LIBRA®

A non-invasive breath test to measure hepatic metabolic capacity

LIBRA® is a breath test designed to measure liver function for a variety of research applications. It is used to target specific disease-relevant metabolic pathways that can be monitored non-invasively using the breath collection device.

LIBRA measures Exogenous Volatile Organic Compounds (EVOCs) associated with chronic liver disease to evaluate related metabolic alterations. The LIBRA Oral Solution contains the EVOCs, limonene, 2-pentanone, and 2-butanol.

As shown in figure 1, limonene is metabolized by the CYP system, especially by CYP2C9 and CYP2C19. 2-butanol and 2-pentanone are metabolized by alcohol dehydrogenase (ADH).

Alterations in liver function induced by chronic liver disease are reflected in variations in the EVOCs breath profile. Notably, breath limonene showed higher levels in patients with cirrhosis compared to healthy controls (mean and 95% confidence interval).

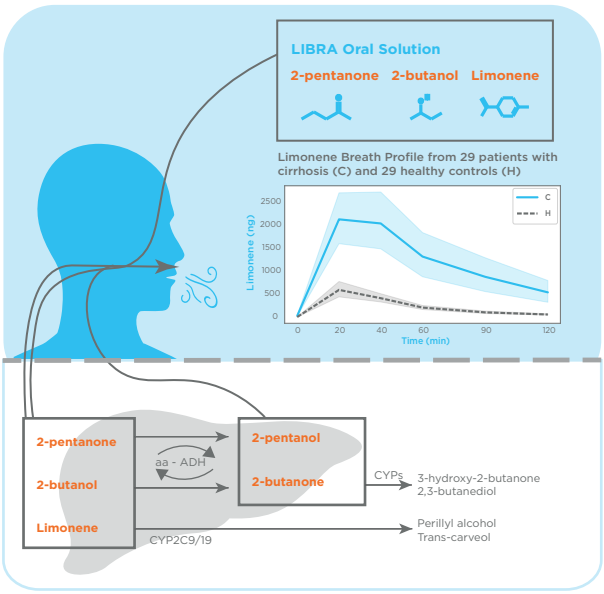
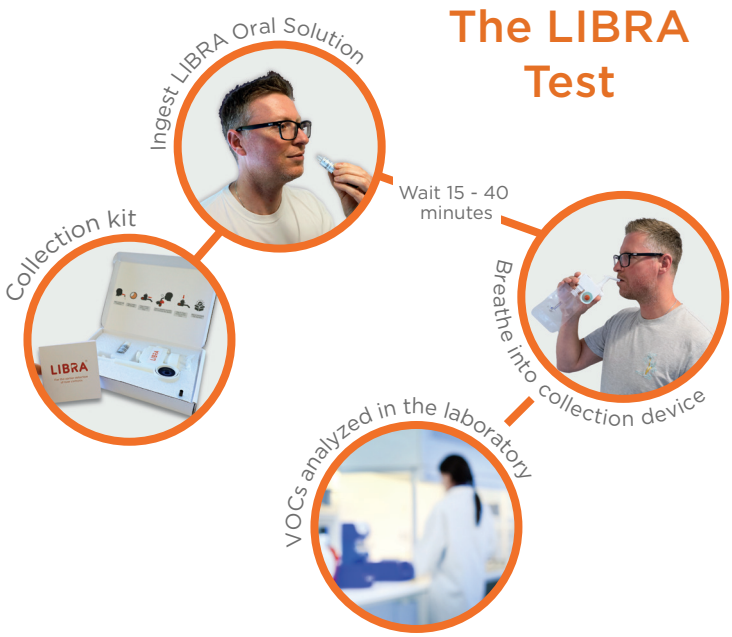


Figure 1: Substrates and bioproducts of the LIBRA Oral Solution



LIBRA Research Applications

Disease Detection

- Cirrhosis
- Portal hypertension
- Chronic liver disease at pre-cirrhotic stages (e.g. MASLD)

Disease Monitoring

- Progression of compensated advanced liver disease
- Assessing liver perfusion vs metabolic function
- Assess hepatic function recovery after liver transplant

Drug Evaluation

- Hepatic metabolic improvements post-treatment
- Evaluate liver function in drug induced liver injury
- Adjusting drug doses in subjects with hepatic impairment
- Assess drug-drug interaction studies

LIBRA® Case Study Examples

Comparing Limonene Breath Profiles in Healthy and Cirrhotic Subjects

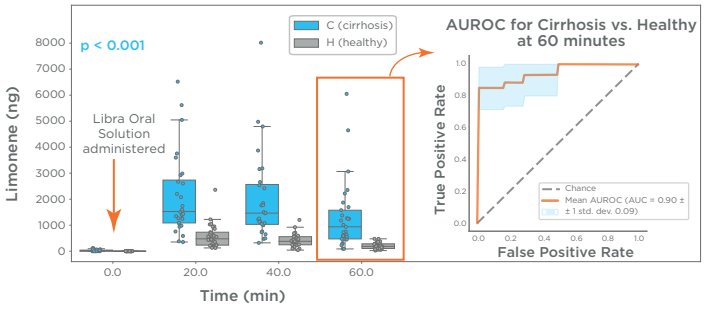


Figure 2: Limonene Breath Profile and Classification Performance. Limonene ingestion elicits a >100-fold spike of breath limonene compared to baseline. The investigated timepoints post-administration showed excellent classification performance. At 60 minutes we measured an area under the roc curve (AUROC) of 0.91, sensitivity of 0.83 ± 0.07, and specificity of 0.9 ± 0.06 (in Ferrandino et al. Biomedicine 2023).

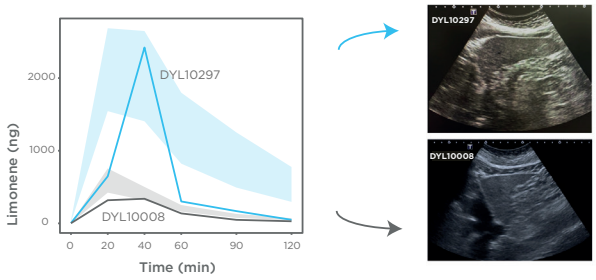
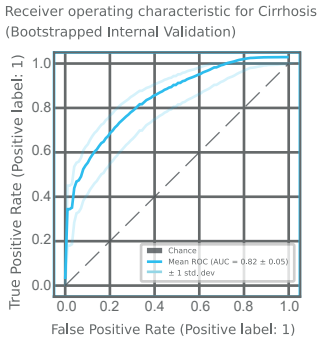


Figure 3: LIBRA test to discriminate subjects with cirrhosis from healthy controls. LIBRA effectively identified subjects who had been incorrectly allocated. Subject DYL10297 was initially recruited as a control but exhibited an abnormal breath profile. A follow-up ultrasound revealed previously unknown liver disease. Similarly, Subject DYL10008, classified in the cirrhosis group based on a three-year-old autoimmune hepatitis diagnosis, displayed a breath profile resembling that of healthy subjects. A further ultrasound confirmed cirrhosis regression, suggesting successful immunosuppressant treatment. These findings highlight LIBRA's potential for both chronic liver disease detection and treatment monitoring.

Detecting Cirrhosis in a High Risk Population

Figure 4: LIBRA classification performance. LIBRA identified subjects with cirrhosis with an area under the curve (AUC) of 0.82, sensitivity of 0.73 and specificity of 0.73 (at Youden index) in a cohort of 147 individuals with risk factor and symptoms of cirrhosis of which 78 were diagnosed with early compensated cirrhosis across Chile, the United Kingdom, and the United States.



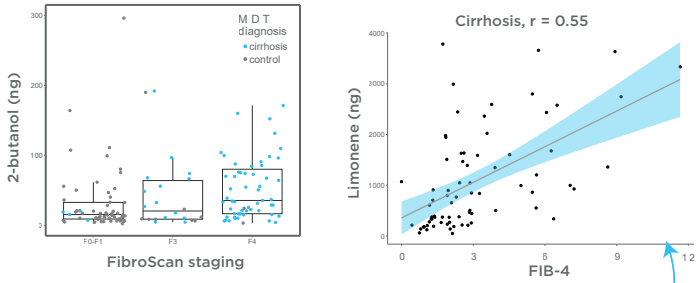


Figure 5: LIBRA in Relation to Other Non-invasive Tests

A progressive increase of EVOCs on breath was observed across the spectrum of liver fibrosis estimated using FibroScan®.

Breath limonene 15 minutes post LIBRA Oral Solution administration showed a correlation with FIB-4 in subjects with cirrhosis.

Limonene is Associated with Signs of Portal Hypertension

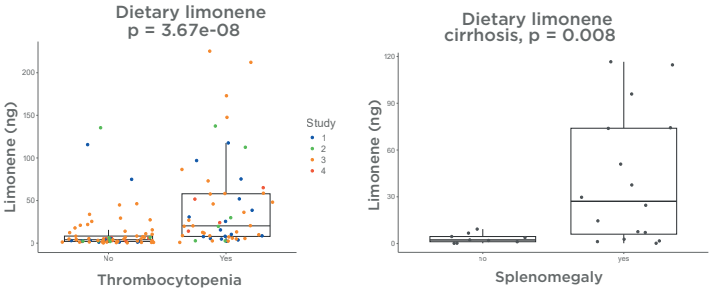


Figure 6: Dietary Limonene and Onset of Portal Hypertension. Left, analysis of 133 cirrhotic patients across four studies revealed higher breath limonene levels derived from dietary exposure in individuals with thrombocytopenia (platelet count <150 × 10^9/L). Right, in an exploratory study of 29 cirrhotic patients, ultrasound evaluation of spleen size showed that those with splenomegaly (spleen >12 cm) exhibited increased breath limonene levels from random dietary exposure. Since thrombocytopenia and splenomegaly are established markers of portal hypertension, these findings suggest LIBRA's potential for longitudinal monitoring, aiding in the early detection of portal hypertension and timely intervention.

Progressive Rise in Limonene through Chronic Liver Disease Spectrum

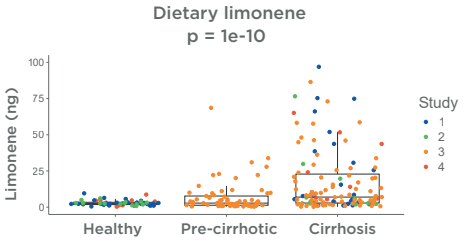


Figure 7 Dietary Limonene in Healthy, Pre-cirrhotic and Cirrhosis Groups. A progressive elevation in breath limonene levels was observed across healthy individuals, pre-cirrhotic patients, and cirrhotic patients. Changes in VOCs are detectable at pre-cirrhotic stages, suggesting early biomarkers for liver dysfunction. The LIBRA test may facilitate early identification of individuals with chronic liver disease before the cirrhosis stage. The progressive nature of VOC alterations could serve for monitoring liver function improvement.

Email us at breathbiopsy@owlstone.co.uk to find out more about incorporating LIBRA into your research.

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