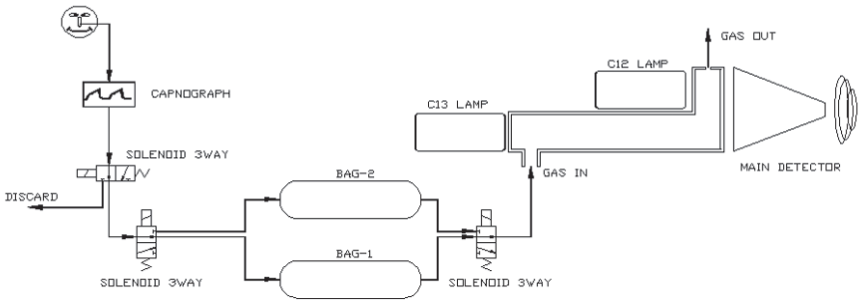
BreathID Technical Overview

The **BreathID®** Breath Test System is a breath-testing platform that automatically measures changes in the $^{13}CO_2$ to $^{12}CO_2$ ratio in a patient's exhaled breath following the administration of ^{13}C-labeled substrates. The test uses laser-like light sources to measure changes in $^{13}CO_2$ to $^{12}CO_2$ ratios. The following document provides an overview of the BreathID® technology that is currently used in the detection of H. pylori. Future applications, which are still under investigational use, include the testing of hepatic impairment, gastric emptying, and pancreatic function.

BreathID® System Schematic Overview



Patient Breath Collection

The BreathID® collects breath that flows through a nasal breathing cannula worn by the patient. This automatic passive breath collection method requires minimal patient cooperation and may be used even in extreme cases, such as in young children or patients requiring artificial respiration. The device includes a capnograph that measures the real-time waveform of each breath. This enables the appropriate parts of a patient's exhaled breath (typically the $ETCO_2$ portion[1]) to be selected. In particular, the device is programmed to collect only breath with a high concentration of CO_2. Therefore, breath from inhalation will not be collected since it has a low CO_2 concentration.

> The built-in capnograph enables to select only the appropriate part of the patient's breath

[1] *$ETCO_2$-End-Tidal Carbon Dioxide*

The Intermediate Cell

The working range of CO_2 concentrations is a critical factor for system accuracy, as false ratio readings are a common problem in breath-testing instrumentation. Patient breath CO_2 concentrations can vary between 2% and 6%. The BreathID® System's intermediate cell assures that the collected breath samples are in the optimal concentration range of 2.0% to 2.5%. This is based on the utility capnograph, which has been designed and built by Oridion, a global leader in the field of capnography. Oridion has been an OEM supplier of capnographs for defibrillators, ventilators, and other medical monitors for many years and provides capnographs to leading companies in the field, including Phillips, Siemens, Drager, Hewlett Packard, and Physio, among others.

Bag Collection System

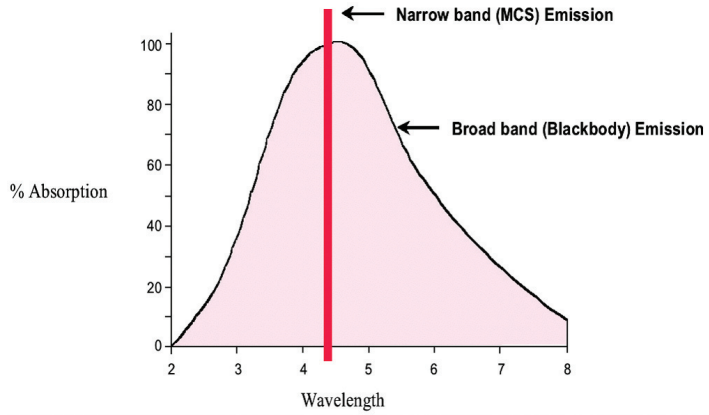
The measuring system of the BreathID® samples continuously, once per second, and the samples are averaged roughly every 70 seconds. A new data point is recorded approximately every 2 to 2.5 minutes.

The BreathID® device continuously collects breath into one of two gas bags. While one bag is being sampled by the measuring system, the other one is being filled by the device's collection system; this process saves time.

Optical Measurement - Molecular Correlation Spectrometry

The BreathID® System measures changes in the ratio between the carbon dioxide isotopes in the exhaled breath using a technology called molecular correlation spectroscopy (MCS™).

Because MCS™ is highly accurate with gas samples, there is no need to create special algorithms and filters to correct for the presence of other gases.



Exalenz
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BreathID Technical Overview

Continued

MCS™ is a unique, laser-like technology. MCS™ creates an infrared emission that precisely matches the absorption spectrum of the isotope-specific CO_2 that the MCS™ is designed to measure. The optic emitter radiates a beam of infrared energy characterized by the narrow region (0.15 μm wide) of the spectrum where CO_2 molecules absorb the infrared radiation. This is significantly more efficient and straightforward than conventional infrared technologies (such as the UBiT by Otsuka), which use a blackbody emitter. A blackbody emission is typically **135 times broader** than the MCS™ emission spectrum, as shown in the graph below.

The highly efficient, CO_2-specific emission source of the MCS™ results in an extremely short light path. This sets the stage for a number of technological advantages and clinical benefits.

- The breath sample cell can be greatly reduced in size, enabling frequent samples during the continuous measurement of the individual patient and a lower flow rate of exhaled air.

- The molecular correlation spectrometer is based on specific optical-radiation emission and absorption by $^{13}CO_2$and $^{12}CO_2$ gases. As the $^{13}CO_2$ and $^{12}CO_2$ are measured by discharging lamps as light sources, light absorption will solely be due to the existence of $^{13}CO_2$ and $^{12}CO_2$ in the gas mixtures. This eliminates the need for filters and correcting algorithms which may affect the results.

- The MCS™ technology enables the detection of very small variations in $^{13}CO_2$ and $^{12}CO_2$ concentrations in the $^{13}CO_2/^{12}CO_2$ ratio. In fact, the BreathID® System can detect variations of less than 1/1000 in the $^{13}CO_2/^{12}CO_2$ ratio.

Device Stability and Calibration

Although the device is designed for very high levels of stability with its thermoelectric cooling and heating control, the device nevertheless constantly checks its own stability using advanced real-time algorithms. It measures two separate references during the course of the measurement to compensate for slight variations in the breath samples and to ascertain that it is measuring the changes in ^{13}C and not external changes or noise.

The BreathID® comes with its own system to ensure it is properly calibrated. After 25 tests are completed, the BreathID® requests that a SystemCheck be performed. A SystemCheck canister, with a known concentration of CO_2 gas, is inserted into a designated compartment in the system, automatically checking the device's calibration. In case the SystemCheck determines that the device needs calibrating, the BreathID® will automatically calibrate itself during the baseline collection process of the next patient's breath test.

Accuracy and Precision

The repetitive precision (reproducibility) and the accuracy of the BreathID® are very high:

- For a measurement range of 0-5 δ [‰]: ±1.0 δ [‰] at 20°C - 30°C, 2°C change within an hour (±0.3 δ under special conditions)
- For a measurement range of 5 δ [‰] and higher: 0.2 x δ [‰] at 20°C - 30°C, 2°C change within an hour
- Typical Standard deviation of single points: 0.3 δ [‰].

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