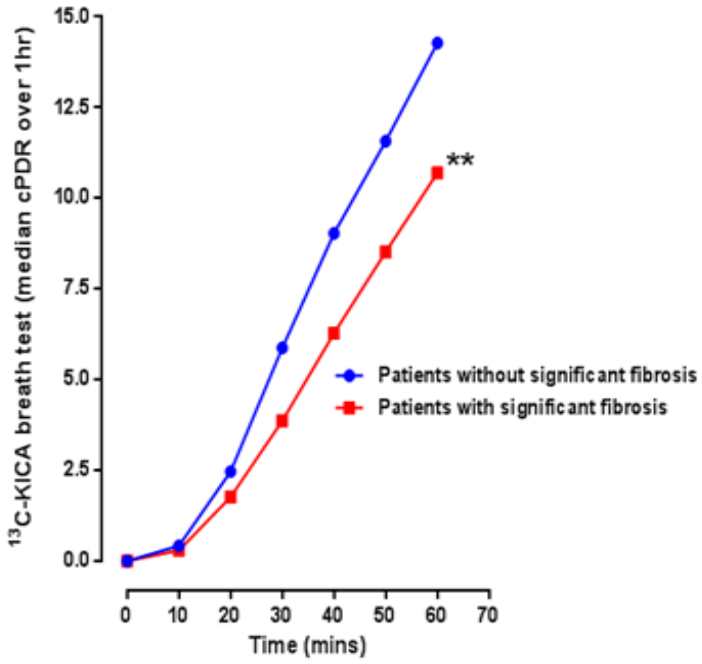


Figure 1. Time course of the recovery of the $^{13}$C on breath ($^{13}$C-KICA breath test) of NAFLD patients expressed as median cumulative percent $^{13}$C-dose recovered over 1hr ** -p<0.05

**This study demonstrates how the ABCA2 can be used in a simple, non-invasive breath test to assess liver damage via hepatic mitochondrial function.**

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