What is Pharmacobreathomics?

In pharmacobreathomics, the breath VOC (volatile organic compound) profile is used to study how a drug interacts with the body. This new field combines pharmacology (the science of drugs) and breathomics (the study of VOCs in breath) to develop precision medicine tools that aim to deliver the right drug, to the right patient, at the right time.

Monitor Changes in Volatile Metabolites in Breath Over Time

Exhaled breath contains thousands of VOCs which are products of metabolic activity taking place in the body. This includes VOCs produced during the metabolism of pharmaceuticals and other xenobiotics.

Observing changes in the type and concentration of metabolites over time after the administration of pharmaceuticals is a useful tool in drug pharmacokinetics and drug compliance studies. Breath Biopsy enables changes in levels of metabolites over time to be investigated non-invasively via breath.

This case study describes how the Breath Biopsy platform can be used to capture multiple breath samples over time, uncovering detailed changes in the concentration of volatile drug-related compounds present in breath.

![Figure 1. Peppermint-related VOCs in breath before and at 30 minute intervals after consumption of a peppermint capsule. Data from a single individual is shown. Breath was collected using the ReCIVA Breath Sampler and analyzed using TD-GC-TOF mass spectrometry.](owlstonemedical.com)
Breath Biopsy for Pharmacokinetics and Dynamics

As metabolite VOCs in the bloodstream are efficiently exchanged with air in the lung’s alveoli, measuring VOCs in exhaled breath allows metabolic processes occurring throughout the body to be analyzed non-invasively (Figure 2).

Single measurements of metabolites provide only a snapshot of an individual’s current state. While this provides useful information, point measurements do not give information about the baseline abundance of metabolites for that individual.

Making multiple measurements over time allows the detection of changes in metabolite concentration that can, for instance, indicate whether a patient is complying with a medication regime or provide information about how a particular drug is being metabolized by the patient.

Breath Biopsy can be used to measure longitudinal changes in exhaled VOCs for monitoring:
- Drug activity
- Drug compliance
- Pharmacokinetics
- Therapy response

Figure 2. Metabolites comprise the products of endogenous cellular metabolism, compounds produced by the body’s own resident microbiome, compounds introduced from the environment, and downstream drug metabolites resulting from therapeutic interventions. Volatile metabolites originating from the entire body can be accessed by continuously sampling breath over a few minutes. Capturing breath VOCs onto the Breath Biopsy Cartridge allows pre-concentration of volatile metabolites originating from the entire body via the circulatory system.
Successful longitudinal measurements require highly reproducible sampling and analysis techniques. The Breath Biopsy platform includes the ReCIVA Breath Sampler, which was designed in collaboration with leading experts to provide a standardized method to collect exhaled breath samples.

By measuring VOCs in breath following ingestion of a surrogate pharmaceutical, in this case a peppermint oil capsule, we show that Breath Biopsy can be used to observe the decrease in target compounds over time using repeated, robust breath collection and analysis over a period of 8 hours.

**Breath Biopsy Workflow**

After ingestion of the peppermint capsule, breath samples were collected from an individual onto a Breath Biopsy Cartridge every 30 minutes for 8 hours using a ReCIVA Breath Sampler and CASPER Air Supply. For comparison, two breath collections were made from the same individual prior to ingestion to provide a baseline concentration for the VOCs of interest. Breath samples were analyzed in Owlstone Medical’s Breath Biopsy Clinical Laboratory where the analytical workflows include FAIMS and mass spectrometry.

Analysis of breath captured 30 minutes after consumption of the peppermint capsule shows a large increase in the VOCs α-pinene, β-pinene, limonene, eucalyptol and (±)-menthol compared to baseline pre-ingestion controls captured immediately prior to taking the capsule (Figure 1). The most abundant of these peppermint-related compounds are α-pinene, β-pinene and limonene. Limonene was present at part-per-trillion (ppt) concentrations.

Breath collections made every 30 minutes after this initial capture show a consistent decrease in the target VOCs over time. (Figure 1). Captures made from 6.5 hours after consumption show the levels of the target VOCs decreasing to baseline levels. All of the target compounds display a similar washout curve over time.

In this study, standard deviations were calculated for the 4 replicate samples collected on the Breath Biopsy Cartridge at each breath collect (Table 1). This gives an indication of the high intra-sample reproducibility of breath sampling and analysis using the Breath Biopsy platform.

<table>
<thead>
<tr>
<th>%RSD</th>
<th>α-pinene</th>
<th>β-pinene</th>
<th>limonene</th>
<th>eucalyptol</th>
<th>(±)-menthol</th>
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<tr>
<td><strong>average</strong></td>
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<td>7.99</td>
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<td>13.02</td>
<td>11.60</td>
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<td>61.83</td>
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</table>

*Table 1. Mean average and range of % relative standard deviation (%RSD) of peak area for compounds shown in Figure 1. Note high max %RSDs are for points close to baseline where VOC concentrations were much lower.*

**Summary**

This study demonstrates that the Breath Biopsy platform can be used to reproducibly capture and analyze breath samples during a longitudinal study. Using a peppermint capsule as a surrogate pharmaceutical, the levels of peppermint-related compounds in breath were found to increase rapidly after ingestion, and subsequently decrease following a washout curve over time. Measuring volatile drug compounds and metabolites in breath over time offers a completely non-invasive way of monitoring drug compliance and analyzing pharmacokinetics.
WE SPEND $1 TRILLION EVERY YEAR ON DRUGS, 40% OF WHICH DON’T BENEFIT PATIENTS

THERE IS A NEED TO UNDERSTAND THE INTERACTION BETWEEN PHARMACEUTICALS AND THE BODY

PHARMACOBREATHOMICS

MONITOR CHANGES IN DISEASE AND DRUG RELATED VOLATILE METABOLITES IN BREATH OVER TIME

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