In the above study, VOCs in breath were monitored following ingestion of a peppermint oil capsule which contains several exogenous VOCs with potential to be used as EVOC Probes. These results illustrate the power of Breath Biopsy to monitor changes in exhaled breath over time (Figure 12).

Analysis of breath captured immediately before and shortly after consumption of the peppermint capsule shows a pronounced increase in the VOCs α-pinene, β-pinene, limonene, eucalyptol and (3)-menthol (Figure 12). The most abundant of these peppermint-related compounds are α-pinene, β-pinene and limonene.

Breath collections made every 30 minutes after this initial capture show a consistent decrease in the target VOCs over time. (Figure 12). Captures made from 6.5 hours after consumption show the levels of the target VOCs decreasing to baseline.

This approach illustrates how Breath Biopsy could be used in a range of medical contexts to monitor disease progression or assess treatment efficacy over time. This could be particularly powerful in identifying suitable treatment regimes for each patient and to detect early signs of treatment resistance in infections and cancers.

What are EVOC Probes?

EVOC Probes enable Breath Biopsy to measure metabolic pathways and organ function in a targeted manner. Find out more about this innovative approach on Page 83.

Untargeted & Targeted Approaches

Technologies such as EVOC Probes support a more targeted approach to VOC analysis on breath. To date, the vast majority of studies have been untargeted biomarker discovery studies that take an unbiased approach to collection and analysis of as many available VOCs as possible. This is typically a slow and high-effort solution requiring advanced technologies and is impractical for point of care clinical applications.

Targeted approaches are more focused and informed, using preceding studies as well as biological knowledge of the mechanisms of disease to identify a small number of candidate VOCs that are most likely to be relevant for a specific goal. For example, evidence suggests that monitoring the exogenous VOC limonene could provide information relevant to liver diseases (see Page 57).

These targeted methods allow sample collection and analysis to be optimized for predetermined targets increasing the opportunity to accurately identify relevant changes and enabling the kind of accessible and portable breath testing technologies that are needed to enable widespread medical applications.

The Breath Biopsy platform is capable of both targeted and untargeted VOC analysis and offers the opportunity to combine approaches. Providing analyses optimized for given target VOCs while still collecting information on the wider variety of VOCs accessible through breath sampling. With the integration of Thermo Fisher Scientific Orbitrap mass spectrometry capabilities, Breath Biopsy offers unrivalled sensitivity for the precise detection of VOCs on breath (see Page 81).

4. Applications of VOC Biomarkers

Exhaled breath represents a vast untapped resource of chemical information. It contains over 1,000 volatile organic compounds, which reflect metabolic activity and the state of cells and tissues. VOCs can therefore act as convenient biomarkers.

The clinical applications for non-invasive, breath-based VOC biomarkers are wide ranging, with numerous applications in precision medicine and early detection.

Breath Biopsy Applications

- Early detection and screening
- Precision medicine
  - Companion diagnostics
  - Complementary diagnostics
  - Patient stratification
  - Therapy response biomarkers
  - Toxicity prediction
- Clinical diagnostics and prognostics
- Disease monitoring

Wide Disease Relevance

VOCs originating from all parts of the body are captured in breath, making Breath Biopsy applicable to a wide range of contexts, These include early detection and precision medicine for inflammatory diseases (e.g. respiratory diseases like asthma and COPD) fatty liver diseases, infectious diseases, metabolic conditions (e.g. diabetes), cardiovascular conditions and cancers.

Research case studies

Discover how academic and clinical partners are applying VOC biomarkers to research across various disease areas.

owlstonemedical.com/case-studies

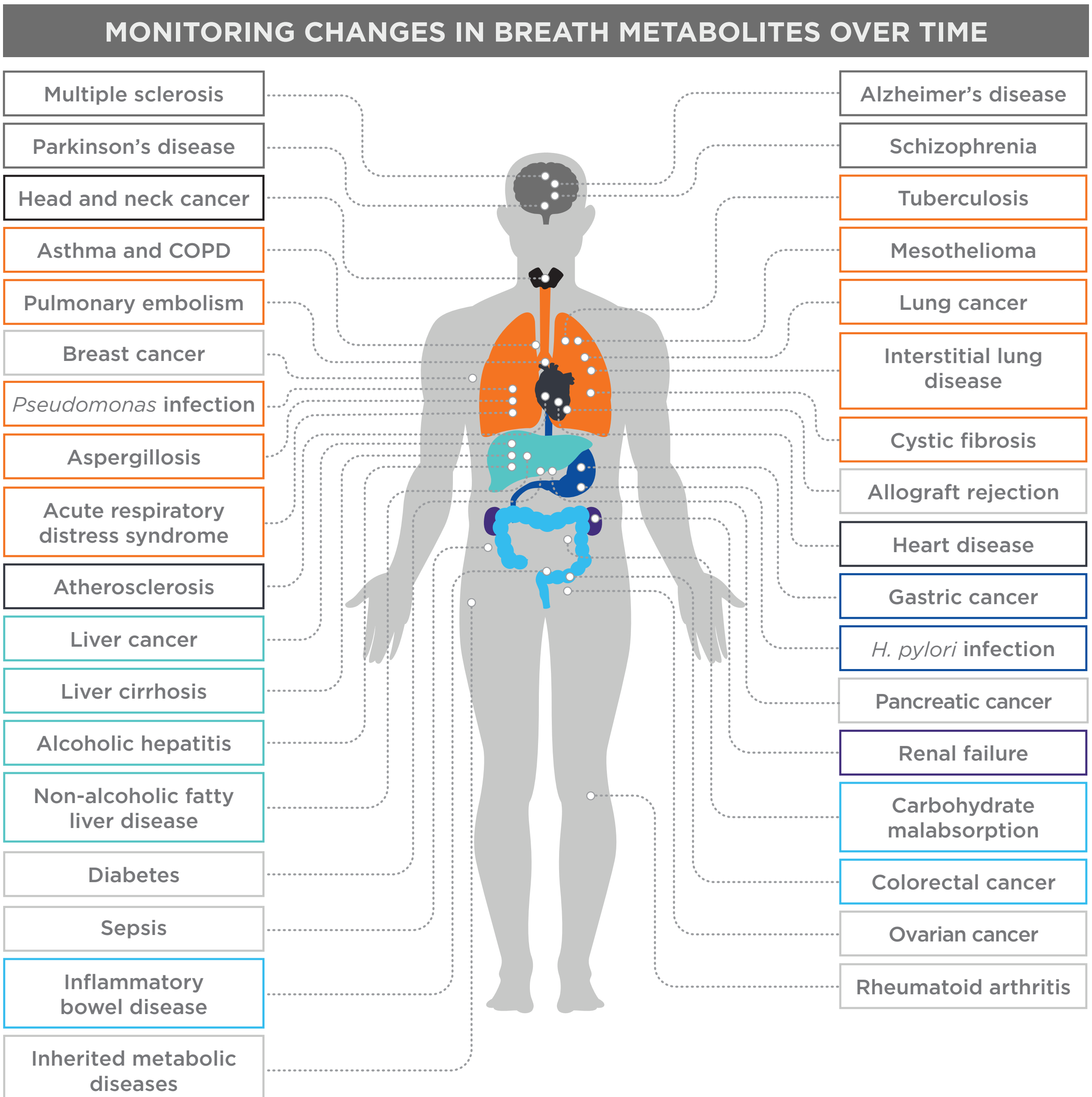

Figure 15. VOC biomarkers in breath have been reported for a large number of diseases in the literature [63,64], highlighting the wide disease relevance of Breath Biopsy. Colours relate to the main organ of disease effect, grey borders indicate diseases linked to other organs or systems.

Novel Biomarkers

Until recently, the identification of robust VOC biomarkers in breath has been hampered by the lack of standardized sampling and analytical methods. Progress is now being made through the advent of new technologies for the reliable collection of patient breath samples (ReCIVA Breath Sampler) and advances in VOC analysis technology (Breath Biopsy platform).

Breath and the metabolome are under-explored in a clinical context, this means VOC biomarkers identified in breath are likely to be novel, which may allow their utilization as companion or complementary diagnostics.

Advances in breath sampling technology allow Breath Biopsy to be embedded into early stage clinical trials. This enables pharmaceutical companies to discover and use biomarkers early in the drug development process and may help to maximize the chance of achieving regulatory approval.

Precision Medicine

Volatile metabolites are closely linked to disease activity, which makes them ideal for capturing the biological variability of disease. As a result, VOC biomarkers have found use in precision medicine applications that depend on a detailed insight into the biological variability that underlies disease processes.

For example, VOCs in breath have been used to stratify asthma patients into groups which are either responsive or non-responsive to a particular therapy (see Page 34). Similarly, VOC biomarkers offer a non-invasive means to accurately stratify inflammatory bowel disease patients to assist with therapy selection (see Page 55).

If VOC biomarkers can be identified that predict therapy response and treatment efficacy it can lead to the development of diagnostic breath tests for identification of responders.