



In the USA, there are more than 50,000 deaths due to liver disease each year. That's more than 137 deaths a day. There has been a four-fold increase in death rates over the last 50 years.



The number of liver disease-related hospital admissions in the USA has increased by 23% from 2012 to 2016, placing an even greater strain on the health service, with >\$30billion/year currently spent on treating liver disease.



Cirrhosis is often asymptomatic with 75% of diagnoses occurring in the emergency room due to the advanced nature of the disease. Treatment options at these later stages can be limited.



Many existing tests have limitations in performance or economics which prevents widescale use in primary care, where the impact of earlier detection of cirrhosis is key.

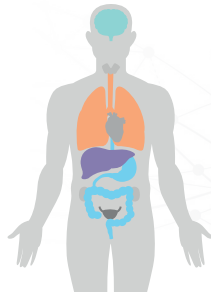
## Our Approach:

EVOC<sup>®</sup>  
Probes

Disease  
Metabolism

Breath  
Biomarkers

Collection  
and Analysis



One or more administered EVOC Probes designed to produce distinctive metabolic products

Metabolic processes characteristic of a disease or phenotype

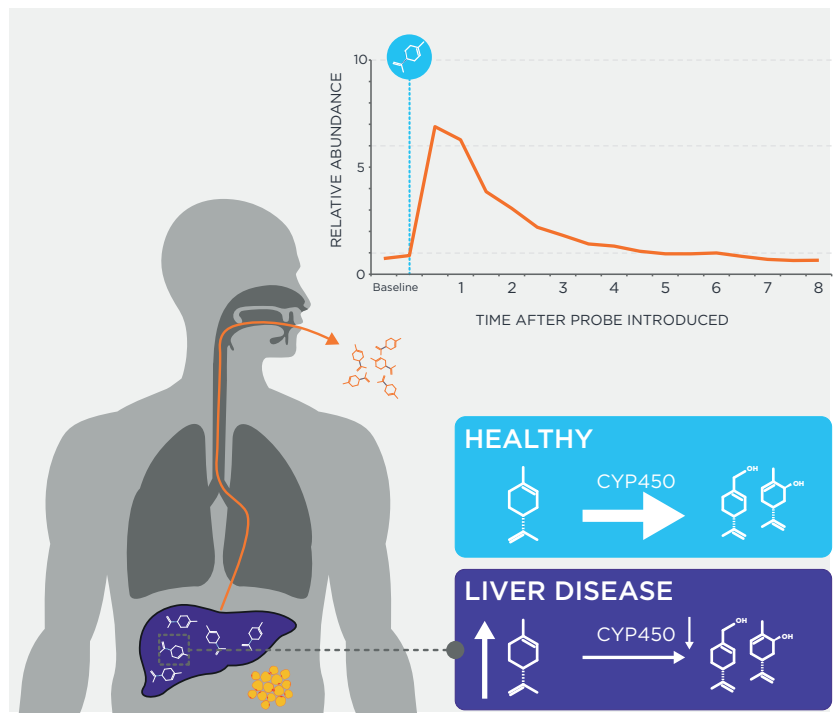
Distinctive metabolic products present in exhaled breath support high signal-to-noise detection

Robust, quantifiable, disease-relevant data and interpretation

## Proof of Concept: Ferrandino et al. (2023)

29 subjects with cirrhosis and 29 controls were enrolled in this study, and breath samples were taken using Breath Biopsy<sup>®</sup> before and at different time points after the administration of 100 mg of limonene. Levels of limonene in the breath samples were measured using our OMNI<sup>®</sup> platform.

The ingestion of 100 mg limonene induced a spike in breath of >100-fold the baseline levels in all subjects. More than 90% of the subjects showed a limonene maximal breath amount (C<sub>max</sub>) within 20 and 40 min (T<sub>max</sub>). The investigated time course in a semi-logarithmic presentation showed single-phase exponential decay of breath limonene with first-order kinetics (R<sup>2</sup> > 0.8) in >90% of the subjects.



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LIBRA<sup>®</sup>



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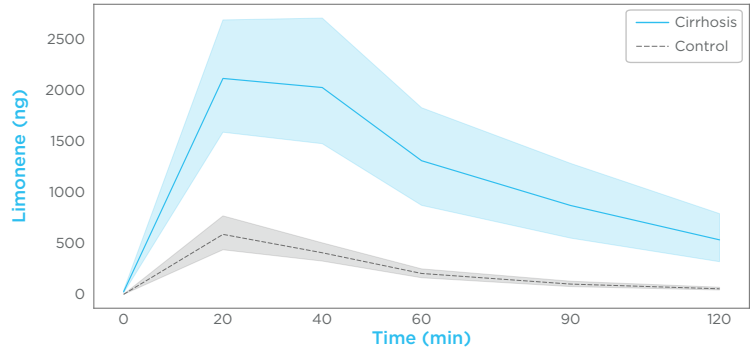
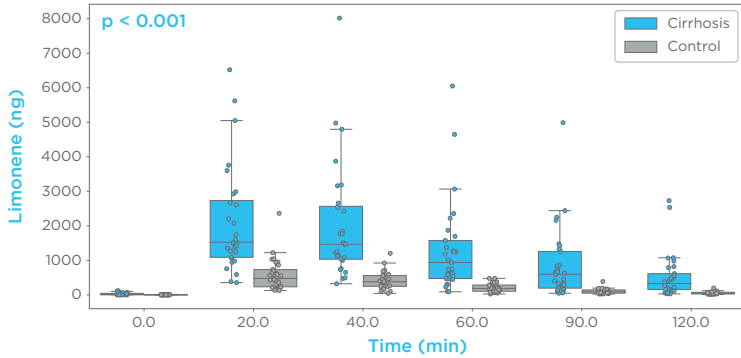
BREATH  
BIOPSY<sup>®</sup>



Comparisons of all the participants showed that subjects with cirrhosis had higher levels of limonene in the breath at each tested timepoint ( $p < 0.001$ ), with the cirrhosis group presenting with a higher Cmax and bioavailability.

With the high levels of sensitivity and specificity achieved in this study, this demonstrates that **a dynamic limonene breath test could maximize the diagnostic performance of a breath test for cirrhosis.**

As breath analysis is non-invasive and well tolerated by patients this approach could complement, or even potentially replace current clinical diagnostic techniques due to the suitability for early detection and implementation into primary care.



Limonene exhalation shows first-order kinetics and increased bioavailability in subjects with cirrhosis.

## Case Study: Subject 10297

A subject enrolled as a control showed no altered blood metrics of liver function. However, an abnormal limonene breath profile was observed. Additional diagnostic work-up established this subject in fact had liver damage. The LIBRA<sup>®</sup> breath test caught a misassigned control case that had liver damage where blood tests failed to catch them. Additional follow-up was recommended.



Parameter	Result from subject 10297	Reference range
Platelets (number/ $\mu$ L)	252000	150000-400000
Bilirubin (mg/dL)	0.5	0.1-1.2
Albumin (g/dL)	4.4	3.5-5.5
INR	1.1	$\leq 1.1$
AST (U/L)	29	8-33
ALT (U/L)	25	7-56
Creatine ( $\mu$ mol/L)	0.72	0.7-1.3
ALP (IU/L)	105	44-147

## Sample LIBRA<sup>®</sup> Test Report

### LABORATORY REPORT: LIBRA<sup>®</sup> TEST



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**PATIENT INFORMATION:**  
Surname: Doe  
Forename: John  
Date of birth: 01/07/1980  
Sex: Male

Sample collected at: St  
Cedar Medical Practice,  
100 Example Street  
Cambridge, CB4 1EE  
Ref. by: Dr. Arnold Smith



Patient identifier: PI001562  
Laboratory: SCM0002

Test performed on 12-10-2025  
Fasting time: 2 hours  
Limonene beverage ingestion time: 11:40  
Breath collection time: 12:00

### TEST RESULTS

**AMOUNT OF LIMONENE: 980 ng**

**HIGH RISK**

**Thresholds:**  
 $\leq 480$  ng limonene: low risk of having cirrhosis, no need for additional diagnostic workup.  
 $>480$  -  $<950$  ng limonene: intermediate risk of having cirrhosis, consider lifestyle modifications and additional diagnostic workup if risk factors present.  
 $\geq 950$  ng limonene: high risk of having cirrhosis, specialist referral recommended for additional diagnostic workup and treatment.

Disclaimer: The results of the LIBRA<sup>®</sup> test should not be used as the sole basis for diagnosing liver cirrhosis. A definitive diagnosis and treatment plan must be determined by a qualified healthcare provider.

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Read the full paper now:

Ferrandino et al. (2023)

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